

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.



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

Pharmaceutical products successfully tested (continued)

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

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