Compounding & Administration Transfer Device Comparison Using Potential Surrogate for NIOSH Protocol

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Objectives

- To compare containment performance of five compounding and administration transfer devices within the NIOSH 2019 draft protocol
- Using a surrogate under evaluation by NIOSH, propylene glycol methyl ether (PGME), applicable to all CSTDs
- To quantify vapor, aerosol, and liquid leaks
- Surrogate concentration was increased to meet sensitivity requirements

Methods

- FTIR gas analyzer (Gasmet DX4040) connected to 125 L chamber as in 2019 draft NIOSH protocol
- Task 1 of the 2019 protocol was performed in replicate
  - 100 ml glass vials charged with 50 ml of 4 M PGME in water
  - 45 ml solution transferred from one vial (Vial 1) to a second (Vial 2) using transfer device
  - Five different transfer devices (n = 6 for each system)
  - Positive controls using needle and syringe (n=2)
  - Devices handled as per IFU
- Limits of detection (LOD) and quantitation (LOQ) determined for each repetition based on blank measurements

Table 1 Transfer devices tested

Transfer Device	Manufacturer	Classification	Pressure equalization	Port connection
Chemfort®	Simplivia	CSTD	Activated carbon drug binding matrix + hydrophobic membrane	Membrane-to-membrane
PhaSeal™	BD	CSTD	Balloon	Membrane-to-membrane
ChemoLock™ vented	ICU Medical	CSTD	Hydrophobic membrane only	Membrane-to-membrane
ChemoClave™ vented	ICU Medical	CSTD	Hydrophobic membrane only	Needle free (Luer)
Mini-Spike® Chemo	B. Braun	Dispensing pin	Hydrophobic membrane only	Needle free (Luer)

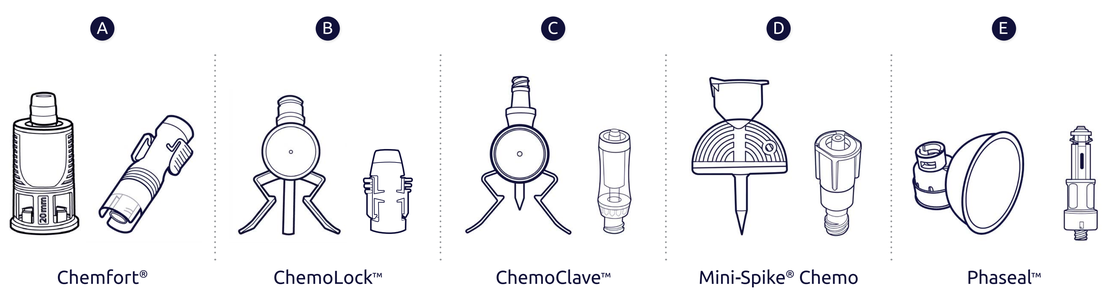

Figure 1 Transfer devices tested: vial and syringe adaptors from each of the 5 systems in Table 1. (A) Chemfort®; (B) ChemoLock™; (C) ChemoClave™; (D) Mini-Spike® Chemo with Puresite; and (E) Phaseal™

Results

- Mean LOD and LOQ per device ranged from 0.18-0.33 ppmv and 1.00-1.13 ppmv, respectively.
- Maximum PGME vapor concentration from five transfer devices in Task 1 of 2019 draft NIOSH protocol using 4M PGME were as shown in Table 2.
- Mini-Spike® Chemo with Puresite displayed visible liquid leaks in some cases (Figure 3).

Table 2 Table showing mean LOD, LOQ, and maximum PGME signal for all repetitions for each type of transfer device.

