3PC-005

CLOSED SYSTEM TRANSFER DEVICE (CSTD) EXTENDS PRACTICAL IN-USE SHELF LIFE TO 28 DAYS AFTER FIRST PUNCTURE OF NON-PRESERVED SINGLE-USE VIALS IN BOTH CONTROLLED AND UNCONTROLLED ENVIRONMENTS

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Background and Importance:

Closed system transfer devices (CSTDs) were initially designed to protect operators from cytotoxic, mutagenic, and reprotoxic agents. Additionally, product protection is necessary to avoid patient infection by microbiological contamination. Therefore, the National Institute for Occupational Safety and Health has defined a CSTD as "a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system".[1]

There is increasing pressure to reduce cost burden by preserving drugs, especially in oncology.[2] Numerous stability studies[3] support extension of the in-use shelf life of parenteral medicines beyond those specified in the Summary of Product Characteristics if the preparation takes place under adequate microbiological conditions. This may be possible through use of the Chemfort® CSTD. To date, Chemfort® can be used for up to 7 days and 10 activations, according to its instruction for use (IFU).[4]

Aim and Objectives:

This study tested Chemfort®'s maintenance of microbiological integrity after 10 withdrawals from vials over 28 days in a controlled and an uncontrolled environment.

Materials and Methods:

Tests were performed in both a controlled GMP Class A environment and an uncontrolled (worse than EU GMP class D) environment (350 vials in each environment). The rubber stoppers of all vials containing tryptic soy broth growth medium were disinfected by wiping with 2-propanol (IPA) before mounting Chemfort® Vial Adaptors (VAs). Statistical samples of each batch of medium were incubated at 30 - 35°C and verified to be sterile. The Chemfort® Syringe Adaptor Lock (SAL) was attached to a 10 mL syringe and subsequently connected to the VA. Handling was according to the device's IFU (Figure 1). The septa of both the VA and SAL were disinfected before every connection.

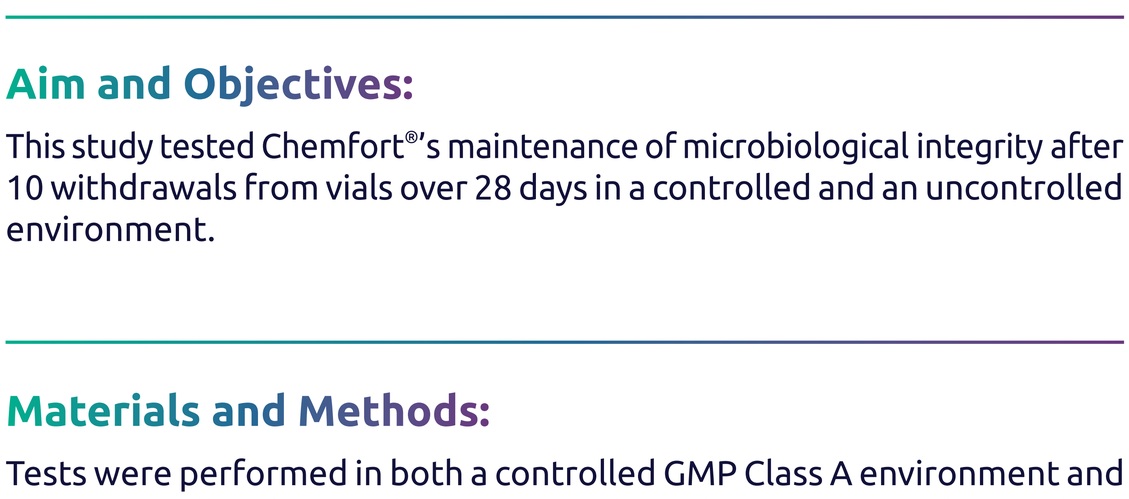

Figure 1. Vial Adaptor and Syringe Adaptor Lock handling procedure

Ten 5 mL aliquots were withdrawn from each vial at 2-week intervals (days 0 / 3 syringes, 14 / 3 syringes, and 28 / 4 syringes) and incubated for 7 days at 20 - 25°C and 7 more days at 30 - 35°C. After 28 days, the vials containing the remaining growth medium were incubated in the same way (Figure 2). Vials and syringes were inspected visually for signs of microbial growth during and after each incubation cycle.

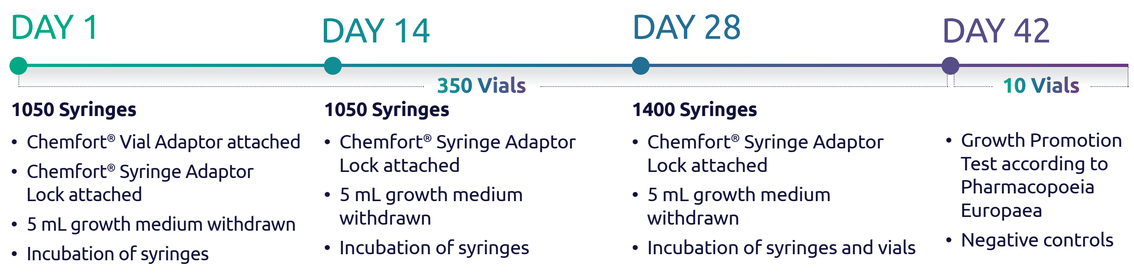

Figure 2. Sampling schedule for each environment (controlled and uncontrolled)

Following the incubation, on day 42, the growth-promoting capability of the medium was tested by inoculating 10 containers with each of 5 test microorganisms (50 containers total), according to Pharmacopoeia Europaea.[5] The positive control required microbiological growth from minimum inoculum (10-100 colony forming units) to be observed in all test containers. Ten unused containers served as negative controls.
Air quality was monitored to ensure that the appropriate environmental conditions were maintained for the relevant test groups.

Results

No signs of microbial growth were observed in any of the 7,000 samples, nor in the growth medium remaining in the vials after transfers were performed in either an uncontrolled or controlled environment.
Microbial growth (turbidity) was observed in all positive controls.

Conclusion and Relevance

The data demonstrate the ability of Chemfort® to maintain microbiological integrity. The results support extension of the practical in-use shelf life of drug products for up to 28 days when used with Chemfort® in either aseptic conditions or uncontrolled conditions.
Thus, drug vial optimization becomes feasible, avoiding costly drug waste.

References:

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