

**Validation of SKC Cat. No. 575-002 Diffusive Sampler for  
Monitoring Halogenated Anesthetic Gases in Workplace Air  
(Isoflurane, Halothane, Desflurane, Enflurane,  
and Sevoflurane)**

## Research Report

### **Validation of SKC Cat. No. 575-002 Diffusive Sampler for Monitoring Halogenated Anesthetic Gases in Workplace Air (Isoflurane, Halothane, Desflurane, Enflurane, and Sevoflurane)**

#### ***Abstract***

The SKC Cat. No. 575-002 diffusive sampler was validated for sampling the halogenated anesthetic gases isoflurane, halothane, desflurane, enflurane, and sevoflurane. This diffusive sampler, which contains 500 mg of Anasorb<sup>®</sup> 747, was fully validated for isoflurane and halothane; and partially validated for desflurane, enflurane, and sevoflurane.

Desorption efficiency (DE) studies were performed at 0.1 to 2 times the in-house threshold limit value (TLV) of 75 ppm for isoflurane, 0.1 to 3 times the American Conference of Governmental Industrial Hygienists (ACGIH) TLV of 50 ppm for halothane, and 0.1 to 2 times the National Institute of Occupational Health and Safety (NIOSH) recommended exposure limit (REL) of 2 ppm (with a 60-minute ceiling) for desflurane, enflurane, and sevoflurane. The DE results were: isoflurane, 96% with a relative standard deviation (RSD) of 4.1%; halothane, 99.9% with an RSD of 1.6%; desflurane, 94.3% with an RSD of 6.9%; enflurane, 101% with an RSD of 3.6%; and sevoflurane, 100% with an RSD of 5.8%.

The sampling rates were determined at 2 to 150 ppm for isoflurane and 2 to 100 ppm for halothane for 15 minutes to 8 hours and 2 to 4 ppm for desflurane, enflurane, and sevoflurane for 30 minutes to 4 hours. All were determined at 20 to 80% relative humidity (RH) and 22 to 40 C. The average sampling rates were: isoflurane, 13.2 ml/min (RSD 10%); halothane, 14.1 ml/min (RSD 8.4%); desflurane, 13.8 ml/min (RSD 5.8%); enflurane, 13.8 ml/min (RSD 6.8%); and sevoflurane, 12.8 ml/min (RSD 5.6%).

The five halogenated anesthetic gases showed less than a 7% loss in recovery when stored for 3 weeks at ambient and freezer (< 4 C) temperatures. There were no reverse diffusion effects. The diffusive sampler was desorbed in 2 ml of carbon disulfide and analyzed by gas chromatography (GC) with a flame ionization detector (FID). The Minimum Reporting Limits (MRLs) for these halogenated gases are about 0.1 ppm for an 8-hour sample and about 0.8 ppm for a 1-hour sample.

#### **Author**

Cynthia Kuhlman

Validation date: May 2015

**SKC, Inc.**  
**863 Valley View Road**  
**Eighty Four, PA 15330**

## ***Introduction***

The halogenated anesthetic gases isoflurane, halothane, desflurane, enflurane, and sevoflurane are colorless, nonflammable liquids that are vaporized for use in operating rooms and dental operatories. (Isoflurane and sevoflurane are also used in veterinary facilities.) Workplace exposure can occur during manufacturing or when these gases escape from components of the anesthetic delivery system, valves left open after use, liquid anesthetic spills, and patients in the post-anesthesia care unit.<sup>1,2</sup>

Isoflurane, halothane, desflurane, enflurane, and sevoflurane have a slight or sweetish odor, depending on the particular gas. They may irritate the skin and eyes, cause serious eye damage, irritate the respiratory tract, damage fertility or the unborn child, and be harmful if swallowed or absorbed through the skin.<sup>3,4,5,6,7</sup> Symptoms of inhalation include headaches, dizziness, drowsiness, unconsciousness, liver damage, and death.<sup>3,4,5,6,7,8,9,10,11,12</sup>

For a specific example, isoflurane, a halogenated ether used for inhalation anesthesia<sup>8</sup>, may cause significant neurodegeneration in infants and young children and postoperative cognitive dysfunction in the elderly.<sup>13,14</sup>

This study was conducted to determine if the SKC Cat. No. 575-002 diffusive sampler is suitable for sampling the above halogenated anesthetic gases in workplace air. Critical parameters included analytical recovery, sampling rate and capacity, storage, and reverse diffusion.

