Chemfort™
Keeps you safe. Simply click

Safe Administration of Hazardous Drugs - Novel Approaches

Introduction

Closed system transfer devices (CSTDs) have been widely used in the last decades to prepare and administer hazardous drugs. The definition of a CSTD, according to the National Institute for Occupational Safety and Health (NIOSH) is, "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, 2004). The purpose of using CSTDs is to protect staff involved in the delivery of hazardous drugs throughout the entire process of drug preparation by pharmacists, administration to the patient by nurses, and disposal of waste (Connor & McDiarmid, 2006). In 2015, NIOSH published a draft protocol to quantitatively evaluate combined liquid, aerosol, and vapor containment performance of CSTDs, which claim to be effective for gas/vapor containment within a controlled test environment (NIOSH, 2015).

Nevertheless, the use of CSTDs during drug administration in the hospital wards remains an unsolved issue. Since the exposure to antineoplastic agents may occur through both inhalation of airborne agents and skin absorption, nurses working in cancer units are prone to this type of exposure daily when spiking intravenous (IV) chemotherapy bags, priming IV tubing, connecting, or disconnecting tubing from patients, or if there is a spill or leakage. For example, doxorubicin, a common hazardous drug used to treat cancer, is usually administered to patients via bolus injection, and small spills are frequently observed by nurses when syringes are connected to, and disconnected from, infusion lines. Results of a study performed in the UK, examining the use of a CSTD (Tevadaptor®, Simplivia) during doxorubicin administration, demonstrated a significant decrease in the number of spills and level of contamination compared with the currently used techniques (Marler-Hausen et al., 2020).

During the last decade, some studies approached this topic with different solutions, where various systems were suggested for improving the safety of nurses during hazardous drug administration. These systems presented an experimental concept of "safe infusion devices", the aim of which was to keep the connections of the IV bags safe, thus preventing the hazardous disconnection of empty bags (Simon, 2010; Lalande, 2012, Forges, 2021). This "safe disconnection" was also recently described as a solution for exposure reduction when using an elastomeric pump for drug infusion (Raphaelle, 2021). However, none of these studies used a truly closed system as defined by NIOSH as a part of a solution to prevent exposure to nurses administering the drug to patients in hospital wards. Therefore, there is still a need for a closed system which is implemented in a drug administration set, providing the required safety for nursing personnel during administration of hazardous drugs in practice.

Chemfort™
Keeps you safe. Simply click

Chemfort™ (Simplivia Healthcare LTD, Israel) is a commercially available Closed System Drug Transfer Device, which allows drug containment by using a unique air-cleaning technology (Toxi-Guard® system), comprised of a 100% activated carbon drug binding matrix and a 0.2 µm hydrophobic and oleophobic membrane (Figure 1). These components serve together as an effective sterile, particulate, and toxic drug vapor barrier.

Results of a recently published study demonstrated that Chemfort™ CSTD can efficiently contain the hazardous vapors of actual chemotherapy drugs (cyclophosphamide or 5-fluorouracil) even in extreme temperature conditions and after a 7-day exposure period (Levin and Sessink, 2021).

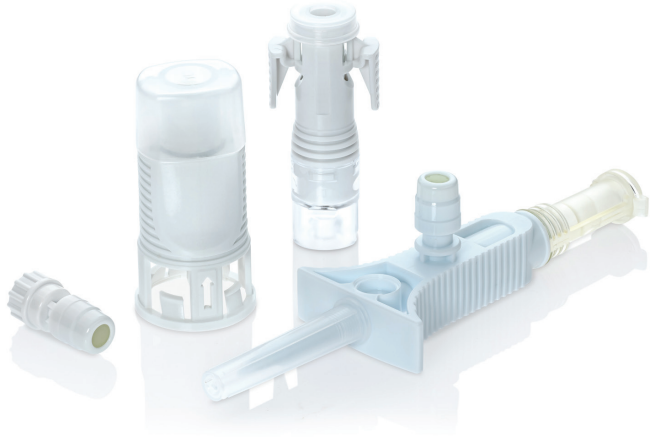
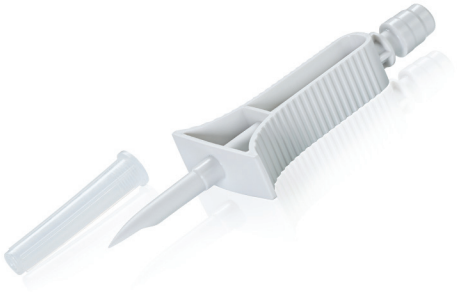


