PRACTICE RESEARCH REPORT

Evaluating Containment Effectiveness of A2 and B2 Biological Safety Cabinets

Authored by

Alex V. Taylor, B.S.
Chemical Engineering,
Technical Safety Services, LLC, Berkeley, CA.

Nicholas Baker,
Pharm.D., M.P.H,
Northern California Pharmacy Operations, Kaiser Permanente, Modesto, CA.

Morgan Hulsey, B.S.
Bioengineering,
Technical Safety Services, LLC, Berkeley, CA.

Corbin C. Bennett,
Pharm.D., M.P.H, National Pharmacy Services and Programs, Kaiser Permanente, Fresno, CA.

Matthew Meiners,
B.A. Chemistry,
Pharmaceutical Industrial Hygiene Laboratory, Maxxam Analytics, Lake Zurich, IL.

Ben A. Gonzales,
B.S., P.E., Technical Safety Services, LLC, Berkeley, CA.

Purpose This study investigates the use of a canopy-connected recirculating class II type A2 biological safety cabinet (BSC) as an alternative to the B2 when preparing volatile, sterile compounded preparations. Selection of the appropriate BSC for processes which use sub gram levels of volatile chemicals is difficult due to a lack of quantitative containment evidence by cabinet type. There is a perception that hazardous compounding must be done in a B2 cabinet due to the potential for vapors, and this study seeks to challenge that perception.

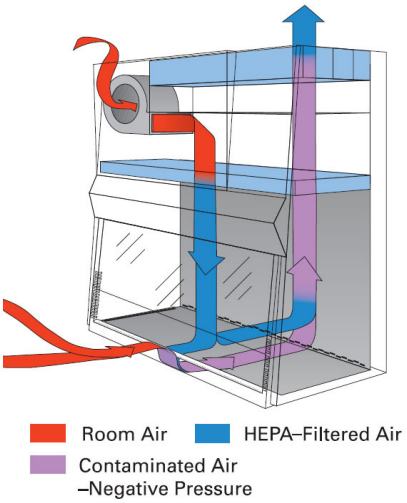
Methods In total, 5 tests, 3 prequalification tests and 2 containment capability tests, were conducted on a single cabinet of each type at sterile compounding pharmacies. Prequalification tests were performed to verify that each BSC was operating properly. Each cabinet was certified to NSFANSI 49–2016, particle counted per ISO 14644-1:1999, and subjected to a qualitative video smoke study. Once these tests confirmed the expected working conditions, 2 containment capability tests were conducted. The containment testing included tracer gas testing per ASHRAE 110:2016 section 8.1.1 through 8.1.13, and cyclophosphamide sampling during sterile compounding of the drug material.

Results Both cabinets passed all the prequalification tests. During the ASHRAE tracer gas testing the A2 cabinet was able to contain a tracer gas 92% to 160% as effectively as the B2 cabinet depending on the position of the gas ejection. During sterile compounding the airborne cyclophosphamide sampling captured samples of less than 1.0 ng at all locations for both the A2 and B2 cabinets.

Conclusion The data generated from this study demonstrate that use of an A2 for hazardous compounding can provide a comparable level of safety for the environment, users, and product while having less stringent airflow requirements relative to a B2.The simpler requirements for an A2 make them an appealing alternative as they have the potential to reduce the overall operating costs associated with a compounding pharmacy while maintaining safe levels of containment.

Keywords Biological safety cabinet, costs and cost analysis, cyclophosphamide, pharmacy, tracer gas testing.

Figure 1: *Airflow for B2 biological safety cabinet. Reproduced with permission from reference 1.*



Class II biological safety cabinets (BSCs) provide 3 levels of protection—for the compounder, for the compounded sterile preparations inside the work area of the cabinet, and for the environment or room that contains the cabinet. There are 2 common types of class II BSCs: a recirculating cabinet (A2) and a fully exhausted cabinet (B2). B2 cabinets use constant-volume exhaust from the facility as the only source of exhaust airflow. Supply air is provided by an internal blower that pulls air from the room, through the BSC supply high-efficiency particulate air (HEPA) filter, down into the work area. The supply blower will not turn on unless there is sufficient exhaust airflow,

meaning that the cabinet must be constantly supplied with sufficient exhaust to cover not only the inflow volume but also the supply airflow (downflow) volume. The airflow also must not be too high, or the balance between inflow and downflow can be disrupted. This leads to the need for very precise control of exhaust airflow for a B2 cabinet. **Figure 1** illustrates the airflow movement within a B2 BSC.[1] A 6-foot-wide B2, manufactured in 2017[a] and located at a Medical Center Ambulatory Care Pharmacy in Modesto, CA, was used for this study.

