# SphereFlash® Colonies Software

## Automatic Measurement of Inhibition Zones

Software Instructions for Use

Doc. No 50007969-05

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# Contents


1. Introduction ..... 5
   1.1. Intended use of the SphereFlash® ..... 5
2. Computer Requirements ..... 6
3. Setting up the application ..... 7
   3.1. Installation of the software ..... 7
   3.2. Log in and enter the activation key ..... 8
   3.3. Changing usernames and passwords ..... 9
   3.4. Management of failed logins ..... 9
4. Overview of the user interface ..... 10
5. The About dialog and access to the manuals and guides ..... 11
6. Calibration and verification ..... 12
   6.1. Automatic calibration of the SphereFlash® instrument ..... 12
   6.2. Verification ..... 12
7. Processing a plate to measure halos diameters ..... 15
   7.1. Launching a halos measurement process ..... 15
   7.2. Obtaining the measurement results ..... 16
   7.3. Manually modifying the process to get better results ..... 17
      7.3.1. Changing threshold value ..... 17
      7.3.2. Interactive graphical modification of halos ..... 17
   7.4. Saving the results in the database ..... 19
8. Creating a customized recipe for your halos plates 20
   8.1. Selecting a default recipe ..... 20
   8.2. Editing the recipe settings ..... 20

8.2.1. Testing the settings on a sample plate ..... 21
8.2.2. Layout settings ..... 21
8.2.3. Image Capture Settings ..... 22
8.2.4. Basic settings ..... 23
8.2.5. Advanced Settings ..... 26
8.2.6. Coloring settings ..... 28
8.3. Management of the recipe ..... 29
8.4. Importing and exporting recipes ..... 29

**9. Managing stored Process Results ..... 31**

9.1. Overview of the Process Result View ..... 31
9.2. Fields displayed by the Process Result View ..... 31
9.3. Sorting, filtering, and selecting results on the Results View ..... 31
9.4. Re-processing the plate image of a stored result ..... 32
9.5. Printing and exporting results ..... 32

**10. Displaying and exporting images ..... 34**

**11. Views Management ..... 35**

11.1. Built-in Views ..... 35
11.2. Customized Views ..... 35
11.3. Actions on the views ..... 36
11.4. Audit Trail ..... 36
11.5. Managing result groups ..... 38

**12. Working with worksheets ..... 39**

12.1. Creating and editing a worksheet ..... 39
12.2. Using a worksheet to measure halos ..... 40
12.3. Importing, exporting, and deleting worksheets ..... 41
12.4. Working with remote file input ..... 42

**13. Antibiotic Potency Test ..... 43**

13.1. Preparation and measurement of the plates ..... 43
13.2. Running the Antibiotic Potency Test ..... 44

13.2.1. General and configuration data ..... 45
13.2.2. Selection of plates to determine the standard line ..... 45
13.2.3. Calculation of the standard line ..... 47
13.2.4. Selection of plates with the unknown(s) ..... 48
13.2.5. Calculation of the potency of the unknown(s) ..... 49
13.2.6. Summarizing and saving the calculation results ..... 50
13.3. Viewing and exporting the data of the Antibiotic Potency Tests ..... 50

**14. General administration of the application ..... 53**

14.1. User Management ..... 53
14.1.1. Roles and permissions ..... 53
14.1.2. View existing users ..... 54
14.1.3. Add new user ..... 55
14.1.4. Other user management operations ..... 55
14.1.5. Changing the active user ..... 55
14.2. Environment and System options ..... 56
14.2.1. System options ..... 56
14.2.2. Expiration times ..... 57
14.2.3. Date and Time format ..... 57
14.2.4. List separator ..... 57
14.2.5. Remote input/output folders ..... 58
14.2.6. Barcode reader ..... 58
14.3. Customizing the logo on the reports ..... 59
14.4. Digital signature of PDF reports and tables ..... 59
14.5. Removing outdated results (purge) ..... 60
14.6. Managing the database files ..... 61
14.6.1. Location and backup of the active database files ..... 61
14.6.2. Location of archived database files resulting from purge operations ..... 61
14.6.3. Temporarily restoring archived databases ..... 61
14.7. Interfacing with a LIMS (Laboratory Information Management System) ..... 62
14.7.1. Remote input file example ..... 63
14.7.2. Remote output file example ..... 63

**15. Regulatory compliance: FDA 21 CFR part11 ..... 64**

# 1. Introduction

Thank you for choosing the SphereFlash®. We are confident that this instrument will become an integral part of your laboratory.

Before using the SphereFlash®, it is essential that you read this user manual carefully. Following the instructions and safety information in this user manual will ensure safe operation and maintain the system in a safe condition.

## 1.1. Intended use of the SphereFlash®

The SphereFlash® is an automatic colony counter that meets all the requirements that may be required in a modern microbiology laboratory.

With its SphereFlash® Colonies LITE Software it performs the colony simply and reliably thanks to its world-class software and its patented built-in lighting system.

For more demanding users the software can be upgraded to the SphereFlash® Colonies PRO Software to increase its capabilities, e.g., setting user's permission levels, LIMS connectivity, worksheets, barcode reading, reporting, audit trail, or CFR21 Part 11.

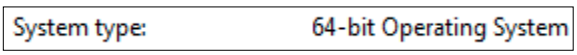
With the optional SphereFlash® Halos PRO Software, the SphereFlash® unit can be transformed to measure inhibition halos, accepting various circle approximation criteria to obtain the corresponding diameters of virtual circle areas.

In all versions, the lighting is done through LEDs that are oriented to the internal wall of a moving spherical chamber. The result is an unprecedented uniform and reflections-free illumination in a colony counter device.

The moving sphere closes the chamber and prevents the area in which the Petri dish is located from any external light. It avoids any reflection or interference from external light, creating a luminous atmosphere without reflections from the walls of the Petri dish or the colonies. For the transparent media, the light by transmission is also available in all versions.

# 2. Computer Requirements

To install and run the SphereFlash® Halos PRO Software, the computer must meet or exceed the following requirements:

| | |
|---|---|
| **Processor** | x64, 2.5 GHz |
| **Operating System** | Microsoft 64-bit Windows 7, 8.1, 10<br>(x64 platforms)<br>  |
| **Interface** | 1 free USB 3.0 port<br> |
| **RAM** | 8 Gigabytes |
| **Free disk space** | Application: 100 Megabytes<br>Database: 10 Gigabytes (for 5000 results stored w/images) |
| **DVD reader** | For the installation of the software[1] |
| **Screen resolution** | Full HD (1920 x 1080px) (recommended) |
| **Screen size** | 24'' (recommended) |
| **Optional third-party applications** | • Microsoft Excel® 2007 or higher, 64bits (to open exported Excel files)<br>• A virtual PDF printer such as PDFCreator (to create PDF reports)<br>• Adobe Acrobat Reader DC® 2015 or higher (to digitally sign PDF reports) |

[1] Alternatively, you may transfer the files from the DVD to a USB memory stick in another computer, and then install the software onto the destination computer from the USB memory stick; see section 3.1.

# 3. Setting up the application

**NOTE 1**: You can skip this section if a IUL representative staff has already installed and set up the application for you.

**NOTE 2**: For the initial set up of the application, you should be authorized by your company's management to act as administrator of the SphereFlash® Halos PRO software.

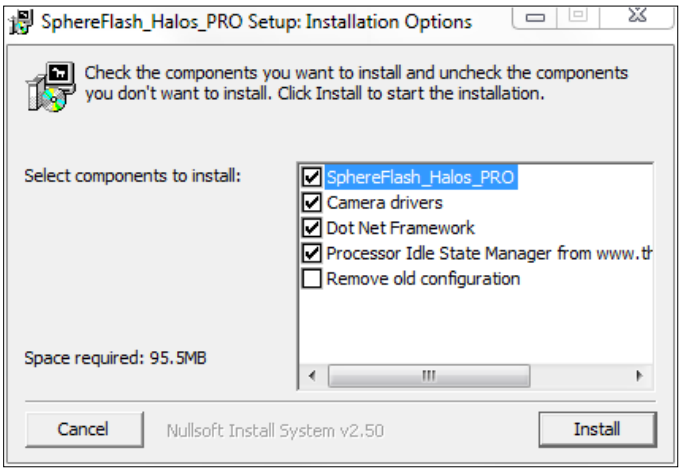
## 3.1. Installation of the software

Insert the supplied DVD into your computer's DVD reader and let it automatically execute the installation procedure. When asked for, select the installation of the Halos PRO software.

Alternatively, obtain the installer executable file:
*SphereFlash_Halos_PRO_Installer_vn.n.n.n.exe*
copy it into a local folder of your computer, and double click on this file.

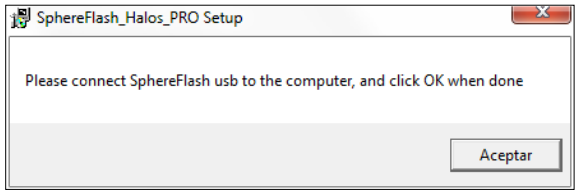
Follow the instructions given on the installer dialog appearing on the screen.

In a first installation, it is recommended that you leave the checkboxes with the default values. If your computer is equipped with an Intel Core i3 processor or similar, we recommend that you keep checking the *'Processor Idle State Manager'* checkbox.




**NOTE:** Do not check the box *Remove old configuration* unless you are aware that all the Halos processing results and recipes previously stored in the database will be erased.

Power the SphereFlash® instrument using the mains adaptor and pressing the on the button, wait until the status lamp of the instrument starts blinking, and plug the USB cable to a free USB 3 port on the computer when required:



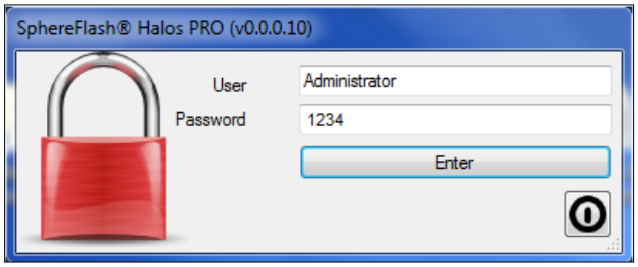
Accept when required and let the installer complete all the required steps until a finish message is displayed.

Now your desktop should contain a new shortcut for the SphereFlash® Halos PRO software:

## 3.2. Log in and enter the activation key

First make sure that the instrument is powered-on, its lamp slow-flashing, and its USB3 cable connected into a USB3 socket of the computer.

Double click the *SphereFlash® Halos PRO* shortcut icon; a login dialog will be displayed. In the *User* box, type in *'Administrator'*, introduce the Password *'1234',* and press enter.




Accept, and a *SphereFlash® Halos PRO* Activation dialog will appear:

To activate the *SphereFlash®* Halos *PRO Software* license, copy or write down the displayed '*system signature'* and send it to a IUL representative along with the serial number of your SphereFlash® instrument. In return, IUL will provide your personalized key, which must be introduced in the *'Activation Key'* field, and then press *OK*.

**NOTE: Communication Issues**
If you get a message warning about communication errors with the instrument, it's advisable that you check whether the computer firewall is blocking the access of the IUL application to the instrument (the SphereFlash® instrument implements a private IP network, with address

192.168.233.1, which is tunneled through the USB 3 connection). Please refer to the Troubleshooting section on the Instrument User Guide.

## 3.3. Changing usernames and passwords

The application, after the first setup, has three default users (*Administrator, Programmer,* and *Operator*), one for each role (permission level), and all of them sharing the same default password *'1234'.*

It is advisable that during the setup you change the name and password of each of them. Later, you will be able to create new users, reassign roles and change passwords.

To change the passwords, see details in section 14.1.4.

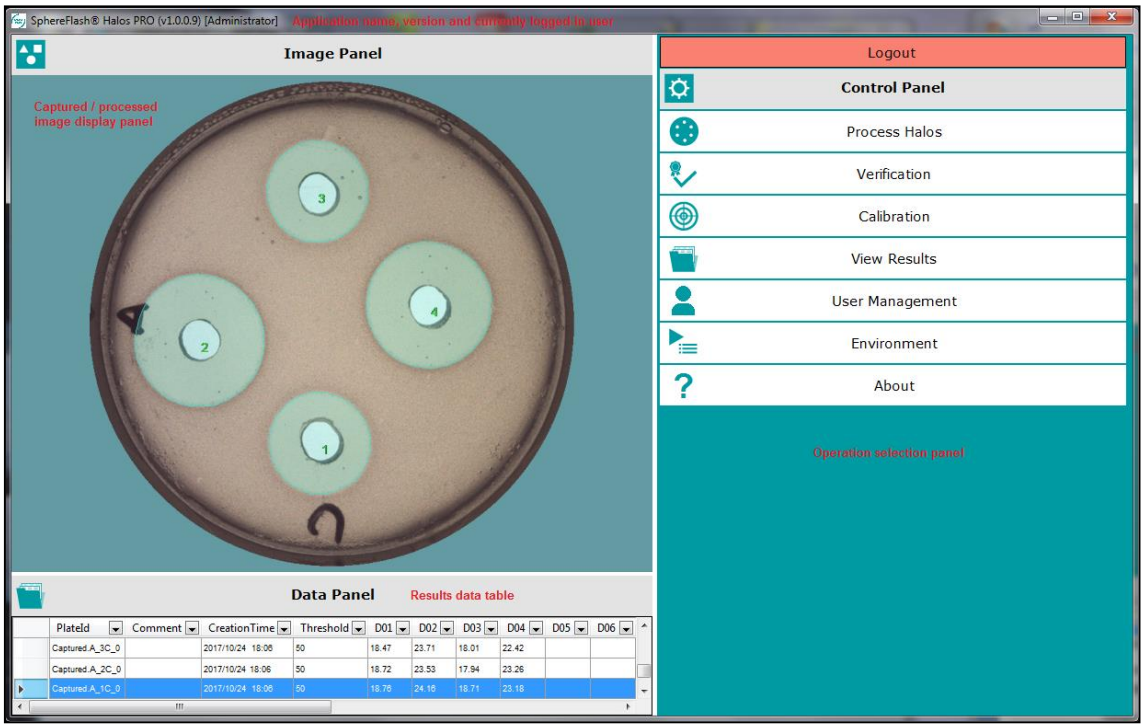
## 3.4. Management of failed logins

When logging in, if the user enters a wrong password, there are two more attempts left until the access is blocked for this user. After blocking, a period must be elapsed until the user is automatically unblocked and will be able to re-try login.

If the user definitively forgets the password, the administrator can create a new password for the user.

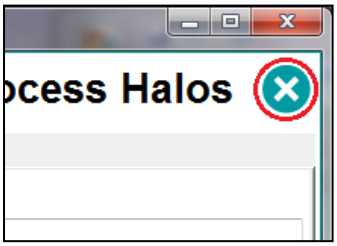
If the administrator forgets his password, please contact IUL technical service to require and arrange a *Remote Recovery Session.* It is highly advisable to register two or more users with the *Administrator* role.

# 4. Overview of the user interface

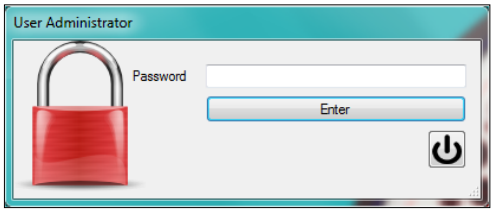



By hovering the cursor over the buttons at the bottom of each operation panel, a tip will be displayed summarizing their function or purpose.

When an operation panel is displayed, you can return to the selection control panel by clicking on the top-right ‘X’ cross icon:

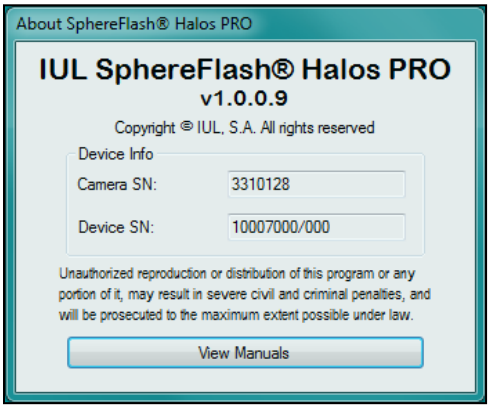



After a time of inactivity, the application becomes blocked, and the user is required to re-enter their password into a re-login dialog:



# 5. The About dialog and access to the manuals and guides

By pressing the *About* button in the *Control Panel,* a dialog appears where relevant information about the instrument and the application can be found. The *View Manuals* button opens a folder that contains the PDF manuals of the instrument and the Halos PRO software application.

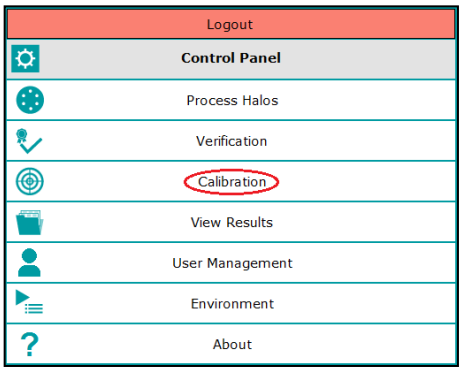


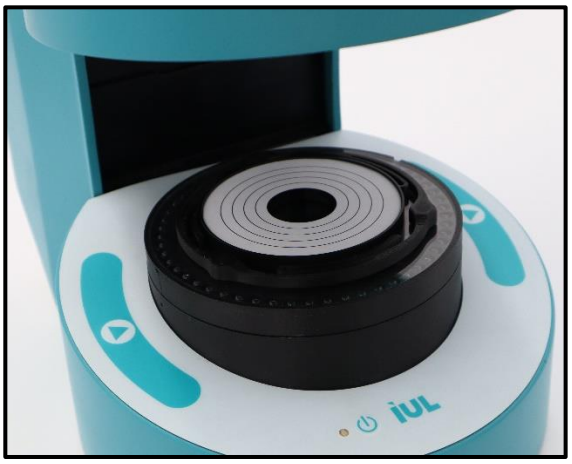
# 6. Calibration and verification

## 6.1. Automatic calibration of the SphereFlash® instrument

Each time the application finds a SphereFlash® instrument that has not been used previously with the Halos PRO Software, a calibration is requested. Calibration must also be timely performed according to the standard procedures of your laboratory.

To perform an automatic calibration, select *Calibrate* in the top-right control panel and insert the calibration disk ref.900010081 on the platform:



Push the *Run* button on the bottom right: . The instrument will proceed to perform several image captures, and finally, an image of the calibration disk will appear on the *Image Panel*.

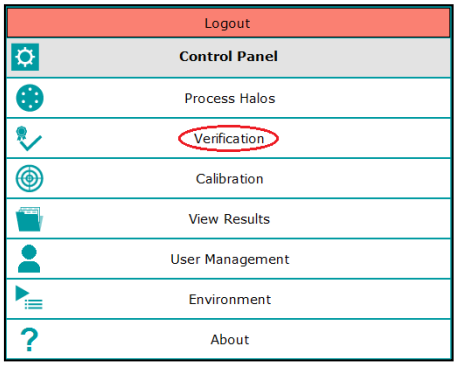
You will be prompted to accept the calibration using the *Accept* button: . The list of previous calibrations is shown in the *Data Panel*. The new accepted calibration is added on top.
After performing a calibration procedure, verification will be automatically requested.

> **NOTE:** If *Calibration* fails, first check whether the surface of the calibration disk is clean and undamaged and that the back of the disk is fully in contact with the transparent base support, removing any particle on the bottom that might tilt the disk, and gently pressing the disk against the base. Then try *Calibration* again.

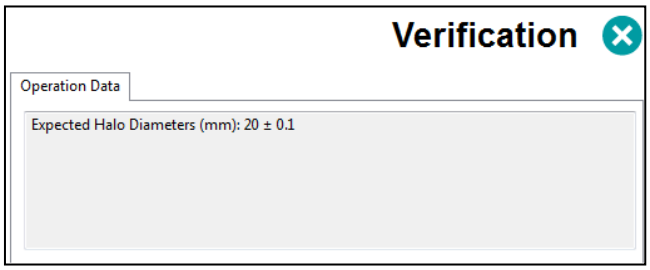
## 6.2. Verification

To assess whether the instrument is correctly measuring the halos, there is a halos verification disk ref. 900011876 which simulates a plate with six halos whose diameters have a standard precise value.

