User Guide

Milliflex® Rapid System 2.0

Detection Tower

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Introduction

The Milliflex® Rapid System 2.0 Detection Tower

This user guide is intended to assist lab personnel in using the Milliflex® Rapid System 2.0 Detection Tower **(Cat. No. MXRDP2DT00)**, a key component of the Milliflex® Rapid System 2.0, with its software. The role of the Milliflex® Rapid System 2.0 Detection Tower is to perform automated, software-based detection, imaging, and quantification of viable microorganisms that have been grown on media plates as microcolonies. Its sCMOS image sensor detects the photons emitted as a result of an enzymatic reaction, and a computer algorithm then processes the collected data to enumerate the microcolonies in colony forming units (CFUs).

The Milliflex® Rapid System 2.0

The Milliflex® Rapid System 2.0 is a solution for the rapid detection and quantification of viable contaminants (bacteria, yeasts and molds) in filterable samples, allowing an earlier response to a contamination issue. Based on highly sensitive adenosine triphosphate (ATP) bioluminescence technology, it delivers faster total viable count results than traditional methods, such as membrane filtration and pour plates. The Milliflex® Rapid System 2.0 is suitable for both rapid sterility and rapid bioburden testing.

The central hardware components of the Milliflex® Rapid System 2.0 are the Milliflex® Rapid Detection Tower and the Milliflex® Rapid 2.0 AutoSpray Station **(Cat. No. MXRP2SPRKT)**, which automatically applies the reagents for the enzymatic reaction to the membrane filter. For an optimal workflow and fastest detection results, we strongly recommend using the Milliflex® Rapid System 2.0 together with the proven Milliflex Oasis® VHP resistant pump **(Cat. No. MMPPLUVHP)** for efficient membrane filtration in an isolator.

The Milliflex® Rapid System 2.0 workflow is performed in three steps:

1. Any microorganisms contained in a liquid sample are captured on a membrane filter (Milliflex Oasis® VHP Pump recommended), which is then transferred onto a media plate and incubated for growth.
2. After incubation, reagents are evenly distributed onto the membrane filter by the Milliflex® Rapid 2.0 Autospray Station to perform an enzymatic reaction that leads to bioluminescence where microcolonies are present.
3. The emitted light allows any microcolonies on the membrane filter to be automatically detected and counted by the Milliflex® Rapid System 2.0 Detection Tower and its software.

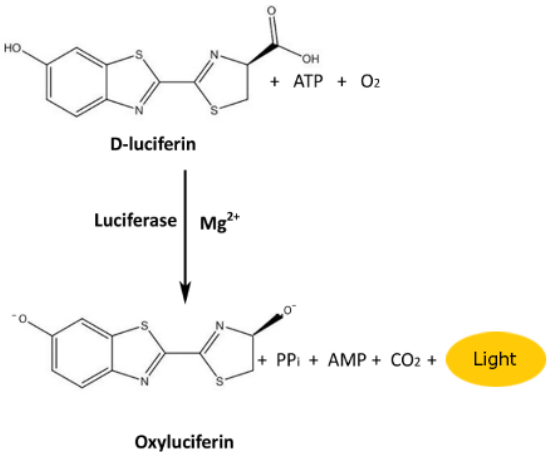
Note: For details on using the Milliflex Oasis® VHP resistant pump and Milliflex® Rapid 2.0 Autospray Station, consult the respective user guides.

ATP bioluminescence reaction chemistry

ATP (adenosine triphosphate), the primary energy carrier of living organisms, is present in all living cells including bacteria, yeasts and molds. To detect the ATP present in the microorganisms that have been captured during the filtration step, the following reagents are applied to the membrane:

- Reagent #1—ATP Releasing Reagent **(MXRPBLRST)**: acts on the microorganisms captured on the membrane surface, making the ATP from the cells available for detection by the system
- Reagent #2—Bioluminescence Reagent (**MXRPBLRST**): reacts with the ATP released by Reagent #1, upon which light (photons) is emitted

The chemical reaction, catalyzed by the enzyme luciferase, is an oxidation described by the equation below:



Legend:

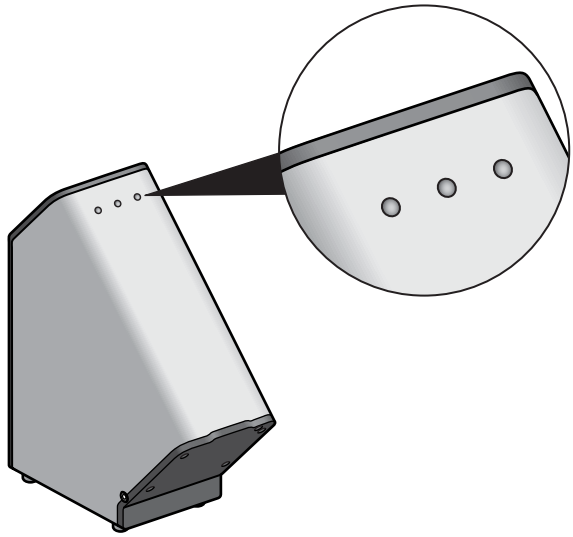
- D-Luciferin: Substrate
- ATP: Adenosine triphosphate
- O_2: Oxygen (from atmosphere)
- Luciferase: Enzyme from a recombinant source
- Mg^{2+}: Magnesium ions (cofactor in trace quantities)
- AMP: Adenosine monophosphate
- PP_i: Pyrophosphate
- OxL: Oxyluciferin (oxidized substrate)
- CO_2: Carbon dioxide

Accessories of the Milliflex® Rapid System 2.0 Detection Tower

The Milliflex® Rapid Detection Tower **(Cat. No. MXRDP2DT00)** comes with a 3-meter USB 3.0 cable and safety instructions, both also contained in the packaging.

