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Airborne Exposure Assessment of Class II, Type A2 Biosafety Cabinets (BSC) at Controlling Workplace Exposures to Volatile Fractions of Select Antineoplastic Agents

Xavier Alcaraz*, Nick Filipp, Michael Peterson, Russell Snyders, Alex Truchot

BSI EHS Services and Solutions, 2150 North First Street, Suite 450, San Jose, Calfornia, USA

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***For Correspondence**

Xavier Alcaraz, BSI EHS Services and Solutions 2150 North First Street, Suite 450, San Jose, Calfornia, USA.

Tel: 408-790-9216

E-mail: xavier.alcaraz@bsigroup.com

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ABSTRACT

Objective: The objective of this study was to evaluate whether Class II, Type A2 Biosafety Cabinets (BSC) that are commonly used for pharmaceutical compounding are effective at controlling potential exposures to the organic vapor fraction of chemotherapy drugs under small and/or large spill conditions.

Methods: This study involved testing for the airborne, vapor fraction of propylene glycol (as a surrogate chemical compound) under two separate conditions to assess the ventilation effectiveness of the Class II A2 BSC. A small amount of propylene glycol (5 ml) was used to simulate a small spill of a chemotherapy agent in solution that could occur during compounding in a BSC using a closed system transfer device (CSTD). Then a large amount of propylene glycol (250 ml) was used to simulate a worst-case spill. Air samples for propylene glycol were collected within each compounding room. Similar air sampling under like conditions was also performed in Class II B2 BSC for comparison purposes.

Conclusion: The data suggest that Class II A2 BSC are similarly effective to Class II B2 BSC at controlling volatile fractions of simulated chemotherapy agents. However, the data also suggest that there may be an exposure risk in both types of BSC should compounding technicians need to access the inside of the BSC for clean-up during small and/or large spills. The study results are relevant to any operations where compounding of chemotherapy drugs is performed in Class II A2 BSC.

INTRODUCTION

Many healthcare facilities, large and small, urban and rural, throughout the United States use Class II biological safety cabinets (BSC) for compounding of antineoplastic agents (chemotherapy drugs, hazardous drugs). Operational parameters of the four different types of Class II BSC vary somewhat with key differences as follows:

1. Recirculating Class II, Type A1 ventilated cabinets have a minimum inflow face velocity of at least 75 fpm; 70% of inflow air is recirculated to the cabinet work area through an integrated high efficiency particulate arrest (HEPA) filter; 30% of air can be exhausted through the HEPA filter back into the room or to building exterior [1].
2. Recirculating Class II, Type A2 (Class II A2) ventilated cabinets have a minimum inflow face velocity of at least 100 fpm [1]; 70% of inflow air is recirculated to the cabinet work area through an integrated HEPA filter; 30% of air is exhausted to the building exterior through a HEPA filter.
3. Class II, Type B1 ventilated cabinets have a minimum inflow face velocity of at least 75 fpm; 30% of inflow air is recirculated to the cabinet work area through an integrated HEPA filter; 70% of air is exhausted through a HEPA filter to the building exterior [1].
4. Class II, Type B2 (Class II B2) ventilated cabinets have a minimum inflow face velocity of at least 100 fpm, and exhaust 100% of all air to the exterior of the building [1].

Class II BSC are commonly used for compounding of hazardous drugs as they are designed to provide personnel, environmental, and product protection [2]. Class II B2 BSC are designed to provide a higher level of worker protection than Class II A2 BSC because they exhaust 100% of the inflow air, thus they are ideal for compounding due to the toxic and sometimes semi-volatile nature of hazardous drugs [2]. Class II A2 BSC have the potential to return volatile organic compounds back into the enclosure because they are not captured through HEPA filtration and are not suitable for compounding of hazardous drugs unless containment devices are used [2] or if only minute quantities are used [1]. In addition, movement of personnel at the BSC and/or in the room can cause increased turbulence within the work area that can disrupt directional airflows and the protective functions of BSC [3]. However, many healthcare facilities are opting to utilize recirculating Class II A2 BSC over Class II B2 BSC for compounding operations for their energy conservation and cost saving benefits.