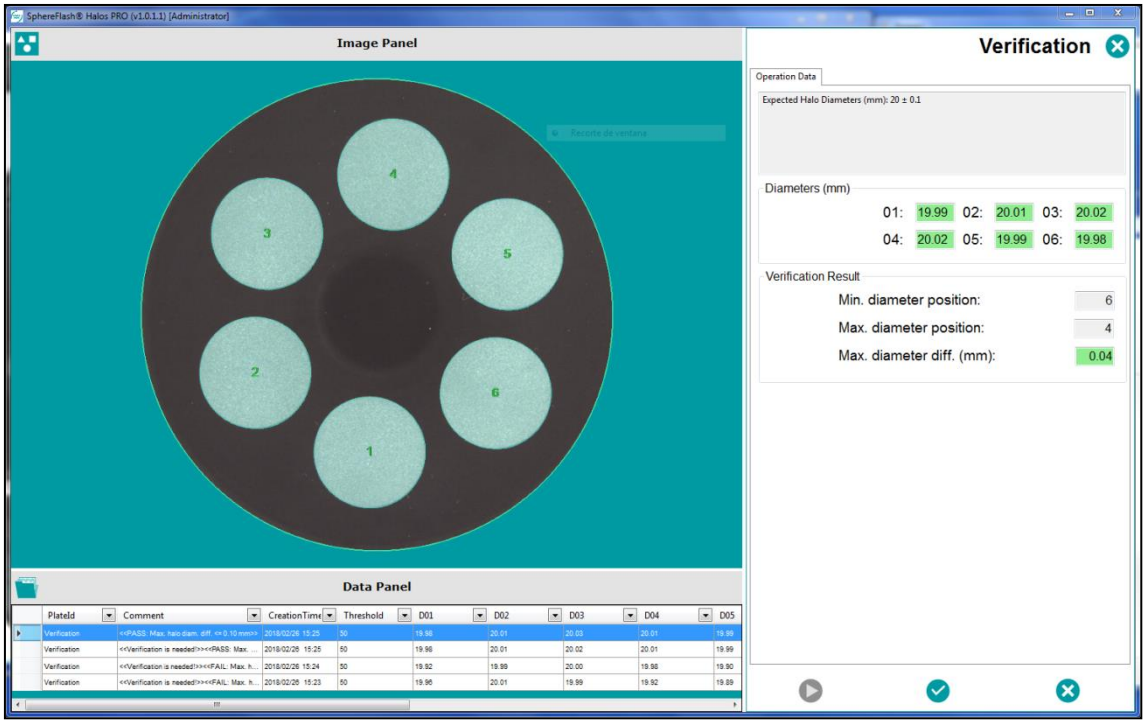
To run a *Verification* operation, insert the verification disk on the platform and select *Verification* in the top-right control panel:




The *Verification* panel will be displayed. At the top of the *Operation Data* tab page there is a comment stating the expected range of the measured halos diameter values:

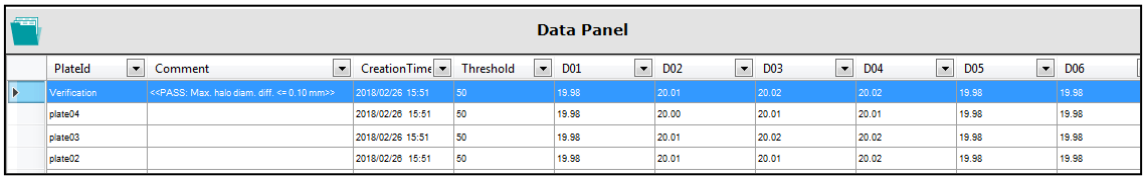



Push the *Run* button on the bottom right: . The instrument will acquire an image of the disk. The image panel will show the acquired image with a greenish mask filling the found halos, each of them being numbered:



The verification panel will display the measured diameters of the halos, the maximum diameter difference among halos, and the positions where the extreme diameter values have been found. Any value outside the prescribed tolerances will be highlighted in red background.

Now you can accept or reject the verification result using the respective buttons or . If accepted, the measured diameters are added in a row at the top of the results list on the *Results* data panel, with the *Plate ID* and *Recipe Name* fields labeled as *Verification.* The comment field will be filled with the *PASS* or *FAIL* outcome and the applied tolerance:



Data Panel

| PlateId | Comment | CreationTime | Threshold | D01 | D02 | D03 | D04 | D05 | D06 |
|---|---|---|---|---|---|---|---|---|---|
| Verification | <<PASS: Max. halo diam. diff. <= 0.10 mm>> | 2018/02/26 15:51 | 50 | 19.98 | 20.01 | 20.02 | 20.02 | 19.98 | 19.98 |
| plate04 | | 2018/02/26 15:51 | 50 | 19.98 | 20.00 | 20.01 | 20.01 | 19.98 | 19.98 |
| plate03 | | 2018/02/26 15:51 | 50 | 19.98 | 20.01 | 20.02 | 20.02 | 19.98 | 19.98 |
| plate02 | | 2018/02/26 15:51 | 50 | 19.98 | 20.01 | 20.01 | 20.02 | 19.98 | 19.98 |

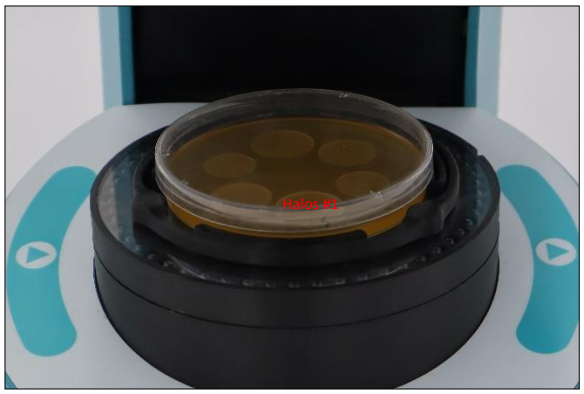
**NOTE:** If *Verification* fails, first perform a *Calibration* operation. Check whether the surface of the verification disk is clean and undamaged and insert the disk on the base in a fashion that the back of the disk is fully in contact with the transparent base support, removing any particle on the bottom which might tilt the disk, and gently pressing the disk against the base. Then, try *Verification* again.

# 7. Processing a plate to measure halos diameters

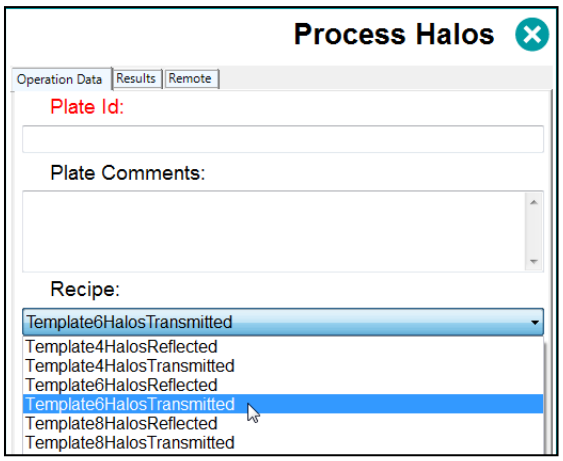
Through ready-to-use recipes, the application is prepared to process standard plate typologies and automatically obtain their halos diameters as a result. Additionally, customized recipes can be created, starting with the supplied ones, to refine the processing of plate typologies (see 8).

## 7.1. Launching a halos measurement process

Insert a halos plate into the instrument platform, aligning the halo #1 with the front mark (given that you have not changed the *1st Halo Orientation* from the default *Front*, as described in 8.2.2).




Go to the *Process Halos* panel, tab *Operation Data*.

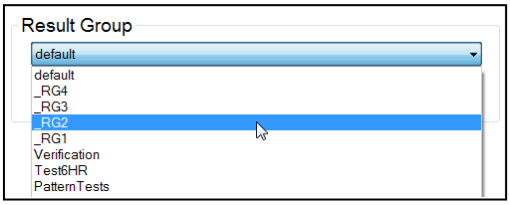



If the *Plate Id* label text is red, it means that you must give a name to the plate by filling in the corresponding box either typing or reading a barcode. With no plate name, it is not possible to run a halos process. You can also introduce an optional comment for the plate in the *Plate Comments* box.

Select in the *Recipe* field the recipe (either ready-to-use or customized) suitable for the plate typology. There are six recipes ready-to-use, based on *Auto Gradient* contour detection mode (see 8.2.4). Choose the most appropriate one according to the number of halos to be measured (4, 6, or 8) and the type of lighting to be applied (transmitted

from below, for the more transparent plates, or reflected from above, for the opaquer ones).

Select in the *Result Group* field the group to apply to the obtained results. The *Result Group* list can be expanded by adding new groups to it. *Result Group* is a label or tag that can be applied to the result, allowing subsequent grouping or filtering of the results in the views based on this label (see 11.5).



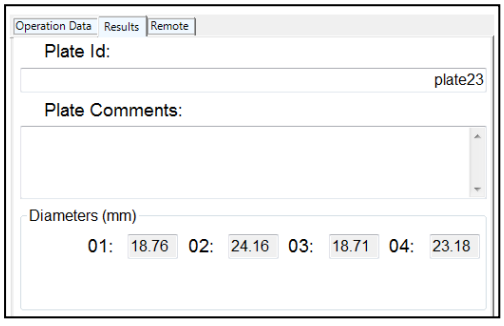

Press the play button, either on the instrument or on the screen .

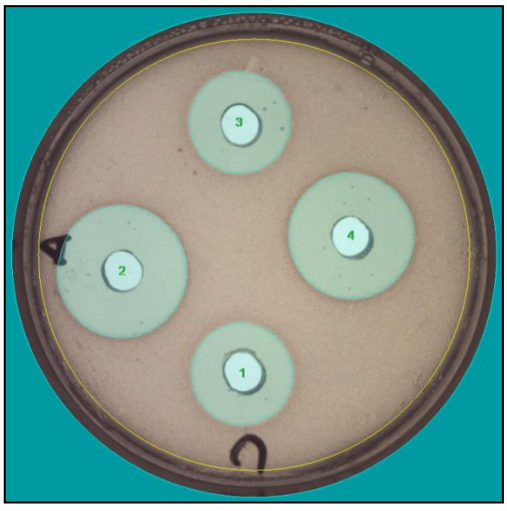
## 7.2. Obtaining the measurement results

The program will proceed to take an image of the plate and process this image until the measurements of all haloes diameters are available. The tab will automatically change to *Results,* showing the resulting diameter values in the *Diameters (mm)* section. If no halo has been detected on a prescribed position, its corresponding diameter is set to 0.

> **NOTE:** Given that halo's shape can be slightly irregular, halo diameters are estimated by fitting the found halo to a perfect circle.

The *Image Panel* will display the plate image with a greenish overlay filling the detected halos and the corresponding number for each halo.

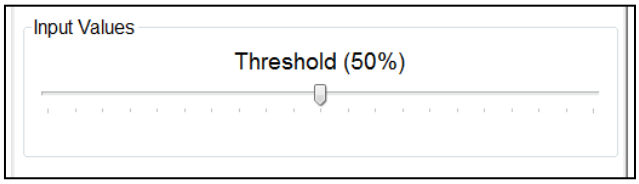


## 7.3. Manually modifying the process to get better results

### 7.3.1. Changing threshold value

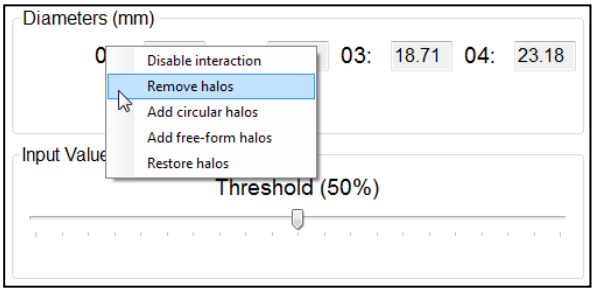
If you do not get satisfactory results (e.g. missing halos or wrong halos outline) you can try to improve them by modifying the *Threshold* slider, away from its recipe default value.




To return to the recipe threshold default value, press the Discard Changes button. If the new threshold value seems to work better than the default value of the recipe, and you have a role with enough permissions as *Programmer* or *Administrator* (*see 14.1.1)*, you can integrate this new value into the recipe by pressing the Save Changes button.

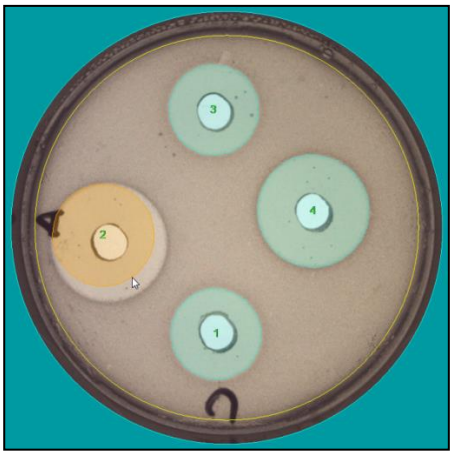
### 7.3.2. Interactive graphical modification of halos

Additionally, you can manually discard or draw a halo; to access this function right-click on the resulting diameter labels, and a drop-down menu will appear for the interactive modification.

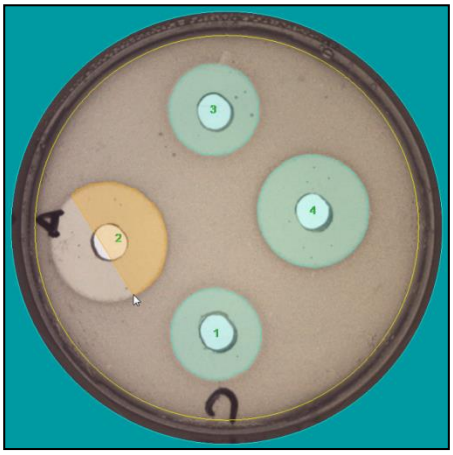



- ***Remove halos:*** Left click on a halo on the image to remove it.

- ***Add circular halos:*** Draw a circular halo by left-clicking over a place on the image belonging to the desired halo contour and dragging the mouse while keeping the left button pressed, until the desired halo position and diameter are reached.




- ***Add free-form halos:*** Draw a halo with arbitrary shape by left-clicking over a place on the image belonging to the desired halo contour, and dragging the mouse while keeping the left button pressed to manually draw the desired halo shape until closing the contour.




- ***Restore halos:*** Discard the manual interactions made so far and restore the automatically processed halos.

- ***Disable interaction:*** Stop allowing the manual interaction but keep the interactive modifications made so far.

If any interactive graphical modification has been made, a warning text informing of this circumstance will be automatically added to the *Comments* field of the plate results.

## 7.4. Saving the results in the database

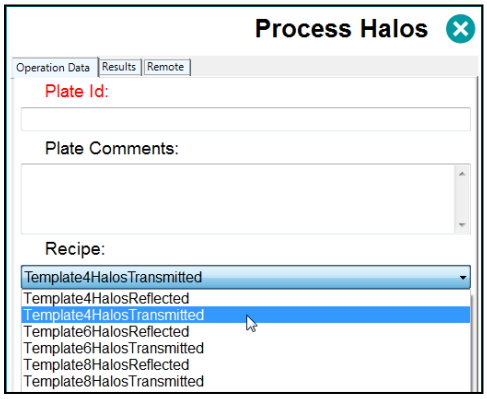
Press the button to accept the results and to save them into the database. If you want to discard the results, press the reject button . You are not allowed to launch a new *Process Halos* without having saved or rejected the previous process.

# 8. Creating a customized recipe for your halos plates

A recipe is a set of settings suited to process a typology of halos plates. If the existing ready-to-use recipes (see 7) do not satisfy your needs, you can create a customized recipe tailored to your plate typology. To create the recipe, you need one or more sample plates of the same typology, following the Layout settings 8.2.2.

## 8.1. Selecting a default recipe

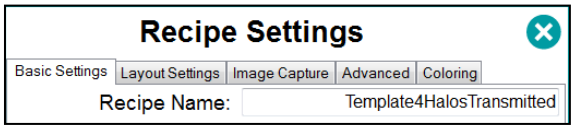
Select *Process Halos* in the top-right control panel; the *Process Halos* panel will be displayed; now select a "*Template"*- started recipe from the recipe drop-down list:




The template recipes contain a set of general-purpose default settings (see 7.1), that you must modify to create the specific recipe for your plates.

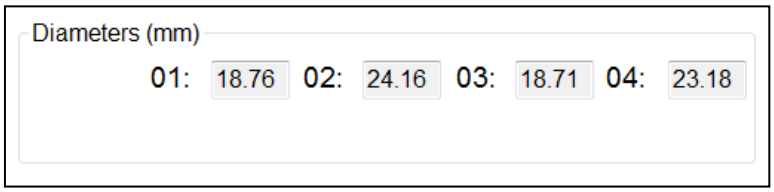
## 8.2. Editing the recipe settings

Press the edition button at the bottom of the *Process Halos* panel. If you do not have a role with limited permissions as *Operator* (*see 14.1.1)*, the *Recipe Settings* panel will appear with five tabs: *Basic Settings, Layout Settings, Image Capture, Advanced,* and *Coloring.*



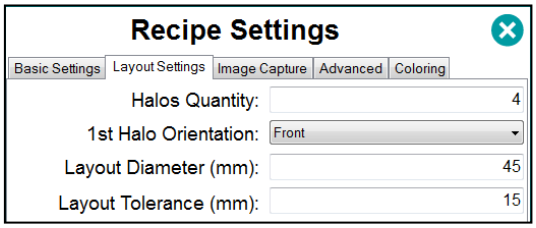
### 8.2.1. Testing the settings on a sample plate

When staying in any of the five tabs of the *Recipe Settings* panel, click the run button at the bottom to apply the current settings to a sample plate. The instrument will take an image, which will be processed to find halos. At the bottom of the panel, the diameters of the halos resulting from processing the plate with the current settings are displayed.




### 8.2.2. Layout settings

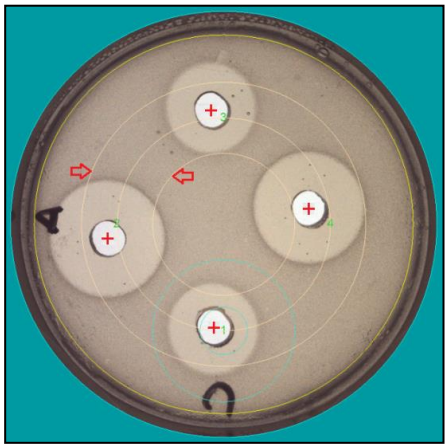
On this tab, the geometrical design layout of the halos in the plate is defined.




- ***Halos Quantity:*** The number of halos that will contain the plate (1-8). It is assumed that halo centers will be evenly spaced on a circumference.
- ***1st Halo Orientation:*** The angular orientation on the plate of the halo that will start the halo count (#1). Halo number count increases clockwise. The default orientation is *Front*, but you can instead specify R*ight, Back,* or *Left*.
- ***Layout Diameter (mm):*** The diameter of the circumference where the centers of the halos must be theoretically placed.

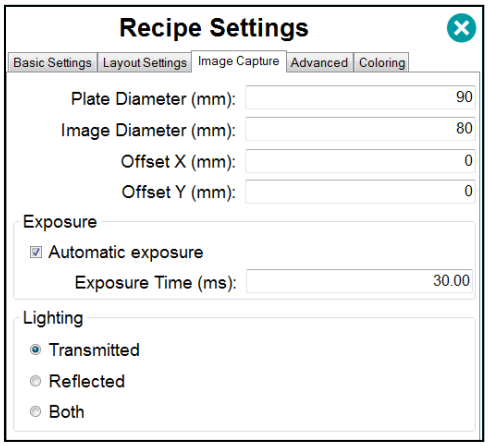
- ***Layout Tolerance (mm):*** The range below and above the *Layout Diameter* where a halo center must be found to be accepted.

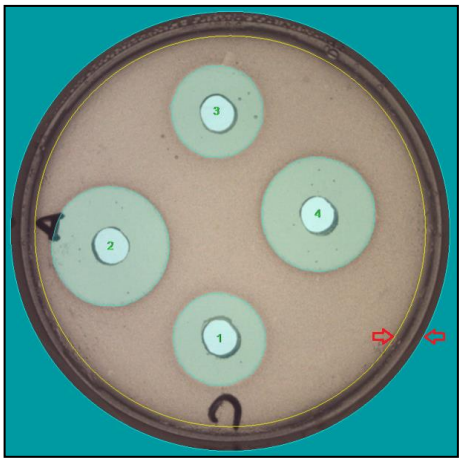
> **NOTE:** When a *defined image* is displayed, by selecting the *View Defined* option in the *Image Panel* context menu (see 10), three overlaid brown circles show the *Layout Diameter* and its tolerance limits. Halos whose center is located outside these limits will be discarded. Two other overlaid cyan circles show the *Max.* and *Min. Halo Diameters* (see 8.2.4).



### 8.2.3. Image Capture Settings

This tab contains the settings relevant to how the image of the plate is acquired.




- ***Plate diameter (mm):*** Diameter of a blue circle, at the edge of the green mask that should be placed over the walls of the plate. It is just a visual aid to assess whether the plate is well centered.

- ***Image diameter (mm):*** Diameter of a yellow circle that defines the region of the plate that will be processed to find halos. You should set an *Image Diameter* slightly smaller than the *Plate Diameter* to avoid the artifacts that sometimes appear close to the edge of the plate.

- ***Offset X / Offset Y (mm):*** If the layout of the halos is not centered concerning the plate, you can re-center the image to the expected layout using these offsets.

**NOTE**: Before try using the offsets perform a calibration. These offsets are not intended to cope with wrong calibrations.

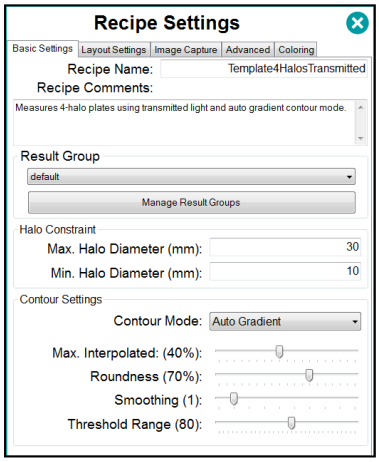
- ***Automatic exposure:*** When checked each time a halos plate is processed, the application will automatically select the most suitable exposure, to achieve a proper image brightness. If unchecked, the application will run each halo process with the fixed value set in the *Exposure time* box.

- ***Exposure time (ms):*** If *Automatic exposure* is unchecked, this is the value that will be applied to all halos plates using this recipe. You can fill in this field and set the proper value by trial-and-error on a sample plate, or you can check and uncheck the *Automatic exposure* checkbox to allow the application to find and fill in the proper exposure value for the sample plate, which later will be applied to all the halos plates being processed by this recipe.

- ***Lighting:*** Select *Transmitted* to use the bottom light (default value); this is suited for the cases when the agar substrate is transparent enough to see the halos clearly defined through the agar. Select *Reflected* to use the upper light; this is suited for the cases where the agar substrate is not transparent enough. You can also select both lights simultaneously.

### 8.2.4. Basic settings

This tab contains the settings that allow discriminating the halo outlines from the background.




- ***Recipe Name:*** Here you should type in the desired name for your recipe. Built-in default recipe names cannot be used for custom recipes.

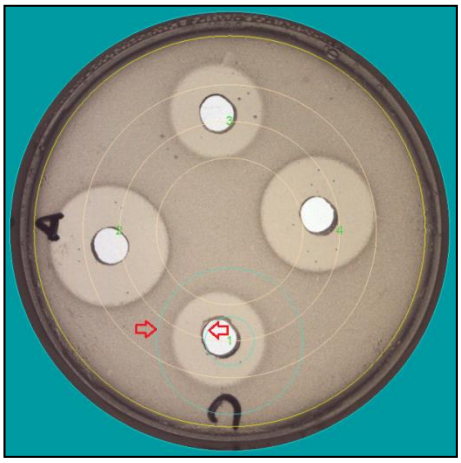
- ***Recipe Comment:*** An optional comment for the recipe can be introduced, describe the purpose or features of the recipe.

