

Milliflex® Rapid Microbiology Detection System

An automated system for rapid, accurate detection of microorganisms

- ▶ *CFU test results correlate with traditional methods*
- ▶ *Consistent performance delivers reproducible results*
- ▶ *Results in approximately one-fourth of the time of membrane filtration or pour plate methods*
- ▶ *Easy to operate and validate*
- ▶ *21 CFR Part 11 compliance ready*

The Milliflex Rapid Microbiology Detection system is an automated solution for the rapid detection, response, and resolution of microbial contamination in filterable samples throughout the manufacturing process. The system improves process control, product yield and the timely release of products. Based on Adenosine Triphosphate (ATP) Bioluminescence technology, the Milliflex Rapid system delivers faster test results than traditional microbial contamination detection methods, such as membrane filtration (MF) and pour plates. The Milliflex Sample Prep method also ensures consistent, reliable results. The Milliflex Rapid system can clearly distinguish between mixed microbial growth of slow growing and fast growing microorganisms, variances in their size and ATP content in water samples.

Results in Hours, Not Days

With the Milliflex Rapid system you can detect bacteria in approximately one-fourth the time of your current method. An intelligent system, the Milliflex Rapid system can detect and count viable microorganisms filtered

onto a membrane down to 1 CFU per sample. The software displays results as familiar colony forming units (CFU) therefore providing a direct comparison with historical data obtained from traditional methods.

Applications

Filterable samples from a wide range of industries including pharmaceutical, beverage, personal care and micro-electronics:

- Raw materials
- Non-sterile final products
- In-process bioburden
- Water
- Mineral water, iced tea, flavored water, beer, wine, and other beverages

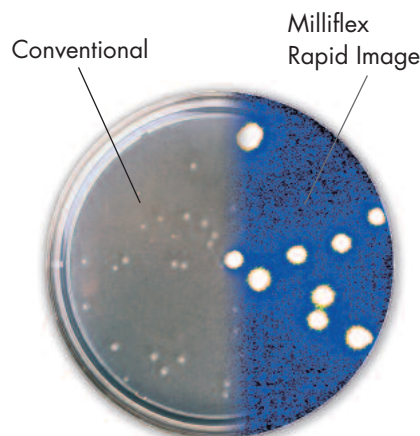


Figure 1. *Conventional vs. Milliflex Rapid image analysis*


Streamlined Detection and Analysis

Fast, reproducible test results in three easy steps:



Step 1

Sample Prep
Filter the desired sample volume through presterilized, disposable Milliflex filter units. Filter a rinse solution to wash away any growth inhibitors (if necessary). Place filter base onto a media cassette and incubate.



Step 2

Apply Reagents
Release filter base from the Milliflex prefilled media cassette and place filter unit on the Milliflex AutoSpray Station for application of reagents. Reagents are automatically sprayed across the membrane in quick succession.



Step 3

Enumerate Microorganisms
Transfer the filter unit to the Milliflex Rapid Detection Tower for enumeration of colonies. From the PC, enter information about the sample and click the Run Test button to enumerate the microcolonies. The colony count in CFUs and an image of the filter/organisms are automatically recorded, displayed, and archived.

Automated Imaging Analysis

The technologically advanced Milliflex Rapid Image Analysis software enables analysts to test water, in-process products, raw materials and final products in a fraction of the time of traditional methods. Access and

editorial privileges are controlled by the system administrator ensuring secure data acquisition and retrieval.

The detection tower scans and develops an image of the microcolonies on the membrane in two minutes.

The system counts each microcolony and stores the data for downloading, printing and retrieval. Within approximately two minutes, the sample analysis and results are displayed (Figure 2) along with the batch history and electronic image of the membrane with CFUs, which can also be viewed three dimensionally.

