Drug sterility is maintained in Luer Lock (LL) syringes fitted with Tevadaptor syringe adaptor lock (SAL) according to NHS yellow cover document (YCD) syringe integrity standards.

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Introduction

Pharmacy technical services aseptically compound chemotherapy drugs within syringes as final container systems for use in dose banding. Syringe integrity must be demonstrated using the syringe and sterile blind hub as container/closure system in accordance with NHS yellow cover document (YCD) requirements [1]. With the increasing use of closed system transfer devices (CSTDs) for preparation and administration of hazardous drugs (HDs) there is great interest in syringes fitted with CSTD syringe adaptor as replacement of the sterile blind hub for the closure of the syringe.

The objective of this study was to conduct syringe integrity testing using Tevadaptor syringe adaptor lock (SAL) as the terminal end closure device for a range of luer lock (LL) syringes in accordance with the NHS yellow cover document syringe integrity test 2nd edition 2013 [1].

Testing was performed using three sizes of luer lock (LL) syringe (1mL, 20mL and 50mL) as container systems in combination with the Tevadaptor syringe adaptor lock (SAL) (n=20) covering the most commonly used sizes of syringe used for dose banded product storage.

The microbiological (Method 1, partial immersion) and physical (Method 3) challenges were applied as described in the YCD with some modifications [1].

Experimental set up: Microbiological apparatus

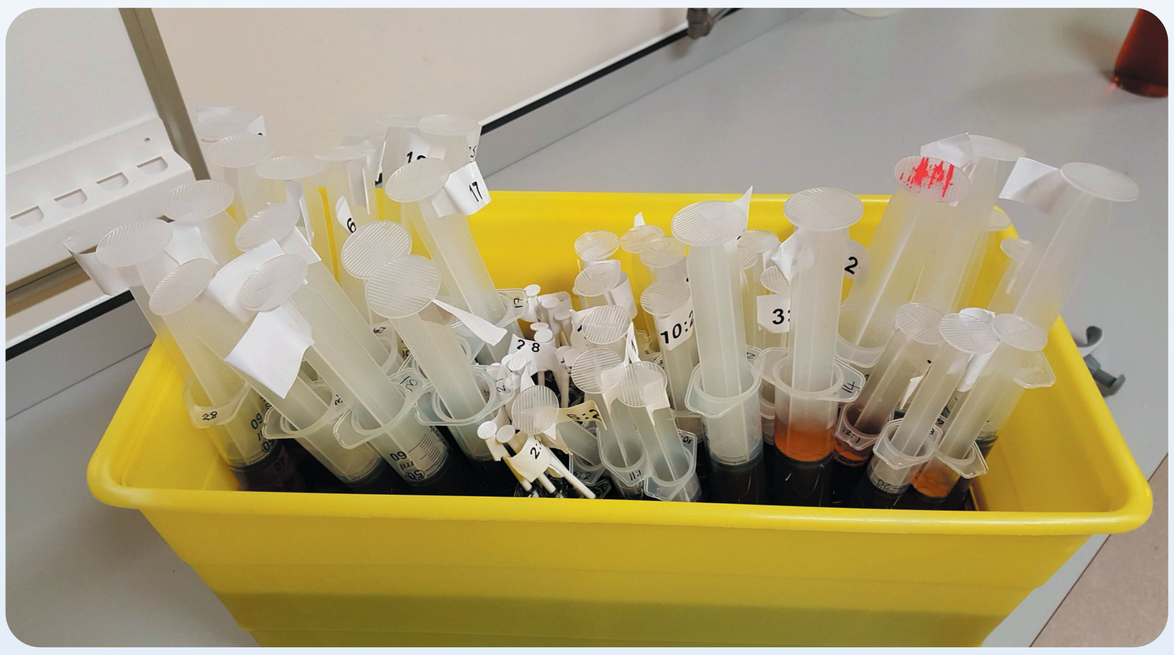

Figure 1. Tevadaptor fitted to 50mL BD syringes and immersed in the tank containing culture media.

Methodology

Twenty syringes at each volume size (1mL, 20mL and 50mL) were fitted with the SAL device (Tevadaptor, Simplivia Healthcare ltd) and were aseptically filled with TSB growth media.

The SAL septa was punctured during the TSB draw up from a vial fitted with Tevadaptor vial adaptor (Simplivia Healthcare ltd) as would happen in clinical practice. All devices incubated for 14 days 30-35°C and checked for growth prior to test.

The devices were immersed in a vessel containing TSB inoculated with a 24hr culture of *Brevundimonas diminuta* in a ratio 100:1 (single strength TSB media:culture) sufficient to cover the SAL to LL syringe hub (partial immersion test), incubated for 14 days at 30-35°C followed by visual examination of the container system for evidence of microbiological growth. Growth promotion testing (GPT) was performed to demonstrate viability of the media to support growth of the challenge organism.

