

Validity Period of Multidose Vials – Sterility Validation after Multiple Withdrawals

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INTRODUCTION

The manufacturing of cytostatic drugs at our institution is centralised, allowing improved protection of the personnel and the pooling of knowledge and infrastructure. The manufacturing process follows GMP-Guidelines, including environmental control and validation of aseptic working processes. According to physicochemical stability data, cytostatic stock solutions are used over several days. The aim of this study was the verification of absence of microbial contamination in multidose vials after multiple withdrawals under aseptic manufacturing conditions over a period of 28 days.

METHODS

The validation of sterility was based on the media fill test by the United States Pharmacopoeia. The test was conducted by replacing the cytostatic drug with a CASO culture medium and by simulating the manufacturing process by making 6 withdrawals over 28 days. Two extraction modes, either by mini spike or by needle, and two storage conditions (2-8°C, clean room class D; 15-25°C, clean room class B) were assessed. Samples were taken in triplets and incubated at 20-25°C (7 days) and at 30-35°C (7 days). The culture medium was visually examined on the absence of turbidity.

Results. No microbial growth could be observed in all taken samples (n = 72).

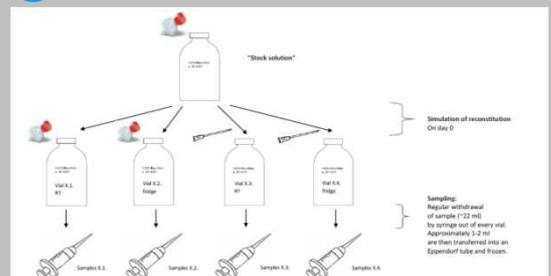
RESULTS

No microbial growth could be observed in all taken samples (n = 72; figure 2).

DISCUSSION - CONCLUSION

The sterility of the multidose vials, from which 6 withdrawals were taken over a period of 28 days, could be confirmed. The results are strengthened by the results of regularly conducted environmental monitoring and personnel validation and are further confirmed by a similarly conducted study.[1] Therefore, our manufacturing process can be maintained. However, these results only apply for the hospital pharmacy of the KSA and must not be transferred to other production sites.

1 Illustration of the sampling process.



2 Culture medium containing syringes (samples 2.1-2.4 of day 3) after the 14 days of incubation.