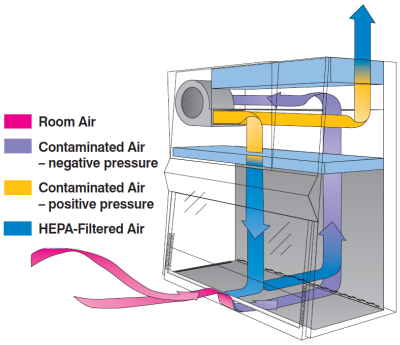
A2 cabinets do not require facility exhaust but when used for handling volatile or hazardous compounds must be ducted to a constant-volume facility exhaust source. A canopy connection, which is the gap in the ducting between the HEPA-filtered exhaust and the facility exhaust that draws in room air, is required on all ducted A2 cabinets. The canopy connection must exhaust enough air to keep the air gap under negative pressure. This makes providing facility airflow for the A2 a much simpler task compared with a B2. Supply and exhaust airflow for the cabinet are provided by an internal blower that pulls air from the room through air grilles on the front and rear of the work area and pushes it through a supply HEPA filter down into the work area. Roughly 70% of the air supplied by the internal blower is returned to the work area inside of the cabinet. The remaining 30% is exhausted from the cabinet through an exhaust HEPA filter, into the canopy connection, and through the associated facility exhaust. **Figure 2** illustrates the airflow movement within an A2 BSC.[1] A 4-footwide A2, manufactured in 1985[b] and located at a Medical Center Ambulatory Care Pharmacy in Sacramento, CA, was used for this study.

When dealing with vapors, volatile compounds, and other potentially gaseous work it has been recommended to use a B2 to ensure containment of gases and vapors that might be created within the BSC by compounding procedures.[2] B2 cabinets are typically used for this type of work as 100% of the airflow within the cabinet is directly and completely exhausted from the cabinet through the associated exhaust system. A2 cabinets recirculate 70% of the airflow within the cabinet, while directly exhausting only 30%. It is unknown if gases or vapors generated in the work

area of an A2 BSC are recirculated in the 70% of airflow that is sent back to the work area, which often results in a conservative decision to use a B2.

Key Points
• A canopy-connected A2 biological safety cabinet contained vapors and aerosols generated from hazardous sterile compounding as effectively as a B2 biological safety cabinet.
• A canopy-connected A2 biological safety cabinet contained gases generated during a tracer gas test as effectively as a B2 biological safety cabinet.
• A canopy-connected A2 biological safety cabinet is simpler to install and requires less facility exhaust airflow than a B2 biological safety cabinet, which can result in lower operating costs per cabinet.

Figure 2: *Airflow for A2 biological safety cabinet. Reproduced with permission from reference 1.*



The main operating cost for a BSC is the exhaust airflow. If the required amount of airflow is reduced, the operating costs will decrease. A typical 6-foot B2 cabinet exhausts approximately 1,969 m^3 of air per hour. A typical 4-foot B2 cabinet exhausts approximately 1,266 m^3 of air per hour. An alternate cabinet with lower exhaust airflow requirements that can demonstrably maintain the same level of containment would result in operational cost savings.

Canopy-connected A2 cabinets also require direct connection to a constantvolume facility exhaust source; however, A2 cabinets require significantly less facility exhaust due to their recirculating airflow design. The required exhaust airflow for a canopy-connected A2 is estimated to be as much as 47% less exhaust airflow than B2 cabinets (**Table 1**).[3] By one estimate of $2.65 annually for each cubic meter of air,[4] use of a canopy-connected 6-foot A2 cabinet provides savings of $2,772/yr comparedwith a 6-foot B2. A 4-foot A2 will provide savings of $1,776/yr versus a 4-foot B2. Additionally, A2 cabinets are less expensive to purchase than their B2 counterparts although the specific cost difference may depend upon contracted manufacturer pricing and cabinet options.

Another benefit of an A2 cabinet is that it is less complicated to provide facility exhaust to the cabinet. Due to the nature of the canopy connection, any excess exhaust airflow will be drawn from the room and will not affect the balance of the cabinet. Conversely, when dealing with a B2, the amount of exhaust airflow must be very precise as too much exhaust can throw off the balance between the supply and exhaust airflow. In some scenarios, this can lead to difficulty maintaining not only the proper air balance in the hood, but also the air balance in the pharmacy room itself.

The purpose of this study was to investigate the relative containment capabilities of A2 and B2 cabinets in pharmacy compounding, where hazards may exist in an aerosol and/or vapor state.

Methods

Study tests were designed and selected to verify proper operation of each BSC prior to assessing the containment capabilities of each unit.