Physical integrity was tested using device combinations at each syringe size (n=20), filled with MilliQ water to 75% of the maximum fill volume. The syringe adaptor lock (SAL) was disconnected from the vial adaptor and internal vacuum was applied to each test unit by drawing back the plunger to 100% of its volume. The plunger was secured in place using a mechanical fixing applied to the plunger to maintain vacuum during test. The syringes were then submerged in a vessel containing 0.4% w/v methylene blue (MB), sealed and rotated at 45rpm for 2 hours. The devices were then cleaned and inspected with absorbances measured at 660nm. A positive control syringe was included in each batch of test syringes. The puncture of the SAL septa during the draw up of MilliQ water from a vial fitted with Tevadaptor vial adaptor replicates what would happen in practice and adds a further challenge to the CSTD.

Conclusions

Tevadaptor SAL is the first closed system transfer device (CSTD) to be tested in combination with luer lock syringes as a final container system for cytotoxic drugs and passes the acceptance criteria of the 2013 NHS QA yellow cover document for syringe integrity testing by both physical and microbiological methods [1].

Physical dye intrusion test

Figure 2. Figure showing the Tevadaptor syringe adaptor lock (SAL) devices subjected to the physical dye intrusion test with MB dye.

Results:

Figure 3. Microbiological integrity test results for test (lower) and control (upper) from left to right: 1mL, 20mL and 50mL syringes.

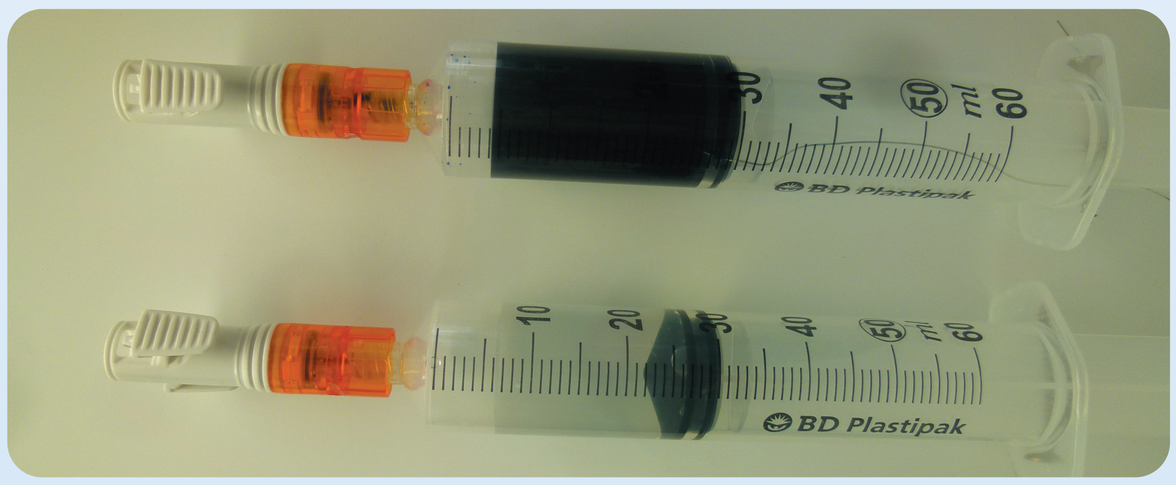

Figure 4. 50mL physical dye intrusion test (lower) versus the 50mL positive control (upper). Presence of MB dye in the positive control syringe only.

1. Microbiological: All combinations of Tevadaptor SAL/syringe (n=20) showed no evidence of microbiological growth demonstrating that sterility was maintained. Positive control tests (n=2) produced growth following inoculation with <100 cfu of *Brevundimonas diminuta* and incubation for 3 days at 30-35°C.
2. Physical integrity: All combinations of Tevadaptor SAL/syringe (n=20) were found to be free of methylene blue dye, recorded as below LOD, indicating no ingress of methylene blue dye at the end of the test period. Positive control tests (n=3) at each size showed ingress of dye with absorbances ≥0.010 (±0.005) mAu as confirmed spectrophotometrically and by visual appearance. Limit of detection (LOD) for the MB dye was determined at 1:10000 dilution of 0.4% w/v stock for both visual and instrumental readout.

Discussion

A stringent microbiological challenge was applied in the study using the motile organism *Brevundimonas diminuta* with an extended contact time of 14 days incubation. A long contact time with the challenge organism coupled with the punctured septa provides a robust test of the CSTD-syringe container system. In the physical dye intrusion testing rotating the CSTD-syringe units for 2 hours in the dye bath provides a robust challenge of the luer lock, syringe plunger and septa against ingress. All test devices passed the test.

References

[1] NHS Pharmaceutical Quality Assurance Committee 2013. Protocols for the integrity testing of syringes. Yellow cover document (YCD) 2nd edition April 2013.

Acknowledgement

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