## ***Experimental***

Isoflurane and halothane (Sigma-Aldrich, St. Louis, MO) and desflurane, enflurane, and sevoflurane (U.S. Pharmacopeia, Rockville, MD) were used to prepare concentrations in the atmospheric chamber. A dynamic atmosphere was generated using a syringe pump and filtered air streams to make the concentration. The atmosphere was fed into an exposure chamber. SKC Cat. No. 575-002 diffusive samplers were used for this study. They were exposed on a rotating bracket inside the chamber to simulate wind velocity. The test system is shown in Figure 1. The sampling rate study was conducted at 2 to 150 ppm for isoflurane and 2 to 100 ppm for halothane for 15 minutes to 8 hours at 20 to 80% RH and 22 to 40 C; and 2 to 4 ppm for desflurane, enflurane, and sevoflurane for 30 minutes to 4 hours at 20 to 80% RH and 22 to 40 C. The concentrations within the atmospheric chamber were verified with SKC Cat. No. 226-81A sorbent tubes.

Desorption efficiency (DE) studies were performed at 0.1 to 2 times the in-house TLV of 75 ppm for isoflurane; 0.1 to 3 times the ACGIH TLV of 50 ppm for halothane; and 0.1 to 2 times the NIOSH REL of 2 ppm (with a 60-minute ceiling) for desflurane, enflurane, and sevoflurane.

In the storage study, 28 samplers were injected with known amounts of isoflurane, halothane, desflurane, enflurane, and sevoflurane. After exposure, samplers were sealed until analysis. Four samplers were analyzed for a Day 0 while 12 samplers were stored at ambient temperatures (22 C) and the remaining 12 samplers were stored in a freezer (< 4 C). Four samplers each from the ambient and freezer lots were analyzed each week for 3 weeks to determine analytical recovery.

In the reverse diffusion study, 8 samplers were exposed to a known concentration of each halogenated anesthetic gas for 1 to 2 hours. Afterwards, 4 of the samplers were removed and capped and the remaining 4 samplers were exposed to 0 ppm for 6 hours.

All diffusive samplers were desorbed in 2 ml of carbon disulfide and shaken on a flatbed shaker for 15 minutes. The extracts were then analyzed by GC with FID. A chromatogram is shown in Figure 2.

Because SKC constantly reviews this data and conducts experiments to provide the most precise sampling rate, the rates published in this validation report are correct.

## ***Results and Discussion***

The DE study results are shown in Table 1. The mean recovery of the diffusive sampler for each gas is listed below:

- Isoflurane: 96% with an RSD of 4.1%
- Halothane: 99.9% with an RSD of 1.6%
- Desflurane: 94.3% with an RSD of 6.9%
- Enflurane: 101% with an RSD of 3.6%
- Sevoflurane: 100% with an RSD of 5.8%

The sampling rate data are shown in Table 2. The results indicate that these five halogenated anesthetic gases can be sampled with the Cat. No. 575-002 diffusive sampler at the following average sampling rates:

- Isoflurane: 13.2 ml/min with an RSD of 10%
- Halothane: 14.1 ml/min with an RSD of 8.4%
- Desflurane: 13.8 ml/min with an RSD of 5.8%
- Enflurane: 13.8 ml/min with an RSD of 6.8%
- Sevoflurane: 12.8 ml/min with an RSD of 5.6%

The data indicate that the diffusive sampler can collect a 15-minute to 8-hour sample of isoflurane at 2 to 150 ppm and of halothane at 2 to 100 ppm; and a 30-minute to 4-hour sample of desflurane, enflurane, and sevoflurane at 2 to 4 ppm. Table 3 shows the MRL for each compound.