There have been many studies documenting the presence of surface contamination of hazardous drugs on interior BSC surfaces, product vials, and employee's hands [4-7]; however, there have been few studies demonstrating whether recirculating Class II A2 ventilated cabinets are similarly effective as Class II B2 ventilated cabinets in protecting employees during hazardous drug compounding activities, in particular for the volatile fraction of hazardous drugs. Similarly, there have been few studies evaluating the risk or potential exposures to the volatile fraction of hazardous agents during compounding activities [7]. One study observed that vaporization of some antineoplastic agents is evident at room temperature, thus a spill could present an inhalation route of exposure to healthcare workers [8]. Greater vaporization was observed at higher temperatures which could be created by heat sources within the BSC (such as compressor motors, lights, etc.), thus creating a higher risk of exposure to personnel during a spill [8]. Another study observed evaporation of cyclophosphamide during compounding activities in BSC and cautioned that commonly used protective systems equipped with particle filters only (such as BSC) do not provide complete protection for workers [9]. The researchers further suggested that the volatile fraction of antineoplastic agents be considered when selecting occupational and environmental control methods [9].

Although the use of recirculating Class II A2 BSC for compounding of hazardous drugs is common and widespread in healthcare facilities across the United States, the known properties of these chemicals and the configuration of recirculating Class II A2 BSC suggests there is a potential risk of inhalation exposure to healthcare workers under normal and/or chemical spill conditions which has not been adequately characterized. This study served to start to close this gap.

Study Purpose and Objectives

The purpose of this study was to evaluate whether the use of Class II, Type A2 BSC used by many healthcare facilities for compounding tasks are effective at controlling potential worker exposures to the organic vapor fraction of hazardous drugs under simulated spill conditions using a surrogate compound.

The objective of this cohort study was to obtain representative air sampling data to evaluate the relative effectiveness of Class II A2 BSC as compared with Class II B2 BSC at controlling potential workplace exposures to the organic vapor fraction of common antineoplastic agents under simulated spill conditions that could occur during compounding using a relatively safe surrogate compound.

This study involved performing airborne sampling for propylene glycol (CAS #57-55-6) as a surrogate chemical for common (low vapor pressure) chemotherapy drugs during a simulated (incidental) spill condition as well as a large (complete) spill condition inside several Class II A2 BSC and Class II B2 BSC (for comparison purposes).

METHODS

Participating Healthcare Facilities

The following five medical centers were requested to volunteer as participants for the study:

- CHI Franciscan Health, Highline Cancer Center Pharmacy, Burien, WA
- CHI Franciscan Health - St. Joseph Medical Center, Tacoma, WA
- Group Health (now known as Kaiser Permanente), Bellevue Medical Center, Bellevue, WA
- Group Health (now known as Kaiser Permanente), Capitol Hill Campus, Seattle, WA
- MultiCare Health System, Tacoma General Hospital, Tacoma, WA.

These facilities have Class II A2 Biosafety Cabinets (BSC) and/or Class II B2 BSC. Participation from five separate facilities in the study served to provide a broader industry comparison rather than limiting sampling to just one facility. The participating facilities were generally located within the greater Seattle-Tacoma metropolitan area and are generally considered larger healthcare facilities. Smaller or rural facilities were not identified for the study.

Antineoplastic Agents Considered For Sampling

Several common hazardous drugs were considered for incorporation into the study because of their common use as hazard-

ous drugs across the participating healthcare facilities including the following:

- 5-Fluorouracil
- Cyclophosphamide
- Ifosfamide
- Methotrexate.

However, there are currently no known validated methods for the capture of the volatile airborne fraction of these compounds. Therefore, a surrogate compound with semi-volatile properties and a validated sampling and analytical method was considered as a substitute for the chemotherapy compounds.

Surrogate Sampling Chemical Selection

Propylene glycol (CAS #57-55-6) was selected as the surrogate chemical for sampling based on the following:

- Low vapor pressure
- Miscible in water
- Relatively low toxicity
- Validated air sampling method for the volatile fraction
- Readily available.

The vapor pressure of propylene glycol at room temperature is several orders of magnitude higher (approximately 1,000x) than that of Cyclophosphamide, 5-Fluorouracil, and several other antineoplastic agents **(Table 1)**. This provides a greater safety factor for use of propylene glycol as a surrogate chemical for sampling.

