Evaluation of Vapor Containment of Closed System Transfer Devices During Reconstitution, Based on NIOSH Methodology

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Objective

Closed system transfer devices (CSTDs) promote safe preparation of hazardous drugs by inhibiting contamination of the drug and environment.

- Attention often focuses on pressure equalization mechanisms in vial and syringe adaptors, overlooking bag adaptors.
- Manufacturer A offers separate bag adaptors for injection and withdrawal.
  - According to its instructions for use, a new syringe must be used for withdrawal of diluent from an infusion container for drug reconstitution.[1]
  - No physical mechanism prevents syringe reuse, and the warning may be overlooked to reduce waste.
- Manufacturers B and C offer single bag adaptors for injection and withdrawal.
  - B offers both "closed" (balloon) and "vented" (membrane) vial adaptors.
  - C offers a single vial adaptor with a mechanical barrier containing activated carbon and a 0.2-micron membrane.

The National Institute for Occupational Health (NIOSH) has released multiple containment testing draft protocols for CSTDs, but none has been finalized.

The aim was to compare containment of three CSTDs (A, B "vented", and C; Figure 1) during simulated 100 ml reconstitution, which requires repeated diluent withdrawals, using a single syringe, applying principles from NIOSH draft protocols.

Figure 1 Vial adaptor, syringe adaptor/unit, and bag adaptor components from manufacturers A, B, and C used in this study.

Methods

Equipment matched the NIOSH 2019 draft protocol.[2] The surrogate was (4 M) propylene glycol methyl ether (PGME), currently under consideration by NIOSH.[3] PGME was transferred between CSTD components inside a closed chamber connected to an FTIR gas analyzer (Figure 2).

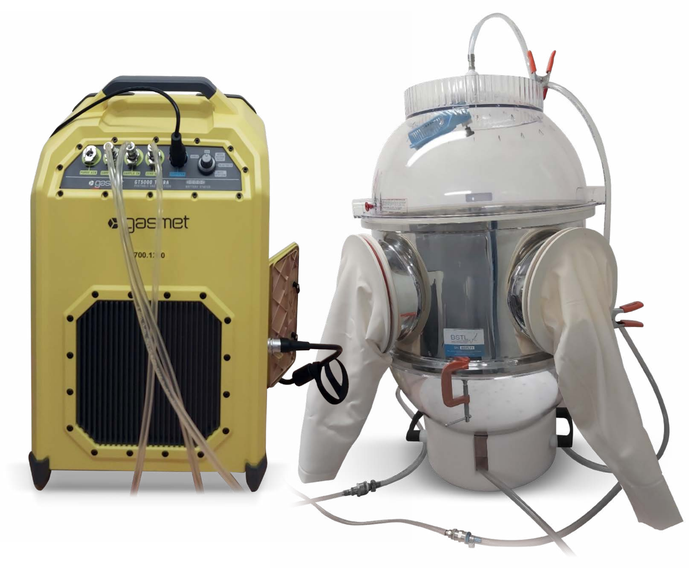

Figure 2 Left: Gasmet GT5000 Terra gas analyzer for online ethanol vapor quantification. Right: sealed glove-box chamber inside which tested CSTD products can be manipulated for vapor containment testing in a closed environment.

The bag adaptor was connected to a saline infusion bag (Figure 3, step 1), and a complementary syringe unit/adaptor was used to "reconstitute" PGME in a vial (Figure 3, steps 2 and 3). A second portion of saline was withdrawn using the same syringe (Figure 3, step 4). PGME vapor concentration was monitored inside the chamber before, during, and after the procedure.

Step 1
Spiked bag

Step 2
Withdrew 50 ml saline

Step 3
Injected saline into vial containing ethanol

Step 4
Withdrew another 50 ml saline with same syringe unit

Figure 3 Illustration of task steps. The same steps were performed for all three CSTD brands.

Results

LOD and LOQ were 0.14±0.04 and 0.32±0.07 ppm, respectively. Within 15 minutes following the procedure, PGME concentrations rose by 0.61±0.10 (>LOQ), 1.12±0.05 (>LOQ), and 0.07±0.02 ppm (<LOD) for brands A, B, and C, respectively (Figure 4).

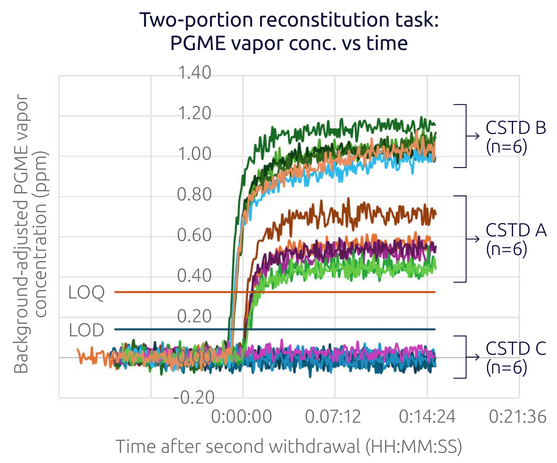

Figure 4 Graphic display of PGME vapor concentrations during the reconstitution task. Each differently colored curve represents a separate repetition.
Time 0:00:00 is defined as the time of disconnection after withdrawal of the second portion of saline from the IV bag.

Discussion & Conclusions

When a syringe was reused to complete a 100 ml reconstitution:

- CSTD A demonstrated quantifiable release of contaminated air during withdrawal of the second portion of saline from the bag.
- CSTD B demonstrated quantifiable release of contaminated air during injection to the vial.
- CSTD C demonstrated full vapor containment (no release detected).

In the absence of a physical mechanism to prevent syringe reuse during 100 ml reconstitution, pharmacists may do so to reduce waste and costs of disposables. The results of this study highlight potential hazardous drug exposure risks for pharmacists when these steps are performed with CSTDs A and B.

Sponsorship

Sponsored by Simplivia Healthcare Ltd, the manufacturer of Chemfort® CSTD.

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References
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[2] "A Containment Performance Protocol for Physical-Barrier Type Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs" NIOSH, 2019. (Shared only with CSTD manufacturers)
[3] Westbrook EG, Doepke A, Steicher RP. *Anal. Methods*, 2022, 14, 4393; CDC National Institute for Occupational Safety and Health 09 February 2024, Closed System Drug-Transfer Device (CSTD) Research website, accessed 11 November 2024, <https://www.cdc.gov/niosh/healthcare/hazardous-drugs/cstd-research.html>.