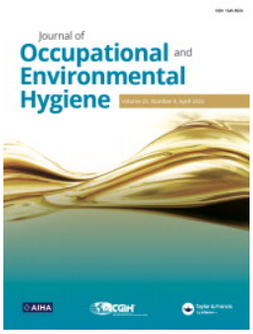

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A novel approach for evaluating the containment of a closed intravenous administration system for hazardous drugs

Elana A. Slutsky Smith and Asaf Alon

Simplivia Healthcare Ltd, Kiryat Shmona, Israel

ABSTRACT

Oncology nurses are routinely exposed to antineoplastic agents through skin absorption or inhalation of airborne agents when administering drugs intravenously. Although safe infusion devices aimed at preventing the hazardous disconnection of empty bags were developed, none of them are completely closed systems per National Institute for Occupational Safety and Health (NIOSH) guidelines. The authors evaluated a closed system administration device developed to prevent exposure of healthcare professionals to cytotoxic drugs during their administration. System components were assembled in various scenarios mimicking intravenous drug administration and then tested in a sealed chamber connected to a gas analyzer. The concentration of 70% isopropanol vapors (as a drug surrogate) was measured continuously in the chamber. The analysis showed no detectable increase in isopropanol vapor concentration in the sealed chamber compared to baseline levels over the course of the tasks, indicating that no leaks of 70% isopropanol occurred when the closed system administration devices were used. Furthermore, the results remained the same regardless of the number of connection cycles the products had undergone, or whether they were newly manufactured or at the simulated end of their shelf-life. This study showed that the use of a closed administration system can minimize the risk of exposure of healthcare professionals to hazardous drugs and potentially reduce environmental contamination.

KEYWORDS

Closed administration system; drug vapors; safe infusion devices; safety

Introduction

Oncology nurses routinely handle antineoplastic agents and are potentially exposed to them through skin absorption or inhalation when spiking intravenous (IV) chemotherapy bags, priming IV tubing, connecting or disconnecting tubing from patients, or in the case of a leak or spill (Friese et al. 2020). Some administration protocols can also present risks of needle stick injuries and exposure to antineoplastic agents through accidental needle sticks. Such exposure has been associated with acute and chronic toxicities, including carcinogenicity, mutagenicity, and reproductive toxicities (IARC 2000; Connor et al. 2014; Liu et al. 2023).

To reduce the risks associated with the handling of cytotoxic drugs, guidelines and recommendations were published by several organizations (Health and Safety at Work etc. Act 1974; The Management of Health and Safety at Work Regulations 1999; EU-OSHA 2004; NIOSH 2004a; OSHA 2006; ASSTSAS 2008; OSHA 2012; HSE 2013; HSE/MHRA 2015; USP 2016; NHS 2018; Power and Coyne 2018; Celano et al. 2019; EBN 2019; ONS/HOPA 2019; HSE 2022; ISOPP 2022). These include the implementation of standard operating procedures, staff training, hygiene measures, exposure monitoring, surveillance of health, safe management of spills, safe disposal of cytotoxic waste, and the use of personal protective equipment (EU-OSHA 2004; NIOSH 2004b; ASSTSAS 2008; HSE 2013; USP 2016; NHS 2018; Power and Coyne 2018; Celano et al. 2019; EBN 2019; ONS/HOPA 2019; HSE 2022; ISOPP 2022). Personal protective equipment protects the healthcare worker wearing it, but does not prevent surface contamination, which can be spread to hospital staff and visitors when they are not donning such equipment (Labrèche et al. 2021). To reduce the risk of environmental contamination during hazardous drug preparation, the use of biological safety cabinets, isolators,

CONTACT Elana A. Slutsky Smith Elana.SlutskySmith@simplivia.com Simplivia Healthcare Ltd., Kiryat Shmona, Israel.

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and/or closed system transfer devices (CSTDs) was recommended (Sessink et al. 2016). The *United States Pharmacopeia (USP) General Chapter <800> Hazardous Drugs—Handling in Healthcare Setting* (USP 2016) has recently become obligatory in the United States. This standard requires the use of closed systems for drug administration whenever the dosage form allows.