The National Institute for Occupational Safety and Health (NIOSH) identified propylene glycol as one of several potential surrogate compounds that could be considered for evaluating the effectiveness of CSTD for protecting workers performing compounding activities [10].

Table 1. Comparison of vapor pressure values for antineoplastic agents [9] and proposed surrogate sampling chemical [11]

Chemical	Vapor Pressure (Pascal) @ 20°C	Molecular Weight (grams/mole)
5-Fluorouracil	0.0014	130
Cyclophosphamide	0.0033	261
Carmustine	0.019	214
Cisplatin	0.0018	300
Etoposide	0.0026	588
Propylene Glycol	9	76

Sampling Conditions

All sampling was performed between February 15, 2017 and February 27, 2017. A total of six BSC ventilated cabinets were identified for inclusion in this study. Three cabinets were Class II A2 BSC and three cabinets were Class II B2 BSC. Both Class II A2 BSC and Class II B2 BSC cabinets were tested at one facility (MultiCare Health System - Tacoma General Hospital). Whereas, only one type of cabinet was tested at the other facilities. BSI performed integrated and direct-read air sampling under the following two unique sampling conditions to evaluate the effectiveness of each type of BSC:

- Simulated Minor Spillage: Propylene glycol was used to simulate minor (incidental) spillage or leakage of an antineoplastic agent in solution that could occur during compounding in a BSC using a closed system transfer device (CSTD). A small quantity of propylene glycol (5 ml) was dispensed onto an absorbent wipe (DSS ChemoSorb pad) using a 5–10 mL syringe and placed inside a single containment tray (18”Wx18”Lx4”H) inside of the cabinet with the cabinet sash position maintained at working height. Air sampling was conducted for at least 30 minutes under this condition.
- Simulated Large Spill Condition: Propylene glycol was used to simulate a worst-case spill condition in each BSC. The maximum volume typically used for compounding (approximately 250 ml) was poured into a single containment tray (18”Wx18”Lx4”H) inside of the cabinet with the cabinet sash position maintained at working height. Air sampling was conducted for at least 30 minutes under this condition. The spilled materials were cleaned using DSS ChemoSorb pads, and all material was deposited in sealed waste bags. Air sampling continued for an additional 30 minutes following spill clean-up activities.

There was approximately 10 minutes between sampling of the two spill conditions to allow for multiple air changes in the compounding room to flush potential residual airborne contaminant in the room and allow return to background levels. The BSCs were allowed to run during this period to facilitate room air changes.

All waste materials were handled in accordance with local, state, and federal requirements following each facility's waste disposal protocols.

Integrated Air Sampling

Integrated air sampling (area and source) was performed to assess airborne concentrations of propylene glycol as a surrogate for common hazardous drugs during simulated minor and large spill conditions in Class II A2 BSC and Class II B2 BSC. Area samples were placed on tri-pods in representative locations within the room at approximate breathing zone level (4 feet high from floor). Due to the relatively small size of compounding rooms, the area samples were generally placed on opposite sides of the BSC. Source samples were placed inside the BSC adjacent to the spill materials. A baseline sample was collected in the room for a minimum of 30 minutes prior to the surrogate compound testing to determine potential background levels in the compounding room/area.

Table 2. Summary of sample number and locations for each sampling event

Sample Type	Outside BSC Sample(s)	Inside BSC Sample(s)
Baseline (prior to compounding) - area sample	1	0
Minor Spillage condition–area sample	2	1
Large Spill condition–area sample	2	1
Field Blanks (per site, per event)	2	Not Applicable
Laboratory Blank (per sample lot)	2	Not Applicable

Each sample was collected by passing a known quantity of air through a XAD-7 OVS tube (13mm glass fiber filter and 200 mg/100 mg × AD-7 sorbent). Airflow through the sampling devices was provided by Sensidyne GilAir-5 portable battery-powered industrial hygiene air sampling pumps and calibrated to approximately 2 liters of air per minute (lpm), before and after the sampling event with a BIOS Dry-Cal DC Lite Primary Flow Meter or similar. Two field blank samples for each sampling event were collected for quality assurance purposes by handling the sampling media in the same manner as the actual air samples, but without passing air through them. In addition, two laboratory blanks were submitted per sample lot.

