Millipore®
Preparation, Separation,
Filtration & Monitoring Products

Application Guide

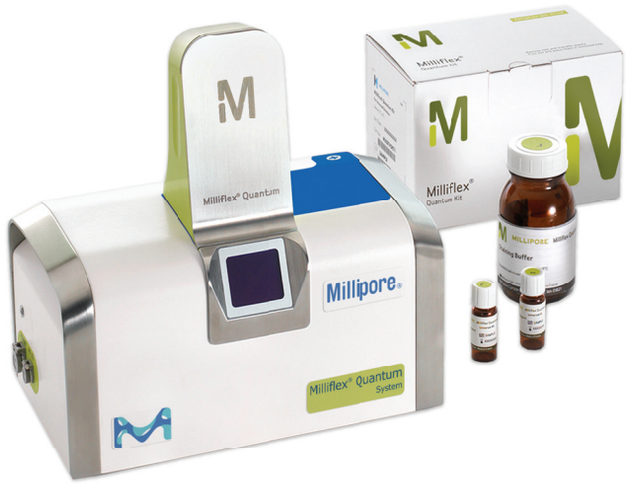
Suitability of fluorescence-based microbial detection technology for pharmaceutical applications

Helping you work smarter

Fluorescence detection technology: the principle

Fluorescence-based technology provides a convenient and a sensitive basis for the **quantitative** and **rapid** detection of contaminants in filterable samples. The principle behind this is the universal enzymatic fluorescent staining of viable and culturable microorganisms. The fluorescent staining procedure is **non-destructive**, allowing the identification of the contaminant following a positive result.

The fluorescence-based technology as used by the Milliflex® Quantum system is not only a **fast** but also a **reliable** alternative for the detection of contaminants. Throughout manufacturing processes, the system enables faster responses and corrective action to be taken earlier if needed. It improves process control and product yield and it permits the final product to be released earlier to the market.



The life science business of Merck KGaA, Darmstadt, Germany operates as MilliporeSigma in the U.S. and Canada.

Sample types suitable with the technology

Any filterable sample such as:

- Raw materials (media, buffers, pharmaceutical ingredients and water)
- In-process samples (bioburden prior to sterilization, CIP/SIP samples, cell culture/fermentation samples, media for fermentation, buffers for manufacturing, and intermediate process samples)
- Final product
- Environmental samples

Examples of microorganisms detectable in various matrices

The following tables list the microorganisms that have proved detectable using the Milliflex® Quantum rapid detection system when present in certain matrices that are typical of production processes in the pharmaceutical and other industries. These findings are based on customer samples which have been successfully tested in our application lab as part of customer feasibility and validation studies. They show that the fluorescence-based Milliflex® Quantum rapid detection system is, in principle, compatible with these kinds of matrices, with some of the tested samples requiring pre-treatment for detection to succeed. However, the findings must be taken to be indicative. Customers are advised to perform their own experiments with the specific matrices relevant to them in order to ensure that detection is possible for their own samples, or to have this performed by us.

Pharmaceutical products successfully tested

Sample source	Matrix tested	Strain recovered	Media
CMO	Vitamin D3	*Escherichia coli*	TSA
	Water	*Staphylococcus aureus*	TSA
Contract lab	Collagen coated implants	Natural contamination	TSA
	Spray	Natural contamination	TSA
	Sterile water	*Aspergillus brasiliensis; Staphylococcus aureus*	TSA
Gene therapy	Cell culture supernatant	*Aspergillus brasiliensis; Candida albicans*	SDA
		Micrococcus sp.	TSA
Immuno therapy	WFI	*Bacillus cereus; Bacillus subtilis; Burkholderia cepacia; Escherichia coli; Methylobacterium extorquens; Pseudomonas aeruginosa; Pseudomonas protingens; Ralstonia pickettii; Staphylococcus aureus*	R2A
Lipids parenteral nutrition	Lipidic emulsion for parenteral nutrition	*Bacillus cereus; Bacillus thuringiensis*	TSA
Medical devices	Rubber tip caps	*Bacillus subtilis; Pseudomonas aeruginosa; Staphylococcus epidermidis*	TSA
Medical imaging products	Contrast agent	*Pseudomonas aeruginosa*	TSA
Parenteral preparations	Water for irrigation	*Bacillus lentus; Kocuria varians rosae*	TSA
		Penicillium chrysogenum; Rhodotorula mucilaginosa	TSA and SDA
		Sphingomonas paucimobilis	TSA and R2A
	Process water	*Deftia acidovorans; Methylobacterium fujisawaense; Natural contamination; Ralstonia pickettii; Staphylococcus saprophiticus*	R2A
		Pseudomonas aeruginosa	Cetrimide
		Ralstonia pickettii	R2A
Pharmaceuticals	Anesthetic gel	*Staphylococcus epidermidis*	TSA
	Anticoagulant	*Aspergillus brasiliensis; Bacillus cereus; Bacillus subtilis subsp. spizizenii; Burkolderia cepacia; Staphylococcus warneri (Corynebacterium)*	TSA
	Blood typing reagent	*Carnobacterium*	TSA and SDA
	Cell culture	*Penicillium; Bacillus; Micrococcus; Stenotrophomonas*	TSA and SDA
	Column eluates	*Penicillium; Bacillus; Micrococcus; Stenotrophomonas*	TSA and SDA
	Cough syrup	*Staphylococcus aureus*	TSA
		Total Microbial Count	TSA and Sabouraud Chloramphenicol
	Empty hard capsules	*Bacillus subtilis; Bacillus coagulans*	TSA
	Fluid A	*Bacillus pumilus; Penicillium spp; Staphylococcus epidermidis*	RSTM
		Methylobacterium radiotolerans	R2A
		Stenotrophomonas maltophilia	R2A and RSTM

