Assessment of the containment performance of closed system drug transfer devices (CSTDs) that either employ a mechanically closed physical barrier or air filtration technology – a Universal Test Protocol for assessment of all CSTD technologies.

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Introduction

January 19th 2016, the National Institute for Occupational Safety and Health (NIOSH) of the Centres for Disease Control (CDC) Department of Health and Human Services (HHS) published a request for information notice in the Federal Register entitled "Request for Information on Development of a Performance Test Protocol for Closed System Transfer Devices that Incorporate Air-Cleaning Technology to Provide Worker Protection During Pharmacy Compounding and Administration of Hazardous Drugs".[1]

In collaboration with the Health and Safety Laboratory UK, BSTL submitted a detailed approach to NIOSH with supporting data for consideration as a Universal Vapour Performance Test for CSTDs.[2]

Data is presented here from a larger study of the containment performance of CSTDs that employ both physical barrier (PhaSeal® and ChemoClave™) and air filtration (OnGuard®) technology. See table 1 below.

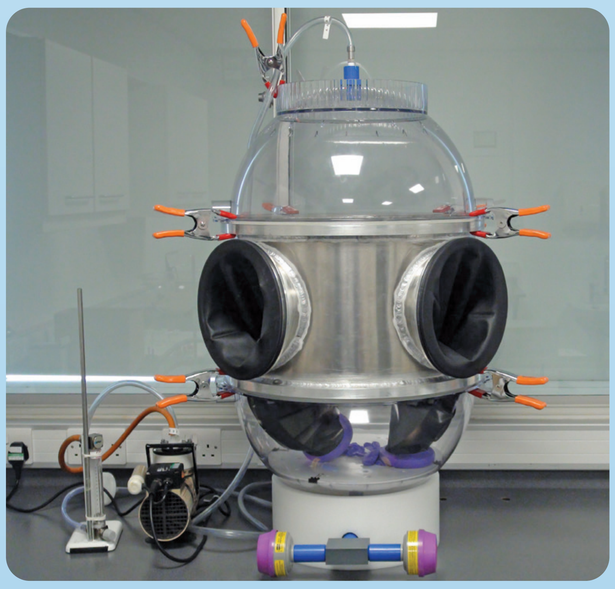


Figure 1. BSTL replica NIOSH experimental chamber used in study.

The BSTL and HSL approach utilises some of the original equipment from the draft NIOSH protocol for use with physical barrier technology CSTDs but with some specific improvements:

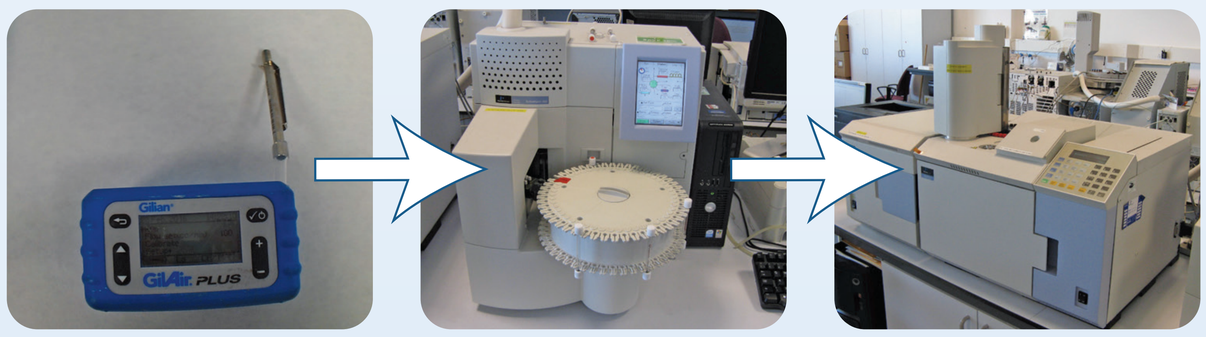
(1) The surrogate 2-Phenoxyethanol (POE) 2.5% in water with a vapour pressure of 1 Pascal at 20°C was selected as being more representative of a Hazardous Drug (HD) solution.