At the completion of the sampling period, the sampling media were labeled, sealed, and submitted for analysis with a 7-day turnaround-time to ALS Environmental (Cincinnati, OH) an independent, American Industrial Hygiene Accredited laboratory. At the laboratory, the samples were analyzed in accordance with the National Institute for Occupational Safety and Health (NIOSH) Method 5523[11] for glycols using Gas Chromatography/ Flame Ionization Detection (GC/FID).

The number of samples and the sample locations collected for each sampling event/location are summarized in **Table 2**. For each of the six BSC cabinets included in the study, approximately 9 samples (including field blanks) were collected. A total of 48 air samples and 12 field/laboratory quality control blanks were collected for the study. Six of the samples were replicate samples. BSI performed replicate air sampling under the large spill condition for the Class II A2 BSC at one facility (Group Health–Belleview). All sample media used were from the same lot; therefore, only two laboratory (lot) blanks were submitted for analysis. The airborne limit of detection for propylene glycol ranged from 0.0026 mg/m^3 to 0.0056 mg/m^3 based on the air sample duration, air sample volume, and the analytical laboratory's limit of quantitation. **Figures 1-3** depict a typical compounding room and the area air sample locations during simulated spill scenarios.

The facility's engineering, administrative, and personal protective equipment controls for compounding activities were observed and noted for each site.

Figure 1. Typical air sampling set-up during a spill condition

Figure 2. Typical air sampling set-up during a spill condition

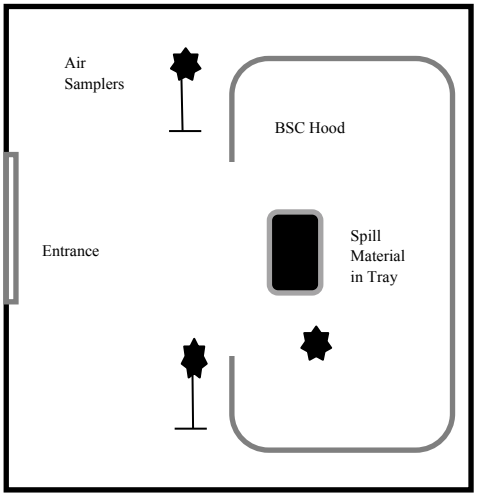

Figure 3. Typical air sampling set-up during a spill condition

Direct-Read Air Sampling

Direct-read air sampling (area and source) was also performed to assess airborne concentrations of propylene glycol as a surrogate for common chemotherapy drugs during simulated minor and large spill conditions in Class II A2 BSC and Class II B2 BSC.

Photo-ionization detectors (PIDs) are broad-band sensors that respond to a large variety of organic and some inorganic compounds. The general class of compounds suitable for detection with PIDs is volatile organic compounds (VOCs).

In addition to integrated air sampling, direct-read air sampling for propylene glycol as total volatile organic compounds (TVOC) was performed using a calibrated ppbRae3000 (RAE Systems) photo-ionization detector (PID) equipped with a 10.6eV lamp configuration. The ppbRae3000 has an instrument resolution of 1 ppb (+2.5%), measurement range up to 9,999 ppb and 3 second response time [12].

Spot measurements for VOC were collected inside and outside the BSC at 5-minute intervals throughout the simulated spill sampling periods for each spill condition. A baseline (background) TVOC measurement was collected prior to initiating each spill event, in between spill events, and following completion of the final spill event.

Measurements were collected at less than 1 inch from the spill; however, these values were not reported as they were only collected to verify operation/response of the direct-read air monitor, but not to serve as representative TVOC accumulation in the BSC.

The final direct-read sampling data was converted using the manufacturer-provided correction factor for propylene glycol (5.5 for ppbRae3000 with 10.6eV lamp). Since the PID is capable of measuring a large variety of VOCs, baseline direct-read PID measurement values were assumed to be background VOC levels not associated with propylene glycol used for the simulated spill

conditions. However, no baseline direct-read air sampling values were measured above the direct-read monitor's lower level of detection (instrument's resolution).