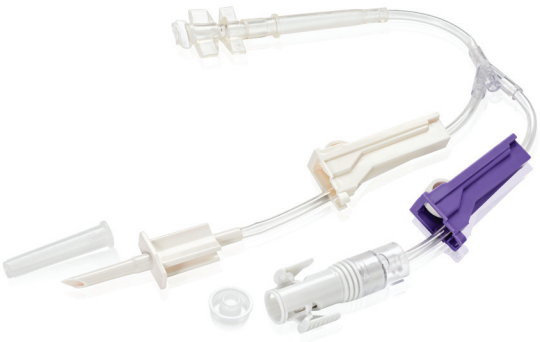
Figure 1 - Chemfort™ CSTD

Using the advantages of Chemfort™ as an efficient CSTD, a novel system combining Chemfort™ with drug administration sets was recently presented to the market. This system, named "Chemfort Closed Administration" (CADM), uses the advantages of Chemfort™ CSTD to protect nurses during administration. Use of the CADM components can minimize the risk of exposure of healthcare professionals to hazardous drugs, and reduce environmental contamination. In addition, the CADM system can eliminate the risk of needle stick injuries. Nevertheless, in order to evaluate this new system according to NIOSH standards, there is a need to examine the efficiency of CADM with regards to the aforementioned NIOSH protocol. The CADM system and its components are depicted in Figure 2.



Bag Adaptor Chemfort™ Port

Closed Adaptor Spike Port



Closed Y-inline Set

Closed Secondary IV Set

Figure 2 - CADM system and Components.

Objective

The objective of this study was to evaluate the CADM system according to NIOSH vapor containment protocol, in order to prove the protection against hazardous drug leakage and escape of aerosols and vapors that can occur during drug administration.

Materials & Methods

As no NIOSH vapor containment testing protocol has been written for closed administration sets, a protocol was developed inspired by the principles of the NIOSH 2015 protocol entitled “A Vapor Containment Performance Protocol for Closed System Transfer Devices Used During Pharmacy Compounding and Administration of Hazardous Drugs.” (NIOSH, 2015). This protocol defines the surrogate used (i.e., the right compound representing chemotherapy drugs), and the trial setup, in which the test is conducted in an environmental test closed chamber and a gas analyzer was used to detect the surrogate levels. In the NIOSH protocol, isopropanol (IPA) is used as a volatile surrogate for hazardous drugs and the acceptance criterion is determined to be <1.0 ppm IPA vapor concentration. The trial setup is presented in Figure 3.

Figure 3 - NIOSH chamber

Three test tasks and one positive control task were developed in order to mimic administration and subsequent disconnection of three different combinations of CADM components and in the absence of closed administrations sets, respectively. The Bag Adaptor Chemfort™ Port (BACP, Figure 2) is the required partner of each of the other three CADM components: Closed Adaptor Spike Port (CASP, Figure 2; task 1); Closed Y-inline Set (Figure 2, task 2); and Closed Secondary IV Set (Figure 2, task 3). In all tasks, a 500 ml IV bag was filled with 70% isopropanol (IPA). The bag was connected in a chain with the following components, according to each task:

Task 1: IV bag-BACP-CASP-non-CADM Secondary IV set (412121)-Chemfort™ Syringe Adaptor (SA)-BACP-empty IV bag

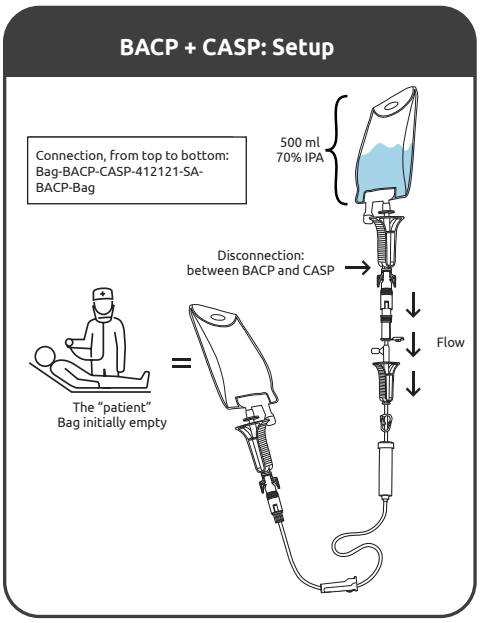
Task 2: IV bag-BACP-Closed Y-inline Set-non-CADM Secondary IV Set (412121)-SA-BACP-empty IV bag