The results of the storage studies, shown in Table 4, indicate that samples can be stored for up to 3 weeks at either ambient (22 C) or freezer (< 4 C) temperatures with less than 5% sample loss for isoflurane and halothane and with less than 7% sample loss for desflurane, enflurane, and sevoflurane.

As shown in Table 5, reverse diffusion does not take place with any of these compounds.

## ***Conclusion***

The SKC Cat. No. 575-002 diffusive sampler was validated for sampling the halogenated anesthetic gases isoflurane, halothane, desflurane, enflurane, and sevoflurane in workplace air. The sampler was fully validated for isoflurane and halothane and partially validated for desflurane, enflurane, and sevoflurane. DE, sampling rate, storage, and reverse diffusion studies were performed.

The mean recovery of the diffusive sampler for each gas was:

- Isoflurane: 96% with an RSD of 4.1%
- Halothane: 99.9% with an RSD of 1.6%
- Desflurane: 94.3% with an RSD of 6.9%
- Enflurane: 101% with an RSD of 3.6%
- Sevoflurane: 100% with an RSD of 5.8%

The diffusive sampler can collect a 15-minute to 8-hour sample of isoflurane at 2 to 150 ppm and of halothane at 2 to 100 ppm; and a 30-minute to 4-hour sample of desflurane, enflurane, and sevoflurane at 2 to 4 ppm. The MRLs for these halogenated gases are about 0.1 ppm for an 8-hour sample and about 0.8 ppm for a 1-hour sample. The average sampling rates were:

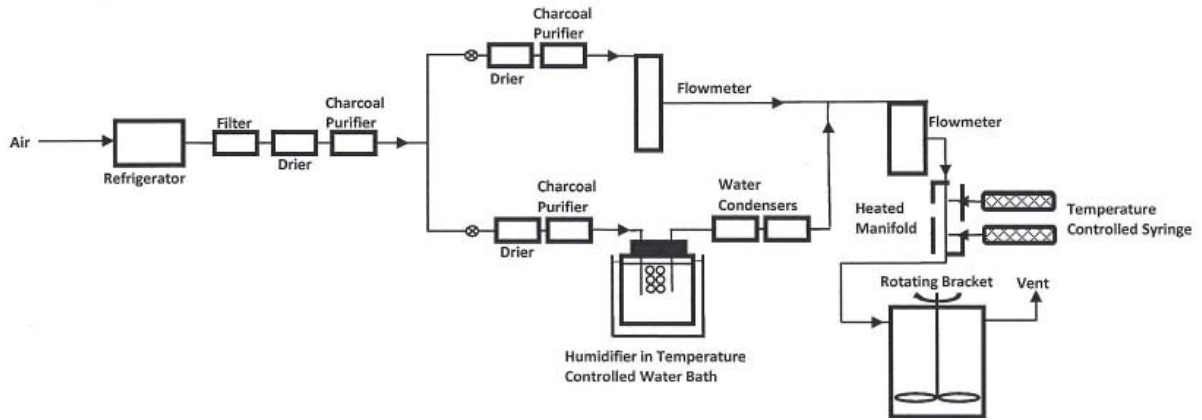
- Isoflurane: 13.2 ml/min with an RSD of 10%
- Halothane: 14.1 ml/min with an RSD of 8.4%
- Desflurane: 13.8 ml/min with an RSD of 5.8%
- Enflurane: 13.8 ml/min with an RSD of 6.8%
- Sevoflurane: 12.8 ml/min with an RSD of 5.6%

Samples of isoflurane, halothane, desflurane, enflurane, and sevoflurane can be stored for up to 3 weeks at either ambient (22 C) or freezer (< 4 C) temperatures with less than 5% sample loss for isoflurane and halothane and less than 8% sample loss for desflurane, enflurane, and sevoflurane. Reverse diffusion does not take place with any of these compounds.

