Somru BioScience Inc.

Biosimilar Software Documentation

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Objectives:

Objective of the software is to allow for automated data analysis with most flexibility. The software will be used for method development and validation.

During method development rules are more “flexible.” And user needs the most flexibility to run analysis various different ways.

For validation: rules are “mostly” set. The configuration function should allow for setting the rules and run the analysis. When exception needs to be made, it should require a reason for exception and electronic signature captured.

Software Design

Figure : Software design

Biosimilar Menu

Biosimilar Menu (v1.1) includes following:

- Standard Comparison Curve
- Quality Control Comparison

Biosimilar Analysis Methods

1. Standard Comparison Analysis

*Figure SEQ Figure * ARABIC 2: Quality Control (QC) Comparison*

Figure : Standard Comparison Flow Chart

2. Quality Control (QC) Comparison Analysis

Data Analysis

1. Experimental Design - Balanced Assay design (recommended)

Table SEQ Table * ARABIC 1: Balanced Assay design table

Assay Dataset	Assay Plate	Validation Serum Sample		
		S_1-S_{20}	S_{21}-S_{40}	S_{41}-S_{60}
R1	P1	✓		
	P2		✓	
	P3			✓
R2	P1		✓	
	P2			✓
	P3	✓		
R3	P1			✓
	P2	✓		
	P3		✓	
R4	P1	✓		
	P2		✓	
	P3			✓
R5	P1		✓	
	P2			✓
	P3	✓		
R6	P1			✓
	P2	✓		
	P3		✓	

R = a dataset P = a plate A = an analyst X= indicates which samples are included in the design

2. Data entry and Definition

2.1. Understand the Study Structure

Figure : Study design

A single study contains multiple analysis method; each analysis type is built up by multiple datasets; each dataset is a container of plates, which plate is the container of sample data. At each level of the structure, users can perform different tasks which the changes in the lowest level will strongly effect its higher level.

A new single study will contain all needed analysis function and users will need to add in the datasets and plate to perform the analysis. To create a dataset, users navigate to the **left side menu** in the study page: **Study Page** > **Select Analysis Type** > **Add New Dataset**

To create a plate, users navigate to the **left side menu** in the study page: **Study page** > **Select Analysis Type** > **Select a Dataset** > **Add New Plate**

2.2. Label Plate

There are total five (5) steps to enter data:

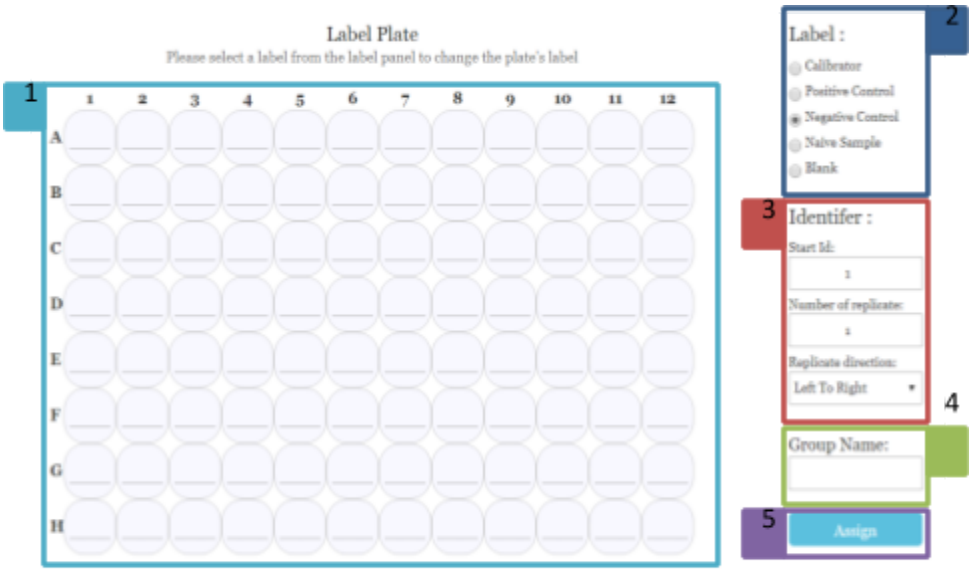


Figure : Sample label plate

1. Select Wells:
   - **Left-Click** on a well will automatically select the well. Hold **Ctrl key** while select will enable multiple selection mode **OR**
   - **Left-Click** on the a well, **hold and drag** to perform mass selection.
2. Select Label on the right-hand side menu indicate the label that will be assigned the label to the selected well(s)
3. Adding identifier to indicate the replicate of samples
   - Assign the Starting Index value; By default, the starting index value assign at 1.
   - Assign the number of replicate per Index. [For example: Number of replicate: 2 means for each index value, there will be 2 replicates]
   - Replicate assign direction has 2 modes: *"Left to Right"* OR *"Top Down"*
4. Assign the sample group name. **NOTE:** this group name will be used to group data to calculate the normality and be involved in the cutpoint analysis.
5. Assign the value to the plate.