Hardware features and operation

Front panel



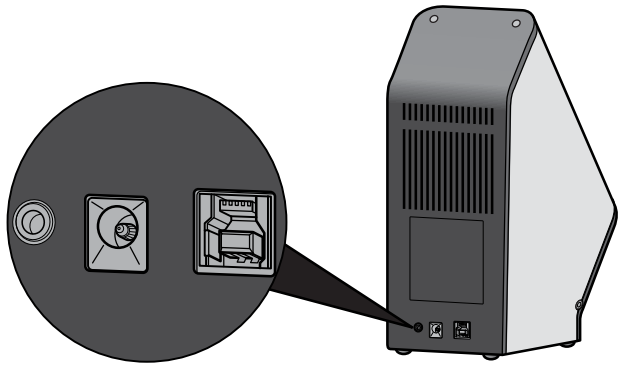
- BLUE LED (on the left in the image above): This LED is ON when the system is initialized. It blinks when the system is in standby.
- GREEN LED (center): The system is ready to scan a membrane filter when this LED is ON. If this LED is OFF the right temperature for scanning has not been reached.
- ORANGE LED (right): The Milliflex® Rapid System 2.0 Detection Tower is in operation when this LED is ON.

Rear panel

Right side in image below: USB port to connect to the computer (USB 3.0 female connector type B)

Center: Power connector for MXRPWRSP--

Left side: Connection to calibration source used for maintenance only



Installing the Milliflex® Rapid System 2.0 Detection Tower

Computer requirements

- Personal computer with Windows 10 and higher version
- RAM: 8 GB
- Disk: 500 GB
- USB 3.0 port type A — female

- Administrator access rights to the computer, to install the software.

Remove the Milliflex® Rapid Detection Tower and the accessories from the packaging.

Other Prerequisites:

- Microsoft Visual C++ 2010 Service Pack 1 Redistributable Package MFC Security Update.
- Ensure Windows Media Feature Pack is installed on the computer.
- The Detection Tower will go to standby 15 min after the computer goes to sleep, to prevent it please adjust the sleep settings on computer. Power & sleep settings from WIN10

To connect to the PC

- Plug the output of the power supply unit into the dedicated DC connector at the back of the Milliflex® Rapid Detection Tower
- Insert the mains plug of the power supply unit into the wall socket
- Insert the USB type B end (plug) into the Milliflex® Rapid Detection Tower
- Insert the USB type A end into an USB3 port of the computer

Installing the software

Note: Administrator access rights are required to install the software on the computer. The login to the Milliflex® Rapid System 2.0 software is managed by Windows accounts.

Download the current version of the Milliflex® Rapid System 2.0 software to a destination folder of your choice from our website.

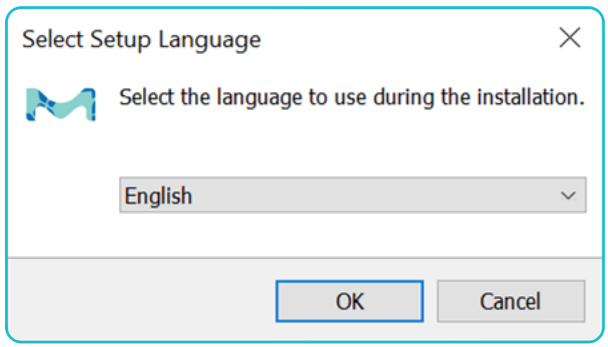
Then access folder and click on its icon to commence with installation of the following software, in that order:

- The Milliflex® Rapid System 2.0 software
- The hardware driver software
- The database

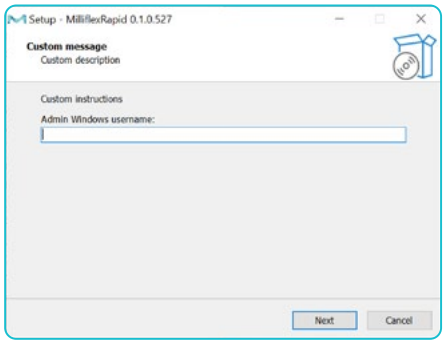
The following screenshots will lead you through the installation process.

Note: An administrator for the Milliflex® Rapid System 2.0 software has to be determined during installation. Only this person will be able to create further users. However, it is possible for this administrator to assign administrator rights to a different user at a later date.

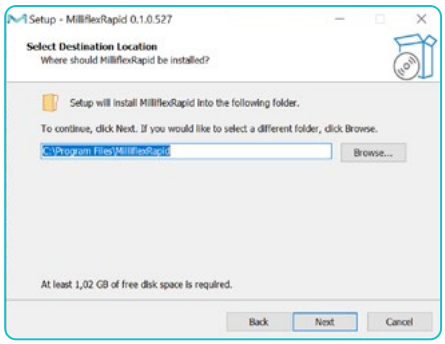
First, select language, then click “OK”



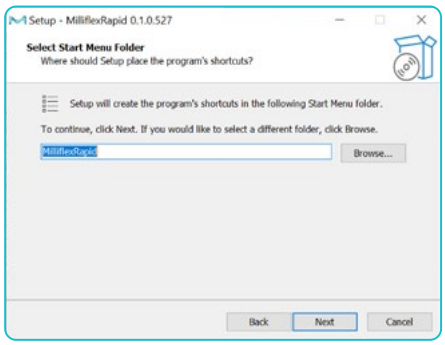
Enter the exact Windows username of the user who will have the administration rights to manage users and tests in the Milliflex® Rapid software.



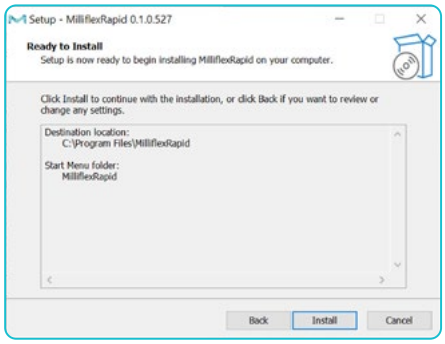
Browse to select where to install the Milliflex® Rapid System 2.0 software. Then click “Next”.



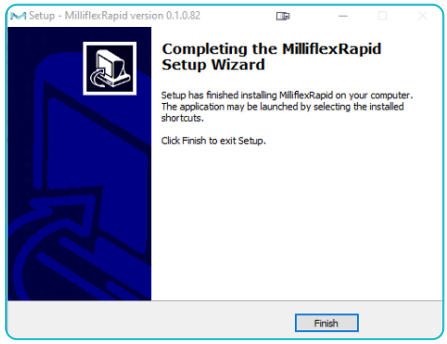
Select the start menu folder in which to place the shortcut icon. Its default name is “MilliflexRapid”. Then click on “Next”.