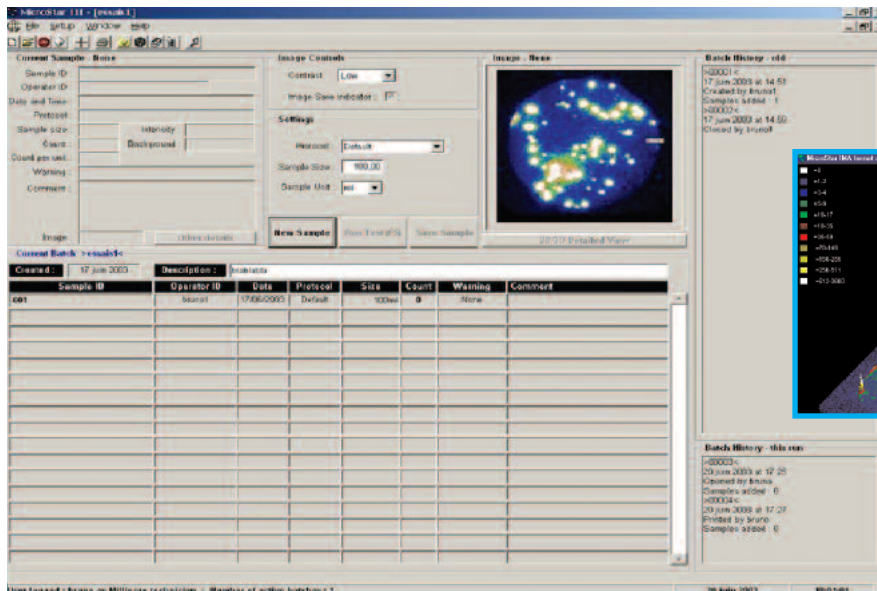


Figure 2. Current sample screen displays results of a test sample batch history. Analysts can view results as two- and three-dimensional images.

21 CFR Part 11 Compliance Ready

Milliflex Rapid Microbiology Detection software meets the requirements of FDA Regulation 21 CFR Part 11 for Electronic Records and Electronic Signatures. The software's powerful batch reporting feature meets the technological requirements of FDA's 21 CFR Part 11 for electronic signatures and electronic batch reporting. The batch reporting feature includes capabilities for electronic signing, performing audit trails, and rendering data files unalterable.

Three Proven Technologies

The Milliflex Rapid system uses proven technologies including membrane filtration, ATP bioluminescence and image analysis for ease of validation.

1. Membrane Filtration

Today's standard for sample preparation. Large volumes of product can be processed and any inhibitor substances are easily rinsed away. Designed to optimize the enumeration of microorganisms, the Milliflex Rapid membrane offers fast filtration and reliable results.

2. ATP Bioluminescence

Found only in living cells, ATP (adenosine triphosphate) is a great indicator of cell viability. Because it is found in all microorganisms, ATP is used in a wide range of applications including raw materials, in-process product, and finished products. Unlike other methods that detect both living and dead cells, the ATP method only detects viable culturable organisms, reducing false positives and improving reliability.

3. Image Analysis for Enumeration of Microorganisms

Unlike traditional methods that require a visual inspection, the Milliflex Rapid system uses a CCD camera to detect and enumerate microcolonies. The concentration

of ATP required for measurement is about 200 attomoles, which is equivalent to one yeast or mold cell or approximately 100 bacterial cells, depending on their metabolic state. The sensitivity of the reagents combined with a charged coupled device (CCD) camera and image processor requires only a short incubation period to generate enough ATP for detection and enumeration.

The system's image analysis software intensifies the bioluminescence from each cell (or microcolony) thousands of times and captures the light signals emitted from the microorganisms on the membrane with a CCD camera. An image processor enumerates the microorganisms and displays them on a computer screen.

Worldwide Regulatory Compliance

ATP bioluminescence technology used by the Milliflex Rapid system is recognized as an alternative detection method by:

- FDA^{1,2}
- PDA Technical Report No. 33: Evaluation, Validation and Implementation of New Microbiological Testing Methods³

Membrane filtration is a recommended methodology in the capture of microorganisms by worldwide pharmacopoeias (US, European and Japan).

The Milliflex Rapid system is calibrated to international light standard [LNE/NIST] and meets electrical conformity to the CE mark.



The Milliflex Rapid Microbiology Detection system



¹FDA draft guidance for industry, PAT — A Framework for Innovative Pharmaceutical Manufacturing and Quality Assurance, August 2004.

²FDA/OPS meeting, April 13, 2004, pages 104–110, 136.

³PDA. May/June 2000. Technical Report No. 33: Evaluation, Validation and Implementation of New Microbiological Testing Methods. PDA Journal of Pharmaceutical Science and Technology 54(3) Supplement TR33.

Specifications

Detection Area	Within the area of the 55 mm diameter Milliflex membrane
Sensitivity of System	1 CFU/sample
PC Configuration	PC with Windows® XP Professional operating system and 256 MB memory and 40 GB hard drive

Dimensions and Weight

<i>Detection tower:</i>	Width: 20 cm (8 in.)
	Depth: 20 cm (8 in.)
	Height: 31 cm (12 in.)
	Weight: 6 kg (13 lb)
<i>Image intensifier controller:</i>	Width: 23 cm (9 in.)
	Depth: 34 cm (13 in.)
	Height: 8 cm (3 in.)
	Weight: 3 kg (7 lb)
<i>AutoSpray station:</i>	Width: 21 cm (8 in.)
	Depth: 40 cm (16 in.)
	Height: 31 cm (12 in.)
	Weight: 10 kg (22 lb)
<i>PC:</i>	Width: 18 cm (7 in.)
	Depth: 45 cm (18 in.)
	Height: 43 cm (17 in.)