A CSTD is defined by the National Institute for Occupational Safety and Health (NIOSH) as "a drug transfer device that mechanically prohibits the transfer of environmental contaminants into the system and the escape of hazardous drug or vapor concentrations outside the system" (NIOSH 2004a). CSTDs can be used to protect staff throughout the process of hazardous drug preparation in the pharmacy, administration to the patient, and waste disposal (Connor and McDiarmid 2006).

To improve the safety of nurses during hazardous drug administration, "safe infusion devices" (SIDs) aimed at preventing the hazardous disconnection of empty bags were developed (Simon et al. 2010; Lalande et al. 2015; Forges et al. 2021). These devices enable the sequential connection of multiple bags on a single infusion line, eliminating the need to disconnect the patient's catheter, which poses a risk of exposure to antineoplastic drugs that may remain in the infusion line. Additionally, they facilitate rinsing of the line to remove concentrated product residues at the end of drug administration. "Safe disconnection" was also described as a solution to reduce exposure when using an elastomeric pump for drug infusion (Raphaëlle et al. 2023). However, none of these studies used a truly closed system as defined by NIOSH to prevent the exposure of the nurses administering the drug to patients in hospital wards. Hence, to ensure the necessary safety for nursing staff when administering hazardous drugs in practical settings, there is a need for a closed system integrated into a drug administration set.

Chemfort (Simplivia Healthcare Ltd., Kiryat Shmona, Israel) is a CSTD that uses a contaminant-trapping technology (ToxiGuard system) comprising a 100% activated carbon drug binding matrix and a 0.2-μm hydrophobic and oleophobic membrane. Together, these components, which include vial adaptors, syringe adaptors, bag adaptors, and Luer lock adaptors, serve as an effective sterile, particulate, and toxic drug barrier (Levin and Sessink 2021). This system can be used for pharmaceutical preparations and some drug administration protocols. In a study that examined the use of Chemfort's predecessor (Tevadaptor) during doxorubicin administration, a significant decrease was observed in the number of spills and extent of contamination compared with currently used techniques (Marler-Hausen et al. 2020).

The Chemfort Closed Administration (CADM) system is another system developed to prevent exposure of healthcare professionals to cytotoxic drugs in liquid, vapor, or aerosol form across a wider range of infusion or administration protocols. The system's components include the Bag Adaptor CP (BACP), the Closed Adaptor SP (CASP), the Closed Y-Inline Set (Y-set), and the Closed Secondary IV Set (Figure 1A–D). The BACP is the required complementary component to each of the other three CADM components, each of which contains a subcomponent identical in structure to the Chemfort Syringe Adaptor (SA; Figure 1E), which forms a reversible closed connection with the BACP's Chemfort Port. This connection is based on membrane-to-membrane contact with no exposed needle and allows dry disconnection for up to 10 connection/disconnection cycles (activations) (Slutsky Smith 2025). Together, the CADM and SA components can convert any IV set spike and any male Luer at the end of an IV set into a closed system.

In addition to CADM devices, several other closed administration devices are commercially available. For example, ICU Medical (San Clemente, CA, USA) has two product lines—ChemoClave and ChemoLock—that correspond to each CADM component. Becton Dickinson (Franklin Lakes, NJ, USA) and Equashield (Tefen, Israel) have devices that are only comparable to the CADM BACP and CASP. However, the current study focused solely on CADM to support verification before regulatory submission.

This study aims to evaluate whether CADM devices can perform as a closed system and prevent leaks of drug surrogates in liquid, vapor, or aerosol form. Both newly manufactured and 3-year accelerated aged products were tested after one and 10 activations of the components.

Materials and methods

Aging of CADM devices

Accelerated aging to mimic 3 years was performed by incubating some of the CADM devices at a temperature of 40 °C for 314 days according to the Standard Guide for Accelerated Aging of Sterile Medical Device Packages (ASTM 2016).