The 3 preliminary, prequalification tests were adapted from standard BSC testing and certification practices, as typical for all pharmacy BSCs. Each cabinet was tested and certified to meet regulatory and manufacturer specifications outlined by the NSF-ANSI 49–2016 field certification standard[5] and ISO 14644- 1:1999 Class 5 criteria[6] and show appropriate airflow patterns in a qualitative airflow visualization study. Containment capability testing would not proceed unless all prequalification tests were conducted and produced acceptable results. Two tests were executed for evaluation of quantitative containment ability for gases, vapors, and aerosols in each cabinet. In the first test, an American Society of Heating, Refrigerating and Air-Conditioning Engineers (ASHRAE) standard 110:2016 tracer gas study was executed in each cabinet to ensure comparable containment capabilities for highly vaporous and gaseous compounds.[7] In the second test, dynamic personal sampling was conducted during cyclophosphamide compounding.

The tracer gas study demonstrates an extreme scenario where nitrous oxide, with many orders of magnitude greater vapor pressure than

Table 1: *Selected Properties of Biological Safety Cabinets*

Cabinet Type	Exhaust Required (m^3/hr)	Annual Operating Cost ($)[4]
4-ft A2	596	1,579.40
A-ft B2	1,266	3,354.90
6-ft A2	923	2,445.95
6-ft B2	1,969	5,217.85

typical compounding materials, is introduced into the cabinet at a high flow rate. Low-volume, low-vapor producing compounds, as typically used, would then be contained at least as well as the high-volume, pure gas. It should be noted that the vapor pressure of nitrous oxide (5.2 × 106 Pa) is approximately 1.58 billion times greater than that for cyclophosphamide (0.0033 Pa),[8,9] and that this test far exceeds any vapor containment conditions that would normally be encountered in a typical sterile compounding pharmacy. **Table 2** depicts vapor pressures of common compounds, as well as the compounds and gases used in this study.[8-11]

Cyclophosphamide was selected for use in this study due to its high vapor pressure relative to other compounds used in compounding,[9] the ability to detect it at 1-ng levels, and its availability at the facilities to be used for the study. Cyclophosphamide's high vapor pressure relative to other commonly compounded hazardous drugs presented a worst-case scenario for possible vapor production in addition to aerosols during compounding. A dynamic cyclophosphamide study was performed in each cabinet using a negative-pressure compounding technique in the absence of a closed-system transfer device to simulate real world conditions. The purpose of this test was to evaluate if any cyclophosphamide was able to escape the cabinet, and at what levels it might be present in the work zone during compounding. Three locations for cyclophosphamide vapors and aerosols were monitored during the simulation. Two of the locations were in the cabinet work area, and one was on the compounder outside of the cabinet. Surface samples were also collected at 5 locations within the cabinet. These surface samples were intended to verify the presence of cyclophosphamide in each cabinet work area after the compounding procedures concluded. Negative controls prior to the testing were used at all vapor, aerosol, and surface sampling locations to establish a baseline level of cyclophosphamide in each cabinet prior to the testing activity. Any surface or air sample that collected the same amount of or less cyclophosphamide than its corresponding negative control was determined to be a zero result. Positive controls were also employed to verify cyclophosphamide would be captured and retained on the sampling media through the duration of the test. Previously published studies using cyclophosphamide have been unable to recover or verify the presence of significant levels of cyclophosphamide.[12] The positive controls also provided a recovery rate for each sampling method. Cyclophosphamide samples, including controls, were collected using both filters for aerosols, as well as sorbent tubes for vapors, in parallel. Collected samples were submitted to a laboratory where they were analyzed with a reporting limit of 1 ng/sample. Temperature and humidity were logged during all sampling to verify the environmental conditions had no adverse effects.

Prequalification field tests.

NSF 49 certification. *Methods*. Tests were conducted per NSF-ANSI49–2016 field certification standard. The field certification used a hot-wire thermoanemometer to verify that the inflow and downflow speeds of the cabinet were operating within manufacturer's and regulatory specifications. The certification uses a polyalphaolefin generator and an aerosol photometer to verify the filter integrity of not only the supply HEPA filter, but also the exhaust HEPA filter. Additionally, site assessments were performed as part of the verification, including assessment of the interlock on the B2 and the exhaust alarm on the canopy- connected A2. Both of these assessments ensure proper exhaust airflow is provided by the facility exhaust system for each cabinet.

Table 2: *Vapor Pressures of Various Compounds*

Compound	Vapor Pressure
Fluorouracil[9]	0.0014 Pa
Etoposide[9]	0.0026 Pa
Cyclophosphamide[9]	0.0033 Pa
Water[10]	2,400 Pa
Isopropryl alcohol[10]	4,400 Pa
Acetone[10]	30,000 Pa
Nitrous oxide gas[8]	5,200,000 Pa
Carbon dioxide gas[11]	5,730,000 Pa

Results and discussion. Both cabinets passed the NSF 49–2016 certification. All HEPA filters were found to have no leaks, rips, or tears. Both cabinets had average inflow face velocities of 100–110 ft/min (FPM). Each cabinet also had appropriate average supply air flow as specified by their manufacturers (55–65 FPM for the B2, and 50–130 FPM for the A2, which has 3 different velocity zones). The interlock worked appropriately on the B2, and the exhaust alarm worked appropriately for the A2.