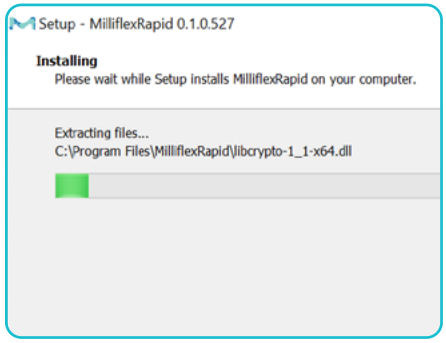
Click on “Install”.



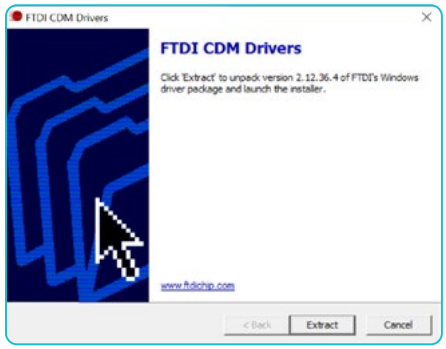
When installation of the Milliflex® Rapid software is completed, click on “Finish”.



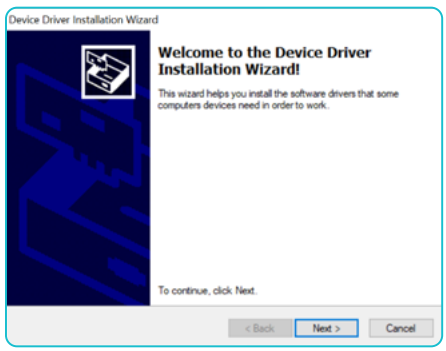
Wait while the software is being installed.



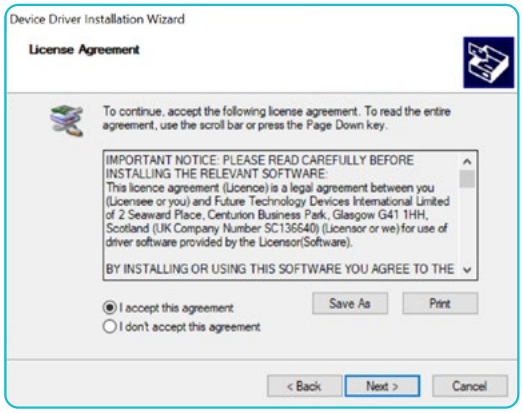
Next is the device driver software. Click on “Extract”.



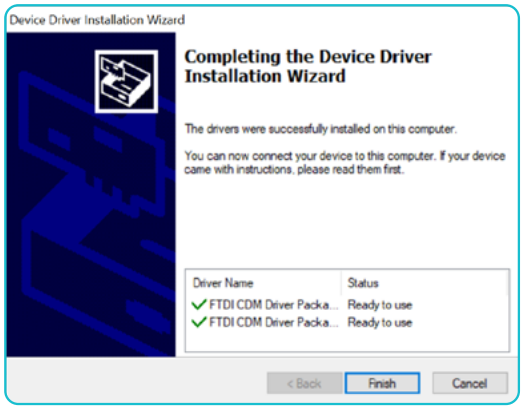
Click on “Next”.



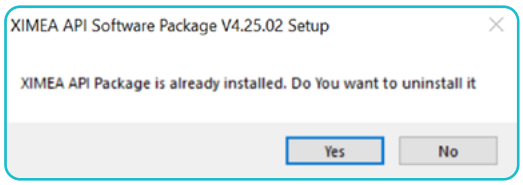
Read the agreement. To accept, select “I accept” and click on “Next”.



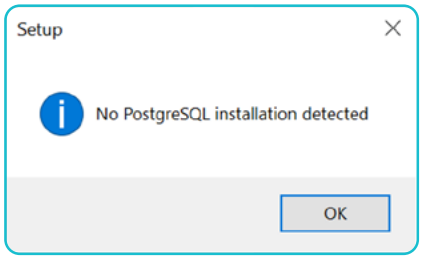
Click on “Finish” to complete driver installation.



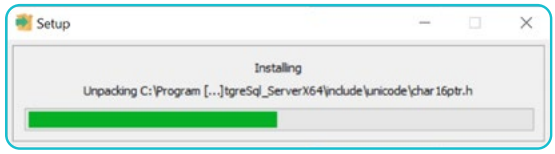
Next the database will be installed. If the screen below appears, click on “Yes”.



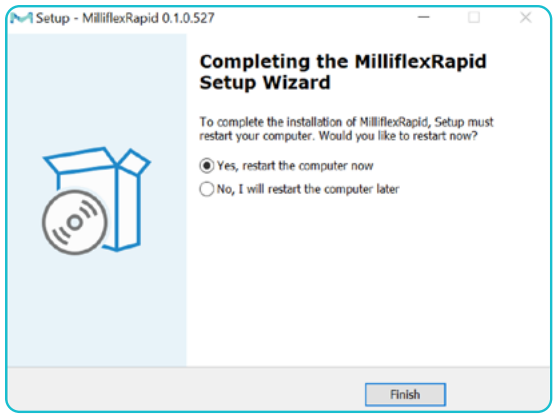
If the screen below appears, click on “OK”.
It appears only if the software has been installed on the computer before. Installation of the database will then commence.



Wait until the end of the installation process.



Finalize the process by clicking “Finish” and restart the computer.