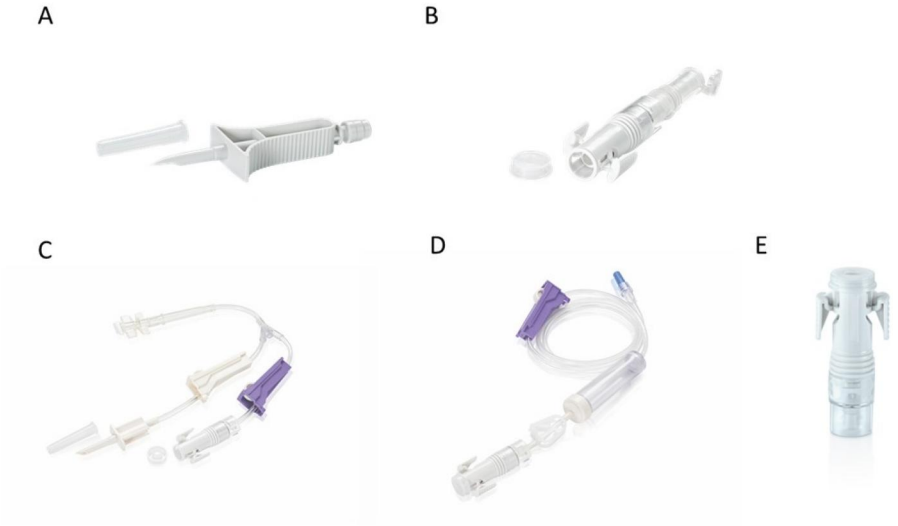

Figure 1. Chemfort Closed Administration (CADM) components: (A) Bag Adaptor CP (BACP); (B) Closed Adaptor SP (CASP); (C) Closed Y-inline Set (Y-set); (D) Closed Secondary IV Set. (E) Chemfort Syringe Adaptor (SA).

Drug surrogate

As no NIOSH vapor containment testing protocol has been written for closed administration sets, the testing protocol was developed according to the principles described in the *NIOSH Draft Protocol: A Performance Test Protocol for Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs* (NIOSH 2016). In the developed protocol, 70% isopropanol (IPA) was chosen as a hazardous drug surrogate due to its high volatility and the commensurate high stringency of the test.

Test groups

CADM devices were tested both at the beginning (time zero) and end of shelf life and upon their first and tenth activation, which is the maximum allowed number of activations according to the CADM system's instructions for use. Each combination of pretreatments was referred to as a test group, for a total of four test groups: (1) time zero, 1st activation; (2) time zero, 10th activation; (3) 3 years accelerated aging, 1st activation; (4) 3 years accelerated aging, 10th activation.

Control groups

Positive control tests utilized a non-closed IV set and mimicked administration and disconnection in the absence of a closed administration system.

Negative control tests were performed on devices from the same test groups described above (1–4) using saline instead of surrogate.

Experimental setup

The testing system comprised a sealed chamber (Figure 2) connected to a Fourier-transform infrared spectroscopy (FTIR) gas analyzer (Gasmet GT 5000 Terra, Vantaa, Finland) in a closed circuit. The Gasmet GT 5000 was within the manufacturer's calibration requirements. Quantification of selected gases was performed automatically using the instrument's proprietary software based on reference spectra at two concentrations per compound. These reference files were provided by the manufacturer and stored locally on the computer controlling the FTIR gas analyzer. At the beginning of each day of measurements, the FTIR gas analyzer was set to zero using nitrogen gas. This procedure generated a background spectrum, which was subsequently subtracted from the spectra measured during the tasks described below. The gas analyzer was set to monitor IPA vapor concentrations with a continuous sampling interval of 20 s. This interval was chosen to allow sufficient temporal resolution for the various steps of each task while minimizing noise relative to shorter measuring times. Immediately before the repetition of each task, background IPA concentrations were measured and recorded for five minutes with all task materials placed inside the sealed chamber. Five measurements were taken (one every minute) to calculate the average background IPA concentration. The test acceptance criterion was defined as an increase <3.06 ppm in IPA vapor concentration. While the NIOSH draft protocol (NIOSH 2016) recommends using the analytical method's limit of quantitation (LOQ) as the acceptance criterion, it describes a slightly different

Figure 2. The sealed chamber developed based on NIOSH guidelines (NIOSH 2016).

apparatus and setup, for which the LOQ was estimated at 1.0 ppm. In the setup described here, the LOQ was estimated to be 3.06 ppm.

To qualitatively verify the absence of leaks or external contamination of the devices before testing, A NEO photo-ionization detector (PID, mPower Electronics, Santa Clara, CA, USA) was used. The PID was within the manufacturer's calibration requirements based on a calibration gas of 10 ppm isobutylene. No IPA correction factor was applied, as quantitative results were not required.