Task 3: IV bag- BACP-Closed Secondary IV Set-SA-BACP-empty IV bag

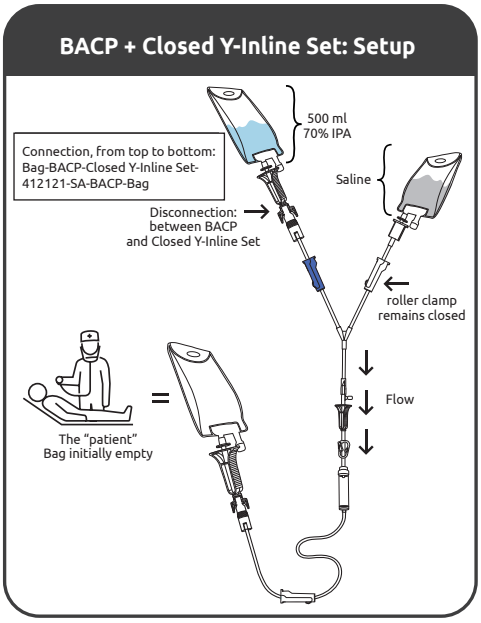
Positive control task: IV bag-non-CADM secondary IV set (412121)-SA-BACP-empty IV bag

The last two components (BACP and empty IV bag) represent the patient receiving the drug infusion and were included as a closed receptable for the IPA after flowing through the CADM components.

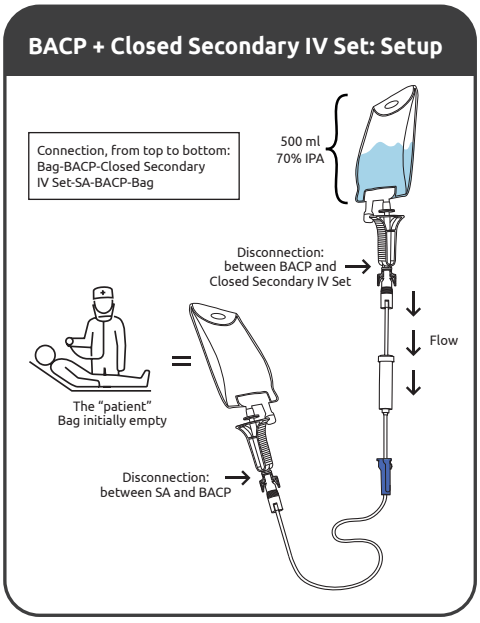
The described tasks are presented in Figure 4.



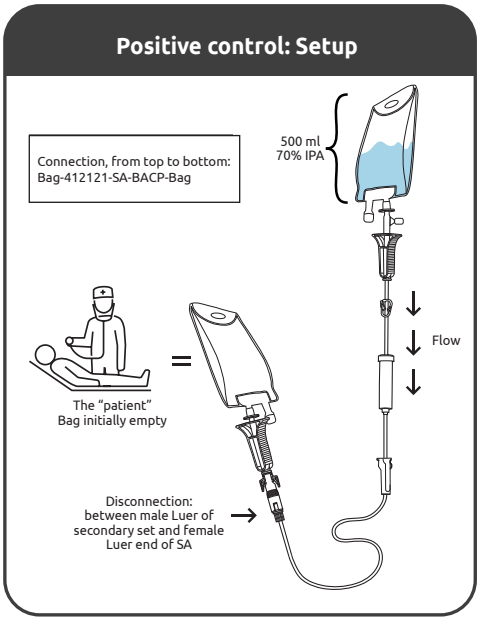
Task 1



Task 2



Task 3



Positive control task

Figure 4

The appropriate chain for a given task was placed inside the NIOSH chamber (Figure 3), which was sealed and connected to a Fourier-transform infrared spectroscopy (FTIR) gas analyzer (Gasmet GT 5000 Terra, Finland) in a closed circuit. The gas analyzer was set to monitor IPA vapor concentrations, and background concentrations were recorded for 5 minutes prior to each experiment. Inside the chamber, IV set clamps were opened to allow flow at a rate of approximately 200-320 ml/hour. After 1 hour, flow was stopped and disconnection was performed between BACP and CASP (task 1), BACP and closed Y-inline set (task 2), BACP and closed secondary IV set (task 3), or SA and BACP, followed by non-CADM IV set and SA (control task). Following these disconnections, IPA levels were monitored in the chamber for 30 minutes. In task 3, an additional disconnection was then performed between the SA and BACP, with subsequent IPA monitoring for an additional 15 minutes.