(2) A Time Weighted Average (TWA) sampling approach was developed using Tenax TA™ sorbent tubes with Automated Thermal Desorption Gas Chromatography Mass Spectrometry Detection (ATD-GCMS).

(3) The NIOSH manipulations Task 1 and Task 2 were retained, however all CSTD manipulations were performed using the manufacturers' Instructions for Use (IFU).

Scientific Approach

Figure 2. Figure showing process flow from TWA air sampling, thermal desorption and detection by MS.



Air was sampled for 30 minutes at a flow of 100mL/minute on to Tenax TA™ from the chamber during manipulation of CSTDs, according to Task 1 and Task 2. Tubes were then analysed using ATD-GC-MS. Negative controls were performed on each day of test using water as surrogate.

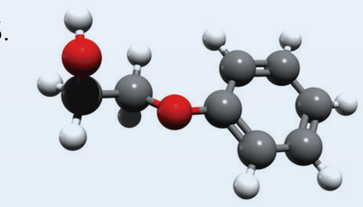


Figure 3. 2-Phenoxyethanol.

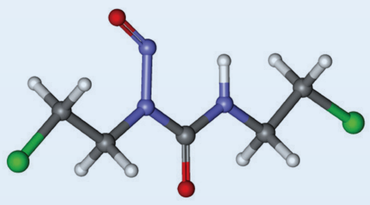


Figure 4. Carmustine.

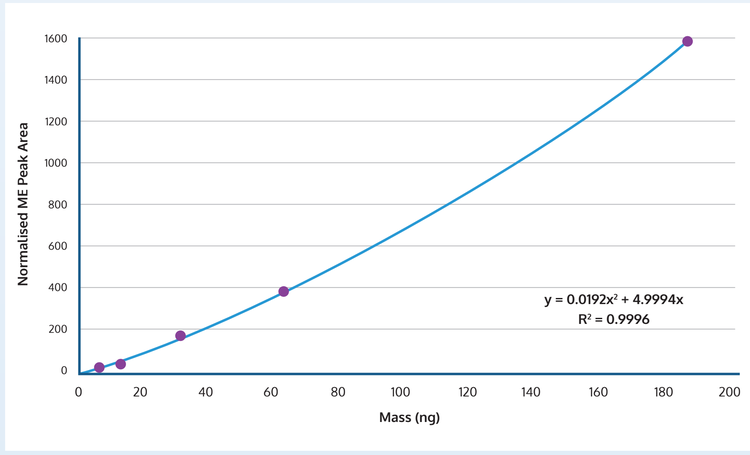
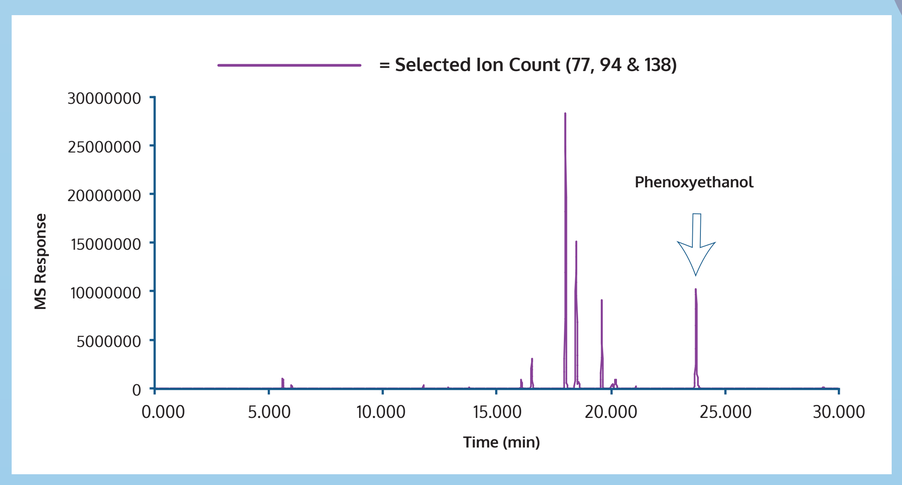


Figure 5. Figure showing response curve for 2-Phenoxyethanol by ATD-GCMS.