To mimic the administration and subsequent disconnection of three different combinations of the CADM components, three test tasks were developed. For all tasks, a 500 mL IV bag was filled with 70% IPA (Bio-Lab Ltd., Jerusalem, Israel). This bag was connected in a chain with test components, according to each task. At the end of each chain, a BACP and an empty IV bag represented the patient receiving the drug infusion and were included as a closed receptacle for the IPA after it flowed through the CADM components. The complete chain of devices for each task was assembled as follows:

Task 1:

- The clamps of a (non-CADM) secondary IV set were closed, and its male Luer end was connected to a Chemfort SA (connection 1, Figure 3A).
- The IV set spike was inserted into a CASP tail (connection 2, Figure 3A).
- A BACP was connected to an IV bag containing 70% IPA (connection 3, Figure 3A).
- An additional BACP, not considered a test item, was connected to an empty 500 mL infusion bag (connection 4, Figure 3A).
- The PID was used to verify the absence of external contamination and/or leaks from the IV bag.
- Then, the SA (already connected to the Luer end of the IV set) was connected to the BACP of the empty IV bag (connection 5, Figure 3A).
- The CASP was connected to the BACP of the IV bag containing 500 mL 70% IPA (connection 6, Figure 3A).

Task 2:

- The clamps of a Y-Set and a (non-CADM) secondary IV set were closed, and the spike of the Y-set (saline path) was inserted into the administration port of a saline-containing IV bag (connection 1, Figure 3B).
- The male Luer end of the secondary IV set was connected to an SA (connection 2, Figure 3B), and the spike of the secondary IV set was inserted into the twist-off port of the Y-Set (connection 3, Figure 3B).
- A non-test item BACP was connected to an empty infusion bag (connection 4, Figure 3B), and a BACP test item was connected to a bag containing 70% IPA (connection 5, Figure 3B).
- The IV bag containing IPA was checked for external contamination/leaks with the PID.
- Then, the SA (already connected to the Luer end of the IV set) was connected to the BACP of the empty IV bag (connection 6, Figure 3B).
- The integral SA of the Y-set (drug path) was connected to the BACP of the IV bag containing 500 mL 70% IPA (connection 7, Figure 3B).

Task 3:

- All clamps of a Closed Secondary IV Set were closed, and its male Luer end was connected to an SA (connection 1, Figure 3C).
- A non-test item BACP was connected to an empty infusion bag (connection 2, Figure 3C), and a