Note: Before installing a new software version:

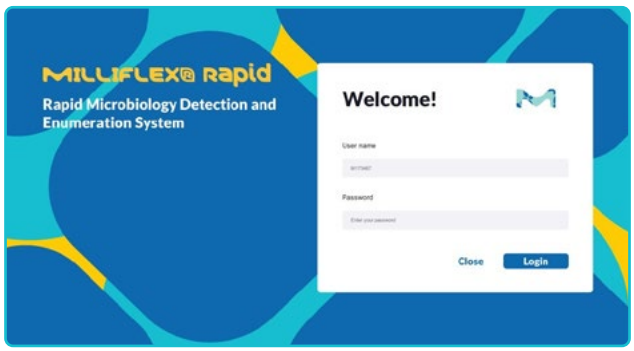
- **Backup the database according to section “Database Management”**
- **Install new software version.**
- **Restore the database from archive according to section ‘Database Management’**

Using the software

Login

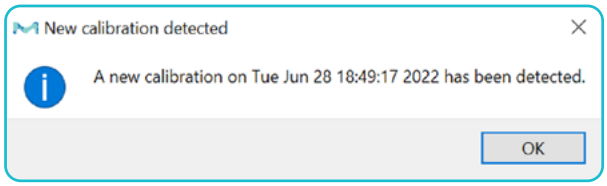
To log in the user shall have his account added in the Milliflex® Rapid software (see § Mange users):

- Double click on the shortcut created during installation of the Milliflex® Rapid software.
- The user name field automatically displays the current user of the Windows session.
- Enter the user's password (it's the same as the Windows session's).
- Click "Login"



Note: For certain activities such as finalizing a batch, exporting a file or importing a file, it is necessary to confirm the user's identity despite already being logged in. This is necessary to remain compliant with existing guidelines.

When a new instrument is connected, or after periodic calibration, the new calibration information is recorded in the software's database. A popup windows appears (see below) to inform about the calibration date. This event is logged in the instrument's audit trail.



Instrument startup

The instrument is not immediately ready for testing, you have to wait a few minutes before it is ready for your work. However, although you cannot perform a test during this time, you can access the other menus.

To know the status of your equipment, you can look on the status bar:

System: A blue flag displays when the instrument is correctly connected to the computer.

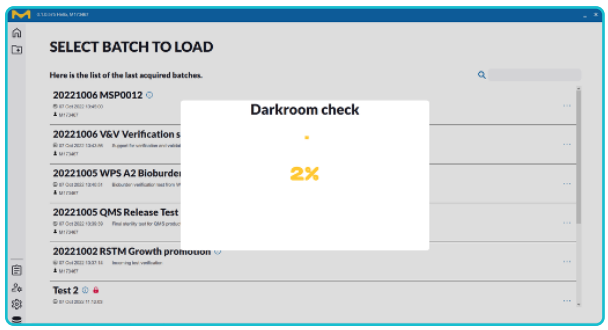
Acquisition: A orange flag displays when a sample is analyzed by the instrument.

Database: A yellow flag displays when the database is connected.

Camera: When not yet ready, progress is displayed. When ready it switches to green.

Dark room verification

During startup, the instrument will perform an automatic test to ensure the tightness of the dark room and the black background lever. During this test, do not open the instrument. This verification will take few minutes to complete.



Manage users

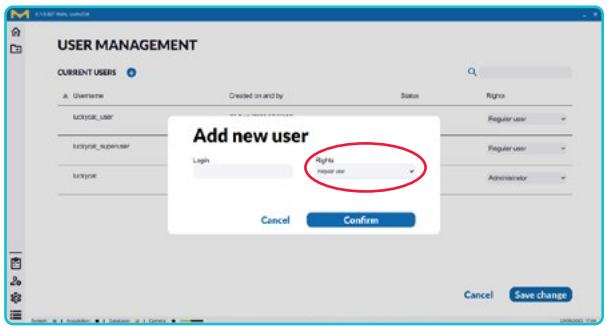
Only the administrator can manage the list of eligible Milliflex® Rapid software users. However, it is possible for this administrator to assign administrator rights to a different user.

Log on with the Windows login of the Milliflex® Rapid software administrator. Go into the User Management by clicking the icon.

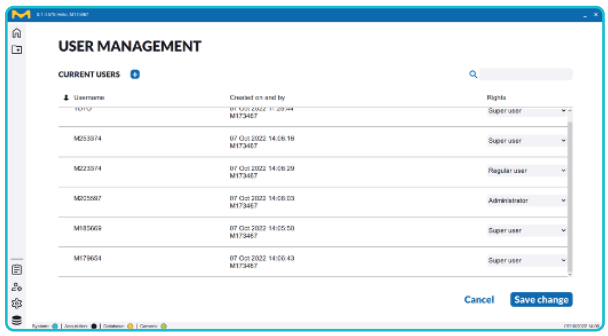
To add a new user, click the "+" button next to "Current Users". A pop-up window appears (see image below). Enter the Windows login of the new user into "Login". From the drop down menu on the right, select from among four choices the access level for the user that will be created:

	Administrator	Super User	Regular user	Inactive
Login	✓	✓	✓	✗
Create Batch	✓	✓	✓	✗
View Batch	✓	✓	✓	✗
Export Batch	✓	✓	✓	✗
Create New Sample	✓	✓	✓	✗
View Sample	✓	✓	✓	✗
Export Sample	✓	✓	✓	✗
Create Test Settings (protocol)	✓	✓	✓	✗
Edit Test Settings (protocol)	✓	✓	✗	✗
Backup and Restore data	✓	✗	✗	✗
Export Audit Trail	✓	✗	✗	✗
User Management	✓	✗	✗	✗

- Regular user: Can only create new batches and perform tests
- Supervisor: Same as Regular user, plus create and modify protocols
- Administrator: Same as Supervisor, plus create and modify users
- Inactive: This user's access to the software is inactivated



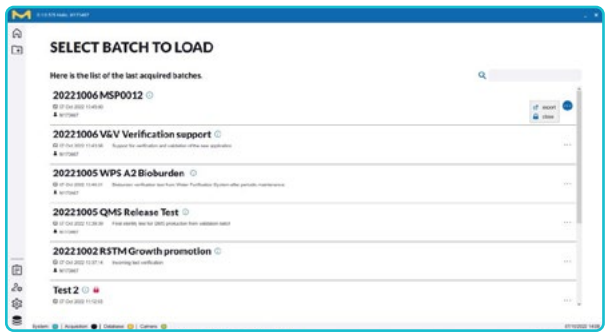
To change the user rights of existing users, go into the User Management and select from the choices in the drop-down menu (circled, red) in the image below. Click "Save change" to save the changed user rights.