Pharmaceutical products successfully tested (continued)

Sample source	Matrix tested	Strain recovered	Media
Pharmaceuticals	Heparin	*Aspergillus brasiliensis; Bacillus cereus; Candida albicans; Staphylococcus aureus; Staphylococcus saprophiticus; Staphylococcus warneri (Corynebacterium)*	TSA
	Human albumin 20%	*Sphingomonas paucimobilis*	TSA
	Human blood derivatives	*Cladosporium cladosporoides*	SDA
	Human plasma	*Escherichia coli; Kocuria rosea; Lysinibacillus sphaericus; Pseudomonas aeruginosa; Stenotrophomonas maltophilia*	TSA
	Lactulose syrup (laxative)	*Aspergillus brasiliensis*	SDA
	Methadone	*Candida lipolitica*	TSA and SDA
		Mold strain	SDA
		Staphylococcus epidermidis	TSA
	Water	*Acidovorax delafieldii; Aquabacterium parvum; Aspergillus brasiliensis; Bacillus cereus; Bacillus licheniformis; Bacillus subtilis; Blastobacter denitrificans; Bradyrhizobium elkanii; Bradyrhizobium japonicum; Bradyrizobium isolate; Brevundimonas vesicularis; Candida albicans; Candida guillerimondi; Cupriavidus basilensis; C. vibrioides; Delftia acidovorans; Escherichia coli; Fusarium oxysporum; M. aquaticum; Moraxella sp; Natural contamination; P. saccharophilia; Stenotrophomonas ritzophila; Pelomonas saccharophila; Penicillium chrysogenum; Phyllobacterium myrcinacearum; Pseudomonas aeruginosa; Ralstonia pickettii; Rhodococcus; S. sanguinis; Sediminibacterium isolate; Sphingobacterium multivorum; Sphingomonas paucimobilis; Sphingopyxis sp; Staphylococcus aureus; Variovorax paradoxus Stenotrophomonas maltophilia; Stenotrophomonas ritzophila*	R2A
		Candida lipolytica	SDA
		Corynebacterium propinquum	Schaedler Blood Agar; TSA and R2A
		Geobacillus	PCA and R2A
		Kocuria rhizophila	Schaedler Blood Agar
		Methylobacterium radiotolerans	Schaedler Blood Agar
		Micrococcus luteus	PCA and R2A
		Rhodotorula minuta	Sabouraud Chloramphenicol
		Serratia marcescens	TSA
		Sporidiobolus salmonicolor	Sabouraud Chloramphenicol
		Staphylococcus epidermidis	R2A and TSA
	WFI	*Aspergillus brasiliensis; Escherichia coli; Mold strain; Natural contamination; Ralstonia pickettii*	R2A
		Penicillium, Bacillus, Micrococcus, Stenotrophomonas	TSA and SDA

Summary

The above findings show that the Milliflex® Quantum basically suitable to detect a wide range of microorganisms in a considerable variety of matrices used or produced in the pharmaceutical, food & beverage and other industries.

If you have any questions or would like your own specific samples to be tested by us on these systems, please contact us.

SigmaAldrich.com/Quantum

MilliporeSigma
400 Summit Drive
Burlington, MA 01803

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