I**SO 14644-1:1999 particle counting.** *Methods.* A dual channel particle counter with fractionation points of 0.5- and 5.0-µm particles/m3 of air was used at 3 locations within each cabinet's work area (left, center, and right). Readings were collected over 60 seconds to determine the total quantity of particles of each size in each location. The flow rate of the particle counter was 75 L/min of air for the B2 samples and 50 L/min for the A2 samples. Both flowrates result in a large enough sample volume to determine ISO Class 5 cleanliness. ISO Class 5 requires an area to have less than or equal to 3,520 particles sized 0.5 µm or larger, and ≤29 particles sized ≥5 µm.[6]

Results and discussion. Both cabinets passed the particle-counting test with no particles of either size present at all locations.

Airflow visualization. *Methods.* A glycol-based aerosol was introduced into each cabinet using a portable fog machine[c]. The aerosol provides a visualization of the airflow, and the path that a potentially hazardous vapor or aerosol would follow. Each cabinet must maintain laminar flow with no swirling or refluxing, demonstrate a split across the work area into the front and back air grilles, and not allow aerosol to escape the cabinet or reflux back into the work area. These qualitative studies were filmed, and the footage was analyzed to verify the results.

Results and discussion. The results are nearly indistinguishable between the 2 types of cabinet. Both cabinets maintained laminar flow and did not show any swirling or refluxing of the aerosol. Both cabinets had a visual airflow split between the front and rear air grilles. Aerosol did not escape from either cabinet. Both cabinets passed this qualitative test.

Containment capability field tests. ASHRAE 110:2016 tracer gas testing. *Methods.* A mannequin was used to simulate the presence of a compounder. The mannequin was held upright by a base with a rod that connected into one of its legs. The mannequin had tubing through its mouth that led back to a gas detector.[d] The gas detector had a minimum detection limit of 0.03 ppm of nitrous oxide according to the manufacturer but was found to be able to achieve 0.01 ppm while stationary in a separate study.[13] The gas detector was connected to a digital input voltage datalogger,[e] which recorded the output as ppm values in a spreadsheet on a connected laptop computer. A nitrogen gas cylinder, a nitrous oxide gas cylinder, a gas ejector, and appropriate regulators and flowmeters for each cylinder were also used. A syringe was used to capture nitrous oxide from the ejector before it mixed with air and transfer it to the gas detector for calibration of the gas sensor.

The gas detector was first calibrated using the calibration procedure described in the manual. The procedures used were from ASHRAE 110: 2016 Section 8.1. It should be noted that the ASHRAE test procedures are intended for fume hoods, which do not have any downward airflow. The only deviation from the procedures was that the gas ejector was placed along the centerline of the work area of each cabinet, which is about 30 cm from the face of the cabinet instead of the 15 cm recommended in Section 8.1.4.2. This was done to better simulate where vapors would be generated during compounding. A tracer gas study was performed at 3 locations for each cabinet: 15 cm from the left side of the work area, the geometric center of the work area, and 15 cm from the right side of the work area, with the ejector and mannequin moving with each change in sampling location. The gas ejector was always inside the cabinet on the centerline of the work area, and the mannequin was always lined up with the ejector, but outside the cabinet with the breathing zone approximately 56 cm above the work surface, and 8 cm back from the glass sash. It should be noted that the A2 was positioned for a standing compounder, and the B2 was positioned for a sitting compounder. The mannequin was put on the lowest height setting but was still higher above the work surface for the B2 than the A2.

The tracer gas study used ejection points on the left, center, and right side of the work area within each cabinet with nitrous oxide as the

tracer gas.[13] ASHRAE does not specify acceptance criteria for acceptable exposure levels, but a similar study performed by Thermo Fisher used an acceptance criteria of less than 100 ppm.[3] In addition to this threshold, a performance factor was calculated for each cabinet that compared the gas levels at the mannequin outside of the cabinet with those inside the cabinet. The levels inside the cabinet were calculated using the gas ejection rate (5 L/min) and the total airflow through each cabinet. After the tracer gas testing concluded, the cabinets were decontaminated, cleaned, and disinfected prior to the dynamic compounding portion of the study.

Results and discussion. The graphs generated by the tracer gas testing can be seen in **Figure 3** (B2) and **Figure 4** (A2). The ASHRAE rating for each position is defined as the maximum ppm that resulted from each positional test. The left side ratings were 0.17 ppm for the B2 and 0.12 ppm for the A2. The center ratings were 0.20 ppm for the B2 and 0.26 ppm for the A2. The right side ratings for both cabinets were 0.13 ppm. All of these values are below the 100 ppm threshold established in the Thermo Fisher paper.[3] In order to account for the size difference between the cabinets a performance factor was calculated.