- ***Result Group:*** The resulting group initially assigned to the recipe can be selected from the dropdown list.

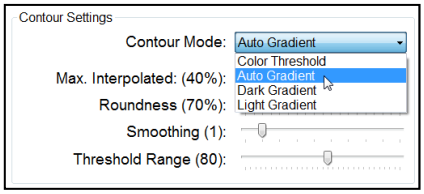
- ***Max Halo Diameter (mm):*** Enter the maximum halo diameter expected for the current plate typology. Objects in the image with higher diameters will be discarded as halo candidates.

- ***Min Halo Diameter (mm):*** Enter the minimum halo diameter expected for the current plate typology. Objects in the image with the lower diameter (such as the antibiotic well or disk) will be discarded as halo candidates.

  **NOTE:** When a *defined image* is displayed, by selecting the *View Defined* option in the *Image Panel* context menu (see 10), two overlaid cyan circles show the *Max.* and *Min. Halo Diameters*. Halos whose diameter exceeds these limits will be discarded. Three other overlaid brown circles show the *Layout Diameter* and its tolerance limits (see 8.2.2).



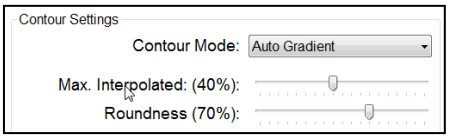
- ***Contour Mode:*** There are four contour detection modes to select; three per gradient (*Auto*, *Dark,* and *Light*) and one per color threshold. *Auto Gradient* mode is the recommended selection to detect any halo with sharp contours clearly outlined. With *Light Gradient* mode, halos lighter than their surroundings are detected. With *Dark Gradient* mode, halos darker than their surroundings are detected. With *Color Threshold* mode, the halo contour is located at the transition between the color of the halo and the color of the surroundings (see 8.2.5).

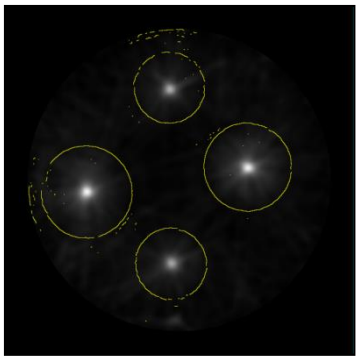



- ***Max Interpolated (%):*** When processing a halo, if part of its contour has not been detected, the program tries to guess by interpolation the missing part. Set this setting to the maximum percentage of the contour that can be interpolated (guessed). Keep this setting low to discard halos having incomplete contours.

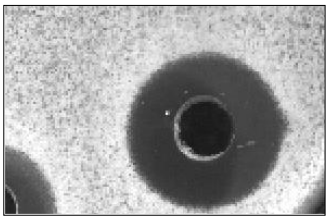
- ***Roundness (%):*** Roundness accounts for the halo shape closeness to a perfect circle (100%). Keep this setting high to discard irregularly shaped halos.

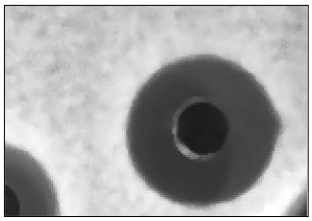
  **NOTE:** When hovering the cursor over the *Max Interpolated*, *Roundness* or the first six Advanced *Settings* labels (see 8.2.5) while the *Processed Image* is displayed, a new image will be displayed showing all the detected edges as yellow segments and the candidate halos centers as white stains.



- ***Smoothing (px):*** If the background of the plate image appears textured in a fashion that prevents correct halos detection, you may increase the smoothing setting from the default value (1) to flatten the background and thus improve the halo detection process.



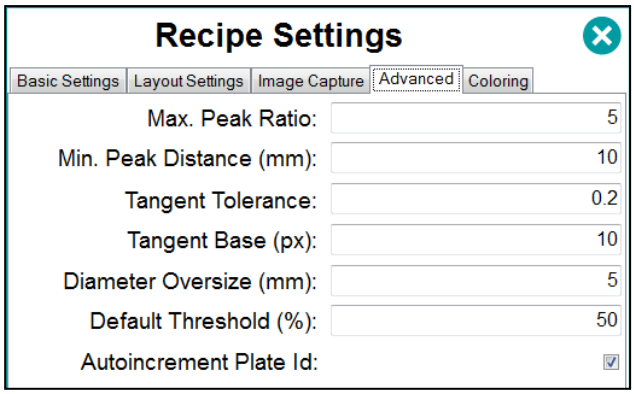


- ***Threshold Range:*** When *Contour Mode* is set to *Color Threshold*, you can fine-tune the results by displacing this setting away from the default value. By rising *Threshold Range* the color acceptation is looser, while lowering it, the color acceptation is stricter. It is useful when using several plates to define a recipe that must work well on all of them.

  **NOTE:** When hovering the cursor over the *Threshold Range* slider, the plate image is overlaid with the purple mask showing the regions that are selected with the current slider value.

### 8.2.5. Advanced Settings

These are settings that are not usually required to be modified from their defaults but can be changed to enhance the performance of some cases.




- ***Max Peak Ratio:*** Candidate halos centers are qualified with a likelihood peak value. One of them will have the maximum peak value; other candidates with lower peak values are discarded if the ratio between the maximum peak and the candidate peak exceeds this setting.

- ***Min Peak Distance (mm):*** Candidate halos centers are discarded if they are closer than this setting to another candidate halos center with a higher peak value.

- ***Tangent Tolerance:*** Contour segments assigned to a halo center are discarded if their tangent deviates from the tangent of a perfect circle more than this setting.

- ***Tangent Base (px):*** The minimum length of a contour segment which is considered to locate a halo center.

- ***Diameter Oversize (mm):*** When searching for candidate halos centers, the *Max* and *Min Halo Diameter* are extended each side by the amount of this setting, to cope with limited cases.

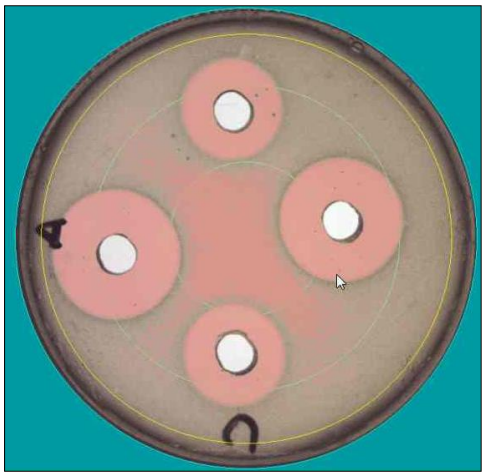
- ***Default Threshold (%):*** It is a multiplicative factor applied to *Threshold Range* that will allow the user to modify it in run time to fine-tune the halos detection performance for plates.

  > **NOTE:** When hovering the cursor over the *Max Interpolated*, *Roundness* (see 8.2.4) or the first six *Advanced Settings* labels while the *Processed Image* is displayed, a new image will be displayed showing all the detected edges as yellow segments and the candidate halos centers as white stains.

- ***Autoincrement Plate Id:*** This checkbox allows you to automatically create a new *Plate Id* after each *Halos Measurement* operation is executed and its results are stored. Successive plate identifiers are created by adding a number to the first *Plate Id* entered by the user or increasing it.

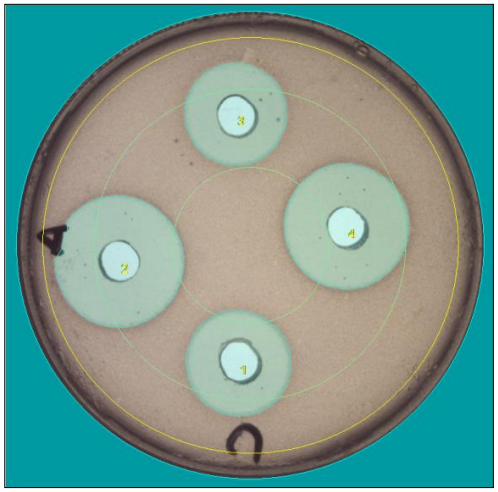
- ***Accepted Colors*:** When *Contour Mode* is set to *Color Threshold* (see 8.2.4) you can click onto this label and it will be highlighted in yellow.

Now hover the cursor over the plate image, inside a halo but very close to its edge. The plate image will be overlaid with a purple mask showing the regions that would be selected if the color under the cursor was chosen.

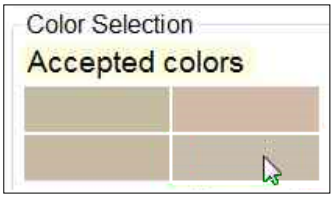


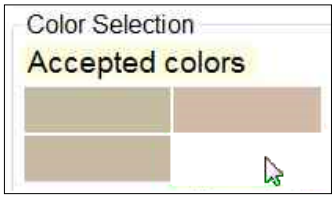
**NOTE:** Not all the inner regions of the halos need to become pink, and all the outer (background) regions are not pink. The goal is that a large proportion of the contour of every halo becomes clearly outlined.

Once a good location has been found, left-click over this location and the selected color will be added as a filled rectangle under the *Accepted Colors* label. By displacing the cursor away from the image, the resulting processed halos for this color selection will be shown as a greenish image overlay filling the detected halos:

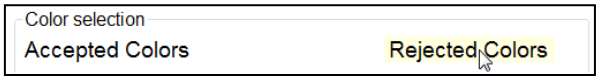


You can add more accepted colors to refine the results, they will be shown as smaller rectangles under the *Accepted Colors* label. By clicking on a color rectangle, you can remove this color:

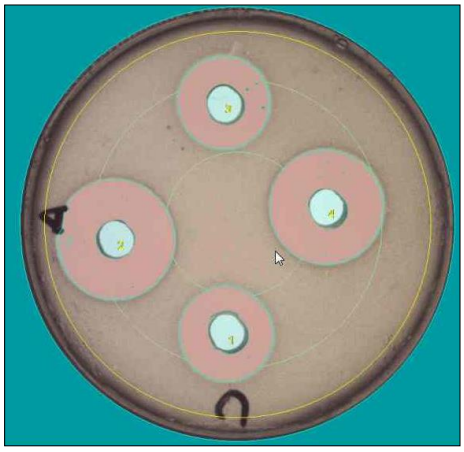



- ***Rejected colors:*** If using only accepted colors the results are not satisfactory enough, you can define in a very similar way colors to be rejected from the selection. Click on the *Rejected Colors* label to highlight it in yellow.

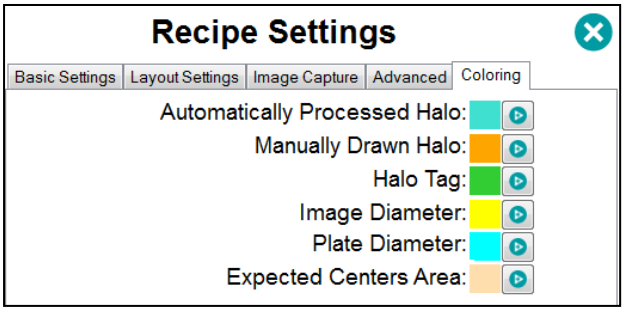



Now hover the cursor over the plate image, outside a halo but very close to its edge, and proceed the very same way that with *Accepted Colors.*



### 8.2.6. Coloring settings

This last category of settings has to do with the preferences of the user about the drawing color of the elements overlaid onto the captured image used to create the processed and defined images.



## 8.3. Management of the recipe

Before saving a recipe, you can restore its previous default settings values by clicking the button .

After editing the settings and achieving the desired results, you can optionally give a new name to the recipe in the box *Recipe Name* of the *Basic Settings* tab, and save the settings to this recipe using the button .

You can delete the current recipe by clicking on the button

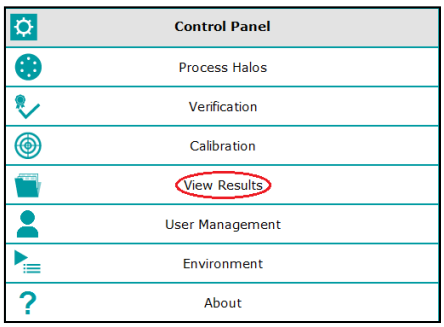
.

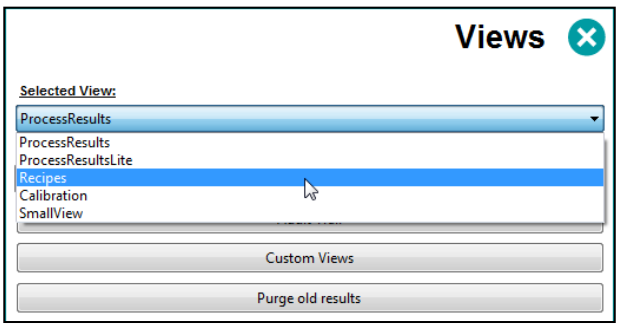
> **NOTE:** You are not allowed to overwrite nor delete the *Template* built-in recipes; instead, save the new settings into a recipe with a new name.

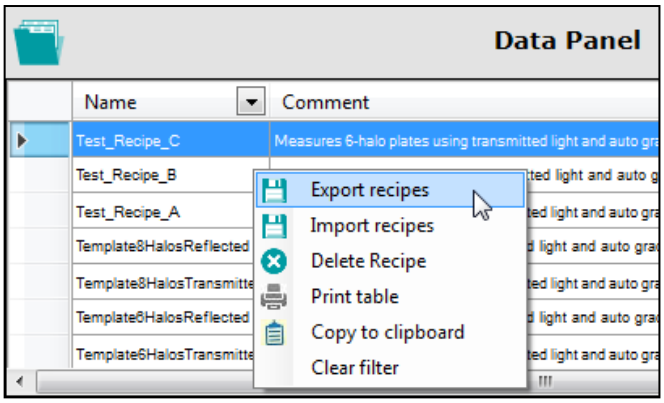
## 8.4. Importing and exporting recipes

If you have several SphereFlash® instruments working in different computers, you may want that some recipes developed on one of these workplaces could be used in the other ones, without the annoyance of manually copying all the settings of the recipe from one workplace to the other.

The *Recipe Export* feature allows you to create on the source workplace an XML file containing the settings of the recipes that you want to copy. To export a recipe, go to *View Results*, select from the drop-down list the view *Recipes*, and you will get in the *Data Panel* a list of all the available recipes. Select all the recipes you want to export, and right-click on the selection to access the context menu; from it select *Export recipes:*

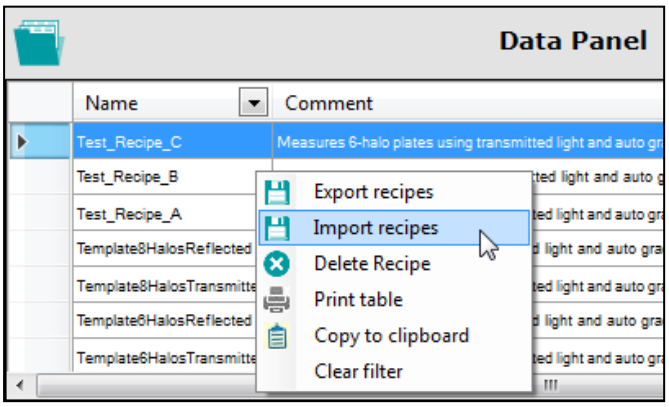





A dialog will be opened, where you can give a name for the exported recipes XML file, and choose the destination folder.

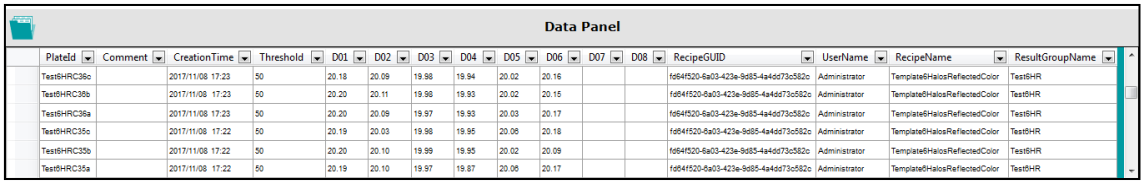
Now copy the generated file onto a folder on the PC of the new workplace where you want to copy the recipes. Proceed similarly as above, but this time select *Import recipes*:




A dialog will be opened to select the recipe file to be imported. Then, if a recipe already exists with the same name as the imported one, you will be prompted to change the name of the imported recipe.

# 9. Managing stored Process Results

## 9.1. Overview of the Process Result View




In the *Data Panel* area (below the *Image Panel)* there is a grid showing for each row one result previously stored. By default, the results are shown ordered by time of execution of the operation, the most recent above.

## 9.2. Fields displayed by the Process Result View

By default, the *Data Panel* shows a view with all the data available for each stored result. That includes the *Plate Id, Comment, Creation Time, Threshold value* used, *D01...D08 measured diameters (of each halo* up to #8*)*, *Username* which operated, *Recipe* used for the measurement, and *Result Group* assigned.

If one result has been interactively modified by the user (see 7.3.2), the comment field will contain a mention of this interactive modification.

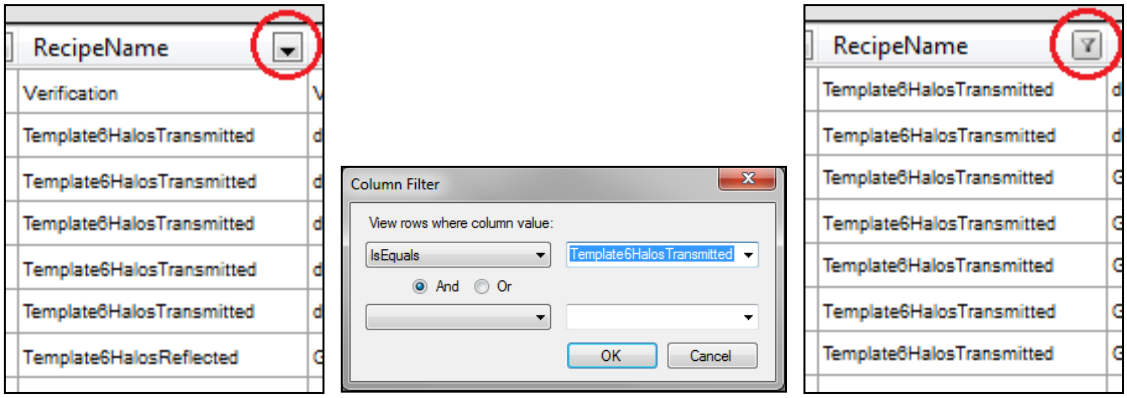
If you click on one result row, the image of the corresponding processed plate will be displayed on the *Image Panel.* Right-click on that panel and select *View Captured* to display the image of the corresponding captured plate (see 10).

## 9.3. Sorting, filtering, and selecting results on the Results View

There are horizontal and vertical scroll bars to aid in displaying all the columns and rows of the view.

By clicking on the header of a column, the view is reordered according to the contents of that column. The direction of ordering toggles each time the header is clicked.

By clicking the down arrow on the header of a column, you can establish the filtering criteria for that column; then the down arrow of the header will turn to a funnel icon and the view will show only the results meeting the criteria:



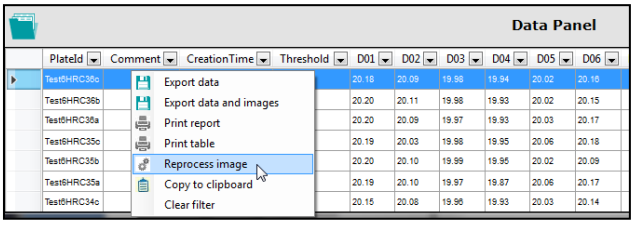

To remove all the applied filters, right-click on the view grid and select *Clear Filter.*

To select one of the results, click its row on the view. To select a contiguous range of results, hold the *Shift* key when clicking the first and the last results of the range. To add or remove one result to the selection, hold the *Ctrl* key and click the result. To select all the results in the (possibly filtered) view, click on the top of the leftmost column.

## 9.4. Re-processing the plate image of a stored result

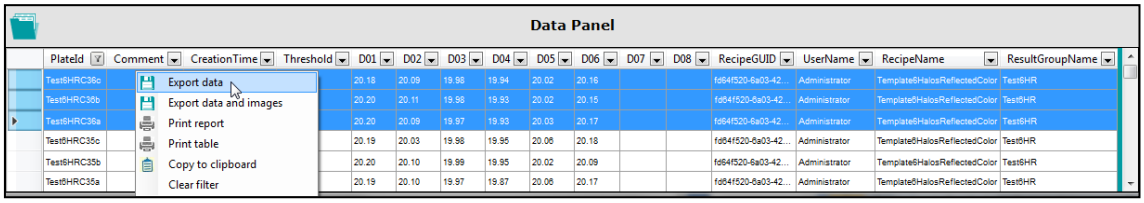
When in the *Process Halos* panel, you can recall the captured image of a stored result to re-process it with possibly different settings, and to store the new result as if its image had been obtained from a real plate with the instrument.

To perform this feature, first, select on the *Process Halos* the desired *Recipe* to be used, then right-click on the *Data Panel* the row corresponding to the resulting plate you want to re-process and select *Reprocess Image*.




## 9.5. Printing and exporting results

After selecting a result of a range of results, you can print or export them in a diversity of ways. To access them, right-click on any of the selected rows:



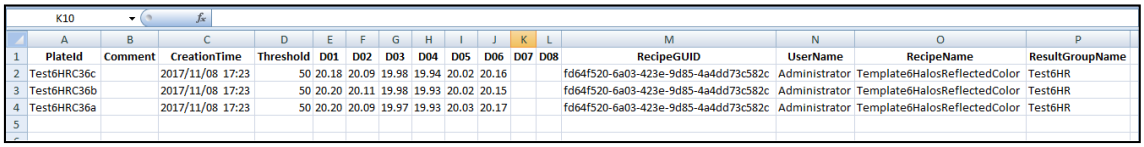
***Export data*** creates a new file containing the headers and the fields of the selected rows. The user is prompted to select the destination folder, the name of the file, and the type of file (XLSX: Excel, CSV: Comma-delimited, and TXT: Tab delimited).