CADM components were tested both for freshly manufactured products, and at the end of shelf-life and upon 1st activation and 10th activation (maximum allowed by IFU). Thus, the tested devices can be divided into four test groups:

1. Freshly manufactured, 1st activation
2. Freshly manufactured, 10th activation
3. End of shelf life (3 years, simulated), 1st activation
4. End of shelf life (3 years, simulated), 10th activation.

Each test task was repeated 4 times for each test group. The control task was similarly repeated 4 times. Additionally, for each test group, 1 repetition of a negative control task similar to task 3 was performed in which IPA was replaced with saline.

Results

The relevant vapor concentration for each repetition was the highest increase in IPA vapor concentration reached over the course of the task, relative to the average background levels before commencement of that task. If subtraction of background led to a negative value, this was corrected to zero to obtain the background adjusted-zero corrected maximum ($BG\text{-}0_{max}$) IPA concentration. The results are presented in Table 1 and in Figures 5-7 below.

Table 1. Analysis of vapor levels for all test groups. Test groups: (1) time zero, 1st activation; (2) time zero, 10th activation; (3) 3 years accel. aged, 1st activation; (4) 3 years accel. aged, 10th activation

Task	Test group or control	Number of $BG\text{-}0_{max}$ Observations	Mean of $BG\text{-}0_{max}$ Observations (ppm)	Lower 95% Confidence Limit (ppm)	Upper 95% Confidence Limit (ppm)	Standard Deviation (ppm)
1	1	4	0.00	0.00	0.00	0.00
	2	4	0.00	0.00	0.00	0.00
	3	4	0.00	0.00	0.00	0.00
	4	4	0.09	-0.08	0.26	0.18
2	1	4	0.00	0.00	0.00	0.00
	2	4	0.05	-0.04	0.13	0.09
	3	4	0.00	0.00	0.00	0.00
	4	4	0.00	0.00	0.00	0.00
3	1	4	0.06	-0.06	0.17	0.12
	2	4	0.00	0.00	0.00	0.00
	3	4	0.08	-0.07	0.22	0.15
	4	4	0.00	0.00	0.00	0.00
Positive control	N/A	4	43.43	34.05	52.80	9.56
Negative control	1	1	0.00	0.00	0.00	0.00
	2	1	0.00	0.00	0.00	0.00
	3	1	0.00	0.00	0.00	0.00
	4	1	0.00	0.00	0.00	0.00

Figure 5. Task 1 results compared to controls. Test groups: (1) time zero, 1st activation; (2) time zero, 10th activation; (3) 3 years accel. aged, 1st activation; (4) 3 years accel. aged, 10th activation.