Note: To prevent losing the administrator user by self-modification the current logged user is not displayed in the list.

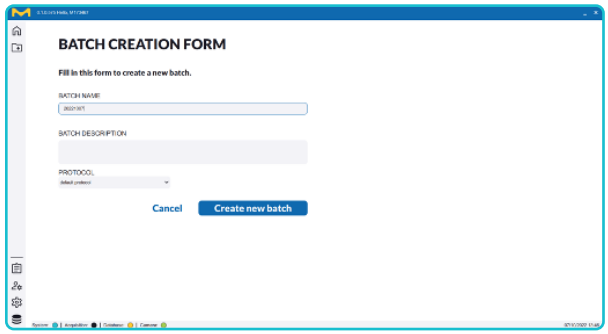
Batch creation

Samples can be created only in open batches. If there is no appropriate batch, a new one must be created before.



To create a batch:

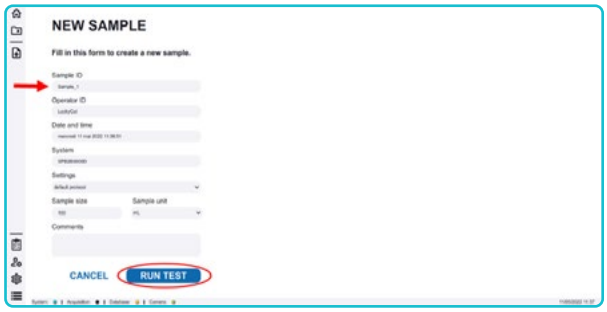
- Click on the icon (top, left) to create a new batch from any page view where it is displayed.
- Enter "Batch name" and "Batch description".
- From the drop-down menu, select the **default protocol** to use for the newly created batch.
- Then click on "Create new batch".



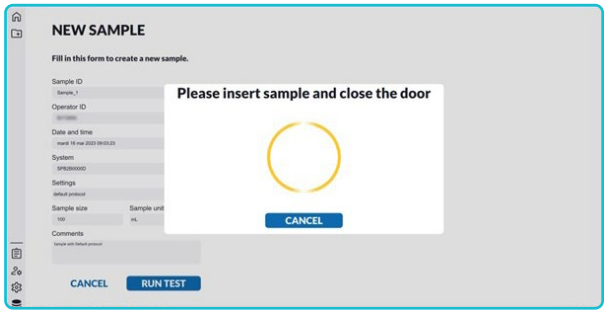
Sample creation, running a test

Go into the Batch Management of the batch into which you want to enter your sample. Then click on “Add sample”.

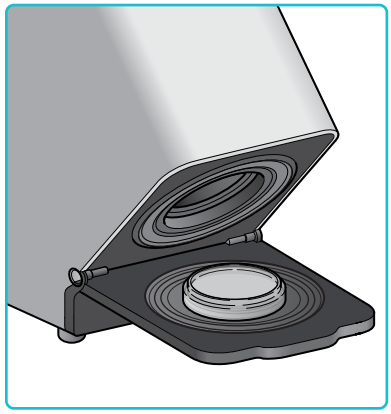
The “New Sample” window appears (see image below) with data about the sample. “Sample ID” suggests an incremental number which, however, can be changed here. If needed, change the protocol and/or the volume of the sample to test. Then click on “Run Test”.



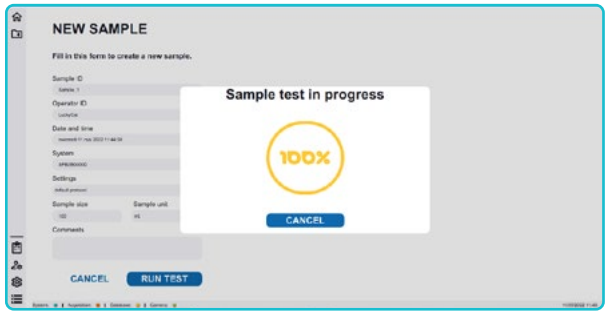
The system is now waiting for the sample to be inserted for starting the analysis.



After the consumable was sprayed using the Milliflex® Rapid 2.0 Autospray station (consult appropriate user guide for guidance), open the door to access the membrane support. Place the membrane onto the membrane support as shown in the image above (narrower circular ledge facing upwards). Push the door up to close the detection tower.



Close the door by lifting it up. Once done, the test runs, and the acquisition of data automatically starts. The message “Sample test in progress” is displayed. A test usually takes about 3 minutes.



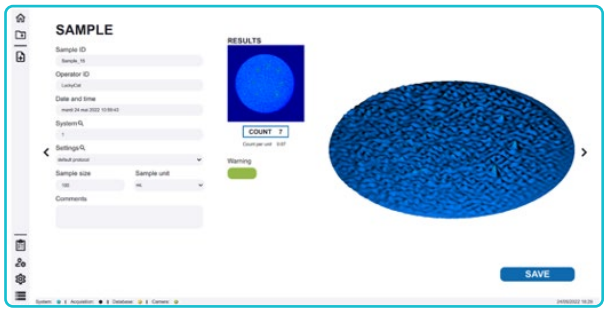
Result analysis

When the test is over, the “Sample” screen displays the results (see below).

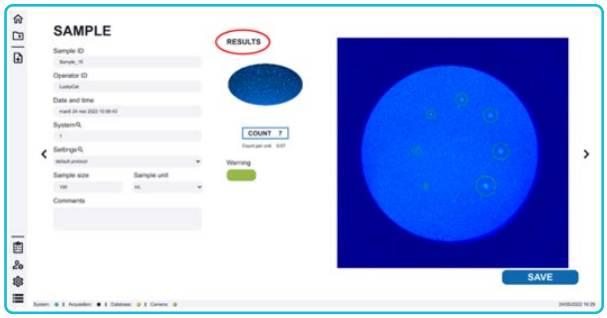
The result view displays:

- Sample ID: Name of the sample
- Operator ID: Username of the person who ran the test (automatic entry)
- Date and Time: Date and time of the test (automatic entry)
- System: Serial number of the system used for test (automatic entry)
  - Click “System” to show the complete information about the instrument
- Setting: Test protocol used for the test
  - Click “Setting” to show all details about the test settings
- Sample Size: Size of the sample tested
- Sample Unit: Unit of the sample tested
- Comments: Field to enter what happened during the test (optional).