Ventilation Assessment

The participating healthcare facilities provided documentation of ventilation performance testing/certification according to the NSF/ANSI 49-2008 Biosafety Cabinetry: Design, Construction, Performance, and Field Certification [13] (or similar) for the Class II A2 BSC and Class II B2 BSC that were selected for the study. The authors requested that the certification be current within 6-months of the scheduled air sampling events.

On the date of the sampling events, the authors performed cursory verification ventilation assessments on each of the Class II A2 BSC and Class II B2 BSC selected for the study. The cabinets were tested for face velocity performance with a calibrated velometer to ensure they met the manufacturer's inward face velocity requirements (typically 100 fpm) with the cabinet sashes adjusted to their proper working positions using the methods established in NSF/ANSI 49-2008 as a guide. If the cabinets did not conform to manufacturer's specifications for proper ventilation performance, the authors requested that the cabinet system be adjusted and re-tested.

The facility heating, ventilation, and air conditioning (HVAC) in each compounding room was allowed to operate according to each facility's standard operating mode. The authors requested information on HVAC performance for each compounding room such as locations of air supplies and returns, make-up air sources, air airflow volumes, room air changes per hour, and relative pressure differentials to adjacent rooms. The facilities provided ventilation data for compounding rooms as air changes per hour. However, availability of Facilities representatives from participating sites was limited; thus, access to additional information was not obtained.

RESULTS

Integrated Air Sampling

The majority of the integrated air sampling results for propylene glycol during simulated incidental (minor) and worst-case spill conditions outside of both Class II A2 BSC and Class II B2 BSC did not exceed the analytical laboratory's limit of quantitation (1 µg/sample). The resulting non-detect exposure values ranged from <0.0026 ppm to <0.0056 ppm. The variation in detection level for the samples was due to differences in sample volumes (i.e., associated with variations in sample time and air-pump flow-rates). However, one of the integrated air samples collected outside of a Class II A2 BSC at Group Health Belleview Medical Center during the simulated incidental (minor) spill condition resulted in a detection of propylene glycol at 0.10 ppm.

One of the two field blanks collected at Group Health Capitol Hill contained a detectable level of propylene glycol (18 µg). All other field blanks and lot blanks were below the analytical laboratory's limit of quantitation (1 µg/sample).

Two integrated air samples collected inside of two separate Class II A2 BSC during the simulated incidental (minor) spill condition resulted in detections of propylene glycol ranging from 0.014 ppm to 0.017 ppm. Similarly, one integrated air sample collected inside of a Class II B2 BSC during the incidental (minor) spill condition resulted in detection of propylene glycol at 0.051 ppm. A comparison of air sampling results for propylene glycol during the simulated incidental (minor) spill condition in Class II A2 BSC vs. Class II B2 BSC across all study sites is provided in **Table 3**.

Table 3. Comparison of air sampling results for propylene glycol during simulated incidental spillage in Class II A2 BSC vs. Class II B2 BSC across all study sites

BSC Type	Sample Type: Location	Sampling Duration Range (min)	Integrated Air Sampling Results–Range (ppm)[ABC]	Direct-Read Sampling Results - Range (ppb)[ABD]
Class II A2	Area: inside cabinet (right)	30	ND, <0.0052	ND, <1.0
			0.014	ND, <1.0
			0.017	ND, <1.0
Class II A2	Area: outside cabinet (left)	30	ND, <0.0052	ND, <1.0
			ND, <0.0052	ND, <1.0
			ND, <0.0053	ND, <1.0
Class II A2	Area: outside cabinet (right)	30	ND, <0.0053	ND, <1.0
			ND, <0.0054	ND, <1.0
			ND, <0.10	ND, <1.0
Class II B2	Area: inside cabinet (right)	30	ND, <0.0054	ND, <1.0
			ND, <0.0056	ND, <1.0
			0.051	ND, <1.0

Class II B2	Area: outside cabinet (left)	30	ND, <0.0051	ND, <1.0
			ND, <0.0054	ND, <1.0
			ND, <0.0056	ND, <1.0
Class II B2	Area: outside cabinet (right)	30	ND, <0.0052	ND, <1.0
			ND, <0.0054	ND, <1.0
			ND, <0.0055	ND, <1.0

Note: [A]NA=Applicable

[B]ND=Non-Detect

[C]ppm=part per million

[D]ppb=part per billion.