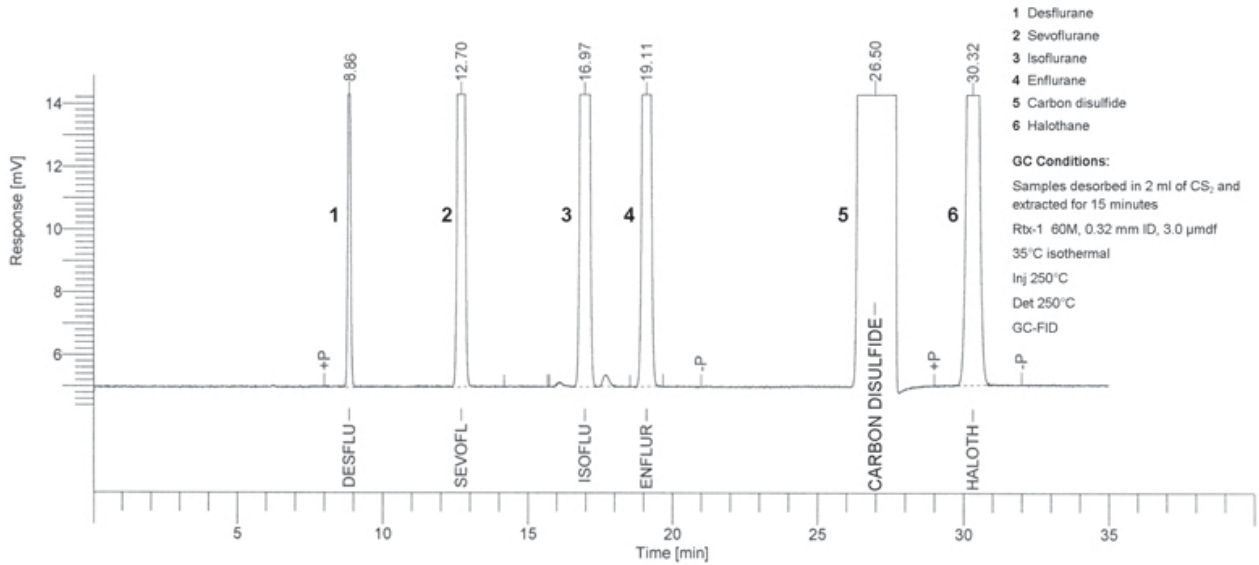
## References

1. “Anesthetic Gases: Guidelines for Workplace Exposures,” OSHA Directorate of Technical Support and Emergency Management, May 19, 2000 (<https://www.osha.gov/dts/osta/anestheticgases/>).
2. “Waste Anesthetic Gases: Occupational Hazards in Hospitals,” Department of Health and Human Services, Centers for Disease Control and Prevention, NIOSH Publication No. 2007-151, September, 2007 (<http://www.cdc.gov/niosh>).
3. Safety Data Sheet: Isoflurane, Sigma-Aldrich, Saint Louis, MO, October 2013
4. Safety Data Sheet: Halothane, Sigma-Aldrich, Saint Louis, MO, October 2013
5. Safety Data Sheet: Desflurane, U.S. Pharmacopeia, Rockville, MD, April 2014
6. Safety Data Sheet: Enflurane, U.S. Pharmacopeia, Rockville, MD, November 2012
7. Safety Data Sheet: Sevoflurane, U.S. Pharmacopeia, Rockville, MD, August 2014
8. Isoflurane, *Merck Index*, 12th Edition, 1996, p. 883
9. Halothane, *Merck Index*, 12th Edition, 1996, p. 786
10. Desflurane, *Merck Index*, 12th Edition, 1996, p. 494
11. Enflurane, *Merck Index*, 12th Edition, 1996, p. 606
12. Sevoflurane, *Merck Index*, 12th Edition, 1996, p. 1457
13. Mellon, R.D., Simone, A.F., and Rappaport, B.A., “Use of Anesthetic Agents in Neonates and Young Children” (<http://www.anesthesia-analgesia.org/cgi/content/full/104/509>). *Anesth Analg* **104** (3), March 2007, pp. 509-20. Doi:10.1213/01.ane.0000255729.96438.b0 (<http://dx.doi.org/10.1213%2F01.ane.0000255729.96438.b0>). PMID 17312200 (<https://www.ncbi.nlm.nih.gov/pubmed/17312200>).