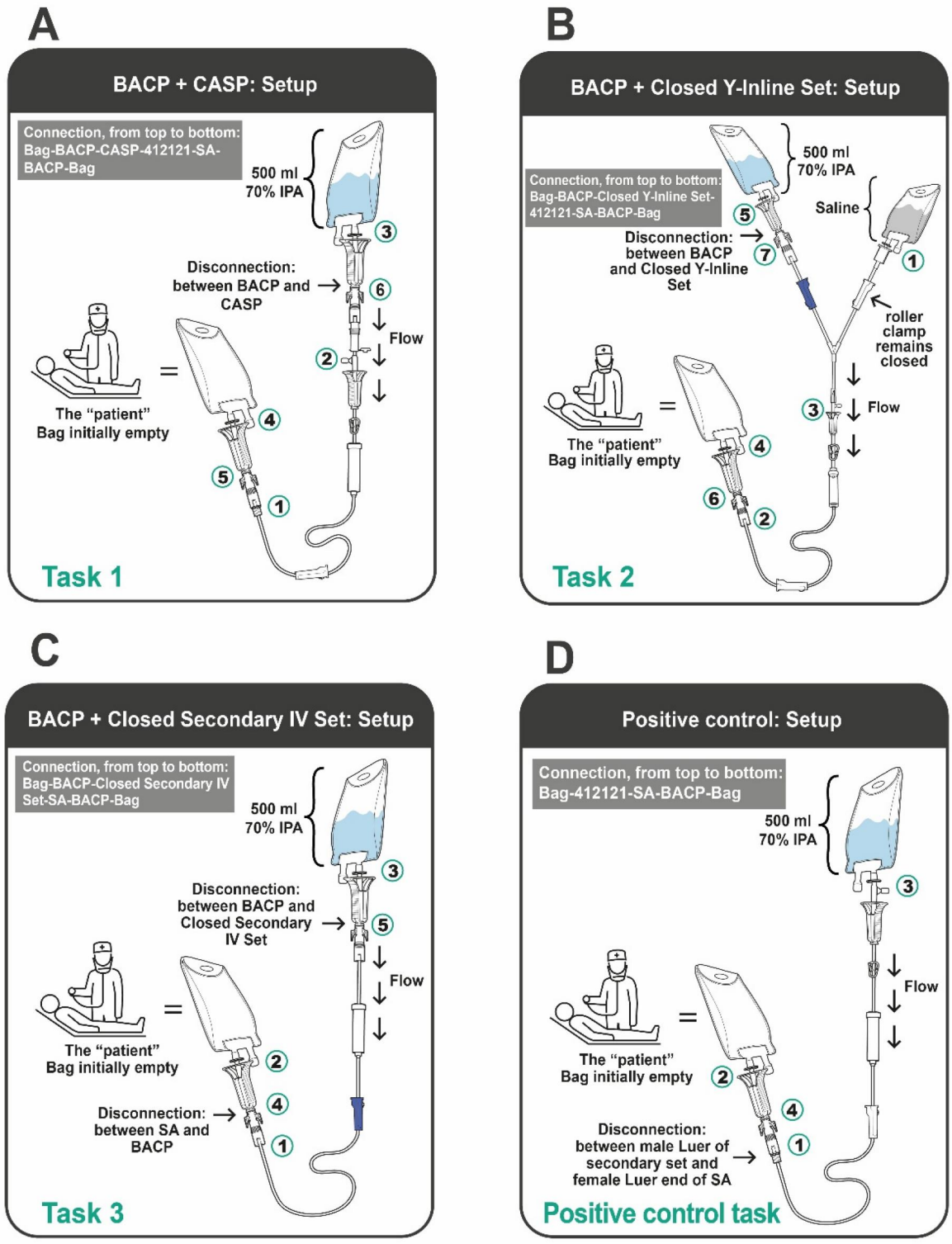

Figure 3. Tasks setup. (A) The Bag Adaptor CP (BACP) + Closed Adaptor SP (CASP). (B) BACP + Closed Y-inline Set. (C) BACP + Closed Secondary IV Set. (D) Positive control with non-CADM products.

BACP test item was connected to a bag containing 70% IPA (connection 3, Figure 3C).

- The IV bag containing 70% IPA was checked for external contamination/leaks with the PID.
- The SA (already connected to the Luer end of the Closed Secondary IV Set) was connected to the BACP of the empty IV bag (connection 4, Figure 3C).

- The integral SA of the Closed Secondary IV Set was connected to the BACP of the IV bag containing 500 mL 70% IPA (connection 5, Figure 3C).

Positive control task: As a positive control, the task was performed without the use of CADM products, except for a (non-test item) BACP that served as part of the collection vessel.

- All clamps on a non-CADM secondary IV set were closed, and its male Luer end was connected to the female Luer end of an SA (connection 1, Figure 3D).
- The BACP was connected to an empty IV bag (connection 2, Figure 3D), the spike of the secondary set was inserted into the bag containing 70% IPA (connection 3, Figure 3D).
- The IV bags were checked for external contamination/leaks.
- The SA (already connected the to Luer end of the secondary IV set) was connected to the BACP of the empty IV bag (connection 4, Figure 3D).

Negative control tasks: As a negative control, Task 3 was performed with saline instead of 70% IPA.

- All clamps of the Closed Secondary IV Set were closed, and its male Luer end was connected to an SA (connection 1, Figure 3C).
- A non-test item BACP was connected to an empty infusion bag (connection 2, Figure 3C), and a BACP test item was connected to a bag containing 500 mL of saline (connection 3, Figure 3C).
- The SA (already connected to the Luer end of the Closed Secondary IV Set) was connected to the BACP of the empty IV bag (connection 4, Figure 3C).
- The integral SA of the Closed Secondary IV Set was connected to the BACP of the IV bag containing saline (connection 5, Figure 3C).