Materials of Construction — AutoSpray Station

<i>Turntable, pad holder, membrane holder:</i>	316L stainless steel
<i>Cover and casing:</i>	polyurethane
<i>Keypad:</i>	polyester

Electrical

<i>Power supply:</i>	230 V, 50 Hz or 110 V, 60 Hz
<i>Consumption:</i>	30 W

Operational Requirements — AutoSpray Station

<i>Ambient temperature:</i>	15 – 40 °C
<i>Relative humidity:</i>	< 90%
<i>Altitude:</i>	< 3000 m (9842 ft)

The AutoSpray station can be used under a laminar flow hood.

Regulatory Information	The AutoSpray Station is compliant with Electromagnetic Compatibility Directive 89/336/EEC, and is CE marked.
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Rapid Microbiology at its Best

For over 10 years, Millipore has set the industry standard for rapid microbiology testing. The development of the Milliflex Rapid Microbiology Detection system is the result of years of communication and collaboration with our customers. The innovative hardware design and control software offers an easy to use, intelligent system for optimizing process control. The system includes a PC, AutoSpray Station, Detection Tower, Image Intensifier Controller, and Image Analysis Software that can be used as a stand-alone test system or within a networked environment.

Millipore's staff of knowledgeable and experienced microbiologists can assist with product filterability and methods development. Validation protocols, as well as on-site IQ/OQ services, service plans and training and up-to-date regulatory compliance information are also available.

Ordering Information

Description	Qty/Pk	Catalogue No
Milliflex Rapid Microbiology Detection System Kit Includes: Detection tower, image analyzer, CCD camera, AutoSpray station, PC with IQV40 PC board and software	110 V 230 V	1 MXRP KT1 10 MXRP KT2 30
Milliflex Rapid AutoSpray Station Includes: AutoSpray station, filter holder, pad holder, 2 needle assemblies with tubing and Millex® FG vent filter, 2 stainless steel caps and universal power supply adaptor		1 MXRP SPR KT
Milliflex Rapid Microbiology Detection System Upgrade kit from MicroStar System Includes: CCD camera, AutoSpray station, PC with IQV40 PC board and software		1 RMMX RP1 10
Milliflex PLUS Pump	Single Head Double Head Triple Head	1 1 1 MXPP LUS 01 MXPP LUS 02 MXPP LUS 03
Milliflex Rapid Funnel, 0.45 µm membrane		24 RMHV MFX 24

Milliflex Rapid Kits

Description	Qty/Pk	Catalogue No
Milliflex Rapid Reagent Kit <i>For 100 tests</i> ATP releasing agent, 2 bottles Bioluminescent reagent, 2 bottles Reconstitution buffer, sterile, 2 bottles 2 syringes, 5 Luer-Lok® caps, 6 vial adapters	1	MXRP BLR ST
Milliflex Rapid Cleaning/Decontamination Kit <i>For 20 cleanings, 2 decontaminations</i> Rinsing agent, 4 bottles Cleaning agent, 4 bottles Decontamination agent, 1 bottle 10 Luer-Lok caps, 9 vial adapters	1	MXRP CLK T1
Milliflex Rapid Cleaning/Decontamination Kit <i>Empty bottle</i> 4 empty 20 mL bottles, 5 empty 10 mL bottles, 10 Luer-Lok caps, 9 vial adapters	1	MXRP CLK TO



A standard reagent kit as well as prefilled and empty cleaning and decontamination kits are available.

Ordering Information (cont.)

Milliflex Rapid Services

Description		Qty/Pk	Catalogue No
Milliflex Rapid Validation Protocol Includes IQ & OQ for AutoSpray station and Milliflex Rapid system	US Letter Format	1	MXRP LTV P1
	A4 Format	1	MXRP A4V P1
Milliflex PLUS Pump Validation Protocol	Single Head	1	MXPP OVG 01
	Double Head	1	MXPP OVG 02
	Triple Head	1	MXPP OVG 03
Milliflex Rapid Calibration and Preventive Maintenance		1	MXRP CLP M1
Milliflex Rapid Setup and Training		1	MXRP SET UP
Service Plans			Contact Millipore
Feasibility Study/Methods Development			Contact Millipore

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In every application, every step and every scale, count on Millipore to be everywhere for you — from monoclonals to vaccines, from clinical through pilot to full-scale manufacturing. Our technologies are used by most of the world's major biopharmaceutical companies. But we deliver more than advanced separation, purification, sterilization and quality control products. With Millipore, you get services to optimize and validate your processes, comprehensive resources to streamline and enhance your operation, unmatched know how forged from 50 years' experience — and solutions that integrate it all. For higher yields, improved process economics and faster speed to market, discover the more in Millipore.

To Place an Order or Receive Technical Assistance

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In the U.S., Canada and Puerto Rico, fax orders to **1-800-MILLIFX (1-800-645-5439)**

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