Containment performance assessment of closed system drug transfer devices (CSTDs) using the NIOSH draft protocol and 2.5% w/v 1,1,3,3-tetraethylurea (TEU) in water as the challenge agent.

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Introduction

In 2016, the National Institute for Occupational Safety and Health (NIOSH) of the Centres for Disease Control (CDC) Department of Health submitted a draft "Performance Test Protocol for Closed System Transfer Devices" that can assess all CSTDs regardless of the technology they employ [1]. HSL and BSTL provided significant input and supporting data to this draft test protocol in response to NIOSH's request for information [2]. BSTL has published improvements to the NIOSH test equipment [3] as well as performance data using two different challenge agents [4,5]. We report here containment performance values for both physical barrier and one air filtration CSTD (Tevadaptor) using the draft NIOSH protocol and TEU as challenge agent.

The challenge agent 2.5% w/v TEU in water was placed in to 100mL glass drug vials. The containment of four CSTDs was assessed by performing pharmacy tasks for drug preparation and administration, Task 1 (n=5) and Task 2 (n=5) according to NIOSH. CSTD release of TEU was captured on Tenax tubes and quantified using Automated Thermal Desorption Gas Chromatography Mass Spectrometry Detection (ATD-GC-MS).

Figure 1. BSTL CSTD test chamber.

Validation of Method

NIOSH suggest that Propylene Glycol (PG) can be used in the test, however we have shown that at clinically relevant concentrations, aqueous solutions of PG do not enter the vapour (undetected) eliminating its use in the test. Incorporation of ethanol can overcome this limitation.

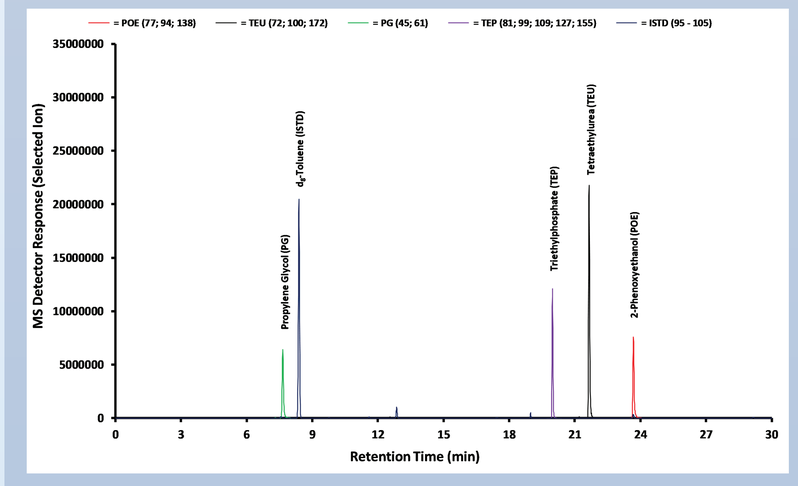

Figure 2. Detector (MS) responses to NIOSH challenge agents: Propylene glycol (PG), Triethyl phosphate (TEP), TEU and 2-Phenoxyethanol (POE) at 35ng each.

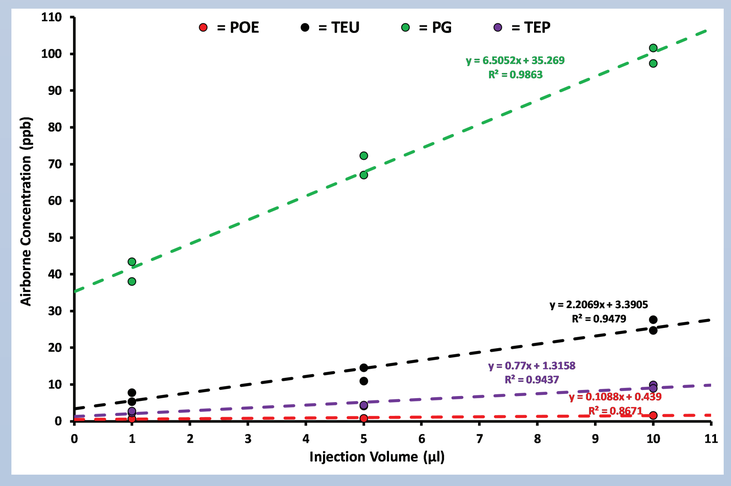

Figure 3. Positive controls for challenge agents in 70:30 water:ethanol: 2.5mM PG, 0.5M TEP, 0.5M TEU and 0.5M POE. Simulated liquid releases in the chamber (1 , 5 and 10 µl).