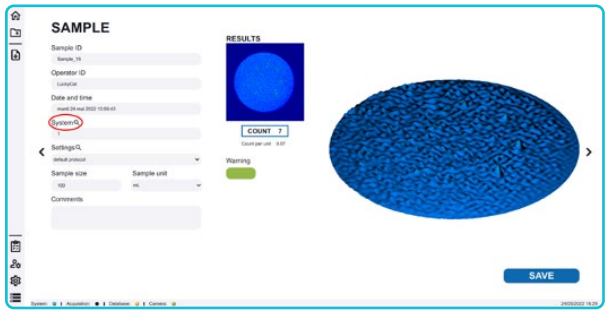
The sample’s parameters are displayed on the left.



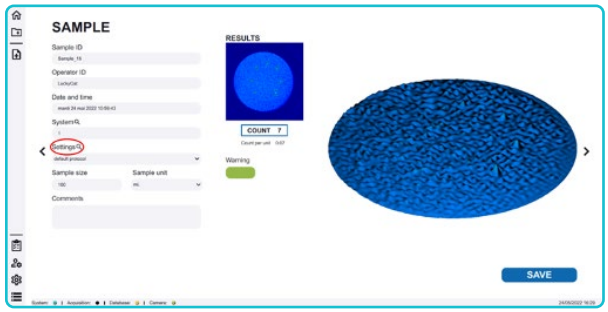
To switch from the default 2D view to the 3D view, click on the small plate image below “Results”.



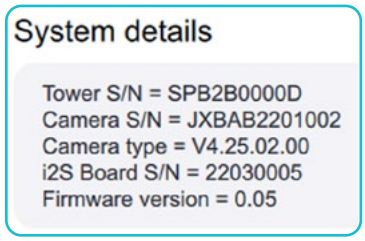
From the “Sample” screen, it is easy to access the parameters of the system and the sample. Click on “System” to display system details.

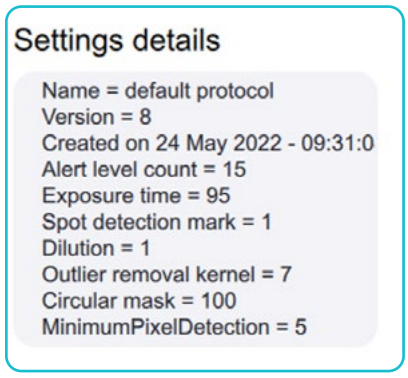


Click on “Settings” to display details about the settings of the performed test.

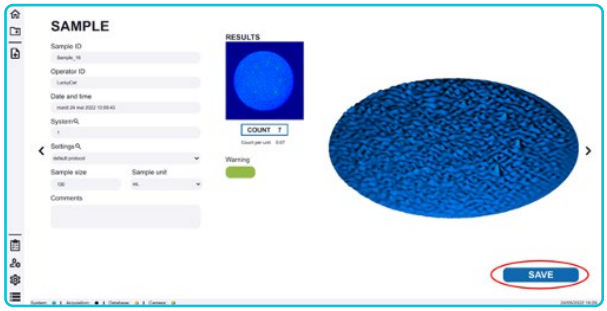


The two images below are examples of what the “System” and “Settings” screens reveal.



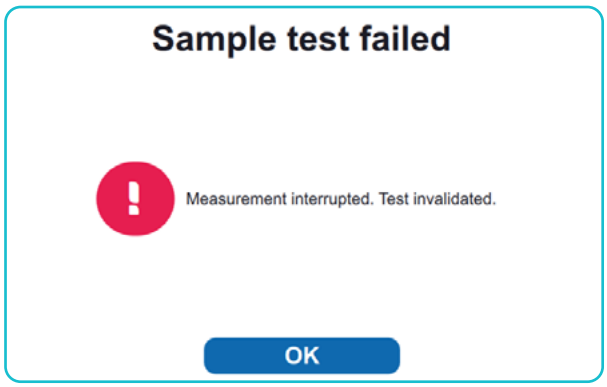


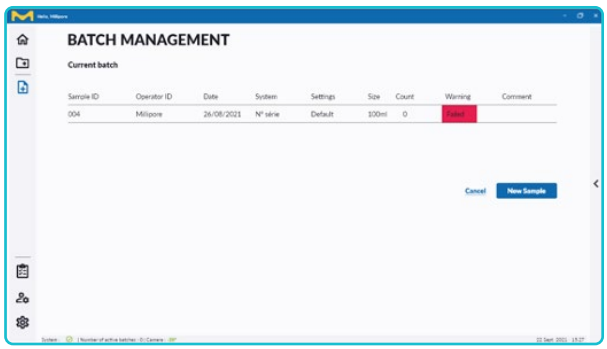
To save the sample's results, click on "Save" in the "Sample" screen. After saving a sample, no changes or additions can be made in the comment field.



Note: The Warning is related to the status of the detection tower.

If the connection between the computer and the detection tower is lost during a test run, a sample test failure screen appears and the "Failed" status of the sample is shown in red in the Batch Management (see images below). Should this occur, restore the connection and repeat the test run. If you want you can add a comment before saving the test result to explain the mistake.





Export results

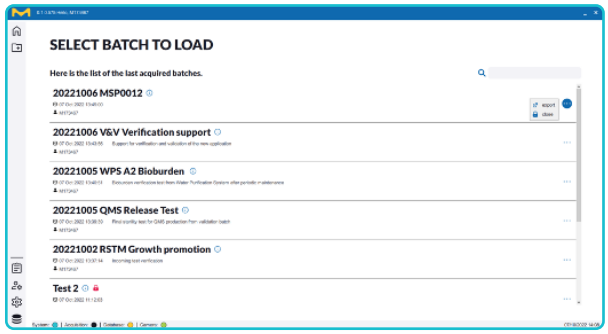
To export results, go into the "Batch Management" view by clicking (top, left). It is possible to export the results of individual samples or of entire batches.