The performance factor measures the gas level inside the cabinet versus that outside the cabinet at the mannequin. A higher number reflects better containment. This performance factor helps account for the size difference between the 2 cabinets. The ppm inside the cabinet was calculated by dividing the flow rate of the gas from the ejector (5 L/min) by the total airflow volume through each cabinet (30,400 L/min for the B2, and 25,400 L/min for the A2). This yields an internal factor of 164.3 ppm for the B2 and 196.8 ppm for the A2. **Table 3** summarizes the tracer gas test results and the associated performance factors. Using the performance factor, the A2 has 160% of the containment on the left side, 92% of the containment in the center, and 120% of the containment on the right side as compared with the B2. Based on these performance factors, the A2 has comparable containment capabilities to the B2. It also does not appear that the recirculating airflow of the A2 caused any reentrainment that significantly affected its containment capabilities.

Dynamic cyclophosphamide sampling.

Methods. Seven total sorbent tubes[f] tubes were used for vapor collection in each cabinet, comprised of 3 dynamic samples,[3] negative controls, and 1 positive control. A total of 7Teflon cassettes[g] were used for aerosol collection, comprised of 3 dynamic samples, 3 negative controls, and 1 positive control. A total of 6 personal sampling pumps[h] were used, with 3 at speeds of 1 L/min for vapor capture and 3 at speeds of 2 L/min for aerosol capture. Two ring stands with clamps were used to hold the sampling media in the cabinets in place for the duration of the sampling. There was 1 surface sampling kiti per cabinet—each with 10 swab samples, comprised of 5 postcompounding samples and 5 postcleaning negative controls. All cyclophosphamide samples were stored in a cooler with several ice packs before and after the

Figure 3: *Tracer-gas graph for the B2 biological safety cabinet using American Society of Heating, Refrigerating and Air-Conditioning Engineers standard 110:2016.7*

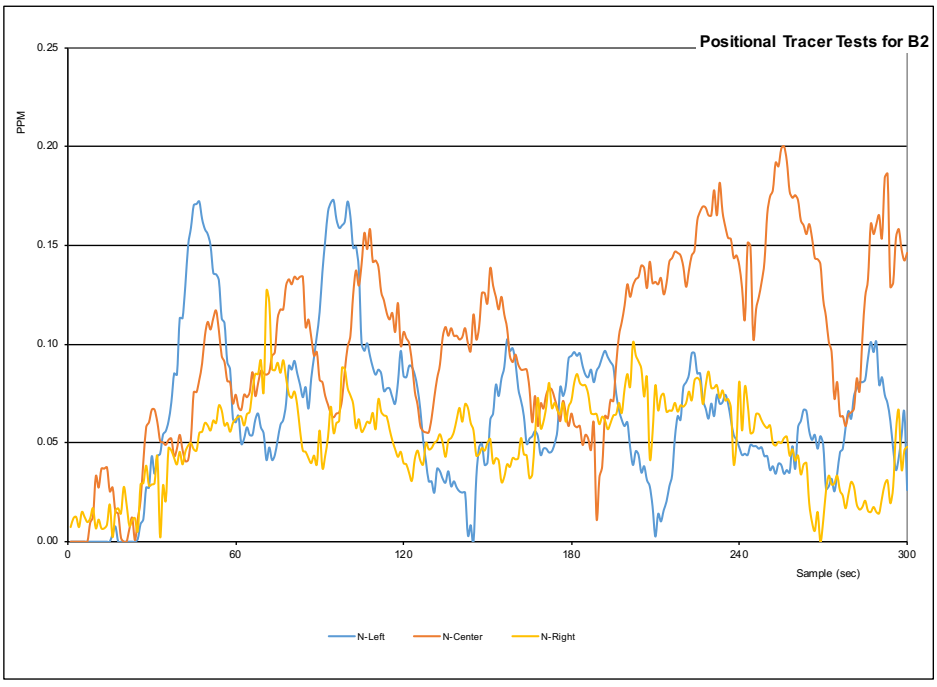


Table 3: *Parts-per-Million Ratings and Performance Factor Results*

Cabinet Work Area and Cabinet Type						
	Left		Center		Right	
Variable	B2	A2	B2	A2	B2	A2
ppm[a] rating	0.17	0.12	0.20	0.26	0.13	0.13
performance factor	1,027	1,640[b]	821	757[c]	1,264	1,514[d]

[a]ppm= part-per-million.
[b]Performance factor for A2 cabinet was 160% that of the B2 cabinet.
[c]Performance factor for A2 cabinet was 92% that of the B2 cabinet.
[d]Performance factor for A2 cabinet was 120% that of the B2 cabinet.

sampling, and positive controls were stored in a freezer after preparation and prior to field use. A temperature and humidity datalogger[j] was used to log the temperature and humidity in the work area of the cabinet.