For each task, the appropriate chain of devices was placed inside the sealed chamber. Inside the chamber, the full IV bag was hung from a hook. Then, IPA monitoring commenced, and background measurements were performed. The IV set clamps were then opened to allow flow at a rate of approximately 200–320 mL/hour. After one hour, the flow was stopped and disconnection was performed between the BACP and the CASP (task 1), the BACP and the Y-set (task 2), the BACP and the secondary IV set (task 3 and negative control), or the SA and the non-test item BACP, followed by the non-CADM IV set (male Luer) and the SA (female Luer) (positive control task). Following these disconnections, IPA levels were monitored in the chamber for an additional 30 min. In task 3, an additional disconnection was performed between the SA and the non-test item BACP, with subsequent IPA monitoring for an additional 15 min. Monitoring times of several minutes allowed IPA that may have leaked in liquid or aerosol form to evaporate and be quantified, along with IPA that may have leaked in vapor form.

For each test group, tasks 1–3 were repeated four times (a total of 16 repetitions per task) and the negative control once (a total of four repetitions). The positive control task was repeated four times. The number of repetitions are designated in the NIOSH draft protocol (NIOSH 2016).

Data analysis

The average of the five background IPA vapor concentration values measured before each repetition of each task was used for background adjustment of the data of that particular repetition. The relevant vapor concentration for each repetition was the highest increase in IPA vapor concentration reached over the course of the task (including the 15–30-minute waiting period after the final task action) relative to the average background levels before commencement of that task. If the subtraction of a background led to a negative value, the negative value was corrected to zero to obtain the background-adjusted-zero corrected maximum (BG-0_{max}) IPA concentration.

An average BG-0_{max} value was calculated for all repetitions of each task. Standard deviation (SD) and 95% confidence upper and lower limits were calculated. One-way analysis of variance (ANOVA) was conducted to evaluate the effect of the five experimental conditions—the three test tasks (1, 2 and 3), the negative control, and the positive control—on BG-0_{max} values.

Results

Mean BG-0_{max} levels for each task and test group are shown in Table 1. All products across all test groups demonstrated BG-0_{max} values well below the acceptance criterion of 3.06 ppm. This threshold is based on the GT 5000 Terra FTIR gas analyzer's limit of detection (LOD) for IPA under ideal conditions (0.92 ppm with 20-second sampling intervals). According to the NIOSH draft protocol (NIOSH 2016), the

Table 1. Background adjusted-zero corrected maximum ($BG\text{-}0_{max}$) IPA vapor concentrations in the sealed chamber.

				$BG\text{-}0_{max}$ (ppm)	
Task	Tested CADM components	Test group or control	Number of repetitions	Mean ± SD	95% Confidence Limits
1	Bag Adaptor CP	Time zero, 1st activation	4	0.00 ± 0.00	0.00, 0.00
	Closed Adaptor SP	Time zero, 10th activation	4	0.00 ± 0.00	0.00, 0.00
		3-years accelerated aging, 1st activation	4	0.00 ± 0.00	0.00, 0.00
		3-years accelerated aging, 10th activation	4	0.09 ± 0.18	−0.08, 0.26
2	Bag Adaptor CP	Time zero, 1st activation	4	0.00 ± 0.00	0.00, 0.00
	Closed Y-Inline Set	Time zero, 10th activation	4	0.05 ± 0.09	−0.04, 0.13
		3-years accelerated aging, 1st activation	4	0.00 ± 0.00	0.00, 0.00
		3-years accelerated aging, 10th activation	4	0.00 ± 0.00	0.00, 0.00
3	Bag Adaptor CP	Time zero, 1st activation	4	0.06 ± 0.12	−0.06, 0.17
	Closed Secondary IV Set	Time zero, 10th activation	4	0.00 ± 0.00	0.00, 0.00
		3-years accelerated aging, 1st activation	4	0.08 ± 0.15	−0.07, 0.22
		3-years accelerated aging, 10th activation	4	0.00 ± 0.00	0.00, 0.00
Positive control	NA	positive control	4	43.43 ± 9.56	34.05, 52.80
Negative control	Closed Secondary IV Set	Time zero, 1st activation	1	0.00 ± 0.00	0.00, 0.00
		Time zero, 10th activation	1	0.00 ± 0.00	0.00, 0.00
		3-years accelerated aging, 1st activation	1	0.00 ± 0.00	0.00, 0.00
		3-years accelerated aging, 10th activation	1	0.00 ± 0.00	0.00, 0.00

Abbreviations: CADM, Chemfort Closed Administration; IV, intravenous; NA, not applicable; SD, standard deviation.