14. Lewis, M.C., Nevoa, I., Paniagua, M. A., et al., “Uncomplicated general Anesthesia in the Elderly results in Cognitive Decline: Does Cognitive decline Predict Morbidity and mortality?” *Medical Hypotheses* **68** (3), 2007, pp. 484-492. Doi:10.1016/j.mehy.2006.08.030 (<http://dx.doi.org/10.1016%2Fj.mehy.2006.08.030>). PMID 17141964 (<http://www.ncbi.nlm.nih.gov/pubmed/17141964>).

**Figure 1**  
**Test System**



**Figure 2**  
**Chromatogram**



**Retention times (minutes):**

<i>Desflurane:</i>	8.86
<i>Sevoflurane:</i>	12.70
<i>Isoflurane:</i>	16.97
<i>Enflurane:</i>	19.11
<i>Carbon disulfide:</i>	26.50
<i>Halothane:</i>	30.32

**Table 1  
Desorption Efficiency Study**

	TLV/REL Range	Spiked µg	Mean	RSD (%)
<b>Isoflurane</b>	0.1 to 2 times	383 to 8582	96.0	4.1
<b>Halothane</b>	0.1 to 3 times	297 to 8814	99.9	1.6
<b>Desflurane</b>	0.1 to 2 times	10.7 to 186	94.3	6.9
<b>Enflurane</b>	0.1 to 2 times	9.97 to 197	101	3.6
<b>Sevoflurane</b>	0.1 to 2 times	9.95 to 197	100	5.8

**Table 2  
Sampling Rate Study**

	Concentration (ppm)	% RH	Recovery Temp C	Time (Hours)	Average Sampling Rate (ml/min)	RSD (%)
<b>Isoflurane</b>	2	80	22	0.5 to 4	15.0	9.6
	7.5	80	22	6	13.7	1.8
	75	80	22	6	12.7	5.7
	75	20	22	6	13.4	3.3
	75	80	40	6	14.7	2.6
	150	80	22	0.25 to 8	13.1	10.3
<b>Halothane</b>	2	80	22	0.5 to 4	16.3	13.0
	5	80	22	6	15.2	6.5
	50	80	22	0.25 to 6	13.7	10.0
	50	20	22	6	14.6	4.4
	50	80	40	6	14.9	3.0
	100	80	22	0.25 to 8	13.8	8.4
<b>Desflurane</b>	2	80	22	0.5 to 4	14.0	5.8
	2	20	22	0.5 to 4	13.5	6.6
	3.2	80	40	0.5 to 4	14.2	4.8
	6.2	80	40	2	12.7	3.7
<b>Enflurane</b>	2	80	22	0.5 to 4	13.5	9.0
	2	20	22	0.5 to 4	13.9	4.4
	2	80	40	0.5 to 4	14.3	4.3
	4.58	80	40	2	12.7	4.6
<b>Sevoflurane</b>	2	80	22	0.5 to 4	12.4	9.0
	2	20	22	0.5 to 4	12.8	4.1
	2	80	40	0.5 to 4	13.0	3.5
	4.4	80	40	2	12.5	3.1