2.3. Input Data

Users may input the data in one of two ways:

- Import an .csv file with a restricted format
- Input the data directly in each well of the given plate

Users also may indicate the unit type of the input data by selecting the options available in the tool box below the plate or selecting the option unit box for custom unit type. By default, the unit value will be **"OD"** value (figure 9).

2.4. Preview and Save

After the data entry, the users will be given a chance to review the plate before saving the data. The preview will show user how the plate will look like after saving with all information of the input data.

3. Data Manipulation

There are two view mode for the data plate. To review the plate's data by navigate to **[Analysis Type] > [Dataset name] > [Plate name] > Plate View** for the virtual plate view or **[Test Type] > [Dataset name] > [Plate name] > Table View** for the table of data view.

3.1. Plate View

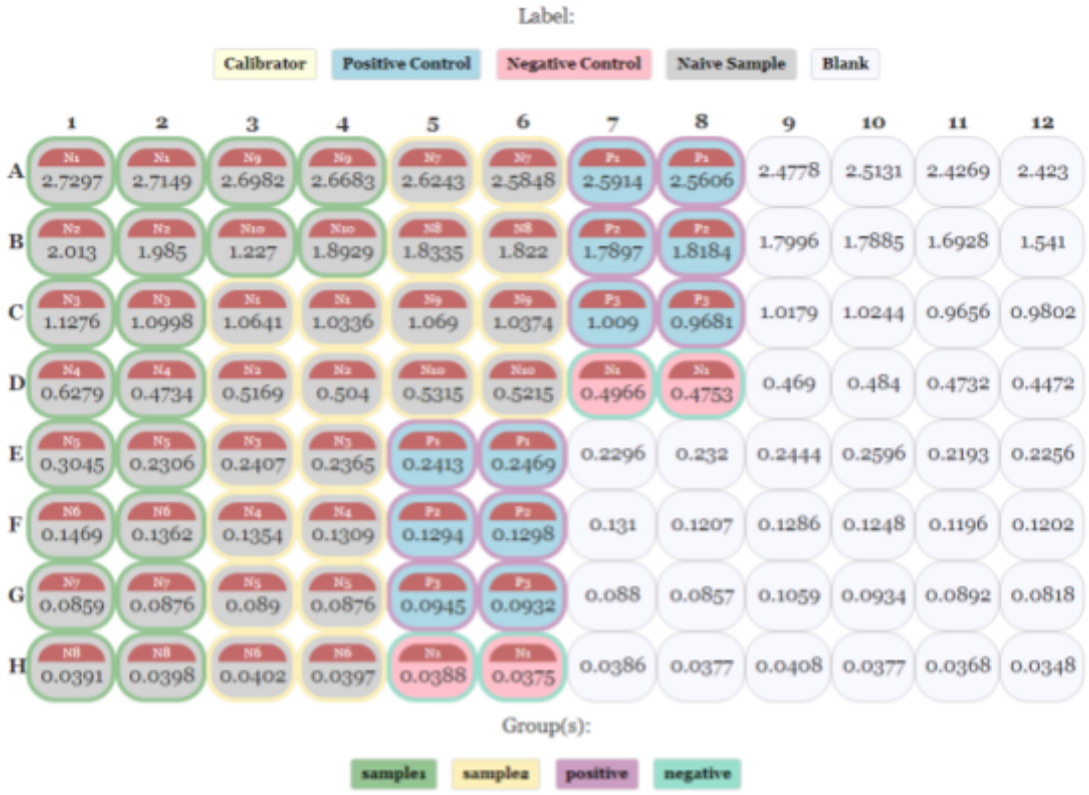


Figure : Plate view

In the **Plate View** mode, the users can review and get full visuallization of the plate along with the reading value. Each well provides four specific pieces of information (figure 11):

- **The group that the sample is belong to** – indicated by the border color of the well
- **The sample type** – indicated by the background color of the well
- **The sample id** – displayed inside the red box in the top half of the well
- **The sample data** – displayed inside the lower half of the well

Figure : Virtual sample well

3.2. Table View

Edit

Group	Sample Id	Replicate 1	Replicate 2	Replicate 3	Replicate 4	Mean	%CV	Comment
sample1	N1	2.73	2.715	0	0	2.722	0	
negative	N1	0.039	0.038	0.497	0.475	0.262	99	
sample2	N1	1.064	1.034	0	0	1.049	2	
sample1	N2	2.013	1.985	0	0	1.999	1	

Figure : Plate's table view

In the **Table View** mode, users can review the plate's data based on the **Sample Id**. The table will display the mean value of each unique identifier as well as the coefficient of variation. Users may edit the data by activating the edit option above the table. In edit mode, users may trigger one or more replicates to exclude or include in the future calculation. User may exclude the whole sample with specific identifier by excluding all replicates in which belong to that identifier.