***Export data and images:*** same as above, but in addition, a sub-folder is created in the selected one, which will contain the *Captured* and *Processed* images of all the exported results, their file names being based on the corresponding fields of each result.

***Print table:*** The current view with the selected results is formatted and printed in tabular form.

***Print report*****:** A report of the results for each processed plate in the selection is printed, one separate page for each plate. The report will include images of the result. In the footer, there is the name of the user who ordered the report, as well as the date and time when it was printed.

***Copy to Clipboard:*** The selection is copied to the clipboard. Then, you can paste the copied results along with the column headers onto an external application such as *Excel*, *Word*, *Notepad*, etc.

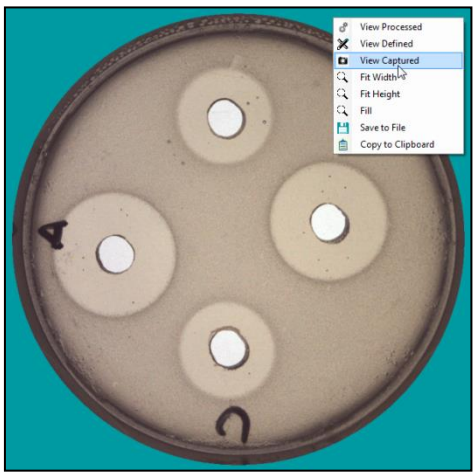


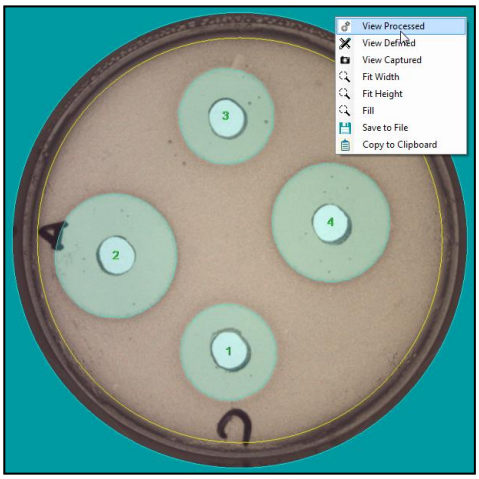
| | A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | PlateId | Comment | CreationTime | Threshold | D01 | D02 | D03 | D04 | D05 | D06 | D07 | D08 | RecipeGUID | UserName | RecipeName | ResultGroupName |
| 2 | Test6HRC36c | | 2017/11/08 17:23 | 50 | 20.18 | 20.09 | 19.98 | 19.94 | 20.02 | 20.16 | | | fd64f520-6a03-423e-9d85-4a4dd73c582c | Administrator | Template6HalosReflectedColor | Test6HR |
| 3 | Test6HRC36b | | 2017/11/08 17:23 | 50 | 20.20 | 20.11 | 19.98 | 19.93 | 20.02 | 20.15 | | | fd64f520-6a03-423e-9d85-4a4dd73c582c | Administrator | Template6HalosReflectedColor | Test6HR |
| 4 | Test6HRC36a | | 2017/11/08 17:23 | 50 | 20.20 | 20.09 | 19.97 | 19.93 | 20.03 | 20.17 | | | fd64f520-6a03-423e-9d85-4a4dd73c582c | Administrator | Template6HalosReflectedColor | Test6HR |
| 5 | | | | | | | | | | | | | | | | |

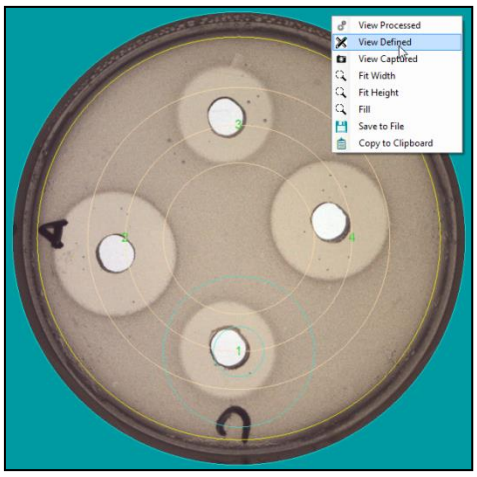
# 10. Displaying and exporting images

By default, the *Image Panel* displays the results image, which shows the captured image overlaid with a turquoise mask showing the detected (or interactively modified) halos and their positional numbers in green figures.

By clicking on the *Image Panel* with the right button of the mouse, a contextual menu will appear allowing to choose the display of the raw captured image without overlays (*View Captured*), the default results image (*View Processed*), or the recipe-defined image (*View Defined*) when being in settings edition (see 8.2.2 and 8.2.4).



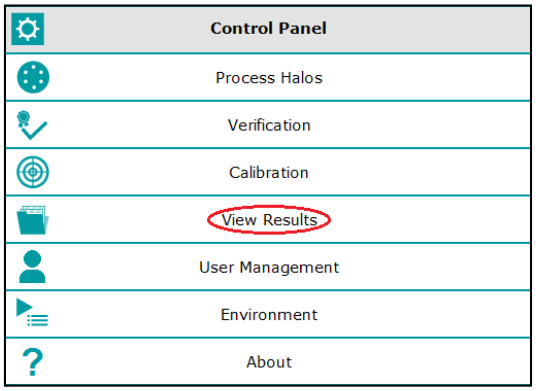

From the contextual menu, you can export both images to files by selecting the option *Save to File* or copy only the displayed image by selecting the option *Copy to Clipboard*.

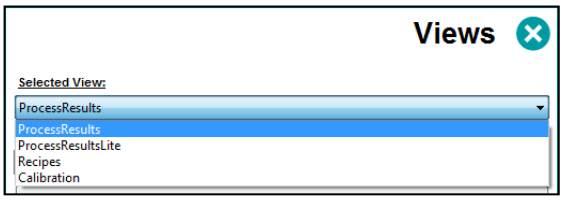
You can also select in the contextual menu to zoom the image: *Fit Width, Fit Height* and *Fill* (fits to width or height, whatever is reached first).

Additionally, you can zoom the image by pressing and rolling the mouse wheel and pan the image by pressing the mouse wheel while displacing the mouse.

# 11. Views Management

You can display in the bottom *Data Panel* several types of views of halos process results, recipes, and calibrations. To select the view to display, go to the *View Results* panel and select from the drop-down list the desired view:




## 11.1. Built-in Views

***ProcessResults:*** Displays all the available information fields of each result.

***ProcessResultsLite:*** Displays a summarized selection of the most relevant fields of each result.

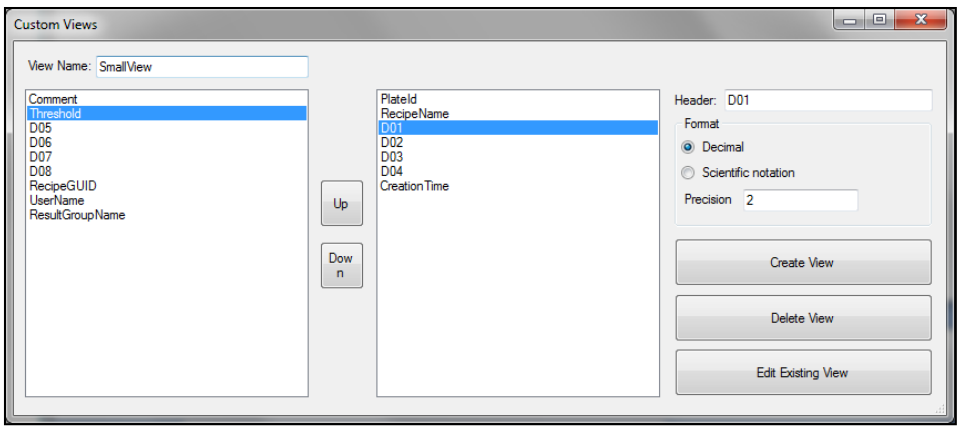
***Recipes:*** Displays a list of all the available recipes. You can select a recipe and delete it if your user has a role with enough permissions.

***Calibration:*** Displays a list of all the available information fields of each calibration.

## 11.2. Customized Views

The users with a role that has permission for it, can create a customized view of the results, by selecting which columns will be shown, in which order, change the heading name of the columns, and define the numeric format to display for numeric, non-integer fields.

Press the *Custom Views* button and a view tailoring dialog will appear:



You must give a name to the view in the upper-left box. In the left panel, there are the available column names, select those you want in your view by double-clicking on each of them, after clicking, the column name will be moved to the right panel.

One in the right panel, you can re-order the columns with the *Up* and *Down* buttons. You can change the header name for the selected column in the top-right box. You can define a numerical format for the fields that admit it (scientific or decimal, with the desired number of decimal places). And you can remove a column from the right panel by double-clicking on it, the column will be moved back to the left panel with its original name.

When you are done, click on the *Create View* button to save the view. Then, this created view will be available in the *Selected View* drop-down list.

To modify an existing custom view, press *Edit Existing View* and select the name of the view to edit. You can delete an existing view when editing it, by pressing the button *Delete View*.

## 11.3. Actions on the views

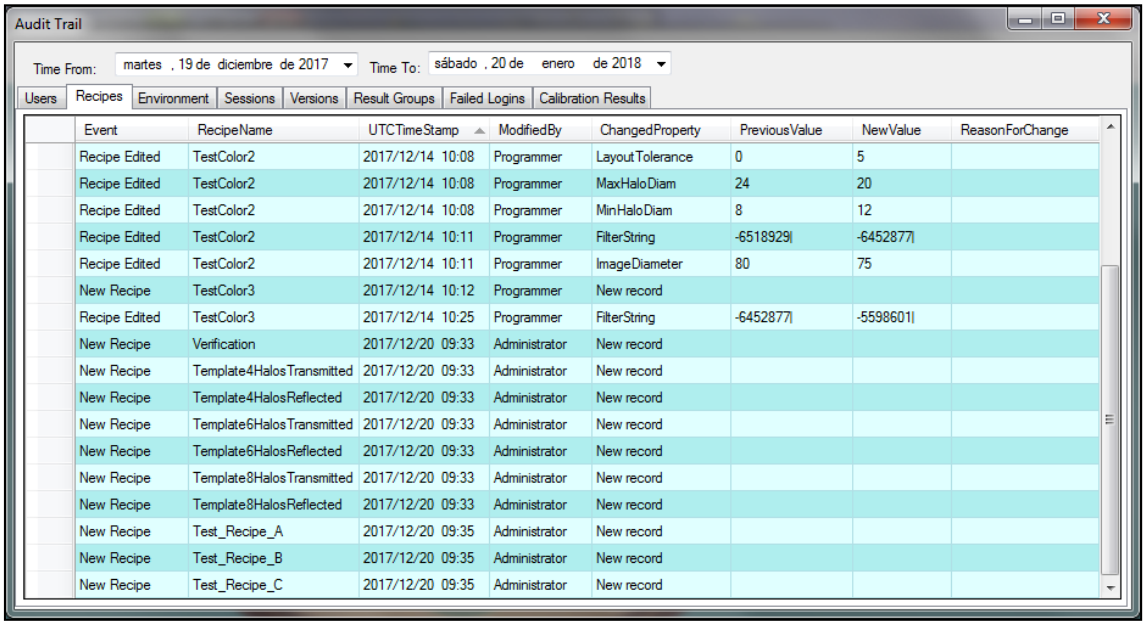
When a view is displayed in the *Data Panel*, you can sort the rows in ascending or descending order by clicking on the header of the column that contains the desired sorting values. A filter can be placed on each column to only select the rows that meet the combined criteria of all the filters. And a manual selection of individual results or a range of them can be established by clicking on the desired rows while holding the *Shift* or *Ctrl* keys as is usual in windows programs.

Once a selection has been established, by left-clicking on it you can export the selected results to a variety of formats, print them as a table or as a report, and copy them to the clipboard. To export to a PDF file of the selected results, you can print them using a third-party virtual PDF printer.

## 11.4. Audit Trail

The *Audit Trail* is a historical record of all the changes and actions that any user has done when using the application. The *Audit Trail* is mandatory under some regulatory schemes, such as the FDA CFR21P11.

To access the *Audit Trail*, go to the *View Results* and click on the button *Audit Trail*. A grid panel with multiple tabs is displayed:




| Event | RecipeName | UTCTimeStamp | ModifiedBy | ChangedProperty | PreviousValue | NewValue | ReasonForChange |
|---|---|---|---|---|---|---|---|
| Recipe Edited | TestColor2 | 2017/12/14 10:08 | Programmer | LayoutTolerance | 0 | 5 | |
| Recipe Edited | TestColor2 | 2017/12/14 10:08 | Programmer | MaxHaloDiam | 24 | 20 | |
| Recipe Edited | TestColor2 | 2017/12/14 10:08 | Programmer | MinHaloDiam | 8 | 12 | |
| Recipe Edited | TestColor2 | 2017/12/14 10:11 | Programmer | FilterString | -6518929\| | -6452877\| | |
| Recipe Edited | TestColor2 | 2017/12/14 10:11 | Programmer | ImageDiameter | 80 | 75 | |
| New Recipe | TestColor3 | 2017/12/14 10:12 | Programmer | New record | | | |
| Recipe Edited | TestColor3 | 2017/12/14 10:25 | Programmer | FilterString | -6452877\| | -5598601\| | |
| New Recipe | Verification | 2017/12/20 09:33 | Administrator | New record | | | |
| New Recipe | Template4HalosTransmitted | 2017/12/20 09:33 | Administrator | New record | | | |
| New Recipe | Template4HalosReflected | 2017/12/20 09:33 | Administrator | New record | | | |
| New Recipe | Template6HalosTransmitted | 2017/12/20 09:33 | Administrator | New record | | | |
| New Recipe | Template6HalosReflected | 2017/12/20 09:33 | Administrator | New record | | | |
| New Recipe | Template8HalosTransmitted | 2017/12/20 09:33 | Administrator | New record | | | |
| New Recipe | Template8HalosReflected | 2017/12/20 09:33 | Administrator | New record | | | |
| New Recipe | Test_Recipe_A | 2017/12/20 09:35 | Administrator | New record | | | |
| New Recipe | Test_Recipe_B | 2017/12/20 09:35 | Administrator | New record | | | |
| New Recipe | Test_Recipe_C | 2017/12/20 09:35 | Administrator | New record | | | |

Each record in all the grid panels includes the name of the user who acted and the timestamp when the action occurred. By clicking on the header of a column, the records can be ordered according to the values of this column. The records can be filtered by the time of occurrence, by introducing the start and end dates on the top boxes *Time from* and *Time to*.

In a very similar way that with the results views, you can manually select a set or range of rows and export, print, or copy them, by left-clicking on the selection.

There are the following tabs available:

***Users:*** Records all the user management actions, such as creation, deletion, role assignment, password change, etc.

***Recipes:*** Records all the events related to the creation, edition, modification, and deletion of recipes.

***Environment:*** Records the changes done in the settings under the *Environment* and *System options* panels.

***Sessions:*** Records each session login and logout data.

***Failed Logins:*** Records the logins that failed because the password was incorrect or the username was wrong.

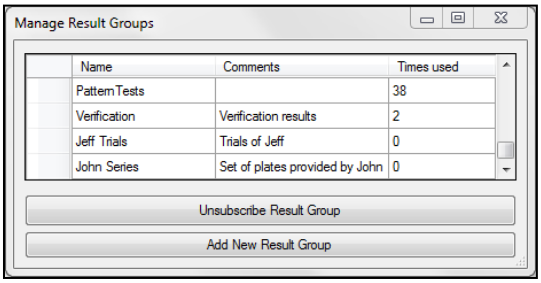
***Versions*:** Records each update done to the application.

***Result Groups:*** Records the creation and deletion of result groups.

***Calibration Results:*** Shows the results of each calibration operation that has been done.

## 11.5. Managing result groups

*Result Group* is a label or tag that can be applied to the result, allowing subsequent grouping or filtering of the results in the views based on this label. To access the management of the groups, click on the *Manage Result Groups* button in the *View Results* panel, and a dialog will open where the existing groups are listed and there are buttons to create a new group or remove an existing one:




The native built-in groups are the *default* group, which is the default for halos measurement operations, and the *Verification* group, which is automatically assigned to the results of the *Verification* operations.

When creating or editing a recipe, you can define the *Result Group* that will be assigned to the results obtained with this recipe (see 14.1.1).

> **NOTE:** A *Result Group* cannot be deleted if there are in the database some results that have this group assigned. Before deletion, you must purge the old results (see 14.5) in a fashion that no remaining results have this group assigned.
>
> **NOTE**: Recipes using a deleted result group, will be automatically re-assigned to the first *Result Group* of the list, the *default* group.

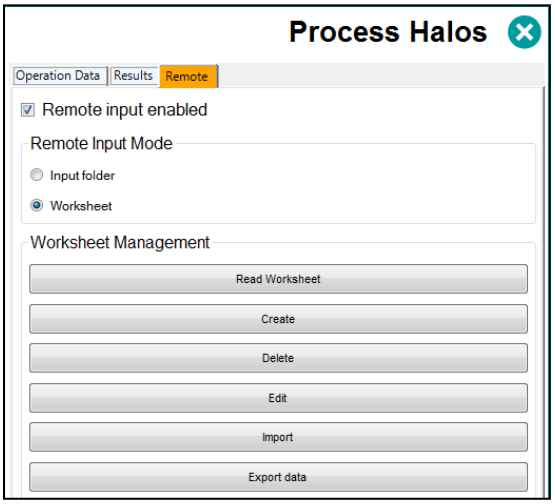
# 12. Working with worksheets

To avoid errors of the operator when selecting the recipe or editing the *Run Data and Input Values* (*Threshold*) required to process each particular plate, a user with (at least) the *Programmer* role can create a table in advance where, for each *Plate Id*, the recipe to be used and the input values can be defined.

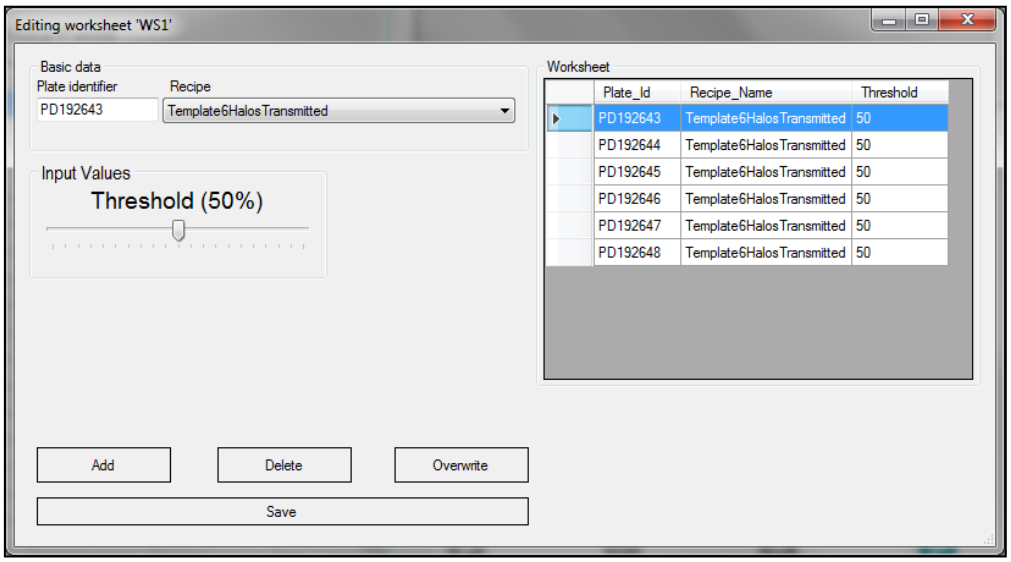
Later when the operator will process a particular plate, by just introducing its *Plate Id* (typing-in it, or better using a barcode reader), if this *Id* exists in the active worksheet, all the required parameters to process it will be automatically loaded.

## 12.1. Creating and editing a worksheet

In the *Process Halos* panel, select the tab *Remote*, and then check the box *Remote input enabled* and the radio button *Worksheet*. The tab *Remote* will be highlighted in orange to indicate that the *Remote* mode is active:



You can create and edit worksheets if you have a role with enough permissions as a *Programmer* or *Administrator* (see 14.1.1). To create a new worksheet, click *Create* and you will be prompted to enter a name for the new worksheet. To edit an existing worksheet, first, click *Read Worksheet*, select the desired one from the list, and then click *Edit.* Then, the worksheet editing dialog will appear:




For each plate you want to include in the worksheet, type-in (or barcode read) its *Plate Id* in the top-left box and select the *Recipe* you want being applied to measure this plate. Optionally, select below the Threshold value you want to apply to this plate.

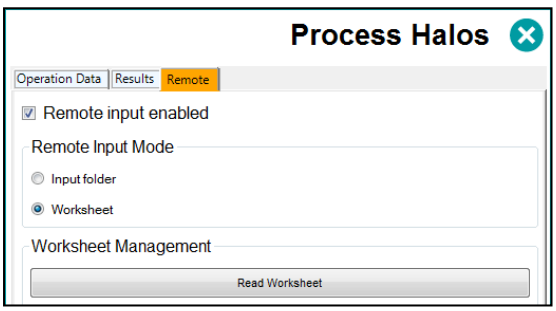
> **NOTE:** The Input values modified for a plate will also apply to the next plate unless you re-load the recipe or use a new recipe for the new plate.