LOQ—commonly defined as 3.33 times the detection limit—serves as the acceptance criterion. Accordingly, for IPA measured by the FTIR gas analyzer with 20-second sampling, the LOQ was 3.06 ppm. In most repetitions of most tasks, IPA levels remained at 0.00 ppm throughout the course of the task. The highest mean $BG\text{-}0_{max}$ reached was 0.09 ppm (Task 1, Group 4); however, the upper 95% confidence limit of 0.26 ppm was still well below the acceptance criterion. $BG\text{-}0_{max}$ values for all other tasks and test groups were lower. In comparison, in each positive control, a non-CADM secondary set was disconnected from the collection vessel by unscrewing the male Luer end of the set that contained 70% IPA from the female Luer of the SA, simulating disconnection from a patient access port in a clinical setting. For these controls, the average ± standard deviation $BG\text{-}0_{max}$ value was 43.43 ± 9.56 ppm—well above the acceptance criterion for vapor concentration increase in the sealed chamber.

One-way ANOVA revealed a statistically significant effect of task condition (1, 2, 3, negative control, or positive control) on $BG\text{-}0_{max}$ ($F(4, 51) = 324.89$, $p < 0.0001$), indicating that the mean of at least one group significantly differed from the others. Descriptive statistics showed that the positive control group had a markedly elevated mean $BG\text{-}0_{max}$ (43.43 ppm)—well above the method's LOQ of 3.06 ppm—confirming a robust measurable response. In contrast, the negative control group and test groups 1, 2, and 3 had mean $BG\text{-}0_{max}$ values that were below the 0.92 ppm LOD (0.00, 0.02, 0.01, and 0.03, respectively), suggesting that these responses were not distinguishable from the background noise. These findings support the specificity of the assay and the effectiveness of the positive control treatment.

Discussion

This study showed that when conventional non-closed administration sets were disconnected from the receptacle representing the patient following drug surrogate administration, IPA vapor concentrations in the sealed chamber increased and exceeded the LOQ. In contrast, when the CADM products were used, IPA vapor concentrations did not exceed the LOQ compared to baseline levels over the course of the tasks, indicating that no leaks occurred according to the predetermined criterion adopted from the NIOSH 2015 protocol (NIOSH 2016).

According to information received from the Gasmet GT 5000 Terra FTIR gas analyzer's manufacturer, the LOD for IPA under ideal conditions with 20-second sampling intervals is 0.92 ppm, such that any nominal concentration below this level is tantamount to instrumental noise. Thus, even the highest $BG\text{-}0_{max}$ values obtained in this study for CADM devices were not only below the acceptance criterion of <3.06 ppm, but also well below the detection limit of the analytical device and the nominal acceptance criterion of <1.0 ppm recommended in the NIOSH draft protocol (NIOSH 2016). In other words, even the non-zero values obtained are within the range of instrumental noise and do not indicate failures in the containment of the devices. Furthermore, the results were the same regardless of the number of activations of the product or whether it was newly manufactured or at the end of its simulated shelf-life.

Notably, the present study setup was not identical to the NIOSH draft protocol (NIOSH 2016) upon which it was based. While the NIOSH draft protocol describes the use of a MIRAN infrared spectrophotometer, this study used the Gasmet GT 5000 Terra FTIR gas analyzer; therefore, the IPA concentrations measured by the two setups cannot be directly compared. For several reasons, the present study setup was more challenging than that described by the NIOSH 2015 protocol (NIOSH 2016). First, the chamber was a completely closed system, as opposed to the system in the NIOSH 2015 protocol, which is semi-closed, constantly drawing in clean air, and essentially diluting any IPA released. In the present study's setup, any IPA released (liquid, aerosol, or vapor) accumulated in the closed space created by the chamber, the FTIR gas analyzer's sample cell, and the tubing connecting them. Notably, preliminary experiments showed that under the study conditions, liquid and aerosols will transfer to the gas phase within minutes and thus be quantified together with vapor leaks. Second, the tasks in the present protocol are 1.5 to 3 h long, whereas the tasks described in the NIOSH 2015 draft protocol (NIOSH 2016) take less than 15 min. Thus, in this study, 70% IPA had more time to potentially escape and accumulate in the gas phase. Despite these more stringent test conditions, the CADM products prevented IPA release, and no IPA was observed above the system's detection limit.