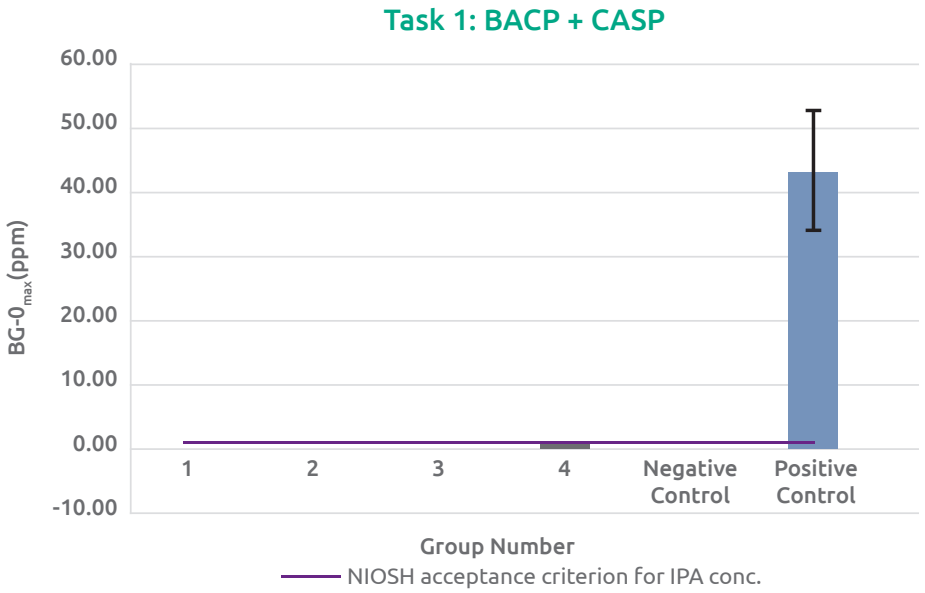


Figure 6. Task 2 results compared to controls. Test groups: (1) time zero, 1st activation; (2) time zero, 10th activation; (3) 3 years accel. aged, 1st activation; (4) 3 years accel. aged, 10th activation.

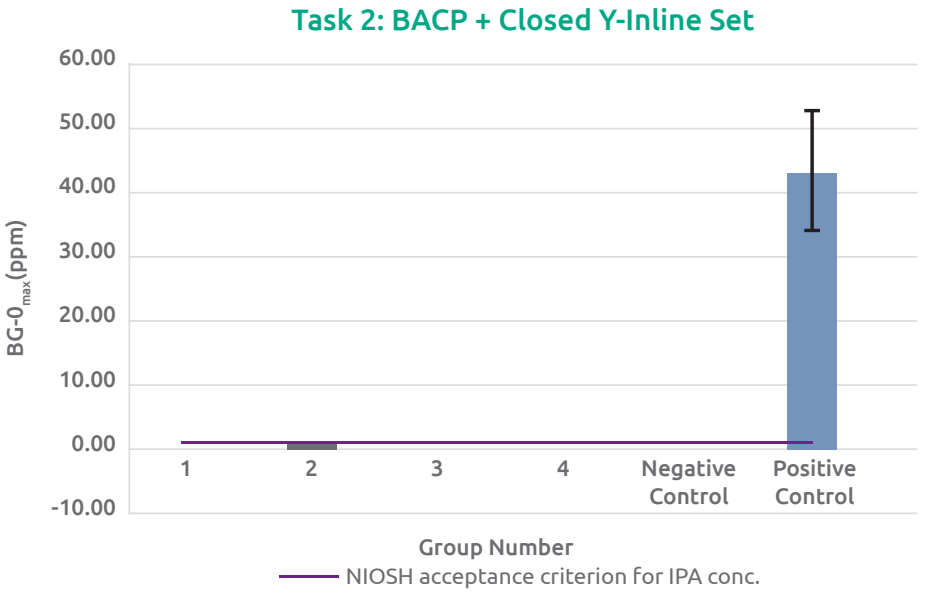
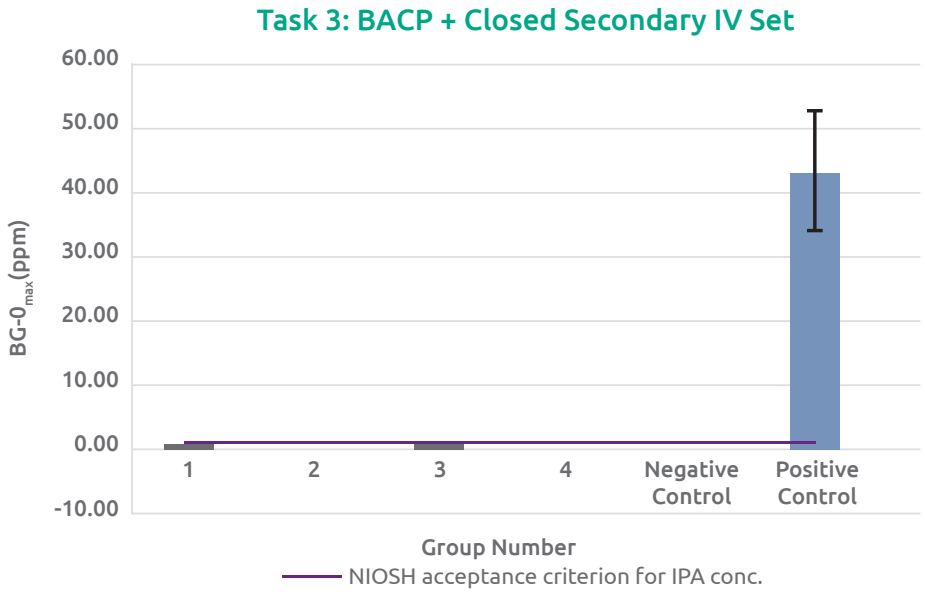


Figure 7. Task 3 results compared to controls. Test groups: (1) time zero, 1st activation; (2) time zero, 10th activation; (3) 3 years accel. aged, 1st activation; (4) 3 years accel. aged, 10th activation.