Press *Add* to include the edited plate in the worksheet list on the right. You can re-edit an existing plate in the list by selecting its row, changing the values, and then pressing *Overwrite*. And you can remove a plate from the list by selecting its row and pressing *Delete.*

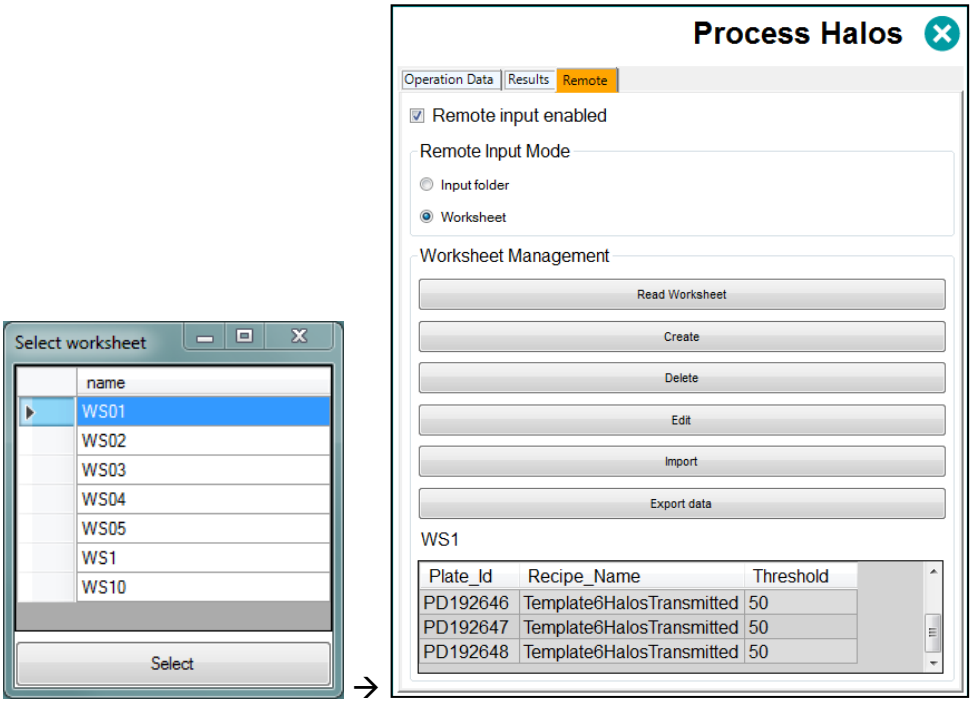
Finally, press *Save* to store the worksheet and its contents in the database.

## 12.2. Using a worksheet to measure halos

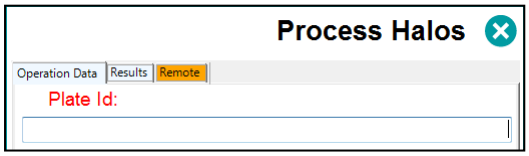
In the *Process Halos* panel, select the tab *Remote*, and then check the box *Remote input enabled* and the radio button *Worksheet*. The tab *Remote* will be highlighted in orange to indicate that the *Remote* mode is active:



Then press *Read Worksheet*, select the worksheet you want to use, and the list of plates included in this worksheet will be displayed at the bottom:




Select the tab *Operation Data*, and type-in (or barcode read) a *Plate Id* in the top-left box:




If this *Id* exists in the worksheet, the *Run* button will turn green and you can proceed to run the halos measurement with the recipe and values specified in the worksheet for this plate.

If the *Id* does not exist in the worksheet, the *Run* button will keep gray and you will be prevented to run a measurement operation.

## 12.3. Importing, exporting, and deleting worksheets

You can create a worksheet in an external application and then import it into the SphereFlash® application for its use. There are three formats supported: Excel, CSV, and XML. Importation is done by clicking on the *Import* button.

To externally create a worksheet to be imported, you may find it helpful to create a sample worksheet with the SphereFlash® application, export it in the desired format, and use the generated file as a template to create your external worksheet with the expected structure and field names. Exportation is done by clicking on the *Export data* button.

To delete an existing worksheet, push the button *Delete* and select from the list the worksheet to be deleted.

## 12.4. Working with remote file input

If you select the *Input folder* radio button instead of the *Worksheet* button, a similar behavior as that of the worksheet will be achieved, but the information concerning which *Recipe* and *Run & Input values* apply to each *Plate Id* will be automatically obtained at each *Halos Measurement* operation, from an XML file located in a remote folder, rather than from a worksheet. See sections 14.2.5 and 14.7.

# 13. Antibiotic Potency Test

You can automatically run the calculations of an Antibiotic Potency Test according to the procedure of the United States Pharmacopoeia (USP <81>: Antibiotics – Microbial Assays, cylinder-plate method). The calculations use as input the previously obtained results of halos measurement on a set of plates properly arranged according to the potency test method.

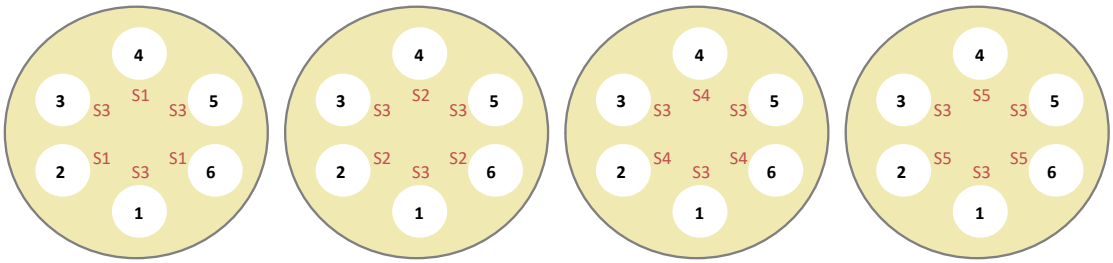
## 13.1. Preparation and measurement of the plates

Plates must be arranged following the schema as specified by USP <81>:

- Use 5 properly spaced known concentrations of the standard, named S1 to S5. Concentration S3 is the central reference standard.

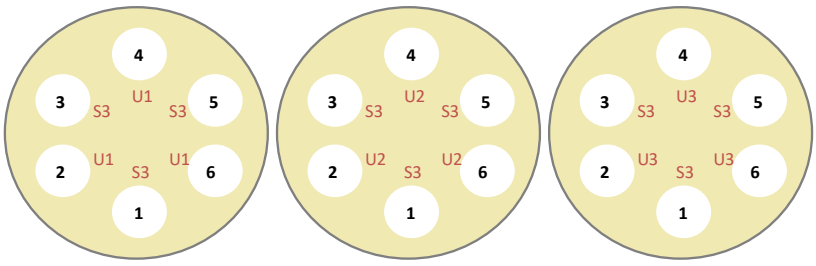
  **NOTE:** It is possible to use only 3 or 4 concentration standards instead of 5, by omitting some of the S1-S5 standards, except the S3 which must be always present because it is the reference.

- For each concentration standard other than S3, prepare one set of repeated plates (typically 3 repeats) with 6 positions each, placing the reference S3 at positions 1,3 and 5, and the other standard at positions 2,4 and 6 (see example in the figure below):




Plates S1-S3 (3 rep.) Plates S2-S3 (3 rep.) Plates S4-S3 (3 rep.) Plates S5-S3 (3 rep.)

- For each unknown sample (U1, U2...) whose potency is to be determined against the standard, prepare one set of repeated plates (typically 3 repeats) with 6 positions each, placing the reference S3 at positions 1,3 and 5, and the unknown at positions 2,4 and 6 (see the example for 3 unknowns in the figure below):




Plates U1-S3 (3 rep.) Plates U2-S3 (3 rep.) Plates U3-S3 (3 rep.)

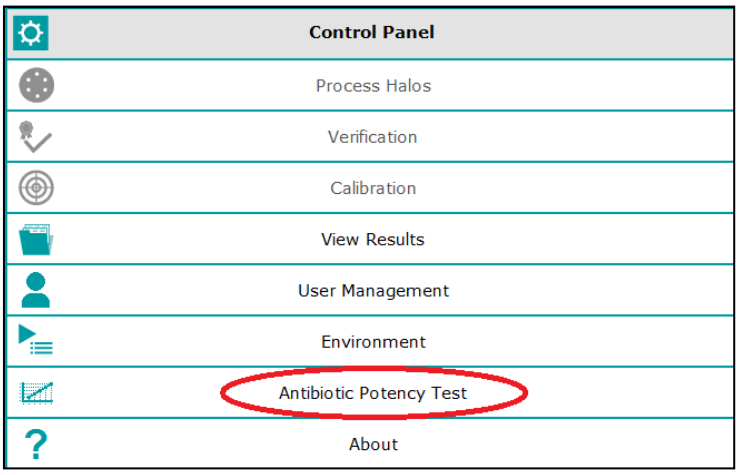
**NOTE:** You can use 1 or more repetitions for each plate set, but ALL the sets must have the same number of repetitions, both the standards sets as well as the unknown sets. It is the responsibility of the user to assess the significance of the calculations when there are few plate repetitions.

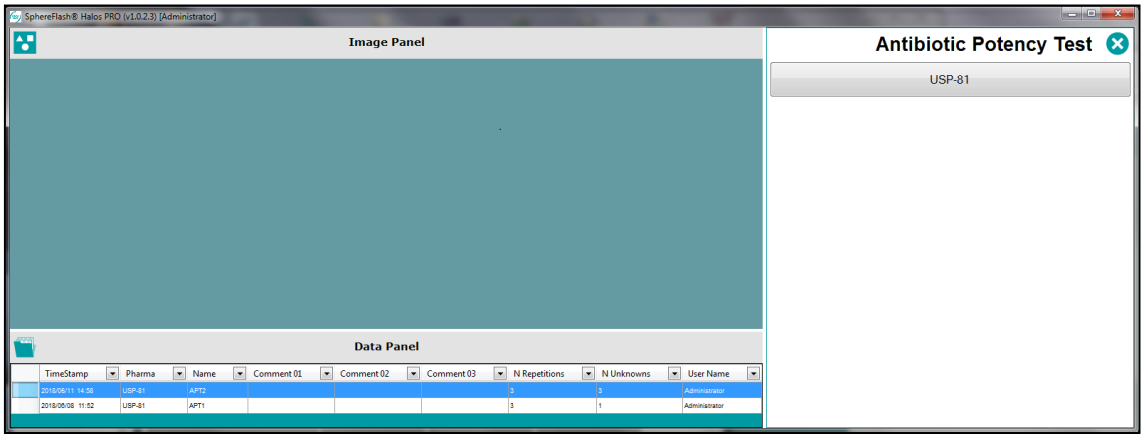
- Proceed to measure the diameter of the halo of all the plates as usual (see section 7.1). Assign a meaningful *Plate ID* to each plate so that later all of them can be easily located and identified in the results table.

  **NOTE**: You may find it useful to define and assign a *Results Group* for all the plates of the same assay (see section 7.1). This way you will be able to easily find and select all the plates of the same assay when performing the potency calculation.

## 13.2. Running the Antibiotic Potency Test

Clicking on the 'Antibiotic Potency Test' access button on the control panel, the 'Antibiotic Potency Test' panel will be shown.



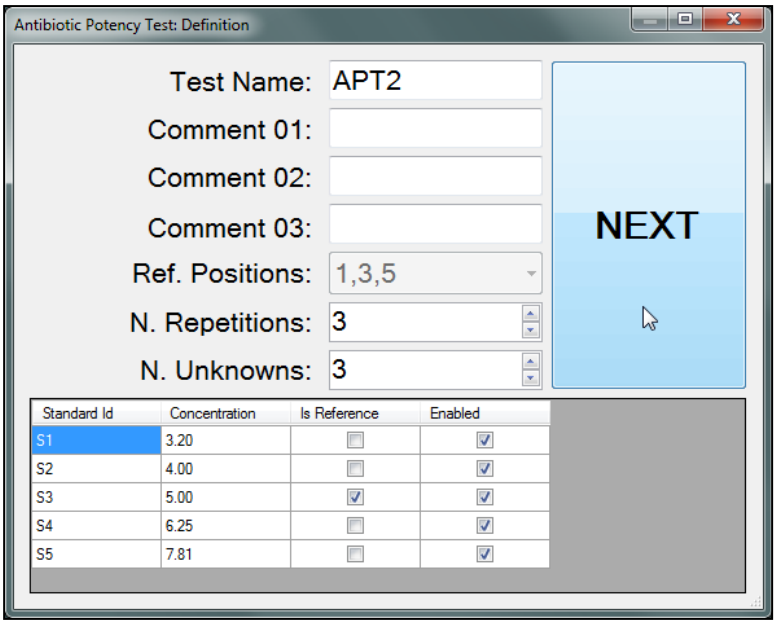




The *Data Panel* displays the list of the antibiotic potency tests previously performed.

Click on the USP <81> button to start a new antibiotic potency test. The test interface is implemented as a wizard-like sequence of dialogs; you can always navigate from one dialog to the next or the previous by clicking on the proper button. If you go to the previous dialog, data entered in the left dialog is lost.

### 13.2.1. General and configuration data

At the first dialog you can enter the general information and configuration about your assay:




- ***Test Name* and *Comments 01* to *03:*** These are general purpose editable text fields. Here you can introduce your data to properly identify the test.
- ***Ref. Position (1,3,5)*:** This is a reminder that all your plates must place the reference standard S3 at positions 1,3 and 5.
- ***N. Repetitions:*** Number of repetitions of each plate type (must be the same for all the plate types).
- ***N. Unknowns:*** Number of unknown samples whose potency is to be determined relative to the same set of standards.
- ***Concentration:*** Enter the concentration for each of the standards in the list.
- ***Enabled:*** By default, all standards S1-S5 are enabled. If you want to use fewer standards, disable the unused standards by unmarking the checkbox. Standard S3 cannot be disabled because it is always the reference.

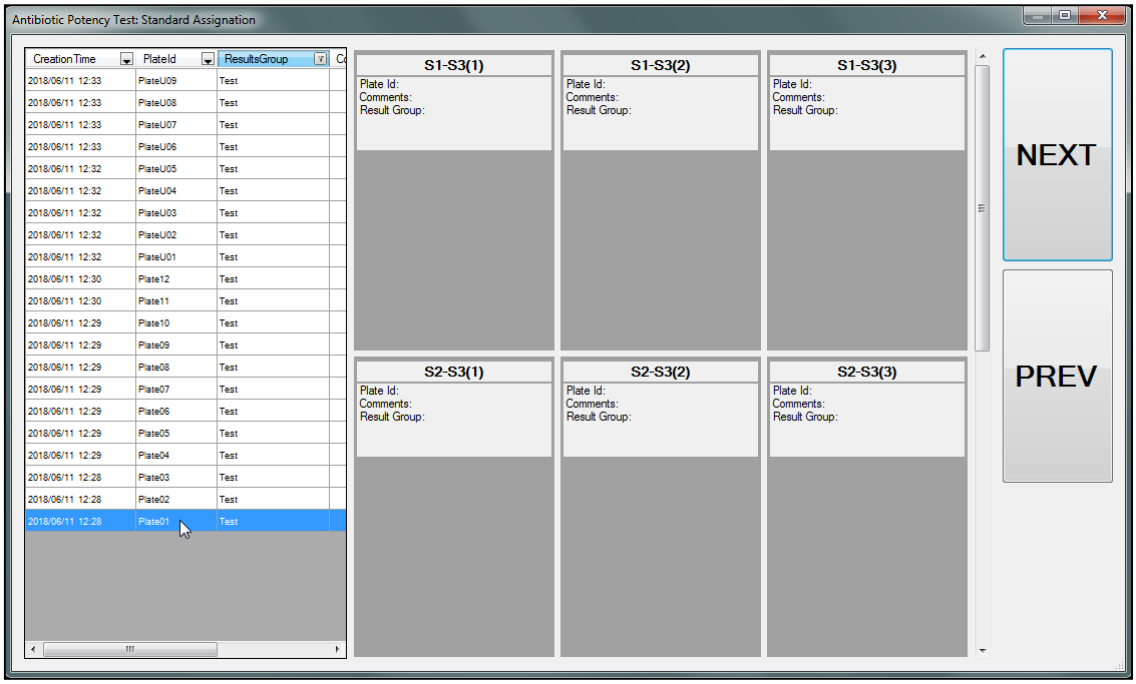
### 13.2.2. Selection of plates to determine the standard line

On the second dialog, you will select the plates that will determine the standard line relating to concentration and response (diameter).

The table at the left shows the stored results of the plates previously measured, showing the *Date and Time, Plate ID, Results Group,* and some other columns. The list displays the most recent results on the top.

You can ease the location of the desired plates by clicking on the right arrow of the header of a column and setting a filter for this field (i.e., a particular result group, a range of dates, or the ID starting with some text). Additionally, by clicking on a column header you can sort the results in ascending or descending order according to the contents of the column.

At the right side of the table, there is one container for each expected plate of the assay, labeled according to the standards in the plate and the repetition number.

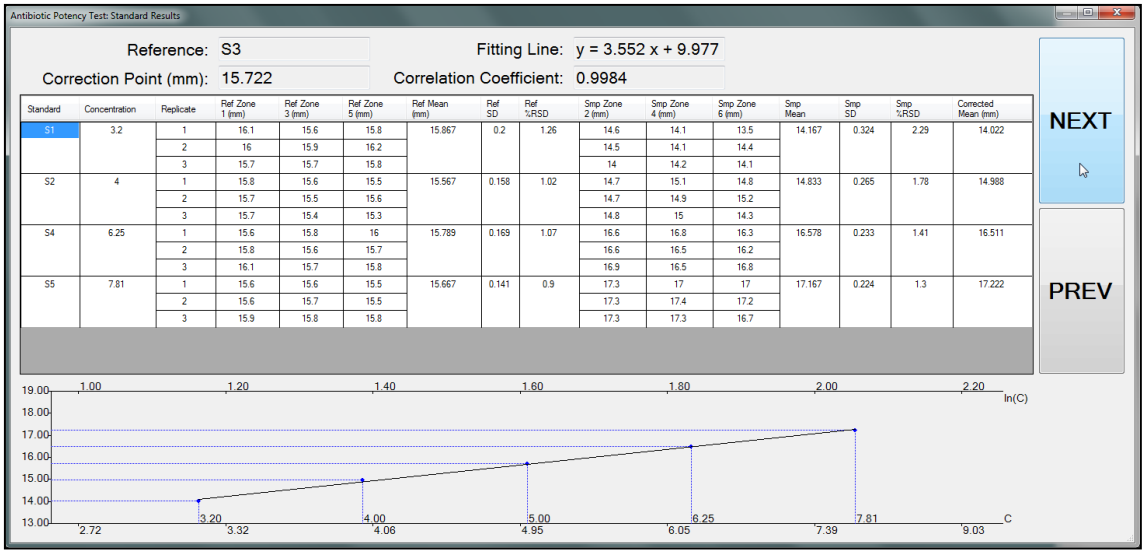



To assign a plate to a particular container, select the row of the plate in the table, click and hold the left button of the mouse, and drag and drop the selected plate into the corresponding container. Then the container will show the processed image of the plate and a summary of its data:

Please, verify that each selected plate matches the title of its container. Press *Next* when done.

### 13.2.3. Calculation of the standard line

Once the plates with the standard antibiotic have been selected, the following screen calculates by the method of the least squares, a log-transformed straight-line that characterizes the behavior of the standard antibiotic at different concentrations:

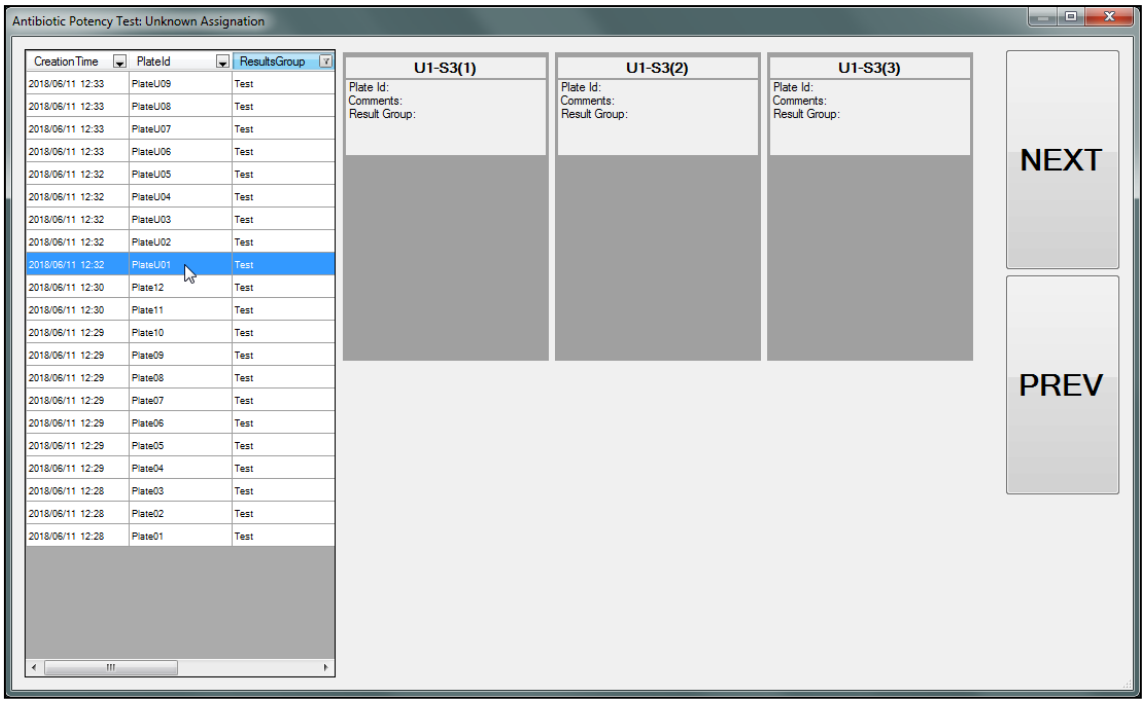


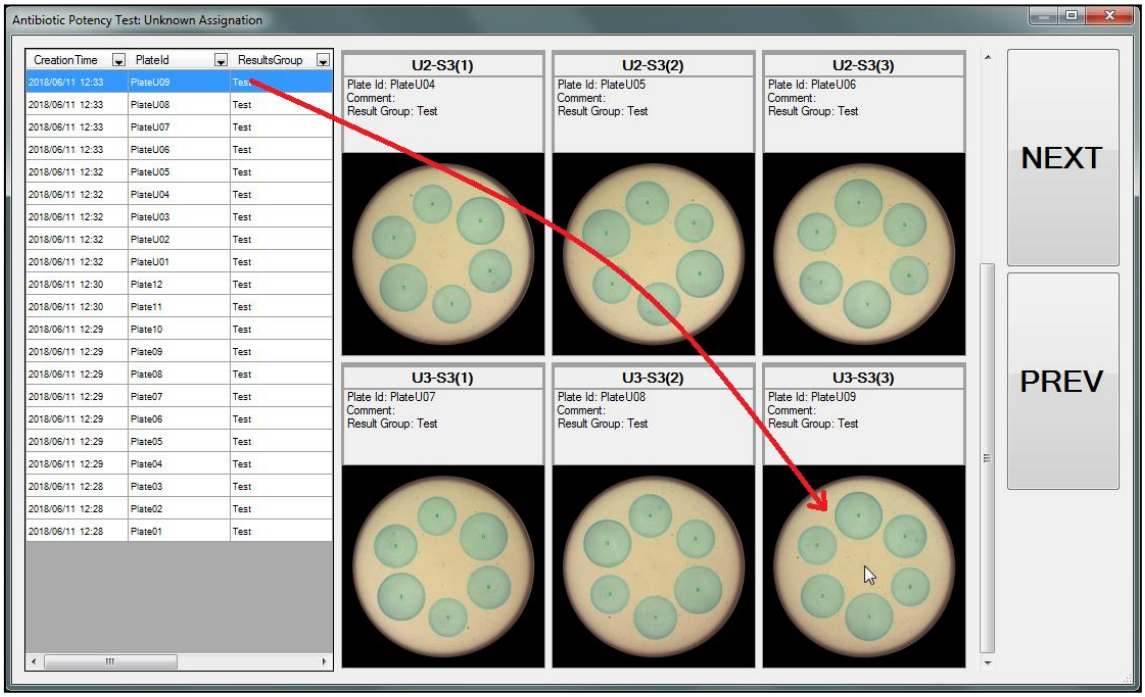

| Standard | Concentration | Replicate | Ref Zone 1 (mm) | Ref Zone 3 (mm) | Ref Zone 5 (mm) | Ref Mean (mm) | Ref SD | Ref %RSD | Smp Zone 2 (mm) | Smp Zone 4 (mm) | Smp Zone 6 (mm) | Smp Mean | Smp SD | Smp %RSD | Corrected Mean (mm) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| S1 | 3.2 | 1 | 16.1 | 15.6 | 15.8 | 15.867 | 0.2 | 1.26 | 14.6 | 14.1 | 13.5 | 14.167 | 0.324 | 2.29 | 14.022 |
| | | 2 | 16 | 15.9 | 16.2 | | | | 14.5 | 14.1 | 14.4 | | | | |
| | | 3 | 15.7 | 15.7 | 15.8 | | | | 14 | 14.2 | 14.1 | | | | |
| S2 | 4 | 1 | 15.8 | 15.6 | 15.5 | 15.567 | 0.158 | 1.02 | 14.7 | 15.1 | 14.8 | 14.833 | 0.265 | 1.78 | 14.988 |
| | | 2 | 15.7 | 15.5 | 15.6 | | | | 14.7 | 14.9 | 15.2 | | | | |
| | | 3 | 15.7 | 15.4 | 15.3 | | | | 14.8 | 15 | 14.3 | | | | |
| S4 | 6.25 | 1 | 15.6 | 15.8 | 16 | 15.789 | 0.169 | 1.07 | 16.6 | 16.8 | 16.3 | 16.578 | 0.233 | 1.41 | 16.511 |
| | | 2 | 15.8 | 15.6 | 15.7 | | | | 16.6 | 16.5 | 16.2 | | | | |
| | | 3 | 16.1 | 15.7 | 15.8 | | | | 16.9 | 16.5 | 16.8 | | | | |
| S5 | 7.81 | 1 | 15.6 | 15.6 | 15.5 | 15.667 | 0.141 | 0.9 | 17.3 | 17 | 17 | 17.167 | 0.224 | 1.3 | 17.222 |
| | | 2 | 15.6 | 15.7 | 15.5 | | | | 17.3 | 17.4 | 17.2 | | | | |
| | | 3 | 15.9 | 15.8 | 15.8 | | | | 17.3 | 17.3 | 16.7 | | | | |

**NOTE:** If there are missing measurements in some plates, the corresponding cells in the upper table will display ‘0‘ and its background will be painted in red, and these cells will not be taken into account for the calculations. Similarly, if the user considers that some measurement is wrong, they can exclude it from the calculations by double-clicking into the value, the cell will then display its background in red. It is the responsibility of the user to assess the significance of the calculations when there are missing values.

### 13.2.4. Selection of plates with the unknown(s)

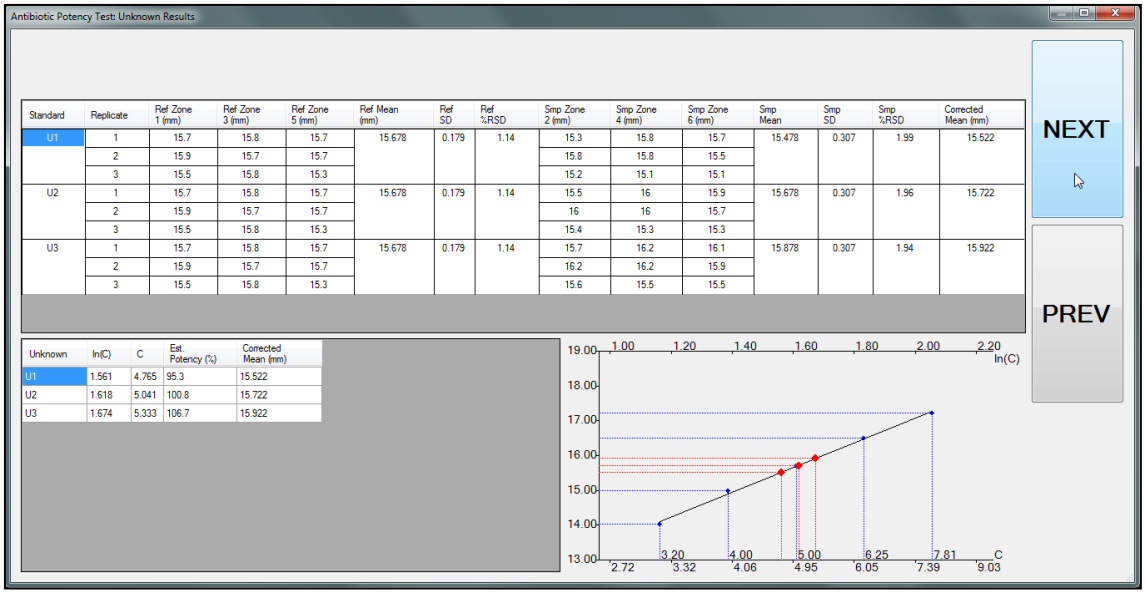
You can now select and assign the plates containing the unknown(s), in the same way as in section 13.2.2:



### 13.2.5. Calculation of the potency of the unknown(s)

Once the plates with the unknown(s) have been selected, the following screen calculates the antibiotic potency of each unknown, by interpolation into the standard curve previously determined:




| Standard | Replicate | Ref Zone 1 (mm) | Ref Zone 3 (mm) | Ref Zone 5 (mm) | Ref Mean (mm) | Ref SD | Ref %RSD | Smp Zone 2 (mm) | Smp Zone 4 (mm) | Smp Zone 6 (mm) | Smp Mean | Smp SD | Smp %RSD | Corrected Mean (mm) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| U1 | 1 | 15.7 | 15.8 | 15.7 | 15.678 | 0.179 | 1.14 | 15.3 | 15.8 | 15.7 | 15.478 | 0.307 | 1.99 | 15.522 |
| | 2 | 15.9 | 15.7 | 15.7 | | | | 15.8 | 15.8 | 15.5 | | | | |
| | 3 | 15.5 | 15.8 | 15.3 | | | | 15.2 | 15.1 | 15.1 | | | | |
| U2 | 1 | 15.7 | 15.8 | 15.7 | 15.678 | 0.179 | 1.14 | 15.5 | 16 | 15.9 | 15.678 | 0.307 | 1.96 | 15.722 |
| | 2 | 15.9 | 15.7 | 15.7 | | | | 16 | 16 | 15.7 | | | | |
| | 3 | 15.5 | 15.8 | 15.3 | | | | 15.4 | 15.3 | 15.3 | | | | |
| U3 | 1 | 15.7 | 15.8 | 15.7 | 15.678 | 0.179 | 1.14 | 15.7 | 16.2 | 16.1 | 15.878 | 0.307 | 1.94 | 15.922 |
| | 2 | 15.9 | 15.7 | 15.7 | | | | 16.2 | 16.2 | 15.9 | | | | |
| | 3 | 15.5 | 15.8 | 15.3 | | | | 15.6 | 15.5 | 15.5 | | | | |

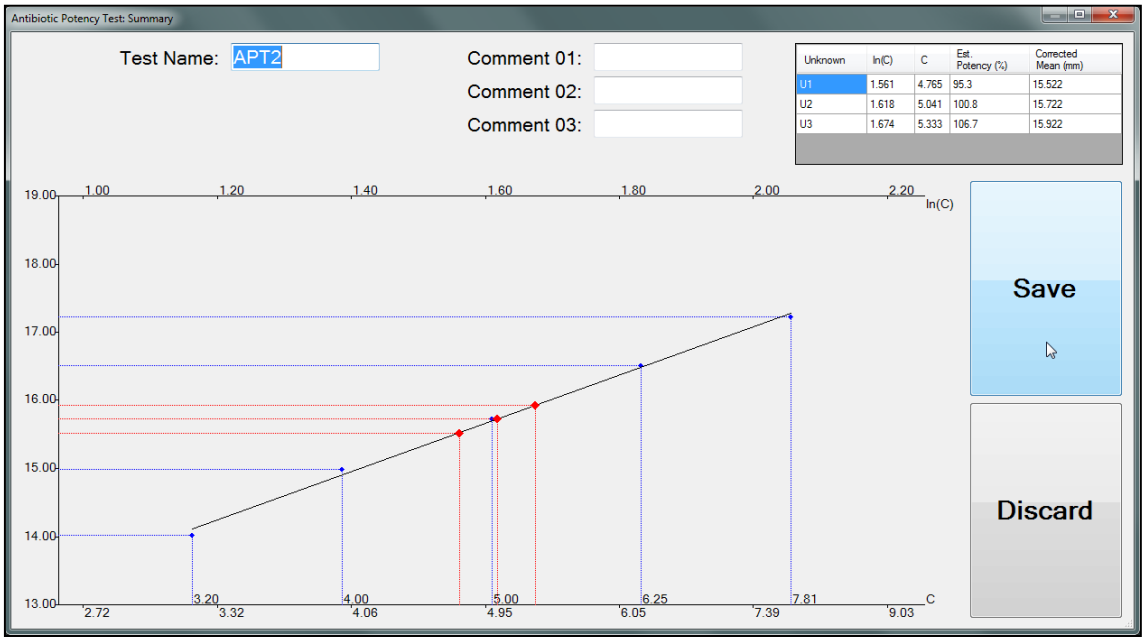
| Unknown | ln(C) | C | Est. Potency (%) | Corrected Mean (mm) |
|---|---|---|---|---|
| U1 | 1.561 | 4.765 | 95.3 | 15.522 |
| U2 | 1.618 | 5.041 | 100.8 | 15.722 |
| U3 | 1.674 | 5.333 | 106.7 | 15.922 |

The bottom-left table shows the results for each unknown, particularly the estimated concentration *C*, and the *Estimated Potency (%)* about the reference standard S3.

> **NOTE:** If there are missing measurements in some plates, the corresponding cells in the upper table will display '0' and its background will be painted in red, and these cells will not be taken into account for the calculations. Similarly, if the user considers that some measurement is wrong, they can exclude it from the calculations by double-clicking into the value, the cell will then display its background in red. It is the responsibility of the user to assess the significance of the calculations when there are missing values.

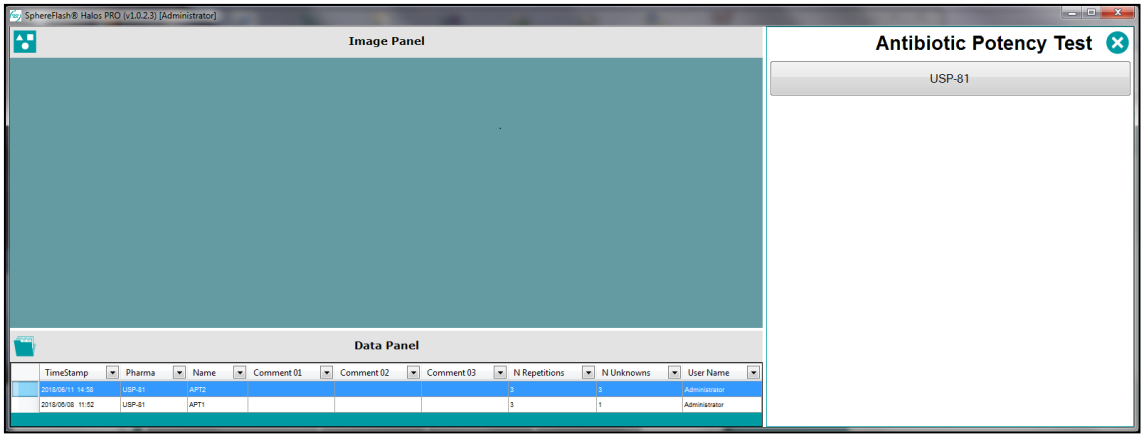
### 13.2.6. Summarizing and saving the calculation results

On the final step, a screen summarizes the calculation results. The user can there modify or add the *Test Name* and the *Comment* fields as required. Then, clicking on the *Save* button, the test data and calculation results will be saved in the database; if clicking on the *Discard* button, the whole calculation data are deleted.



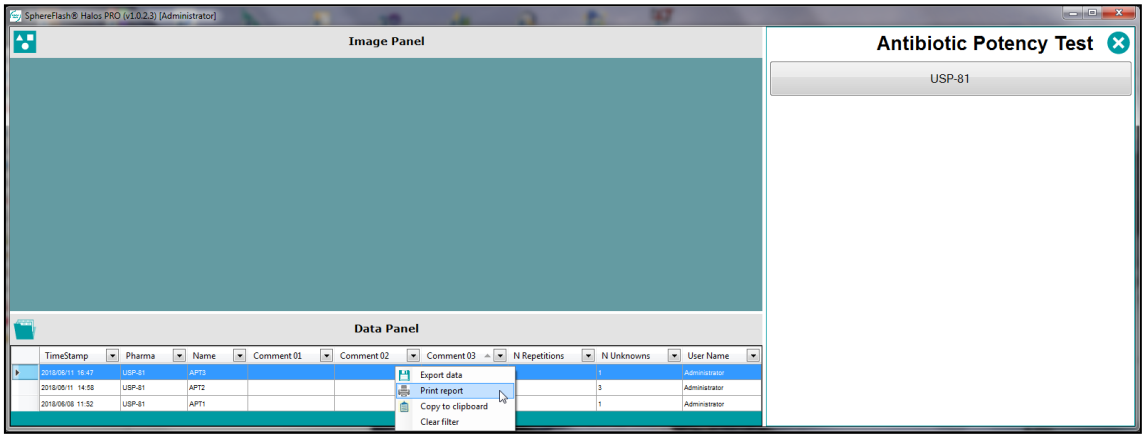

## 13.3. Viewing and exporting the data of the Antibiotic Potency Tests

When in the *Antibiotic Potency* Test panel, the *Data Panel* displays the list of the potency tests previously performed, ordered by time/date with the most recent on top.

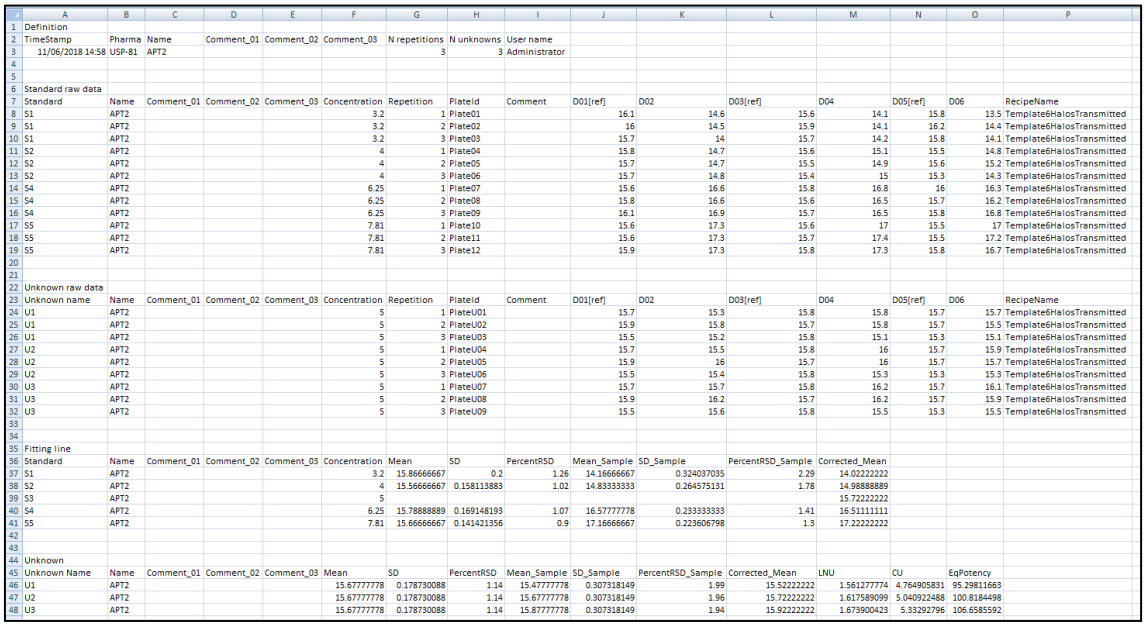



You can filter, sort, and select the tests in the *Data Panel* in the same way as it is done with the halos measurement results view (see section 9.3).

By right-clicking the mouse on a selected row, a context menu appears, allowing several functions to be performed:

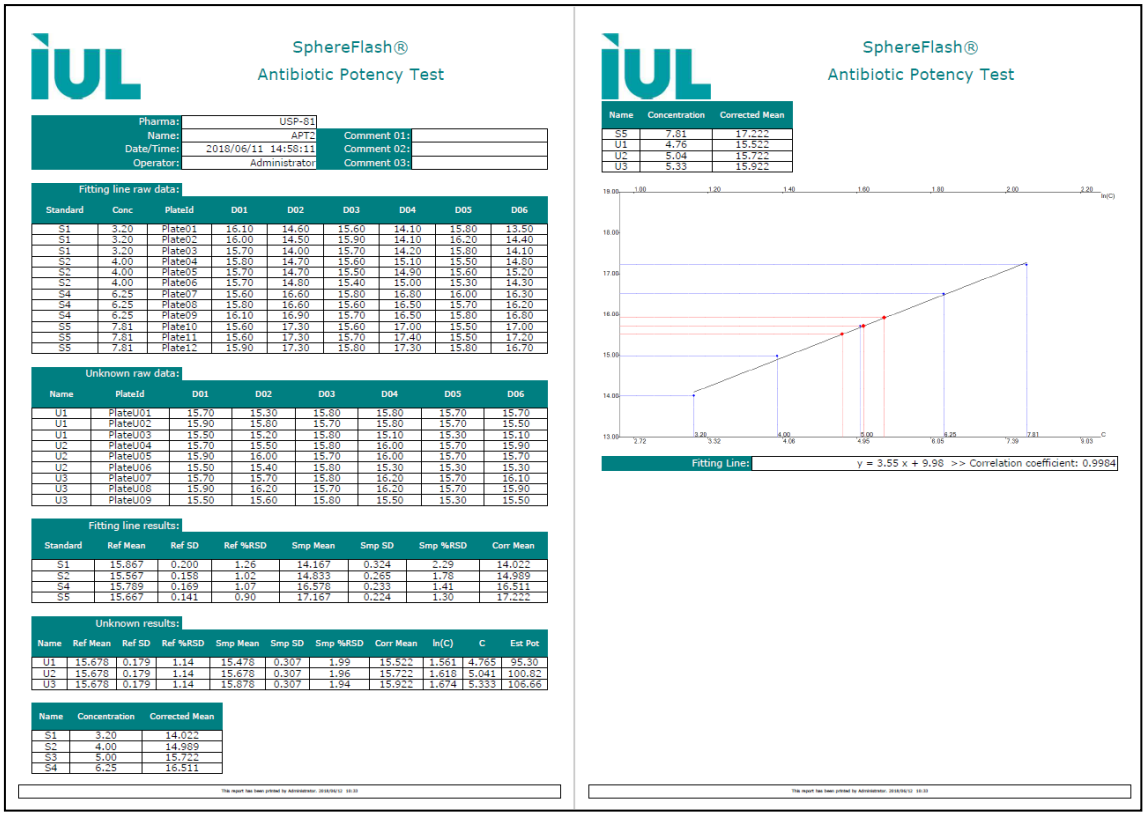



- ***Clear filter:*** Removes all the filters that the user has applied to the columns.
- ***Copy to clipboard:*** Copies to the clipboard just the header line and the data shown on the selected rows. Then the user can paste them onto an external spreadsheet or text-processing application.
- ***Export data:*** This allows the user to export all the data and test calculation tables and results of the selected tests to a text file, either CSV (comma delimited) or TXT (tab-delimited). Then the file can be opened with a spreadsheet application, and the user can perform their calculations if required:



| | A | B | C | D | E | F | G | H | I | J | K | L | M | N | O | P |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Definition | | | | | | | | | | | | | | | |
| 2 | TimeStamp | Pharma | Name | Comment_01 | Comment_02 | Comment_03 | N repetitions | N unknowns | User name | | | | | | | |
| 3 | 11/06/2018 14:58 | USP-81 | APT2 | | | | 3 | 3 | Administrator | | | | | | | |
| 4 | | | | | | | | | | | | | | | | |
| 5 | | | | | | | | | | | | | | | | |
| 6 | Standard raw data | | | | | | | | | | | | | | | |
| 7 | Standard | Name | Comment_01 | Comment_02 | Comment_03 | Concentration | Repetition | PlateId | Comment | D01[ref] | D02 | D03[ref] | D04 | D05[ref] | D06 | RecipeName |
| 8 | S1 | APT2 | | | | 3.2 | 1 | Plate01 | | 16.1 | 14.6 | 15.6 | 14.1 | 15.8 | 13.5 | Template6HalosTransmitted |
| 9 | S1 | APT2 | | | | 3.2 | 2 | Plate02 | | 16 | 14.5 | 15.9 | 14.1 | 16.2 | 14.4 | Template6HalosTransmitted |
| 10 | S1 | APT2 | | | | 3.2 | 3 | Plate03 | | 15.7 | 14 | 15.7 | 14.2 | 15.8 | 14.1 | Template6HalosTransmitted |
| 11 | S2 | APT2 | | | | 4 | 1 | Plate04 | | 15.8 | 14.7 | 15.6 | 15.1 | 15.5 | 14.8 | Template6HalosTransmitted |
| 12 | S2 | APT2 | | | | 4 | 2 | Plate05 | | 15.7 | 14.7 | 15.5 | 14.9 | 15.6 | 15.2 | Template6HalosTransmitted |
| 13 | S2 | APT2 | | | | 4 | 3 | Plate06 | | 15.7 | 14.8 | 15.4 | 15 | 15.3 | 14.3 | Template6HalosTransmitted |
| 14 | S4 | APT2 | | | | 6.25 | 1 | Plate07 | | 15.6 | 16.6 | 15.8 | 16.8 | 16 | 16.3 | Template6HalosTransmitted |
| 15 | S4 | APT2 | | | | 6.25 | 2 | Plate08 | | 15.8 | 16.6 | 15.6 | 16.5 | 15.7 | 16.2 | Template6HalosTransmitted |
| 16 | S4 | APT2 | | | | 6.25 | 3 | Plate09 | | 16.1 | 16.9 | 15.7 | 16.5 | 15.8 | 16.8 | Template6HalosTransmitted |
| 17 | S5 | APT2 | | | | 7.81 | 1 | Plate10 | | 15.6 | 17.3 | 15.6 | 17 | 15.5 | 17 | Template6HalosTransmitted |
| 18 | S5 | APT2 | | | | 7.81 | 2 | Plate11 | | 15.6 | 17.3 | 15.7 | 17.4 | 15.5 | 17.2 | Template6HalosTransmitted |
| 19 | S5 | APT2 | | | | 7.81 | 3 | Plate12 | | 15.9 | 17.3 | 15.8 | 17.3 | 15.8 | 16.7 | Template6HalosTransmitted |
| 20 | | | | | | | | | | | | | | | | |
| 21 | | | | | | | | | | | | | | | | |
| 22 | Unknown raw data | | | | | | | | | | | | | | | |
| 23 | Unknown name | Name | Comment_01 | Comment_02 | Comment_03 | Concentration | Repetition | PlateId | Comment | D01[ref] | D02 | D03[ref] | D04 | D05[ref] | D06 | RecipeName |
| 24 | U1 | APT2 | | | | 5 | 1 | PlateU01 | | 15.7 | 15.3 | 15.8 | 15.8 | 15.7 | 15.7 | Template6HalosTransmitted |
| 25 | U1 | APT2 | | | | 5 | 2 | PlateU02 | | 15.9 | 15.8 | 15.7 | 15.8 | 15.7 | 15.5 | Template6HalosTransmitted |
| 26 | U1 | APT2 | | | | 5 | 3 | PlateU03 | | 15.5 | 15.2 | 15.8 | 15.1 | 15.3 | 15.1 | Template6HalosTransmitted |
| 27 | U2 | APT2 | | | | 5 | 1 | PlateU04 | | 15.7 | 15.5 | 15.8 | 16 | 15.7 | 15.9 | Template6HalosTransmitted |
| 28 | U2 | APT2 | | | | 5 | 2 | PlateU05 | | 15.9 | 16 | 15.7 | 16 | 15.7 | 15.7 | Template6HalosTransmitted |
| 29 | U2 | APT2 | | | | 5 | 3 | PlateU06 | | 15.5 | 15.4 | 15.8 | 15.3 | 15.3 | 15.3 | Template6HalosTransmitted |
| 30 | U3 | APT2 | | | | 5 | 1 | PlateU07 | | 15.7 | 15.7 | 15.8 | 16.2 | 15.7 | 16.1 | Template6HalosTransmitted |
| 31 | U3 | APT2 | | | | 5 | 2 | PlateU08 | | 15.9 | 16.2 | 15.7 | 16.2 | 15.7 | 15.9 | Template6HalosTransmitted |
| 32 | U3 | APT2 | | | | 5 | 3 | PlateU09 | | 15.5 | 15.6 | 15.8 | 15.5 | 15.3 | 15.5 | Template6HalosTransmitted |
| 33 | | | | | | | | | | | | | | | | |
| 34 | | | | | | | | | | | | | | | | |
| 35 | Fitting line | | | | | | | | | | | | | | | |
| 36 | Standard | Name | Comment_01 | Comment_02 | Comment_03 | Concentration | Mean | SD | PercentRSD | Mean_Sample | SD_Sample | PercentRSD_Sample | Corrected_Mean | | | |
| 37 | S1 | APT2 | | | | 3.2 | 15.86666667 | 0.2 | 1.26 | 14.16666667 | 0.324037035 | 2.29 | 14.02222222 | | | |
| 38 | S2 | APT2 | | | | 4 | 15.56666667 | 0.158113883 | 1.02 | 14.83333333 | 0.264575131 | 1.78 | 14.98888889 | | | |
| 39 | S3 | APT2 | | | | 5 | | | | | | | 15.72222222 | | | |
| 40 | S4 | APT2 | | | | 6.25 | 15.78888889 | 0.169148193 | 1.07 | 16.57777778 | 0.233333333 | 1.41 | 16.51111111 | | | |
| 41 | S5 | APT2 | | | | 7.81 | 15.66666667 | 0.141421356 | 0.9 | 17.16666667 | 0.223606798 | 1.3 | 17.22222222 | | | |
| 42 | | | | | | | | | | | | | | | | |
| 43 | | | | | | | | | | | | | | | | |
| 44 | Unknown | | | | | | | | | | | | | | | |
| 45 | Unknown Name | Name | Comment_01 | Comment_02 | Comment_03 | Mean | SD | PercentRSD | Mean_Sample | SD_Sample | PercentRSD_Sample | Corrected_Mean | LNU | CU | EqPotency | |
| 46 | U1 | APT2 | | | | 15.67777778 | 0.178730088 | 1.14 | 15.47777778 | 0.307318149 | 1.99 | 15.52222222 | 1.561277774 | 4.764905831 | 95.29811663 | |
| 47 | U2 | APT2 | | | | 15.67777778 | 0.178730088 | 1.14 | 15.67777778 | 0.307318149 | 1.96 | 15.72222222 | 1.617589099 | 5.040922488 | 100.8184498 | |
| 48 | U3 | APT2 | | | | 15.67777778 | 0.178730088 | 1.14 | 15.87777778 | 0.307318149 | 1.94 | 15.92222222 | 1.673900423 | 5.33292796 | 106.6585592 | |

- ***Print report:*** Sends to the printer (or to a PDF file if a virtual PDF printer is used) all the data, test calculation tables, results, and plots of the selected tests, formatted as a report:



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| | | | |
|---|---|---|---|
| Pharma: | USP-81 | | |
| Name: | APT2 | Comment 01: | |
| Date/Time: | 2018/06/11 14:58:11 | Comment 02: | |
| Operator: | Administrator | Comment 03: | |

Fitting line raw data:

| Standard | Conc | PlateId | D01 | D02 | D03 | D04 | D05 | D06 |
|---|---|---|---|---|---|---|---|---|
| S1 | 3.20 | Plate01 | 16.10 | 14.60 | 15.60 | 14.10 | 15.80 | 13.50 |
| S1 | 3.20 | Plate02 | 16.00 | 14.50 | 15.90 | 14.10 | 16.20 | 14.40 |
| S1 | 3.20 | Plate03 | 15.70 | 14.00 | 15.70 | 14.20 | 15.80 | 14.10 |
| S2 | 4.00 | Plate04 | 15.80 | 14.70 | 15.60 | 15.10 | 15.50 | 14.80 |
| S2 | 4.00 | Plate05 | 15.70 | 14.70 | 15.50 | 14.90 | 15.60 | 15.20 |
| S2 | 4.00 | Plate06 | 15.70 | 14.80 | 15.40 | 15.00 | 15.30 | 14.30 |
| S4 | 6.25 | Plate07 | 15.60 | 16.60 | 15.80 | 16.80 | 16.00 | 16.30 |
| S4 | 6.25 | Plate08 | 15.80 | 16.60 | 15.60 | 16.50 | 15.70 | 16.20 |
| S4 | 6.25 | Plate09 | 16.10 | 16.90 | 15.70 | 16.50 | 15.80 | 16.80 |
| S5 | 7.81 | Plate10 | 15.60 | 17.30 | 15.60 | 17.00 | 15.50 | 17.00 |
| S5 | 7.81 | Plate11 | 15.60 | 17.30 | 15.70 | 17.40 | 15.50 | 17.20 |
| S5 | 7.81 | Plate12 | 15.90 | 17.30 | 15.80 | 17.30 | 15.80 | 16.70 |

Unknown raw data:

| Name | PlateId | D01 | D02 | D03 | D04 | D05 | D06 |
|---|---|---|---|---|---|---|---|
| U1 | PlateU01 | 15.70 | 15.30 | 15.80 | 15.80 | 15.70 | 15.70 |
| U1 | PlateU02 | 15.90 | 15.80 | 15.70 | 15.80 | 15.70 | 15.50 |
| U1 | PlateU03 | 15.50 | 15.20 | 15.80 | 15.10 | 15.30 | 15.10 |
| U2 | PlateU04 | 15.70 | 15.50 | 15.80 | 16.00 | 15.70 | 15.90 |
| U2 | PlateU05 | 15.90 | 16.00 | 15.70 | 16.00 | 15.70 | 15.70 |
| U2 | PlateU06 | 15.50 | 15.40 | 15.80 | 15.30 | 15.30 | 15.30 |
| U3 | PlateU07 | 15.70 | 15.70 | 15.80 | 16.20 | 15.70 | 16.10 |
| U3 | PlateU08 | 15.90 | 16.20 | 15.70 | 16.20 | 15.70 | 15.90 |
| U3 | PlateU09 | 15.50 | 15.60 | 15.80 | 15.50 | 15.30 | 15.50 |

Fitting line results:

| Standard | Ref Mean | Ref SD | Ref %RSD | Smp Mean | Smp SD | Smp %RSD | Corr Mean |
|---|---|---|---|---|---|---|---|
| S1 | 15.867 | 0.200 | 1.26 | 14.167 | 0.324 | 2.29 | 14.022 |
| S2 | 15.567 | 0.158 | 1.02 | 14.833 | 0.265 | 1.78 | 14.989 |
| S4 | 15.789 | 0.169 | 1.07 | 16.578 | 0.233 | 1.41 | 16.511 |
| S5 | 15.667 | 0.141 | 0.90 | 17.167 | 0.224 | 1.30 | 17.222 |

Unknown results:

| Name | Ref Mean | Ref SD | Ref %RSD | Smp Mean | Smp SD | Smp %RSD | Corr Mean | ln(C) | C | Est Pot |
|---|---|---|---|---|---|---|---|---|---|---|
| U1 | 15.678 | 0.179 | 1.14 | 15.478 | 0.307 | 1.99 | 15.522 | 1.561 | 4.765 | 95.30 |
| U2 | 15.678 | 0.179 | 1.14 | 15.678 | 0.307 | 1.96 | 15.722 | 1.618 | 5.041 | 100.82 |
| U3 | 15.678 | 0.179 | 1.14 | 15.878 | 0.307 | 1.94 | 15.922 | 1.674 | 5.333 | 106.66 |

| Name | Concentration | Corrected Mean |
|---|---|---|
| S1 | 3.20 | 14.022 |
| S2 | 4.00 | 14.989 |
| S3 | 5.00 | 15.722 |
| S4 | 6.25 | 16.511 |

SphereFlash®
Antibiotic Potency Test

| Name | Concentration | Corrected Mean |
|---|---|---|
| S5 | 7.81 | 17.222 |
| U1 | 4.76 | 15.522 |
| U2 | 5.04 | 15.722 |
| U3 | 5.33 | 15.922 |

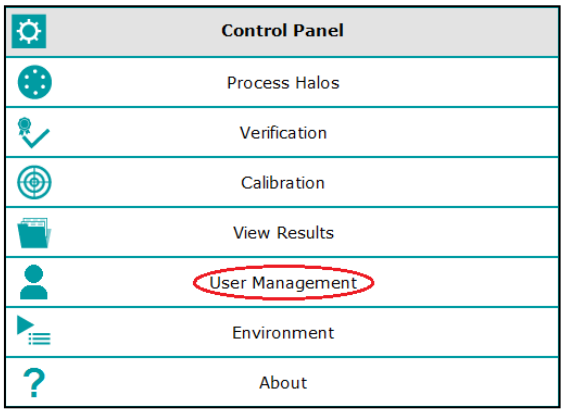
Fitting Line: y = 3.55 x + 9.98 >> Correlation coefficient: 0.9984

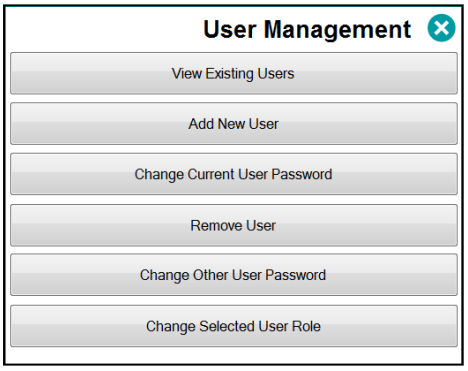
# 14. General administration of the application

**NOTE:** To manage the features of this section your user needs a role level of *Administrator*. Given that some of these features could have implications on the compliance of some regulatory frameworks, you should be authorized by your company's management to act as administrator of the SphereFlash® software.

## 14.1. User Management

In the control panel, select the option *User Management*; then the corresponding panel will be shown with several options:




### 14.1.1. Roles and permissions

Every user has been assigned a role, and this role determines which features of the application are permitted to the user.

There are three different roles:

***Administrator:*** This role has exclusive access to:

- Manage users (view, create, remove, assign role and password).
- Change environment and general settings.
- Purge outdated results from the database.
- Create, edit, and delete custom views.
- View, sort, filter, select, export, and print Audit Trail tables and records.

Besides, *Administrator* role has full access to all the features allowed to the *Programmer* and *Operator* roles.

***Programmer:*** This role has privileged access to:

- Delete *Result Groups.*
- Create, edit, delete and import recipes.
- Save into a recipe the *Threshold* value modified during a halos measurement operation.
- Create, edit, and delete worksheets.

- Re-process the image of a previously stored result of a halos measurement operation.

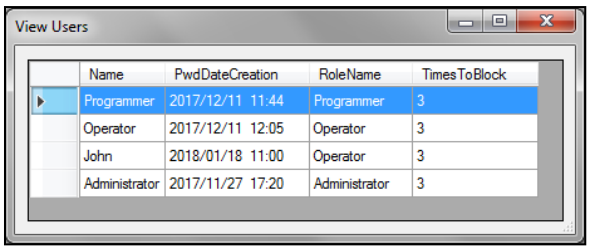
Additionally, *Programmer* role has full access to all the features allowed to the *Operator* role.

***Operator:*** This role has access to all the remaining features not listed above, particularly:

- Run *Calibration* and *Verification* operations.
- Run *Halos Process* operations, select the *Recipe* and *Result Group* to use, change the *Threshold* and interactively modify the measurement results.
- Create *Result Groups.*
- Select and use an existing worksheet or *Remote Input.*
- *Import* and *export* worksheets.
- Select which type of result *View* is displayed.
- Sort by column, filter, select, export, print, and copy to clipboard results from the currently displayed *View.*
- Export recipes.
- Change his password.
- Access the *About* menu item.

### 14.1.2. View existing users

A table is displayed showing a list of all registered users, their name and permission role when their password was changed last time, and how many remaining failed logins are permitted until the user being blocked:

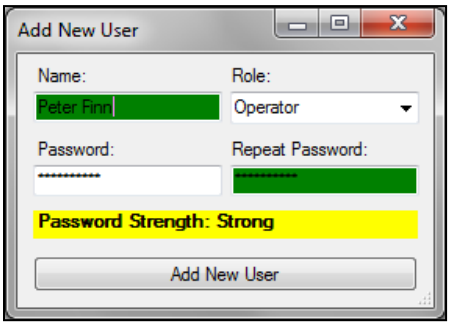



A user is blocked after 3 consecutive failed logins (wrong password). To unblock the user, either wait for a while or ask the administrator to solve the issue (either changing the user's password or removing the user and adding it again).

**NOTE:** The record of all failed logins can be seen in the *Audit Trail* (see 11.4).

### 14.1.3. Add new user

The administrator can create a new user by assigning a name and a role, and entering a password for them:




**NOTE:** The first time a new user accesses the application, they should change the password assigned by the administrator to a new one only known to them.

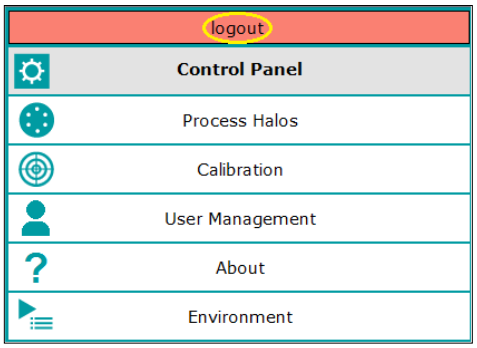
### 14.1.4. Other user management operations

The administrator can also change the password of other users, remove existing users, and change the role of an existing user.

Additionally, any user, regardless of its role, can change their own password.

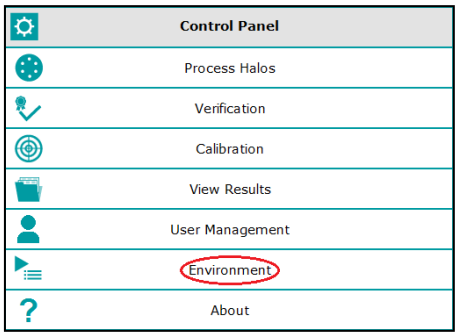
### 14.1.5. Changing the active user

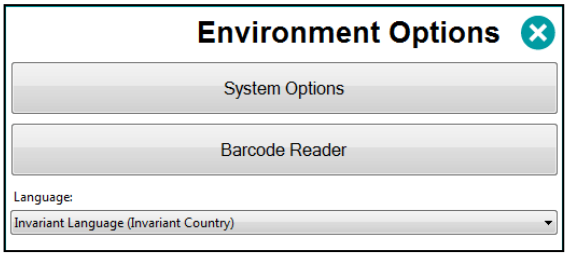
By clicking onto the *Logout* button on top of the *Control Panel*, the current user is logged out, and a dialog appears allowing a new user to login into the application.



## 14.2. Environment and System options

In the *Control Panel*, select the *Environment* option, and the corresponding panel will open:

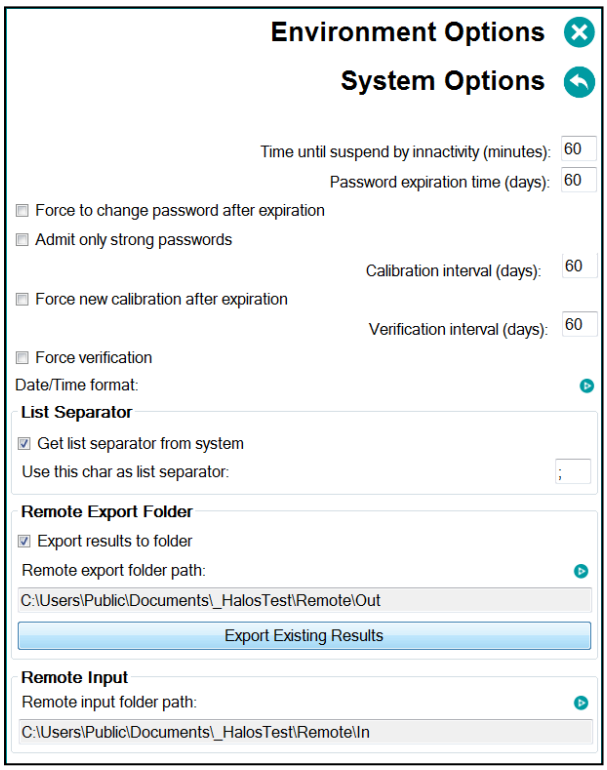



You can choose the language of the user interface among those that have been shipped along with the installation package or added later.

By clicking on the respective button, you can access to change the *System Options,* and define the *Barcode Reader* settings.

### 14.2.1. System options



### 14.2.2. Expiration times

***Time until suspend by inactivity:*** After this time elapsed since the last interaction between the user and the application, the application will freeze, and a re-login will be requested to continue.

***Password expiration time:*** After this time elapsed since the last password change of the current user, the application will warn the user to change its password.

***Force to change the password after expiration:*** If this box is checked, when the change password message is displayed, the user cannot go on using the application until they change their password.

***Admit only strong passwords:*** If this box is checked, only strong passwords will be allowed.

***Calibration interval:*** After this time elapsed since the last calibration, the application will request the user to perform a calibration.

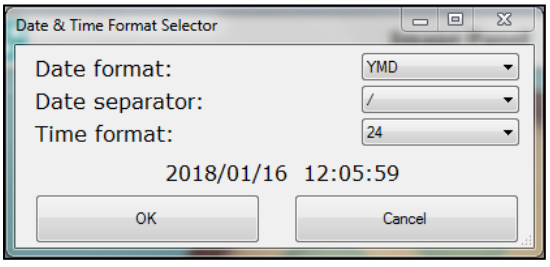
***Force new calibration after expiration:*** If this box is checked, when the calibration requested message is displayed, the user cannot go on using the application until they perform a new calibration.

***Verification interval:*** After this time elapsed since the last verification, the application will request the user to perform a verification.

***Force verification:*** If this box is checked, when the verification requested message is displayed, the user cannot go on using the application until they perform a new verification.