	LOD (ppmv)	LOQ (ppmv)	Maximum signal (ppmv)	Outcome
Chemfort®	0.25	1.02	0.17	<LOD
PhaSeal™	0.33	1.08	0.31	<LOD*
ChemoLock™	0.27	1.05	1.16	>LOQ
ChemoClave™	0.32	1.13	1.35	>LOQ
Mini-Spike® Chemo + PureSite	0.26	1.00	3.86	>LOQ
Needle & syringe	0.18	1.08	3.14	>LOQ

* in 2/6 reps >LOD

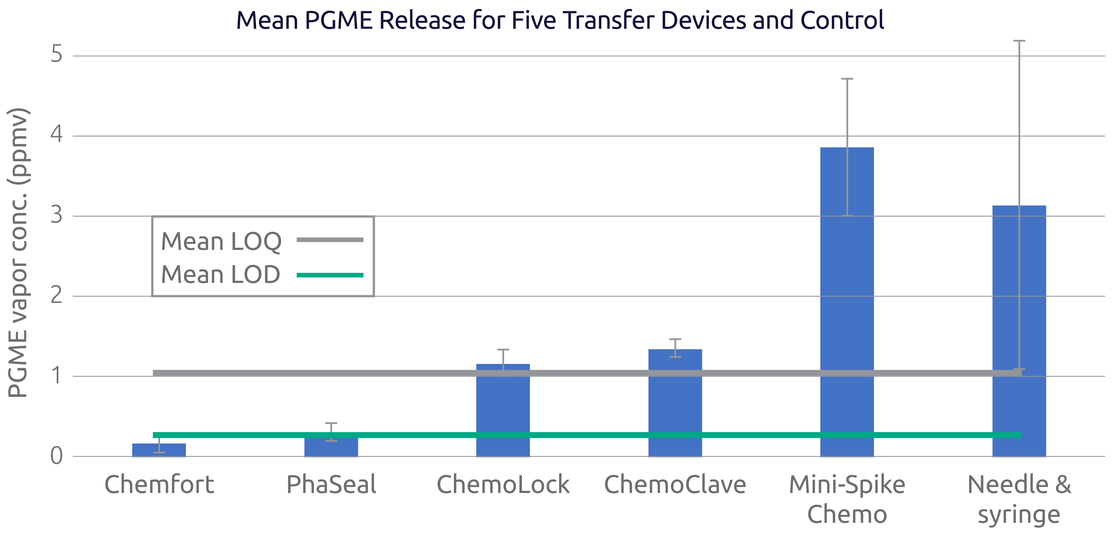

Figure 2
Graph showing mean maximum signals for all repetitions for each type of device, compared to overall mean LOD and LOQ. Error bars represent ± one standard deviation.

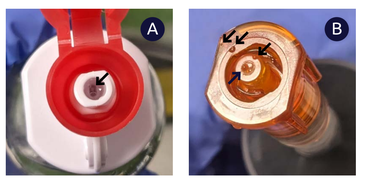

Figure 3
Photographs showing droplets on connecting ports of (A) Mini-Spike® Chemo and (B) PureSite male connector after completion of Task 1 from the 2019 NIOSH draft protocol.
The images are typical of all six repetitions.
→ Arrows indicate source of droplet release.

Discussion & Conclusions

The results indicate three levels of containment:

- Activated carbon drug-binding matrix (Chemfort®) or balloon-containing (PhaSeal™) devices with membrane-to membrane connectors provide full vapor, aerosol, and liquid containment.
- Vial adaptors utilizing hydrophobic membranes alone for pressure equalization (ChemoClave™ & ChemoLock™) may not be sufficient for vapor containment.
- Open systems (spikes and needles) may not be sufficient for liquid droplet containment.

PGME (4M) was shown to be a suitable challenge agent for use in the 2019 draft NIOSH protocol for assessment of CSTD containment.

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References
[1] "NIOSH [2019], A Containment Performance Protocol for Physical-Barrier Type Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs." (Shared only with CSTD manufacturers)
[2] E. G. Westbrook, A. Doepke and R. P. Streicher, "Evaluation of propylene glycol methyl ether as a potential challenge agent for leak detection of liquid and headspace from closed system drug transfer devices using Fourier transform infrared spectroscopy," *Anal. Methods*, vol. 14, pp. 4393-4407, 2022.

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