Chemfort™
Keeps you safe. Simply click

Discussion

In this trial, CADM system components were evaluated, testing each of the four CADM components - BACP, CASP, Closed Y-Inline Set, and Closed Secondary IV Set. Furthermore, the components were tested in four different scenarios: fresh products without pre-activations, fresh products at 10th activation, 3 years (simulated) aged products without pre-activations and 3-year aged products (simulated) at 10th activation. This allowed a full examination of the efficiency of the CADM system to contain vapors, in accordance to the acceptance criterion defined by the NIOSH 2015 containment performance protocol, upon which the test protocol for this study was based. As the defined level of allowed IPA was <1.0 ppm, IPA concentrations observed for all products in all test groups was well below this criterion. In fact, in most repetitions of most tasks, IPA levels remained 0.00 ppm throughout the course of the task. The highest mean BG-0_{max} reached was 0.09 ppm (Task 1, Group 4) with the upper 95% confidence limit of 0.26 ppm, was still well below the acceptance criterion. BG-0_{max} for all other tasks and test groups were even lower (Table 1). In comparison, when a non-CADM secondary set was disconnected from the collection vessel representing a patient in a clinical setting by unscrewing the Luer end of the set which IPA was inside the tubing (positive controls), the average BG-0_{max} value was 43.43±9.56 ppm. Examining negative controls, in which no IPA was present inside the chamber, led to no rise in detected IPA levels.

Conclusions

Chemfort™ Closed Administration system was evaluated according to a NIOSH-based protocol for closed-system devices for administration of hazardous drugs, and proved to provide protection against escape of hazardous aerosols and vapors that can occur during drug administration.

References

1. NIOSH Alert. Preventing occupational exposures to antineoplastic and other hazardous drugs in health care settings. Available at: https://www.cdc.gov/niosh/docs/2004-165/pdfs/2004-165.pdf
2. Connor TH, McDiarmid MA. Preventing occupational exposures to antineoplastic drugs in health care settings. CA Cancer J Clin. 2006 Nov-Dec;56(6):354-65
3. National Institute for Occupational Safety and Health. A vapor containment performance protocol for closed system transfer devices used during pharmacy compounding and administration of hazardous drugs. www.cdc.Gov/Niosh/Docket/Review/Docket288/Pdfs/a-Vapor-Containment-Performance-Protocol-for-Closed-System-Transfer-Devices.Pdf.
4. Marler-Hausen T, Holt C, Headley C, Sessink P. Use of a closed-system drug transfer device reduces contamination with doxorubicin during bolus injection. Br J Nurs. 2020 May 28;29(10): S15-S21.
5. Simon N, Décaudin B, Lannoy D, Danicourt F, Barthélémy C, Odou P. Technical evaluation of a new sterile medical device to improve anticancer chemotherapy administration. Oncol Nurs Forum. 2010 Nov;37(6): E370-6.
6. Lalande L, Galy G, Dussossoy E, Noyel JE, Pivot C. Evaluation of Safe Infusion Devices for Antineoplastic Administration. J Infus Nurs. 2015 Nov-Dec;38 Suppl 6: S29-35.
7. Forges F, Blanc E, Raymond B, Menguy S, Macé A, Hugues M, Macron C, Bouleftour W, Tinquaut F, Guitton J, Simoëns X. Evaluation of a safe infusion device on reducing occupational exposure of nurses to antineoplastic drugs: a comparative prospective study. Contamoins-1. Int Arch Occup Environ Health. 2021 Aug;94(6):1317-1325.
8. Raphaëlle P, Elodie P, Nathalie J, Odile A, Paul S, Isabelle M, Hélène L. Safe disconnection of 5-fluorouracil elastomeric pumps: The benefit of a closed-system-transfer device designed for cytotoxic drug administration/perfusion. J Vasc Access. 2021 Sep 18:11297298211044017.
9. Levin G, Sessink PJ. Validation of chemotherapy drug vapor containment of an air cleaning closed-system drug transfer device. J Oncol Pharm Pract. 2021 Jul 6:10781552211030682. doi: 10.1177/10781552211030682.