The dynamic cyclophosphamide test uses 6 samples at 3 locations for each cabinet, designed to capture both vapors and aerosols released during compounding using cyclophosphamide. The 3 locations are (1) at the rear of the cabinet near the air intake grille, (2) at the centerline of the cabinet near the compounding area, and (3) in the compounder's breathing zone. Sampling near the rear of the cabinet (location 1) captured cyclophosphamide that was generated during compounding and pulled from the work zone to the rear grille. Sampling near the centerline (location 2) in the work area captured cyclophosphamide that was generated from compounding and also captured any cyclophosphamide that was recirculated through the A2 cabinet. Sampling near the compounder's breathing zone (location 3) captured cyclophosphamide that possibly escaped the cabinet and presented a potential inhalation exposure to the compounder. Each sample location had 2 pump connections for collection of aerosol and vapor in parallel. One pump was connected to a tube for vapor capture, and the other pump was connected to a cassette for aerosol capture. Five surface samples were collected in each hood using sampling kits and following the manufacturer's sampling instruction.[14]

The surface sample locations were located at the front (F), back (B), left (L), right (R), and center (C) of the work area.

Prior to any sampling, the cabinets were decontaminated, cleaned, and disinfected per facility procedures. Negative controls were collected after this process concluded. Negative controls for vapor and aerosols were placed in the same locations used for the dynamic sampling, and were connected to the same pumps, which ran for 25 minutes prior to any compounding taking place.

The pumps were run for the duration of the sampling and were connected to an aerosol capture cassette and a vapor capture tube, collected in parallel, at each location. The

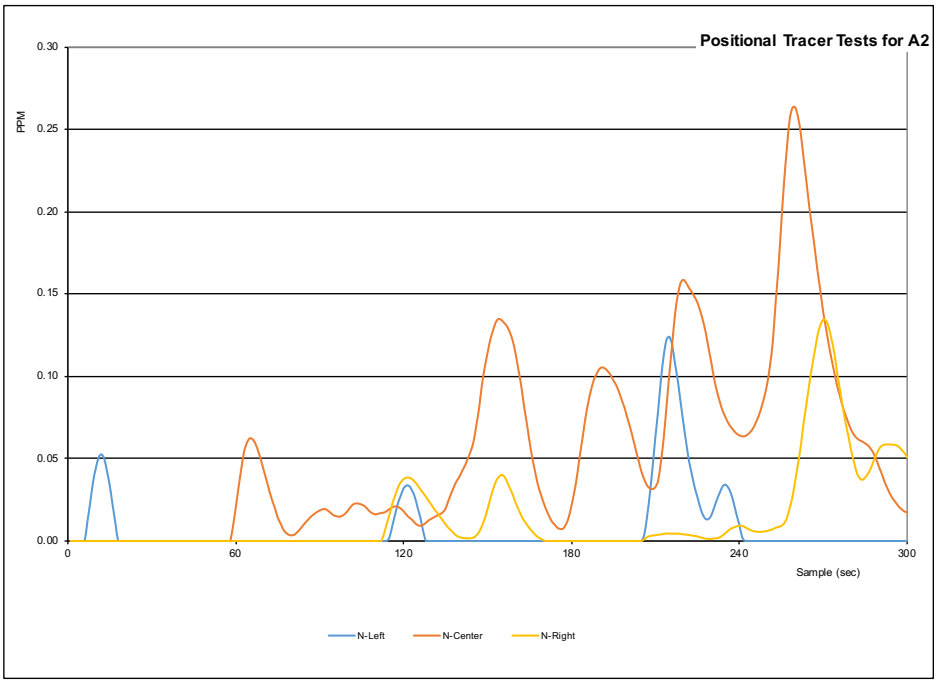


Figure 4: *Tracer-gas graph for the A2 biological safety cabinet using American Society of Heating, Refrigerating and Air-Conditioning Engineers standard 110:2016.7*

dynamic compounding took place for 35 minutes for the B2 cabinet and 41 minutes for the A2 cabinet. During the compounding in the A2 a small amount of cyclophosphamide solution (1–2 mL) was spilled on the work surface. Once compounding was completed another round of surface samples were collected using the same sample locations as the negative controls.

After the dynamic samples were taken, the positive controls were sampled. Before sampling, 1 tube and 1 cassette for each study were spiked with a known quantity of cyclophosphamide. These spiked samples were connected to the pumps at location 2 for 25 minutes. All cyclophosphamide samples were sent to a lab for analysis. Analysis of both air and surface samples for cyclophosphamide was performed by LC/MS/MS multiple reaction monitoring (MRM) with external calibration, employing isotopic cyclophosphamide as an internal standard. The temperature and humidity were logged for the duration of all sampling to rule out the possibility of room conditions impacting the sampling.