Export of entire batch

Click on the three-dot icon (top, right) to open an additional batch menu, then Export the batch. A Windows Explorer window opens and prompts for the location on your computer where to save the batch export.

Select the appropriate location on your computer then click the Select Folder button.

The batch is exported in PDF format in the folder.



Export of individual sample

To export the results of samples within a batch, double-click the batch to open it, the screen displays the samples in the batch. Click the export icon next to the sample to export. To export the results of all shown samples, click "Export all".

Then select the folder into which to store the results. The sample is exported in PDF format in the folder.

Finalizing a batch

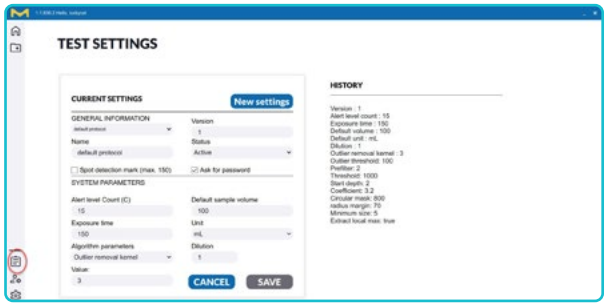
When all testing for a batch is finished, the batch can be finalized (i.e., closed permanently) by clicking on the three dots icon on the top right of the screen, then click "complete". To be able to close a batch, it is necessary to reconfirm identity. Once closed, no more modifications can be made to a finalized batch, neither can further tests be added.

Note: When a batch is closed, a red lock is displayed.

Settings management

Click on (circled in image below) to enter “System Settings” from any view where this icon appears.

This opens the “Test Settings” view.



Two Test settings are available:

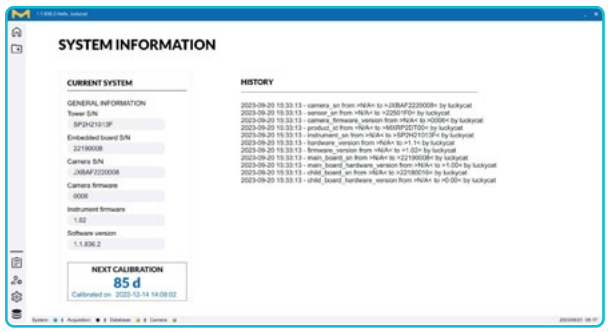
- Default protocol: use this protocol for all the standard readings of Milliflex Oasis® membranes.
- Positive control: use this protocol to read the membranes spotted with ATP using the positive control tool.

Test Settings allows the creation or modification of test parameters (Protocols).

Click the box “Spot detection mark” for detected microcolonies on the image of the plate to be circled (note: the maximum number of highlighted microcolonies is 150)

- Status: activate or deactivate the protocol for use in a batch
- Alert Level Count: threshold (in CFU) when the result displays a warning on the counts.
- Exposure Time: exposure time for picture acquisition. By default it is 150 seconds.
- Default volume: default sample volume for the protocol
- Unit: default sample unit
- Dilution: dilution of sample
  - These parameters are used to calculate the count per unit count/volume/dilution.
- Algorithm parameters:
  - Outlier kernel: size of the kernel for outlier detection
  - Outlier Threshold: threshold for the outlier detection
  - Prefilter: initial filter for preprocessing
  - Start depth: starting scale for wavelet reconstruction
  - Coefficient: threshold for wavelet coefficient filtering
  - Threshold: threshold for the event detection
  - Minimum Size: minimal size of the event to detect
  - Circular mask: size of the consumable mask

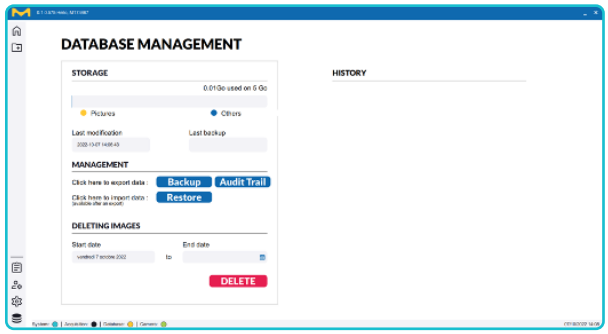
Click on to enter on the “System Informations” view for information about the system, the remaining days until the next calibration becomes necessary, and the history.



Database Management

It is possible not just to not export individual samples or batches (see “Export results”) but to create a backup of the entire database containing all its batch and sample results. In case of a system failure the data can be recovered and reinstalled by importing the stored database file. To export or import database files, it is necessary to confirm user identity.

Click on the bottom icon to go to the “Database Management” view.



To create a backup of the database, click on “Export” to export a database file.

If the data needs to be recovered, click on “Import” to import a database file. Then go to the folder containing the database file to import and click on “Open”.

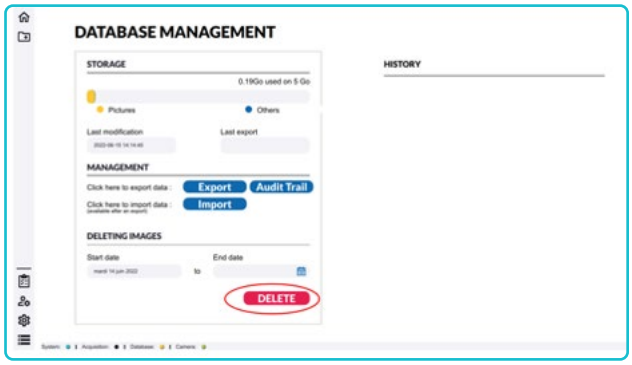
Audit trail

The software records each modification of internal data and maintains a timestamped list of creations and modifications with the name of the person who made the modification, the previous and the new value of the considered fields. The readable export in CSV (coma separated values) can be opened using Microsoft Excel for inspection.

The following events are logged in this audit trail:

- User creation or modification
- Test settings creation or modification
- Test batch creation
- Test sample creation
- Database backup and restoration

When the hard disk or database is full, it is possible to delete no longer needed images to free up storage capacity. To do so, select the start date and end date of the image files to delete, then click “DELETE”.