**Table 3**  
**Minimum Reporting Limits**

<b>Halogenated Anesthetic Gas</b>	<b>ppm based on 8-hour sample</b>	<b>ppm based on 1-hour sample</b>
<b>Isoflurane</b>	0.10	0.82
<b>Halothane</b>	0.09	0.74
<b>Desflurane</b>	0.11	0.89
<b>Enflurane</b>	0.10	0.81
<b>Sevoflurane</b>	0.10	0.81

**Table 4**  
**Storage Study (3 Weeks)\***

<b>Compound</b>	<b>Ambient Temp (22 C) % Loss</b>	<b>Freezer Temp (&lt; 4 C) % Loss</b>
<b>Isoflurane</b>	0	< 2
<b>Halothane</b>	< 5	0
<b>Desflurane</b>	< 4	< 2
<b>Enflurane</b>	< 4	< 3
<b>Sevoflurane</b>	< 5	< 7

\* Acceptance criteria:  $\leq 10\%$



**Table 5**  
**Reverse Diffusion Study**

<b>Isoflurane</b>			
<b>Exposed for 2 hours to 100 ppm Isoflurane (µg)</b>		<b>Exposed for 2 hours to 100 ppm and 6 hours to 0.0 ppm Isoflurane (µg)</b>	
1174		1101	
1121		1157	
1232		1166	
1219		1251	
<b>Mean</b>	1186	<b>Mean</b>	1169
<b>Standard Deviation</b>	50.2	<b>Standard Deviation</b>	61.6
<b>RSD (%)</b>	4.0	<b>RSD (%)</b>	5.0

<b>Halothane</b>			
<b>Exposed for 1 hour to 100 ppm Halothane (µg)</b>		<b>Exposed for 1 hour to 100 ppm and 6 hours to 0.0 ppm Halothane (µg)</b>	
496		530	
500		566	
522		489	
524		519	
<b>Mean</b>	510	<b>Mean</b>	526
<b>Standard Deviation</b>	14.6	<b>Standard Deviation</b>	32.0
<b>RSD (%)</b>	4.0	<b>RSD (%)</b>	4.0

<b>Desflurane</b>			
<b>Exposed for 2 hours to 2 ppm Desflurane (µg)</b>		<b>Exposed for 2 hours to 2 ppm and 6 hours to 0.0 ppm Desflurane (µg)</b>	
21.94		20.92	
22.72		22.33	
22.13		21.88	
22.62		22.35	
<b>Mean</b>	22.4	<b>Mean</b>	21.9
<b>Standard Deviation</b>	0.377	<b>Standard Deviation</b>	0.671
<b>RSD (%)</b>	1.7	<b>RSD (%)</b>	3.1

<b>Enflurane</b>			
<b>Exposed for 2 hours to 1.6 ppm Enflurane (µg)</b>		<b>Exposed for 2 hours to 1.6 ppm and 6 hours to 0.0 ppm Enflurane (µg)</b>	
20.47		19.99	
20.50		19.38	
21.33		19.13	
18.81		20.90	
<b>Mean</b>	20.3	<b>Mean</b>	19.9
<b>Standard Deviation</b>	1.057	<b>Standard Deviation</b>	0.787
<b>RSD (%)</b>	5.2	<b>RSD (%)</b>	4.0

<b>Sevoflurane</b>			
<b>Exposed for 2 hours to 1.6 ppm Sevoflurane (µg)</b>		<b>Exposed for 2 hours to 1.6 ppm and 6 hours to 0.0 ppm Sevoflurane (µg)</b>	
13.0		13.1	
12.9		13.3	
13.2		12.9	
12.6		12.9	
<b>Mean</b>	13.0	<b>Mean</b>	13.1
<b>Standard Deviation</b>	0.358	<b>Standard Deviation</b>	0.280
<b>RSD (%)</b>	2.8	<b>RSD (%)</b>	2.1