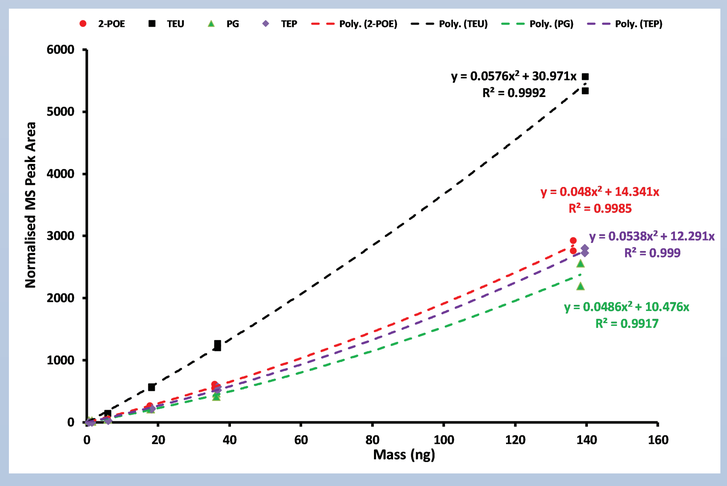

Figure 4. Detector (MS) response curves for challenge agents: PG, TEP, TEU and POE showing calibration data 0-140ng.

ICU Medical employed 100% PG as challenge agent to assess the ChemoClave device using 1mL "drip" of neat PG as positive control with LOQ (1g) [6]. No attempt was made to validate signal response versus release amount. The data supported the FDA 510k approval [7]. Massoomi published similar data on ChemoLock at HOPA in the US [8].

Figure 3 shows positive controls for liquid leakage of PG with LOQ 3.68 ppb (34ng) determined by BSTL, this is 10^8 times more sensitive than the ICU Medical test [8]. Demonstrating the correlation between signal and challenge agent release volume is a critical parameter that MUST be included as part of the method validation (see **Figure 3**). ICU Medical released 1g of PG in the positive control but only detected 820ng of this. Due to the poor sensitivity of the test the result showed equivalent efficacy of containment for ChemoClave and the open system needle and syringe (they both gave <LOQ (820ng)) [6,8].

Results

CSTD product	NIOSH task	TEU LEAKAGE ± 95% CI (ppb)
Tevadaptor®	1	< LOQ
	2	< LOQ
PhaSeal™ (BD)	1	< LOQ
	2	< LOQ
ChemoClave® Vial Shield with Spiros (ICU Medical)	1	5.21 ± 0.82
	2	5.21 ± 1.85
Equashield®	1	< LOQ
	2	< LOQ
Needle and syringe	1	13.6 ± 0.04
	2	55.50 ± 1.31
Blank (n = 74)	_	0.16 ± 0.07

Table 1. Containment performance data using 2.5% w/v tetraethylurea (TEU) in water as challenge agent according to draft NIOSH protocol and defined tasks: task 1 (n = 5) and task 2 (n = 5)

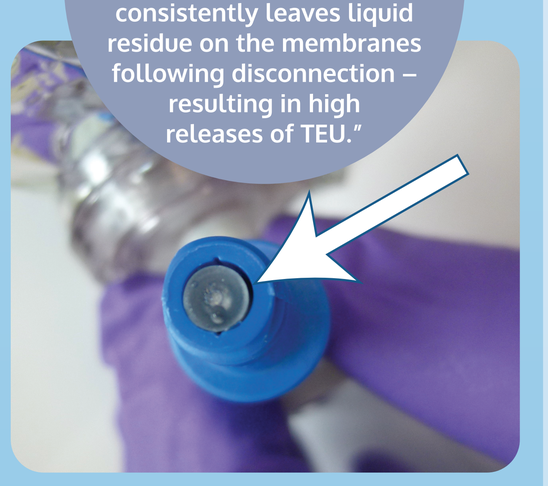

Figure 5. Liquid droplets of TEU are visible on the ChemoClave membrane after use.

Conclusions

- BSTL & HSE present a validated method based on ATD-GC-MS and TEU as challenge agent for containment performance testing CSTDs with a LOD of 0.3 ppb and LOQ of 0.7 ppb.
- BSTL and HSE evaluated a range of commercial CSTDs and found that one device Vial Shield with Spinning Spiros (ChemoClave) produced leakage of 5.21 ppb for both NIOSH tasks.
- Release levels obtained with ChemoClave are similar in size to a positive control of needle and syringe i.e. not using a CSTD.
- BSTL & HSE data from containment performance testing CSTDs using TEU are consistent with results obtained using 2-Phenoxyethanol which is another NIOSH challenge agent [4,5].

"The BSTL & HSE protocol detected TEU at 0.3 parts in a billion (ppb) and quantified at 0.7 ppb making it a sensitive marker for CSTD containment performance. Using TEU [4] and POE [5] in the NIOSH test ChemoClave consistently generates above LOQ liquid leakage – this is an ONB device recently cleared under 510k by the FDA"

References

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