Cleaning & Maintenance

The following surface sanitizers have been tested to be suitable for cleaning the Milliflex® Rapid System 2.0 Detection Tower:

Surface sanitizer tested: Active ingredients	Dilution
Ethanol (N°CAS 64-17-5 : 226 mg/g) Chlorhexidine digluconate (N°CAS 18472-51-0:0.64 mg/g) Didecyldimethylammonium chloride (N°CAS 7173-51-5 : 0.53 mg/g), excipients.	Ready to use
Propane-2-ol (70%), deionized water solution (30%)	Ready to use
Ethanol (70%)	Ready to use
Quaternary ammonium: Benzalkonium chloride (between 0.25–0.5%) Poly(hexamethylene biguanide) hydrochloride (between 0.1–0.25%)	Ready to use
Sodium hypochlorite (2.6% active chloride)	250 ppm
Isopropyl alcohol (N°CAS 67-63-0 10%) Didecyldimethylammonium chloride (N°CAS 7173-51-5:0.15936%)	Ready to use
Hydrogen peroxide (1%) and acetic acid (5.2%)	Ready to use
Peracetic acid (0.08%), hydrogen peroxide (1%), and acetic acid (<10%)	Ready to use
Quaternary ammonium: Ethanol <25%, Didecyldimethylammonium chloride <0.5% N-(3-aminopropyl)-N-dodecylpropane-1,3-diamine <0.5%	Ready to use
Alkaline disinfectant: Potassium hydroxide (CAS 1310-58-3) Tetrasodium ethylenediaminetetraacetate (CAS 64-02-8)	47 mL/L

The Milliflex® Rapid System 2.0 Detection Tower must be cleaned once per day. The cleaning procedure is as follows:

1. Use a wipe moistened only with a surface sanitizer listed in this Cleaning & Maintenance section (see above).
2. Clean all external surfaces with the wipe, except connectors and plugs.
3. Open the door and gently wipe the membrane support, taking care not to press on it.
4. Keep parts drying as long as needed
5. Close the door

Note: Power supply can be cleaned with wipe moistened with 70% ethanol. Ensure the power supply is disconnected during the cleaning.

IMPORTANT NOTE:

Cleaning the lens is unnecessary:

- Under normal environmental conditions in a laboratory, hardly any dust will stick on the lens.
- Even if traces of dust do stick on the optics, the ratio between the area impacted by the dust and the lens area tends to be so small that any interference is likely to be insignificant.
- Cleaning the lens risks that chemical residues degrade and create blur on the images taken.
- Inappropriate chemicals and/or wipes can damage the lens coating.

Specifications and Operating Requirements

Dimensions	Width	297 mm
	Depth	126 m
	Height	348 mm
	Weight	5.2 kg
Material of Construction	Housing material	ABS
	Rear panel	ABS
	Door	Aluminum
Electrical Specifications	External power supply input	100–240 V ±10% ; 50/60 Hz ±2% Hz ; 0.6 A max
	Power supply output	24 VDC 50 W max
	Transient overvoltage	Overvoltage category II
	Tower input (DC IN)	24 VDC 30 W max
	USB	5 V 940 mA max, connect only to class 2 USB host
Environmental Conditions	Altitude	Less than 3000 m
	Temperature	
	1. Storage:	1. 0 °C to +40 °C and –20 °C to +60 °C for 24 hrs.
	2. Operation:	2. 15 °C to 30 °C
	Relative humidity	Max. 80% RH for temperatures up to 31 °C, non-condensing
	Ingress protection rating	2X
	Pollution degree	II

Troubleshooting

This section offers solutions to some issues that might arise when operating the Milliflex® Rapid Detection Tower, along with troubleshooting procedures to be followed should such events occur.

Issue	Solution
The detection tower doesn't turn on (BLUE LED is OFF)	Verify the power supply is well plugged on the detection tower. Verify the USB cable is correctly plugged in at both ends. Ensure the computer's port is USB3 standard.
The detection tower is turned on, nevertheless the system is not ready (GREEN LED is OFF)	Verify the software is running. Verify the USB cable is correctly plugged in at both ends. Ensure the computer's port is USB3 standard. Restart the Detection Tower and ensure the power supply unit is plugged in before connecting via USB. Once the detection tower has restarted wait 15 minutes for the camera to cool. If GREEN LED is still OFF ensure that the lab temperature is below 30 °C.
The instrument remains in standby mode and is thus impossible to use (BLUE LED is blinking)	Verify the USB cable is correctly plugged in at both ends. Ensure the computer's port is USB3 standard. Verify the software is running properly.
The detection tower is turned on, nevertheless the system doesn't perform image acquisition (ORANGE LED is OFF)	Open and close the door: the system should then perform image acquisition, with the ORANGE LED initially turning on and, once the image is taken, off again.
The detection tower is not going to ready state	Ensure instrument is plugged in USB 3.0 at least. Ensure software prerequisites are met.

Accessories and Services

Hardware

Milliflex® Rapid 2.0 Detection Tower	1	MXRDP2DT00

Accessories

Power supply for Milliflex® Rapid System 2.0, needed for the AutoSpray Station and the detection tower	1	MXRPWRSP--
Positive Control Tool for fast and reliable reagent and Milliflex Rapid System efficiency verification	1	POSITCONT1
Milliflex® Rapid System 2.0 USB connection cable for connecting the detection tower to PC	1	MXRP2USBC

Services

Digital validation protocol on Val@M™ Application	1	MXRPIQOQEP
IQ & OQ execution service (protocol not included) combined without Essential PQ consultancy on Milliflex® Rapid system 2.0 at customer site	1	MXRPVAL11
IQ & OQ execution service (protocol not included) combined with Essential PQ consultancy on Milliflex® Rapid system 2.0 at customer site	1	MXRPVAL12
Essential PQ consultancy at customer site	1	RSC0NSUL11
Advanced Operator Training at customer site	1	RSTRAIN12

Terminological Glossary

Acronym	Definition
ATP	Adenosine triphosphate
CFU	Colony-forming unit
HMI	Human-machine interface
LED	Light-emitting diode
sCMOS	Scientific Complementary Metal Oxyde Semiconductor
USB	Universal serial bus

Standard Product Warranty

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