The results from positive control tests, which consisted of a task similar to the tasks with the CADM products but without closed administration sets, confirmed that the test method has the required sensitivity to detect the gas phase of the drug surrogate (70% IPA) if it were to leak from the administration sets during the prescribed task steps, specifically during disconnection from the female Luer of the SA representing the patient access device. In the absence of closed administration sets (positive controls), not only was there significant IPA vapor and liquid leakage following disconnection, but the amount of such leakage was highly variable, as indicated by the large SD and 95% confidence interval among repetitions of the positive control task. In the absence of CADM products, the user has little or no control over dripping or vapor escape from secondary sets following disconnection. The leakage of IPA when using a non-closed administration set in this study represents potential exposure of healthcare workers and the surrounding environment to hazardous drug (liquid, vapor, and/or aerosols) when tubing is disconnected from a patient following IV administration. The use of CADM products in conjunction with compatible Chemfort syringe adaptors prevented this escape and provided consistent performance. Considering that IPA is meant to represent the hazardous (active) ingredient in a drug product solution, its concentration of 70% is much higher than that of typical hazardous drugs (usually ~1% w/v of active ingredient before further dilution into an IV bag for administration). Additionally, IPA is at least five orders of magnitude more volatile (based on vapor pressure) than any common hazardous drug (Wilkinson et al. 2018). Thus, it can be concluded that the containment performance of the Chemfort CADM products is sufficient for drug containment.

Limitations

While the method developed in this study can be directly applied to any other comparable system, a limitation of the present study is that it describes application to only one closed administration system, namely the Chemfort CADM.

The study was performed under controlled laboratory conditions. While this helps isolate containment of the devices tested from environmental interference, it is also a limitation, because it does not fully represent clinical conditions in which the devices are used.

The study utilized a surrogate solution to represent hazardous drugs. This can be considered a strength, as the surrogate is a worst-case representative of real hazardous drugs, in terms of containment, but may also be a limitation because it does not directly mimic clinical use.

Conclusion

The results of this study indicate that the use of CADM components may potentially improve hazardous drugs' containment, thereby minimizing the risk of exposure of healthcare professionals to hazardous drugs and potentially reducing environmental contamination. Further potential benefits of CSTDs and closed administration systems not covered by this study include prevention of needle stick injuries and elimination of the need for a new IV set for each drug/saline administered in sequence to individual patients. Bags can be prepared with BACPs in the pharmacy, eliminating the need for spiking in administration areas. Moreover, the CADM sets can be disconnected from a BACP on one bag, briefly disinfected at the membrane port, and connected to a BACP on a different bag in a completely closed

manner. A study in clinical practice conditions is warranted to further confirm the results of this study.

Recommendations

The authors recommend that readers use this study to raise awareness among clinicians regarding potential exposure to hazardous drugs during administration as well as potential solutions to minimize this exposure. Developers of other administration systems may choose to apply the method described herein to evaluate the containment abilities of devices at various stages of development. Finally, healthcare workers can apply the method to compare containment abilities of various administration systems available for hazardous drugs, to minimize exposure and maximize safety.

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A generative AI language model (Microsoft Copilot [GPT-4o], July 2025 version) was used to assist in describing statistical data analysis (one way-ANOVA) in the methods and results sections.

Disclosure statement

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Ethics declarations

Not applicable (*in vitro* study).

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ORCID

Elana A. Slutsky Smith http://orcid.org/0000-0001-9277-1395

Data availability statement

Data that support the findings of this study are available from the corresponding author upon reasonable request.

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GLOSSARY OF TERMS

ANOVA	Analysis of Variance
BACP	Bag Adaptor CP
BG-0_{max}	Background-adjusted zero-corrected maximum concentration
CADM	Chemfort Closed Administration
CASP	Closed Adaptor Spike Port
CSTD	Closed System Transfer Device
FTIR	Fourier-Transform Infrared Spectroscopy
IPA	Isopropanol
IV	Intravenous
LOD	Limit of Detection
LOQ	Limit of Quantitation
NIOSH	National Institute for Occupational Safety and Health
PID	Photo-Ionization Detector
SA	Syringe Adaptor
SD	Standard Deviation
SID	Safe Infusing Device
Y-set	Closed Y-Inline Set