Two integrated air samples collected inside of two separate Class II A2 BSC during the simulated large spill condition resulted in detections of propylene glycol ranging from 0.040 ppm to 0.044 ppm. One integrated air sample collected inside of a Class II B2 BSC during the large spill condition resulted in detection of propylene glycol at 0.0070 ppm. A comparison of air sampling results for propylene glycol during simulated large spill conditions in Class II A2 BSC vs. Class II B2 BSC across all study sites is provided in **Table 4**.

Table 4. Comparison of air sampling results for propylene glycol during simulated large spill conditions in Class II A2 BSC vs. Class II B2 BSC across all study sites

BSC Type	Sample Type: Task, Location	Sampling Duration Range (min)	Integrated Air Sampling Results–Range (ppm) [ABC]	Direct-Read Sampling Results - Range (ppb)[ABD]
Class II A2	Area: inside cabinet (right)	60	ND, <0.0026 x 3 (repeat sampling)	ND, <1.0
			0.04	ND, <1.0
			0.044	ND, <1.0
Class II A2	Area: outside cabinet (left)	60	ND, <0.0026 x 3 (repeat sampling)	ND, <1.0
			ND, <0.0026	ND, <1.0
			ND, <0.0027	ND, <1.0
Class II A2	Area: outside cabinet (right)	60	ND, <0.0026 x 3 (repeat sampling)	ND, <1.0
			ND, <0.0027	ND, <1.0
			ND, <0.0027	ND, <1.0
Class II B2	Area: inside cabinet (right)	60	ND, <0.0026	ND, <1.0
			ND, <0.0028	ND, <1.0
			0.007	ND, <1.0
Class II B2	Area: outside cabinet (left)	60	ND, <0.0026	ND, <1.0
			ND, <0.0027	ND, <1.0
			ND, <0.0027	ND, <1.0
Class II B2	Area: outside cabinet (right)	30	ND, <0.0026	ND, <1.0
			ND, <0.0027	ND, <1.0
			ND, <0.0028	ND, <1.0 - 0.70 /3.85*

Note: [A]NA=Applicable

[B]ND=Non-Detect

[C]ppm=part per million

[D]ppb=part per billion

Direct-Read Air Sampling

All baseline (background) TVOC measurement collected using the direct-read PID air sampling monitor prior to initiating each spill event, in between spill events, and following completion of the final spill event were below the instrument's lower level of detection (instrument's resolution) of 1 ppb.

Following set-up of spill materials, propylene glycol measurements were collected by placing the direct-read monitor's probe at less than 1 inch from both minor and major spill materials at all sites to verify a response from the instrument. An immediate response was detected for all spill events (as expected) and measured values were observed to return to background when the direct-read monitor probe was retracted to greater than 1 inch from the spill materials. These measurements were not reported with other sampling measurements as they were meant for quality control purposes to verify the direct-read PID was operating as expected.

Direct-read PID air sampling measurements collected for propylene glycol during simulated worst-case spill conditions out-

side of a Class II B2 BSC (Multi-Care Health–Tacoma General) detected values from non-detect to 700 ppb (calculated to be 3,850 ppb with the 5.5 x instrument correction factor). It was observed that cleaning activities were being performed in an adjacent room concurrently with our air sampling. Because the compounding room is under negative pressure, the cleaning solvent used in the adjacent room may have contributed or may have been the sole source of the direct-read PID measurements. All other direct-read PID air sampling results for propylene glycol during simulated incidental (minor) and worst-case spill conditions inside and outside of both Class II A2 BSC and Class II B2 BSC were below the instrument's lower level of detection (instrument resolution) of 1 ppb.

Ventilation Assessment

The results from the ventilation assessments of BSC performed prior to air sampling events are summarized in **Table 5.**

Table 5. Comparison of ventilation assessment results of class II A2 BSC and Class II B2 BSC across all study sites.