Save Cancel

Editing Data

Select the replicate(s) that will be exclude or include from future calculations.

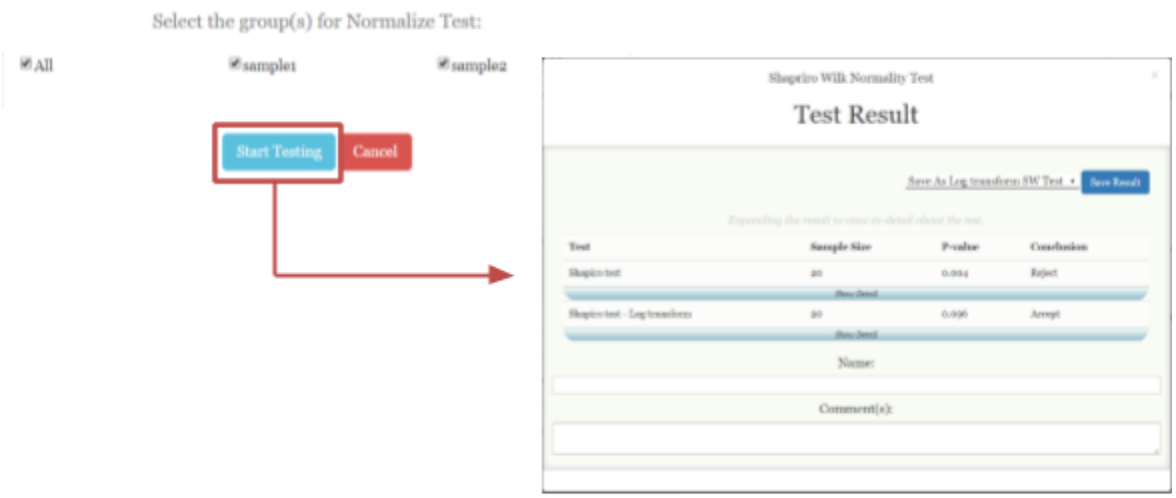
Group	Sample Id	Replicate 1	Replicate 2	Replicate 3	Replicate 4	Mean	%CV	Comment
sample1	N1	2.73	2.715	0	0	2.722	0	

4. Normality Test

To perform Normality Test, users may navigate to: **[Analysis Type]** > **[Dataset Name]** and go to **Shapiro Wilk** tab (figure #). On this tab, users will see the table of save Shapiro Wilk result as well as tool box for generating a new test.

Figure : Shapiro Test

To generate a new Shapiro Test, users may click on the button "**New Shapiro Wilk Normality Test**". Users then will choose the group of samples that will be used to run the test and start the test. A new window will open to run the test. The normality test will be run automatically one the "**Start Testing**" got hit and will choose the most optimal path for the data to test which it will take less than a minute to do the test (as discuss in section #). For detail calculation of each test, users may click on the "**show detail**" button below each result line. Name and comments are optional input to help users to identify the save result easier.



5. Comparison Calculation

5.1. Standard Comparison Curve

Standard comparison test is done on each plate level. The standard comparison test will compare the biosimilar sample and the innovator sample by performing the regression curve on the input data. The curve will be plot using the input data as well as some predict data. F-test and EC50 value will be generate after the curve is defined and plot. To generate a standard comparison curve test, navigate to the **Study page** > **Std Curve Comparison** > **[Dataset name]** > **[Plate name]** > **Standard Comparison** tab.

5.2. Data Extrapolation

Data extrapolation is a testing sample for fitness method that is required before performing the quality control comparison test. This test is done on the plate level and mainly focusing on the calculated concentration of each control sample in the input plate. Navigating to the **Study page** > **Std Curve Comparison** > **[Dataset name]** > **[Plate name]** > **Data Extrapolation** tab to get the test done.

5.3. Quality Control Comparison

This test is done on the dataset level. Quality control comparison is focusing mostly on the control sample of the input data. The control samples of each plate will be categorized depend on its concentration and the calculated concentration from the **Data Extrapolation** and group together for comparison test. The result of the test will be the interbatch and Interbatch percentage of coeficience of all the same group of control. To generate the quality control comparison test, navigate to the **Study page** > **QC Curve Comparison** > **[Dataset name]** > **QC Comparison** tab

6. Report

Report for each analysis can be generated and exported into a **Portable Document Formatted (PDF)**.

The report includes the target analysis calculation and the data processing information such as data removal and data normalization.