### 14.2.3. Date and Time format

Click on the symbol to configure how the dates and times are formatted (order of year, month and day, separator, and 24 or 12 am/pm time format):




### 14.2.4. List separator

For exporting and importing files in CSV format, you can define the list separator symbol, or let the application use the symbol that is defined in the Operating System regional settings.

### 14.2.5. Remote input/output folders

To interface with LIMs (see 14.7) you need to define the path to the folders where the input and output XML files will be located.

***Export results to folder:*** check this box if you want that the result of each halos measurement operation to be exported to a folder.

***Remote export folder path:*** Click on the symbol to access the dialog to choose the destination folder of the individual result files. The chosen path will appear in the box.

***Export pending results:*** If the *Export results to folder* box are checked, but there is no destination path assigned or it is unreachable, the results to be exported are marked as pending. After solving the issue, the administrator can press this button to bulk transfer all the pending result files to the remote folder.

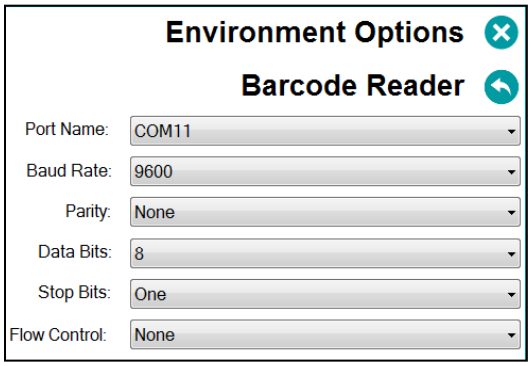
***Remote input path:*** Click on the symbol to access the dialog to choose the destination folder of the input plate-recipe association files (where the recipe and input values are defined for each plate ID). The chosen path will appear in the box. The activation of the input from a remote file using a button in the *Remote* tab of the *Halos Process* panel (see 12.4).

***Remote export folder path:*** Click on the symbol to access the dialog to choose the destination folder of the remote result files. The chosen path will appear in the box.

### 14.2.6. Barcode reader

You can use a serial (RS-232) barcode reader to scan the plate ID from a label with a barcode.

Click on the symbol to access the configuration of the barcode reader serial interface, and fill in or select the proper values according to the reader manufacturer indications. You can find the port name where the reader is connected to the computer using the Windows *Device Manager* dialog.



## 14.3. Customizing the logo on the reports

The printed reports and tables appear with the logo of IUL. If you want that your logo appears instead, replace it in a .jpg image file with the same path and filename at:

```
%ProgramFiles%\IUL\SphereFlash_Halos_PRO\logo\logo.jpg
```

## 14.4. Digital signature of PDF reports and tables

You can apply a digital signature to the PDF reports and tables using third-party applications properly linked to the SphereFlash® application.

**Configuring the digital signature feature:**

a) Install in the computer a virtual PDF printer such as *PDFCreator.*

b) Configure the virtual printer to automatically open the document after the PDF file has been created.

c) Install in the computer *Adobe Acrobat Reader DC®*.

d) Associate the file type PDF to be automatically opened by *Adobe Acrobat Reader DC®*.

**Applying the digital signature to a PDF report or table:**

e) Select or filter the desired rows from the current view.

f) Left-click on them and select *Print Report* or *Print Table.*

g) On the print dialog, select the virtual PDF printer (*such as PDFCreator*).

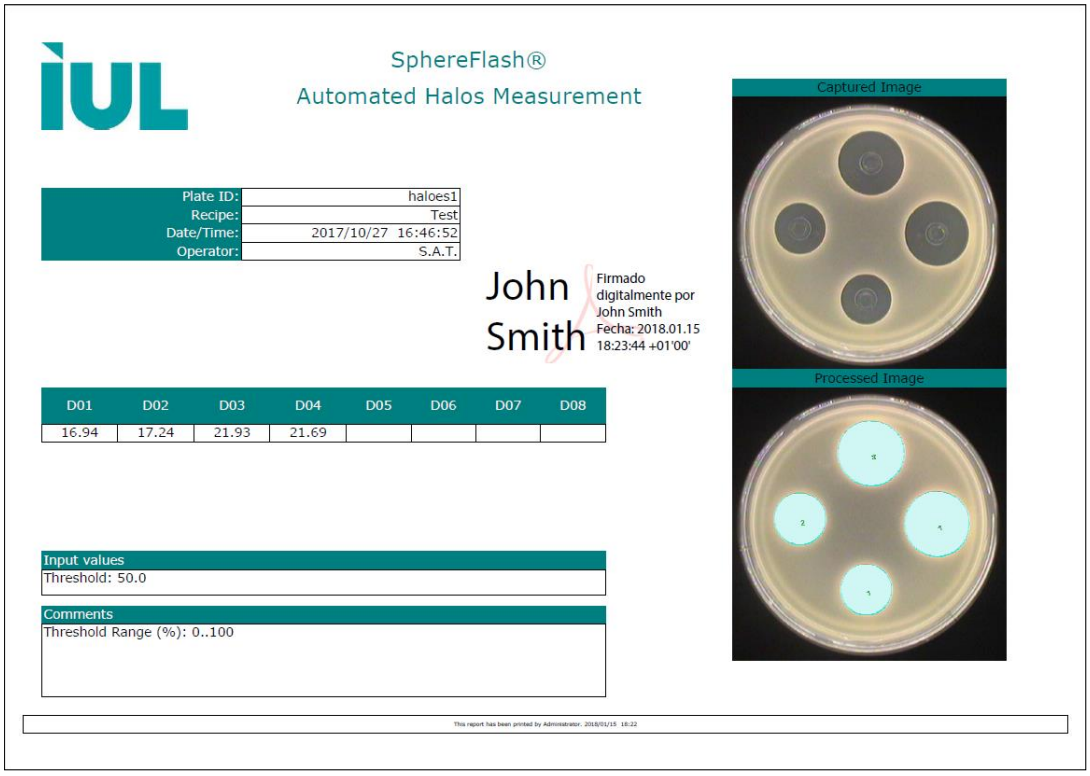
h) When asked for, select the destination folder, and give a name to the unsigned PDF file to be created.

i) When the file has been automatically opened by *Adobe Acrobat Reader DC®*, in this application go to *Tools > Certificates > Digital Signature.*

j) You will be prompted to define an area on the document where the digital signature will be printed.

k) You will be prompted to use an existing certificate or to create a new one.

l) Select the destination folder and give a name to the digitally signed PDF file to be created.



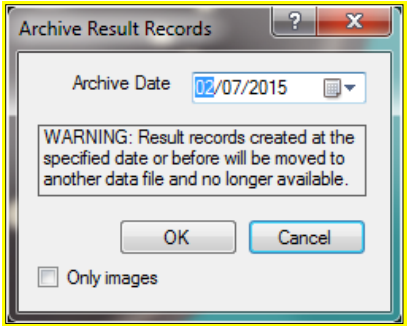

## 14.5. Removing outdated results (purge)

When there are in the database old results and their images that you no longer need to review, using a purge operation you can remove them from the database, moving them into a historic archive file. This way the database will not grow indefinitely, compromising the performance of the application.

Your user role must be that of *Administrator* to being allowed to perform this purge operation.

Before the purge, you have to make sure that you have exported or printed all the old results from which you need to keep their information in external support (Excel, prints, or PDF reports...).

To purge the results, click on the *Purge old results* button in the *View Results* panel, and a dialog will appear where you can define the limit date where the results older than this will be removed. There is also a checkbox allowing to purge only the images but keeping the results (images take a lot of disk space).



You will be warned that **the purge process can take a long time**, in extreme cases it can last up to one hour. It is advisable that you launch the purge at the end of the working day, leaving the purge operation being run overnight. Please be patient and do not try to shut down the application using the Windows *Task manager* or resetting the computer.

> **NOTE:** There are regulatory frameworks that require keeping the information for a prescribed minimum period of time; it is the responsibility of the administrator user to take the proper measures to make sure that these regulations are not broken when purging the database.

## 14.6. Managing the database files

### 14.6.1. Location and backup of the active database files

It is the responsibility of the client's Systems Administrator to perform a reliable regular backup copy of the active database files where the settings and results created by the application are stored.

The path where these active database files are stored is:

```
%ProgramData%\IUL\Halos
```

All the files inside this folder are to be backed up regularly, as prescribed by the client's policies, and by the regulatory frameworks that must be fulfilled.

### 14.6.2. Location of archived database files resulting from purge operations

The archived databases resulting from purge operations are stored in the same path above, inside a folder whose name starts with '@' followed by the date and time corresponding to the purge limit date of the archive:

### 14.6.3. Temporarily restoring archived databases

If the results contained in an archived database must be reviewed or exported/printed, the Systems Administrator can proceed this way:

1. Close the application.
2. Back up the active database files (section 14.1).
3. Locate the desired archive folder (section 14.6.2).
4. Copy the contents of the archive folder to the active database path (section 14.1).
5. Open the application, and perform the review, export, or print off the desired archived results.
6. Close the application and restore the active database files previously backed up in step 2.

## 14.7. Interfacing with a LIMS (Laboratory Information Management System)

The SphereFlash® application can interface in a corporate network with a LIMS to automatically and in real-time:

- Send to the LIMS the Halos Measurement results after processing each plate (*Remote Out* to a folder).
- Get from the LIMs which recipe and which *Threshold* value must be applied to process each plate, similarly, as working from worksheets (*Remote In* from a folder).

To implement these features, the following subjects must be addressed:

a) Two folders have to be designated as the *Remote In* and the *Remote Out* folders; they may be located either in the computer containing the application or in some server reachable through the network.

b) The systems administrator must grant the proper access permissions to both folders by the *SphereFlash®* application as well as the LIMS system.

c) The systems administrator must ensure the rules of privacy and restricted access to the data in these folders, as mandated by the company policies and any regulatory framework that would be applicable.

d) In the *System Options* panel (section 14.2.5) define the paths to the respective remote folders.

e) In the *System Options* panel (section 14.2.5) check the *Export results to folder* checkbox.

f) In the *Remote* tab of the *Process Halos* panel, check the *Remote input enabled* checkbox, and select the button *Input folder* (section 12.4).

g) Each plate must have a unique identifier (*Plate ID*), it is advisable to use a barcode to avoid operator errors.

h) The LIMS must create in advance, for each *Plate ID*, an XML file containing the settings (recipe and *Run / Input Values*) required to process the plate and place this file into the *Remote In* folder.

i) The LIMS must collect from the *Remote Out* folder each XML file that will appear after each *Halos Measurement* operation, parse it, and transfer the measurement results to its database.

j) The LIMS should delete from both *Remote In* and *Remote Out* folders the files corresponding to the plates already processed.

### 14.7.1. Remote input file example

File name:

`RI01.xml`

(where *RI01* is the plate ID to be processed with the settings in the file)

File contents:

```
<?xml version="1.0" standalone="yes"?>
<plate>
  <Plate_Id>RI01</Plate_Id>
  <Recipe_Name>Template6HalosTransmitted</Recipe_Name>
  <Threshold>50</Threshold>
</plate>
```

**NOTE:** Only nodes `<Plate_Id>` and `<Recipe_Name>` are compulsory.

### 14.7.2. Remote output file example

File name:

`00000370.xml`

(where *00000370* is an incremental unique number, not the Plate ID)

File contents:

```
<?xml version="1.0" standalone="yes"?>
<DocumentElement>
  <Results>
    <ResultGroupName>default</ResultGroupName>
    <Id>370</Id>
    <CreatedByGUID>724910d6-4653-4058-873c-f1baea2e0b0f</CreatedByGUID>
    <RecipeName>Recipe1</RecipeName>
    <UserName>Administrator</UserName>
    <CreatedBy>11</CreatedBy>
    <RecipeGUID>aa3f5c4c-8795-4def-9d6b-b1fe091805ab</RecipeGUID>
    <RecipeId>214</RecipeId>
    <D06>16.8182430267334</D06>
    <D05>16.825345993041992</D05>
    <D04>16.817695617675781</D04>
    <D03>16.870086669921875</D03>
    <D02>16.823160171508789</D02>
    <D01>16.8193359375</D01>
    <ScaledImageWidth>768</ScaledImageWidth>
    <ProcessedImage>44123e23-c09c-42a4-9825-f3f44b989abf</ProcessedImage>
    <CapturedImage>d2c97dc0-3341-42de-8ef3-2b840abe6c82</CapturedImage>
    <Threshold>50</Threshold>
    <CreationTime>2016-01-01T00:01:11.336+01:00</CreationTime>
    <Comment />
    <PlateId>Plate1</PlateId>
    <GUID>f7dc11b1-642b-4b10-882d-cd58beaa5156</GUID>
  </Results>
</DocumentElement>
```

# 15. Regulatory compliance: FDA 21 CFR part11

The SphereFlash® Halos PRO application software is designed to enable the customer to comply with FDA regulations related to 21 CFR part 11, allowing the use of electronic records instead of paper records.

Summary of the key elements of compliance:

- The original electronic records are encrypted and protected to ensure authenticity, integrity, confidentiality, and readily retrieval throughout the retention period (§11.10 a, c).
- The software can generate accurate and complete copies of records both in human-readable and electronic form (§11.10 b).
- The access to the software, its use, and operation, is limited to authorized individuals (§11.10 d, g).
- The software automatically generates an Audit Trail that records all the user actions that create, modify, or delete electronic records. This Audit Trail is time-stamped and encrypted and cannot be altered by the users (§11.10 e).
- The correct and appropriate sequence of operations, steps, and events is enforced by the software and cannot be altered by the user (§11.10 f).
- Data input from the user is checked or limited to valid and appropriate values (§11.10 h).

## Features of SphereFlash® software related to FDA 21CFR part 11 compliance:

| # | section of FDA 21CFR part 11 | Topic | Requirement | SphereFlash® software implementation | Customer action is required to comply | Comments |
|---|---|---|---|---|---|---|
| 1 | 11.10 (a) | Validation. | The system must be validated for the intended use. | | X | The customer is responsible for the validation of the system in which the SphereFlash® is integrated, according to the particular use intended by the customer. |
| | | | | X | | The SphereFlash® software provides standard template recipes to be used for customer validation. |
| 2 | 11.10 (a) | Changes on records. | It must be possible to discern invalid or altered records. | X | | The results of all the operations and the settings of recipes are recorded in an encrypted database, which prevents any modification of its contents neither from the application nor form outside it.<br>If an operator re-processes the same plate or the image of a previously processed plate, both the old and new results records are kept, being distinguishable by their respective timestamps.<br>All the operator actions, changes, and entries to the operation results, system settings, and operation recipes, that are relevant for the validity of the results of the operations, are automatically recorded in an Audit Trail which includes the date, local and UTC time, user, and change that has been performed.<br>If the date/time of the computer has been manipulated, so that there are stored records with a timestamp apparently in the future, a warning comment is automatically added to each new halo measurement record. |
| | | | | | X | The customer must ensure that, on the computer where the SphereFlash® software is installed, the date and hour cannot be modified by unauthorized individuals. |

| # | section of FDA 21CFR part 11 | Topic | Requirement | SphereFlash® software implementation | Customer action is required to comply | Comments |
|---|---|---|---|---|---|---|
| 3 | 11.10 (b) | Report, printout, electronic record, FDA review. | The system must be able to produce accurate and complete copies of the records on paper as well as in electronic form, allowing for their review by FDA. | X | | Records data can be exported to Excel, CSV, and text files. The results data of each operation can be automatically exported in real-time to an XML file when *Remote Out* mode is active.<br>Record data can be printed to paper or PDF files in table and report formats.<br>Generated PDF reports and tables can be automatically linked to a third-party application, to be digitally signed to ensure its authenticity, integrity, and authorship.<br>When exporting or printing reports, the exact data contents of the records in the database are automatically transferred to the file or printout; there is no possibility to modify the data. |
| | | | | | X | After exporting to a file outside the application, it is the responsibility of the customer to ensure the integrity of its contents. |
| 4 | 11.10 (c) | Protection of records, retention period. | The records must be readily available throughout their retention period. | X | | The results of all the operations and the settings of recipes are kept in an encrypted database, which prevents any modification of its contents neither from the application nor from outside of it.<br>All the records of the active database are directly available for review, export, and print until the authorized user performs a purge of the outdated records into an archive file.<br>Even in the archive file, the outdated records are still safeguarded under encryption, and they can be retrieved for their consultation if needed. |
| | | | | | X | It is the responsibility of the customer to perform periodic back-ups of the database files |

| # | section of FDA 21CFR part 11 | Topic | Requirement | SphereFlash® software implementation | Customer action is required to comply | Comments |
|---|---|---|---|---|---|---|
| 5 | 11.10 (d) | Login, access authorization | The system must limit access to the system to only authorized individuals. | X | | The SphereFlash® software is provided with a login feature that limits access only to authorized individuals using a username and a password.<br>Each user is assigned a role that defines the subset of features for which they have permission.<br>The users with administrator role have the responsibility to create or delete users, and to assign them the proper role.<br>The system can be configured by the administrator to request the users a periodical change of their password.<br>After several successive failed login attempts, a user becomes blocked, and the intervention of the administrator is required to unblock them.<br>All the changes to the users and their roles, as well as the login events, successful or not, are recorded in the Audit Trail.<br>If the operator leaves the computer unattended for more than a scheduled time, the application will be blocked, requiring a new login. |
| | | | | | X | The customer has the responsibility to designate and empower a staff member to act as administrator of the SphereFlash® software application |
| 6 | 11.10 (e) | Audit trail, timestamps. | The system must automatically generate a secure, time-stamped audit trail, that logs the date and time of user entries and actions which create, modify, or delete electronic records. | X | | All the operator actions, changes, and entries to the operation results, system settings, and operation recipes, that are relevant for the validity of the results of the operations, are automatically recorded in an Audit Trail which includes the date, local and UTC time, user, and change that has been performed. |
| | | | | | X | The customer must ensure that, on the computer where the SphereFlash® software is installed, the date and hour cannot be modified by unauthorized individuals. |

| # | section of FDA 21CFR part 11 | Topic | Requirement | SphereFlash® software implementation | Customer action is required to comply | Comments |
|---|---|---|---|---|---|---|
| 7 | 11.10 (e) | Overwriting data. | When modifying electronic records, the previously recorded information must still be available in the system, not being overwritten by the modification. | X | | All the operation results data, after being recorded, are kept in the database with no possibility of further modification. If an operator re-processes the same plate, or the image of a previously processed plate, both the old and new results records are kept, being distinguishable by their respective timestamps.<br>All the modifications of the settings of recipes or the general system settings are recorded in the Audit trail, where the user, date, and time, and changed values can be seen. |
| 8 | 11.10 (e) | Audit Trail, retention period. | The Audit Trail of an electronic recording must be retrievable throughout the retention period of the record. | X | | The Audit Trail entries are kept in the same encrypted database as the results records, which prevents any modification of its contents neither from the application nor from outside of it.<br>All the Audit Trail entries of the active database are directly available for review until the authorized user performs a purge of the outdated records into an archive file.<br>Even in the archive file, the outdated records are still safeguarded under encryption, and they can be retrieved for their consultation if needed. |
| | | | | | X | It is the responsibility of the customer to perform periodic back-ups of the database files |
| 9 | 11.10 (e) | Audit Trail, FDA review. | The Audit Trail must be available for review and copying by the FDA. | X | | Audit Trail PDF reports can be generated and automatically linked to a third-party application, to be digitally signed to ensure its authenticity, integrity, and authorship.<br>When exporting or printing those reports, the exact Audit Trail contents in the database are automatically transferred to the file or printout; there is no possibility to modify the data. |
| | | | | | X | After exporting the Audit Trail to a file outside the application, it is the responsibility of the customer to ensure the integrity of its contents. |

| # | section of FDA 21CFR part 11 | Topic | Requirement | SphereFlash® software implementation | Customer action is required to comply | Comments |
|---|---|---|---|---|---|---|
| 10 | 11.10 (f) | Sequence of steps. | The system must use operational checks to enforce the permitted sequence of steps and events as appropriate. | X | | The sequence and setting values required for each operation type are enforced by the recipe definition, which doesn't allow the operator to modify any of the steps or settings except those data that purposely have been decided that will be entered by the operator.<br>Additionally, the *Remote In* and *Worksheet* features will enforce the application of the recipe and setting values required for each particular plate ID.<br>Only users having assigned *Programmer* or *Administrator* role are able to define recipe settings, and to associate in a worksheet each plate ID with the recipe and settings required for its processing. |
| | | | | | X | The customer has the responsibility to designate and empower suitable staff members to act as *Programmers*. |
| 11 | 11.10 (g) | User permissions. | The system must ensure that only authorized individuals can use the system, access the functions, modify a record, or perform other operations. | X | | The SphereFlash® software is provided with a login feature that limits access only to authorized individuals using a username and a password.<br>Each user is assigned a role that defines the subset of features for which they have permission.<br>The users with administrator role have the responsibility to create or delete users, and to assign them the proper role.<br>The system can be configured by the administrator to request the users a periodical change of their password.<br>After several failed login attempts, the user becomes blocked, and the intervention of the administrator is required to unblock them.<br>All the changes to the users and their roles, as well as the login events, successful or not, are recorded in the Audit Trail.<br>If the operator leaves the computer unattended for more than a scheduled time, the application will be blocked, requiring a new login. |

| # | section of FDA 21CFR part 11 | Topic | Requirement | SphereFlash® software implementation | Customer action is required to comply | Comments |
|---|---|---|---|---|---|---|
| | | | | | X | The customer has the responsibility to designate and empower a staff member to act as administrator of the SphereFlash® software application. |
| 12 | 11.10 (h) | Validity check of input data. | The system must determine, as appropriate, the validity of the source of data input or operational instruction. | X | | The *Activation Key* for the *Halos PRO* license is linked to the serial number of the SphereFlash® instrument of the client. No plate images acquired with devices other than this instrument will be admitted being processed.<br>The values that the operator is allowed to introduce manually, are either limited to a selection list that contains only the possible meaningful values or are numerical values that are restricted to lie within a range of valid values, hardcoded in the application.<br>Additionally, the *Remote In* and *Worksheet* features will enforce the application of the recipe and setting values required for each particular plate ID. |

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