Facility	Cabinet Type	Face Velocity[A] (fpm)	Flow Rate (cfm)	Facility Reported Room ACH[B]	Certified in Last 6 months?
Group Health–Bellevue	Class II A2	141.4	653	40	Yes
CHI - Highline	Class II A2	145	704.8	36	Yes
MultiCare Health	Class II A2	114.3	499.7	38	Yes
Group Health–Capitol Hill	Class II B2	135.4	526.6	55	Yes
St. Joseph Medical Center	Class II B2	154.1	599.5	69	Yes
MultiCare Health	Class II B2	130.2	291.6	73	Yes

[A]At working sash height/arrow
[B]ACH=Air Changes per Hour

All BSC cabinets evaluated in the study were of stainless-steel construction with an adjustable sash. The BSC cabinets were equipped with integrated airflow monitoring devices that alarm when they fall below a minimum performance level. The compounding rooms were designed to maintain a negative air pressure in relation to the adjacent rooms.

All BSC had average face velocity measurements above 100 fpm (with no value single measurement value below 75 fpm) when the sash was at working height (i.e., at indicator arrows). The BSC at all sites appeared to be well-maintained and storage of items that could impede the ventilation-performance of the cabinets was observed to be minimal. All BSC cabinets were performance-tested and certified by an independent ventilation test contractor within 6 months prior to each sampling event.

DISCUSSION

Minor Spill Scenario

The integrated air sampling results for propylene glycol during the simulated incidental (minor) spill condition in Class II A2 BSC vs. Class II B2 BSC were generally similar across all study sites. Two of the three air samples collected inside Class II A2 BSC had detectable values as compared to one of the three air samples collected inside Class II B2 BSC.

However, the detectable value measured in the Class II B2 BSC (0.051 ppm) was somewhat higher than the detectable values measured in the Class II A2 BSC (0.014 ppm to 0.017 ppm). Review of the direct-read air monitoring data did not reveal any propylene glycol detections inside any of the Class II A2 BSC or Class II B2 BSC across all study sites.

A review of the ventilated cabinet face-velocity test data did not reveal any obvious or notable influence from air flow on propylene glycol concentration for air samples inside the cabinets with detectable values in Class II A2 BSC vs. Class II B2 BSC, and/or those cabinets with non-detect values under simulated incidental (minor) spill conditions. All ventilation face velocities were above 100 fpm (range: 115 fpm–152 fpm).

The majority of the integrated air sampling results was non-detect for propylene glycol during simulated incidental (minor) and worst-case spill conditions outside of both the Class II A2 BSC and Class II B2 BSC across all sites. However, one of the integrated air samples collected outside of the Class II A2 BSC at the Group Health Belleview Medical Center during the simulated incidental (minor) spill condition resulted in a detection of propylene glycol at 0.10 ppm. This was the highest air concentration of propylene glycol measured for an integrated air sample in the study. The integrated air sample collected on the left side of the same ventilated cabinet was non-detect and the direct-read air sample results on both the left and right sides of the same ventilated cabinet were non-detect. The integrated air samples and field blanks collected inside the same cabinet for both spills were also non-detect. At researcher's request, the analytical laboratory performed an internal quality control review including repeat analysis of the sample in question. The laboratory's analytical result of repeat analysis for this sample was very similar. There were no known reports of propylene glycol contamination on the sampling media and it is unlikely that cross-contamination occurred during field sampling; however, these possibilities cannot be ruled-out.

Large Spill Scenario

A comparison of air sampling results during the simulated large spill conditions identified propylene glycol concentrations ranging from 0.040 ppm to 0.044 ppm inside the Class II A2 BSC. These were somewhat higher than the propylene glycol concen-

tration of 0.0070 ppm detected inside of the Class II B2 BSC. Other than the cabinet type, there were no observed factors that could account for the variation of propylene glycol concentrations for air samples inside the cabinets with detectable values in Class II A2 BSC vs. Class II B2 BSC, and/or those cabinets with non-detect values under the same simulated large spill conditions.

Repeat sampling at one site (Group Health - Bellevue Medical Center) to assess the potential variability of air sampling exposure data for the large spill condition. All repeat air sampling data were non-detect and no variability in propylene glycol concentrations was observed for the repeat samples collected.