Results and discussion. **Tables 4–6** summarize the results of the surface and air sampling. With the exception of positive controls, all vapor and aerosol samples submitted to the lab were found to have collected less than 1 ng of cyclophosphamide. This included the negative controls as well as the dynamic samples, which indicates that all locations captured negligible amounts of airborne cyclophosphamide. Both cabinets were able to limit the airborne cyclophosphamide levels both inside and outside of the cabinets.

With the exception of negative controls, all surface swab samples collected inside each of the evaluated cabinets following compounding were positive for cyclophosphamide. The surface samples returned a higher amount of cyclophosphamide for the A2 (100,200 ng) than the B2 (2,879 ng), attributed to a small spill that occurred and was recorded during compounding.

Results for the B2 positive air sampling controls were 59.2% cyclophosphamide recovery of the reference quantity from the vapor tube, and 82.2% recovery of the cyclophosphamide from the aerosol cassette. Results for the A2 air sampling positive controls were 93.2% cyclophosphamide recovery from the vapor tubes, and 86.0% of the cyclophosphamide from the aerosol cassettes. The low recovery rate for the B2 vapor tubes indicates that the samples may have warmed at some point between removal from the freezer, use in the field, and shipment to the lab. All other positive controls retained greater than 80% of their reference level of cyclophosphamide. The recovery data of the positive controls indicates that the majority of the cyclophosphamide that was captured in the tubes and cassettes was successfully recovered.

The temperature and humidity for the sampling remained consistent within each work area, and it is unlikely that the environmental conditions affected the sampling.

Table 4: *Cyclophosphamide Sampling Results in B2 and A2 Cabinets*

	B2 Cabinet		A2 Cabinet	
Sample	**Total ng**	**Reported ng**	**Total ng**	**Reported ng**
Tube 1	0.482	<1.0	0.308	<1.0
Tube 2	0.0328	<1.0	0.01428	<1.0
Tube 3	0.056	<1.0	0.0336	<1.0
Cassette 1	0.1	<1.0	0.1034	<1.0
Cassette 2	0.0656	<1.0	0.01156	<1.0
Cassette 3	0.0814	<1.0	0.0386	<1.0
Back Surface	147.8	147.8	42.6	42.6
Center Surface	340	340	100,200	100,200
Front Surface	504	504	4,960	4,960
Left Surface	488	488	3,120	3,120
Right Surface	2,880	2,880	15,340	15,340

Discussion and conclusion

The results of testing presented in this study indicate that a canopy-connected A2 BSC is a viable alternative to a B2 BSC for use in compounding pharmacies. The overall results of the study for each cabinet can be seen in **Table 7.** The 3 prequalification tests, NSF certification, ISO particle counting, and qualitative airflow visualization, were passed by each cabinet, indicating they were operating within specification. The ASHRAE gas testing, which far exceeds any vapor containment conditions encountered in pharmacy sterile compounding, yielded similar results for each cabinet, with the A2 performing anywhere from 92% to 160% as well as the B2. The cyclophosphamide sampling showed that both types of cabinet were able to prevent any measurable airborne cyclophosphamide from reaching the compounder, and surface swab results demonstrated that cyclophosphamide was present and controlled within the cabinets. Both containment capability tests demonstrated equivalent results between the 2 cabinets. The A2 cabinet was 30 years older, had a smaller work area, had a spill during the compounding, and still delivered equivalent containment compared to the B2. It can be concluded that the canopy-connected A2 is a viable cabinet to consider when working with volatile compounding materials, with the added benefit of less complex airflow requirements and a potential for up to 50% less exhaust airflow cost per cabinet, as compared to its B2 counterpart.

It should be noted that this study was performed on only a single cabinet of each type, and further testing may be warranted to come to a definitive conclusion. It should also be noted that the choice of cabinet is only one of many factors that contribute facility should consider their own risk assessment and training programs when selecting a cabinet.

Table 5: *Negative Control Sampling Results in B2 and A2 Cabinets*

	B2 Cabinet		A2 Cabinet	
Sample	**Total ng**	**Reported ng**	**Total ng**	**Reported ng**
Tube 1	0.0992	<1.0	0.01928	<1.0
Tube 2	0.0662	<1.0	0.01588	<1.0
Tube 3	0.069	<1.0	0.1032	<1.0
Cassette 1	0.056	<1.0	0.073	<1.0
Cassette 2	0.0384	<1.0	0.0504	<1.0
Cassette 3	0.0284	<1.0	0.204	<1.0
Back Surface	4.34	4.34	0.978	<1.0
Center Surface	0.908	<1.0	0.952	<1.0
Front Surface	0.502	<1.0	0.508	<1.0
Left Surface	0.952	<1.0	0.824	<1.0
Right Surface	0.274	<1.0	0.156	<1.0

Table 6: *Positive Control Sampling Results in B2 and A2 Cabinets*

Sample	B2 Cabinet (% Recovery)	A2 Cabinet (% Recovery)
Positive control tube	59.2	93.2
Positive control cassette	82.2	86.0

