BWT
BEST WATER TECHNOLOGY

FACTSHEET

Primary Validation of AQU@Sense MB

WHAT IS THE PRIMARY VALIDATION?

The Primary Validation is a set of experiments to prove the capabilities and limitations of a method in a scientifically sound way. According to the Pharmacopoeias the Primary Validation by the manufacturer is an essential part for completing the validation of an alternative or rapid microbiological method (RMM). It is the basis for the PQ-phase conducted by the customer and helps to reduce the workload for the validation and implementation of a RMM.

Activity	Normaly carried out by: supplier	user
Primary validation	+	–
URS (instrument, application)	–	+
Description of the technique	+	–
Risk benefit analysis	–	+
Design qualification (DQ)	–	+
Installation qualification (IQ)	–	+
Operational qualification (OQ)	–	+
Performance qualification (PQ):	–	+
▪ verification of primary validation data given by the supplier;	–	+
▪ verification for the intended use (e. g. sterility testing. TAMC/TYMC, ...);	–	+
▪ method suitability test	–	+

Figure 1: Tasks to be undertaken during the validation process according to Ph. Eur. 5.1.6

WHAT IS THE AQU@Sense MB?

The AQU@Sense MB is an automated instrument for the continuous detection of bacteria in pharmaceutical water. It uses the principle of flow cytometry.

WHAT WAS TESTED?

Multiple bacterial and fungal strains were tested with the AQU@Sense MB and compared to the official plate counting method proposed by the Ph. Eur. (membrane filtration, R2A, 30–35°C for 5 days). Furthermore, the AQU@Sense MB was challenged by artificial particles and by dead cells. The Validation Master Plan was written based on customer and expert input. The data was evaluated against criteria defined in the relevant documents by acknowledged experts for biostatistics.

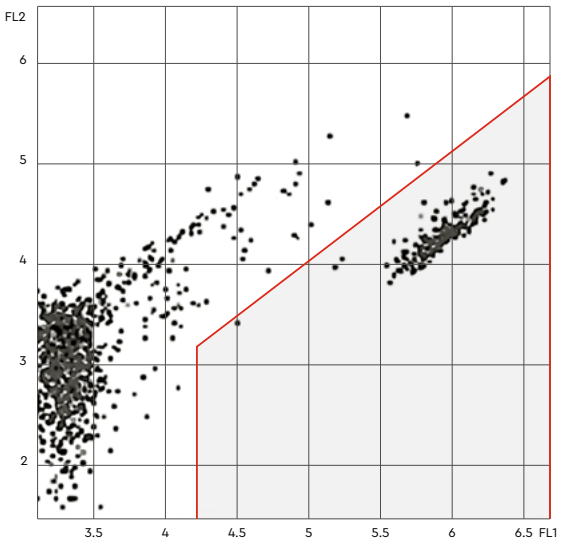

Figure 2: Sample of Staphylococcus aureus analyzed with the AQU@Sense MB. Every dot in the red polygon corresponds to one intact cell (ICC). FL1 shows the green and FL2 the red fluorescent intensity.

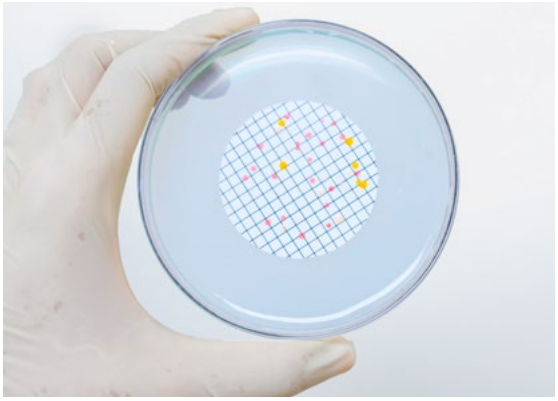

Figure 3: Microorganisms grown on an agar plate. Every colony is counted as one colony forming unit (CFU).

RESULTS

Parameter	Result	Details
Accuracy	✓	non-inferior to HPC
Precision	✓	RSD < 30%; non-inferior to HPC
Specificity	✓	all species detected
Limit of quantification	✓	non-inferior to HPC
Limit of detection	✓	non-inferior to HPC
Linearity	✓	non-inferior to HPC
Range	✓	non-inferior to HPC
Robustness	✓	unaffected by change

SPECIFICITY

For the parameter of Specificity, it was evaluated if all relevant species can be detected by both methods. The panel of microorganisms was chosen in a way to reflect typical contamination in pharmaceutical water plants and cover pharmacopoeial strains and potential external contamination of samples.

Species	Result
Pseudomonas aeruginosa	✓
Bacillus subtilis	✓
Staphylococcus aureus	✓
Stenotrophomonas maltophila	✓
Ralstonia pickettii	✓
Burkholderia cepacia	✓
Penicillium expansum	✓
Sphingomonas paucimobilis	✓
Escherichia coli	✓
Candida albicans	✓

ACCURACY, PRECISION, LINEARITY, RANGE

The parameters Accuracy, Precision, Linearity, Range were assessed for multiple species in a combined experiment. One example of this study can be seen in Figure 4.

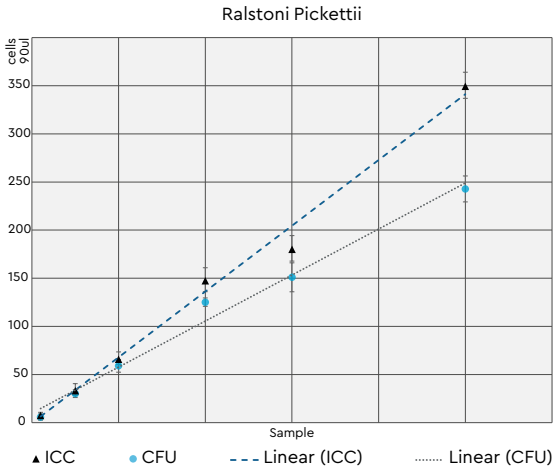

Figure 4: Comparison of results of Ralstonia pickettii of the AQU@Sense MB and plate counting method. Recovery of the AQU@Sense MB was 113–149%.

CONCLUSION

The AQU@Sense MB is the first alternative method for the continues monitoring of pharmaceutical water that was successfully validated during a primary validation. The method used is scientifically proven to work satisfactory for this application. Therefore, the AQU@Sense MB can be used effectively to improve product safety and support a Contamination Control Strategy as demanded by the EU-GMP Annex 1.

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