One of the two field blanks collected at Group Health Capitol Hill contained a detectable level (18 µg) of propylene glycol. Interestingly, the mass of propylene glycol for this field blank was similar to that found on sample #0226-3 noted above (19 µg). However, the air samples were collected on different days. At BSI's request, the analytical laboratory performed an internal quality control review including repeat analysis of this sample. The laboratory's analytical result of repeat analysis for this sample was very similar. There were no known reports of propylene glycol contamination on the sampling media and it is unlikely that cross-contamination occurred during field sampling; however, these possibilities cannot be ruled-out.

Compounding activities were not performed for the Phase 2 air sampling because the partner healthcare facilities were not prepared to use a surrogate chemical, such as propylene glycol, for compounding in this manner. Furthermore, exposure risk from particulate or volatile fractions of chemotherapy agents during compounding is reduced by use of CSTD methods. Instead, the Phase 2 sampling focused only on characterizing potential volatile fractions from higher exposure risk conditions, namely simulated minor (incidental) spills and simulated large (worst-case) spill events.

The number of integrated air samples collected for each unique spill condition was small (generally limited to 3 for each location), and the number of study sites was limited (three Class II A2 BSC and three Class II B2 BSC). As such, the study sample set did not allow for robust statistical analysis of the data. Furthermore, many of the air sample results were non-detect, which also limited the comparative analysis across BSC types.

CONCLUSION

Air sampling results for propylene glycol during the simulated incidental (minor) spill condition in Class II A2 BSC vs. Class II B2 BSC were somewhat similar across all study sites, but not without variations in number of detections and concentration. However, there were no clear factors that could account for the variations of propylene glycol concentrations detected inside the cabinets of Class II A2 BSC vs. Class II B2 BSC.

The majority of the integrated air sampling results for propylene glycol during simulated incidental (minor) and worst-case spill conditions outside of both the Class II A2 BSC and Class II B2 BSC across all sites were non-detect. The Phase 2 air sampling data suggest that there is no notable difference in effectiveness of control of volatile fractions of propylene glycol outside of Class II A2 BSC as compared to Class II B2 BSC. These results suggest that there does not appear to be an inhalation exposure risk to volatile fractions of hazardous drugs to individuals who are simply occupants in compounding rooms.

The air sampling data also suggest that during minor and/or large spills, there is a potential for inhalation exposure risk to volatile fractions of hazardous drugs inside the ventilated cabinets for both Class II A2 BSC and Class II B2 BSC. For this exposure risk to be realized, the compounding technicians would need to lift the ventilated cabinet sash and insert their face/breathing zone into the cabinet. This scenario could occur if a spill requires extensive cleaning of the interior surfaces of the cabinet. Thus, it is advised that detailed hazardous drugs spill clean-up procedures be developed to incorporate methods that limit workers placing their breathing zone across the plane of the BSC sash and/or providing them with skills and appropriate personal protective equipment under these conditions. This may be accomplished by keeping the sash height as low as possible during a spill clean-up, using extension wands for cleaning inside hoods, using respiratory protection with appropriate chemical and particulate filtration, using other protective garments such as gloves and disposable coveralls, and providing spill clean-up training for realistic and worst-case conditions.

It should be noted that the small study data set did not allow for robust statistical analysis of the results. Furthermore, many of the air sample results were non-detect, which also limited the comparative analysis across BSC types.

Based on the results of this study, further assessment is warranted to validate the conclusions of this study and/or provide additional insight. Recommendations for further study to evaluate the relative effectiveness of Class II A2 BSC as compared with Class II B2 BSC at controlling workplace exposures to select antineoplastic agents are as follows:

- Develop and/or validate a sampling and analytical method(s) for the volatile fraction of representative/common antineoplastic agents to evaluate potential exposure risk to compounding technicians during compounding activities.
- Alternatively, consider developing a sampling strategy to involve the use of a semi-volatile surrogate chemical during typical hazardous drug compounding activities.
- Perform additional sampling events to increase the data set so that robust statistical and comparative analysis of the results can be made. This should include additional sampling events at new sites and repeat sampling events at the

same sites.

- Perform sampling events at small metropolitan facilities and small rural facilities to document potential variations in procedures, equipment, and/or facilities.
- Further evaluate the relative volatile chemical properties of antineoplastic agents and how they are handled in Class II A2 BSC to screen their potential exposure risk.

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