Table 7: *Overall Test Results in B2 and A2 Cabinets*

Test	B2 Cabinet	A2 Cabinet
Prequalification field tests		
NSF 49 certification	Pass	Pass
ISO 5 particulate level	Pass	Pass
Airflow visualization	Pass	Pass
Tracer gas testing		
Left ppm[a] rating	0.17	0.12
Center ppm rating	0.20	0.26
Right ppm rating	0.13	0.13
Dynamic cyclophosphamide sampling		
Vapor	<1.0 ng	<1.0 ng
Aerosol	<1.0 ng	<1.0 ng
Maximum surface value (location)	2,880 ng (right)	10,200 ng (center)

[a]*ppm= part-per-million.*

Disclosures

The authors have declared no potential conflicts of interest.

Footnotes

[a]NU-430-600, NuAire, Plymouth, MN, USA.
[b]VBM-400, The Baker Company, Sanford, ME, USA.
[c]M-1 Mobile Fogger, Antari, Taoyun City 338, Taiwan.
[d]MIRAN SapphIRe Portable Ambient Analyzers, Thermo Fisher Scientific, Waltham, MA, USA.
[e]DI-245, DATAQ Instruments, Akron, OH, USA.
[f]Anasorb 708 Sorbent Tube, Maxxam Analytics, Lake Zurich, IL, USA.
[g]TFE-3A 25 mm 1 micron PTFE filter, Maxxam Analytics, Lake Zurich, IL, USA.
[h]Libra Pump L-4 with 120 VAC Charger, A.P. Buck Inc., Orlando, FL, USA.
[i]ChemoAlert(TM), Maxxam Analytics, Lake Zurich, IL, USA.
[j]MPRF Humidity Data Logger, Mesa Labs, Lakewood, CO, USA.

References

1. The Baker Company. Types of class II biosafety cabinets, 2012. http://www.aroundlabnews.com/en/wp-content/ uploads/2013/11/type-ii-biosafetycabinet-overview.pdf (accessed 2019 Mar 11).

2. U.S. Department of Health and Human Services. Primary containment for biohazards: selection, installation and use of biological safety cabinets, 2nd ed. Washington, DC: U.S. Government Printing Office; 2000:14-5.

3. Thermo Fisher Scientific. White paper on the containment of gases in Class II biological safety cabinets. Arnold, MD; 2007

4. Mills E, Sartor D. Energy use and savings potential for laboratory fume hoods. Energy. 2005; 30:1859-64.

5. NSF International Sanitation Foundation/ American National Standards. NSF/ ANSI 49-2016 Annex E. Biosafety cabinetry: design, construction, performance, and field certification. https://www.nsf.org/ newsroom_pdf/NSF_49-2016_Annex_E. pdf (accessed 2019 Mar 13).

6. International Organization for Standardization (ISO).International Standard 14644-1:1999. Cleanrooms and associated controlled environments – Part 1: classification of air cleanliness.Geneva, Switzerland; 1999. https://www.iso.org/standard/25052.html

7. American Society of Heating Refrigerating and Air Conditioning Engineers (ASHRAE). ANSI/ASHRAE standard 110–2016, methods of testing performance of laboratory fume hoods, (2016). https://webstore. ansi.org/Standards/ASHRAE/ANSIASHRAEStandard1102016 (accessed date 2019 Mar 13).

8. Cameo chemicals. Chemical datasheet: nitrous oxide. https://cameochemicals.noaa.gov/report?key=CH8909 (accessed 2018 Feb 15).

9. Kiffmeyer T, Kube C, Opiolka S et al. Vapour pressures, evaporation behaviour and airborne concentrations of hazardous drugs: implications for occupational safety. Pharm. J. 2002; 268:331-7.

10. Engineering ToolBox. Vapor pressure common liquids (2006). https://www.engineeringtoolbox.com/vapor-pressure-d_312.html (accessed 2018 Feb 27).

11. Dortmund Data Bank. Vapor pressure of carbon dioxide. http://www.ddbst. com/en/EEDPCP/VAP_C1050.php (accessed 2018 Mar 05).

12. Sessink PJM, Trahan J, Coyne JW.Reduction in surface contaminationwith cyclophosphamide in 30 US hospital pharmacies following implementation of a closed-system drug transfer device. Hosp Pharm. 2013; 48:204-12.

13. Burke M, Wong L, Gonzales BA et al. Nitrous oxide as a tracer gas in the ASHRAE 110–1995 atandard. J Occup Environ Hyg. 2014; 11:32-9.

14. Maxxam Analytics. ChemoAlert sampling instructions. https://www.maxxamlabs.com/resource/chemoalert-usp-800-hd-surface-wipesampling-instructions/ (accessed 2017 Dec 01).