Results

Figure 6. Figure showing a typical GC signature for 2-Phenoxyethanol (POE), detection by MS employing selected ion mode (SIM).



"The liquid release is seen easily by eye and this correlates with the chemical vapour detection values for POE release."

"As has been previously shown in the original NIOSH work with IPA[3], the ChemoClave™ CSTD leaves liquid residue on the membranes following disconnection – resulting in high vapour release for POE."

Positive control values obtained using a standard needle and syringe were 4.15±1.14 ppb and 5.13±0.87 ppb for Task 1 and Task 2 respectively (n=2). Blanks (n=74) gave 0.16±0.07 ppb and were used to set the LOD and LLOQ for the method.

CSTD Product	Task	Average Result (ppb)
Tevadaptor™	1	≤0.71
	2	≤0.71
Phaseal®	1	≤0.71
	2	≤0.71
Chemoclave™	1	2.70±0.98
	2	7.30±9.66
Needle & Syringe	1	4.15±1.14
	2	5.13±0.87
Blank (n=74)	---	0.16±0.07

Table 1. Table showing CSTD performance for devices tested using the challenge agent 2.5% 2-Phenoxyethanol (POE) according to the NIOSH defined tasks:Task 1 and Task 2 under IFU conditions.

Vapour containment values for PhaSeal® and OnGuard® (Tevadaptor™) were <LLOQ for both tasks (n=5). ChemoClave™, however, produced higher release values of between 5 and 25 x LOD and one release of 120 x LOD.

Conclusions from BSTL/HSL Universal CSTD Performance Test Protocol

IFU conditions must be used for all manipulations of CSTD systems. The original NIOSH draft protocol compromised CSTD function.

- 2-Phenoxyethanol is a more realistic surrogate for hazardous drugs (HDs) given its vapour pressure of 1 Pascal.
- Automated Thermal Desorption Gas Chromatography Mass Spectrometry (ATD-GCMS) has sub ppb detection capability allowing much smaller releases of hazardous drug to be detected than can be achieved using affordable real time chemical detection equipment such as infra-red or PID.
- Using a Time Weighted Average (TWA) approach allows both air filtration and physical barrier CSTDs to be assessed using the same Universal Containment Performance Test Protocol. This represents a paradigm shift from the original draft NIOSH vapour containment test protocol.

Using the developed BSTL/HSL Universal Performance Test Protocol for CSTDs we have demonstrated that, by appropriate selection of surrogate, CSTDs that employ air filtration technology are able to prevent both vapour and liquid release of hazardous drugs during manipulations performed in Pharmacy for compounding and administration.

- Where CSTD equipments fall short of their claims, testing of the vapour concentration following release of either liquid or vapour is able to report the maximum total exposure levels when these devices are used to handle HDs, using the Universal Performance Test Protocol described in this study.

"This study provides a proof of principle for the concept of a Universal Performance Test Protocol that is capable of assessing containment performance for All CSTDs regardless of their containment technology."

References

[1] National Institute for Occupational Safety and Health (NIOSH) of the Centers for Disease Control and Prevention (CDC), Department of Health and Human Services (HHS) notice in the Federal Register on the 19th January, 2016 entitled "Development of a Performance Test Protocol for Closed System Transfer Devices That Incorporate Air-Cleaning Technology To Provide Worker Protection During Pharmacy Compounding and Administration of Hazardous Drugs". Docket CDC–2015–0075; NIOSH– 288, Vol 81, No. 11, 2016.

[2] Recommendations for Testing Protocol for Closed System Transfer Devices. CBRU/2016/017.submitted 030816 Docket No. CDC-2015-0075 NIOSH.

[3] A. Wilkinson et al. Vapour Containment performance of CSTDs. Hospital Pharmacy Europe Summer 2016: volume 082, 25-32pp.

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