Evaluation of Ortho-phthalaldehyde in Eight Healthcare Facilities

Lilia Chen, MS, CIH
Judith Eisenberg, MD, MS
Charles Mueller, MS
Nancy Clark Burton, PhD, CIH

HHE Health Hazard Evaluation Program

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Contents

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The cover photo is a close-up image of sorbent tubes, which are used by the HHE Program to measure airborne exposures. This photo is an artistic representation that may not be related to this Health Hazard Evaluation. Photo by NIOSH.

Highlights of this Evaluation

The Health Hazard Evaluation Program received management requests for eight healthcare facilities nationwide to participate in the field evaluation component of the NIOSH Hazard Assessment of Ortho-phthalaldehyde (OPA) study.

What We Did

- We evaluated OPA-specific work practices, assessed employee exposure to OPA, and evaluated potential health effects from OPA.
- We invited employees who worked in areas where OPA was used (exposed group) and not used (comparison group) to participate. The evaluation included the following components:
  - Questionnaires on work history, practices, and symptoms
  - Skin tests for allergic reactions to common allergens and OPA
  - Blood tests for antibodies to OPA
  - Skin examinations of their hands and forearms before and after each of three shifts
  - Symptom surveys after each of three shifts
  - Personal air samples for OPA and glutaraldehyde
- We took surface wipe samples for OPA on surfaces where OPA was used including counter tops and sinks.
- We observed air movement and ventilation controls in areas where OPA was used.
- We reviewed OPA-related training programs and observed personal protective equipment use.

We documented exposure to OPA in a variety of healthcare settings. Reported work-related skin and respiratory symptoms were rare, and skin sensitization to OPA was not confirmed. Facilities should follow recommended ventilation standards and guidelines for rooms where OPA is used, update training programs, and enforce personal protective equipment use among employees.

What We Found

- Most participants in the exposed group used OPA in basins or containers, not in automated machines.
- About half the participants in the exposed group used OPA every day.
- Very few participants in either group reported symptoms related to work.
- No participants had skin staining from OPA.
- Five participants had positive allergy skin tests to OPA. One of the five was from the OPA exposed group. No participants had OPA-specific antibodies.

- Air concentrations of OPA were similar to or higher than those in other studies.
- OPA was found in most personal breathing zone samples from the comparison group; the average concentrations were lower than in samples from the exposed group.
- Surface concentrations of OPA were generally highest around basins and lids.
- Most rooms where OPA was used were under negative pressure relative to adjacent areas.
- Training material and content varied across and within facilities.
- Personal protective equipment requirements were inconsistent across facilities. Employees did not always follow their departments' personal protective equipment use requirements.
- Most employees wore gloves and eye protection when handling OPA.

What Employers Can Do

- Train employees on how to use and handle OPA safely.
- Ensure employees always use proper personal protective equipment when they handle OPA.
- Maintain proper ventilation in areas where OPA is used.
- Update training materials and make sure they contain accurate information.

What Employees Can Do

- Always wear nitrile or butyl rubber gloves and eye protection when handling OPA.
- Use appropriate handling procedures with OPA when pouring OPA solution and opening the containers with OPA.
- Report any respiratory symptoms or skin irritation that occurs when you handle OPA to your supervisor immediately and seek medical attention.

Abbreviations

µg/m^3	Micrograms per cubic meter
ACGIH®	American Conference of Governmental Industrial Hygienists
ACH	Air changes per hour
CFR	Code of Federal Regulations
GM	Geometric mean
GTA	Glutaraldehyde
HHE	Health hazard evaluation
HLD	High level disinfection
HSA	Human serum albumin
IgE	Immunoglobulin E
IgG	Immunoglobulin G
LEV	Local exhaust ventilation
LOD	Limit of detection
LOQ	Limit of quantitation
MDC	Minimum detectable concentration
mg/mL	Milligram per milliliter
mL	Milliliter
MQC	Minimum quantifiable concentration
NA	Not Applicable
ND	Not detected
NIOSH	National Institute for Occupational Safety and Health
OEL	Occupational exposure limit
OPA	Ortho-phthalaldehyde
OSHA	Occupational Safety and Health Administration
PBZ	Personal breathing zone
PST	Puncture skin test

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Introduction

In 2009 and 2010, we conducted health hazard evaluations (HHEs) at eight healthcare facilities to evaluate exposures to ortho-phthalaldehyde (OPA) and potential health effects among employees using this disinfectant. We received support for this work from the National Institute for Occupational Safety and Health (NIOSH) as part of the National Occupational Research Agenda. This report includes the results from the following HHE Nos: 2006-0238, 2008-0059, 2008-0060, 2008-0212, 2008-0285, 2009-0091, 2009-0132, and 2009-0242.

Ortho-phthalaldehyde and High Level Disinfection

Instruments that are not disposable and are fragile or sensitive to normal heat or steam sterilization procedures must be disinfected by low temperature chemical methods, such as high level disinfection (HLD). HLD kills all microorganisms in or on an instrument, except for small numbers of bacterial spores. Instruments requiring HLD usually contain electronic and fiber optic components, heat-sensitive glues, or flexible tubing. Examples include flexible endoscopes, laryngoscopes, respiratory therapy equipment, anesthesia equipment, rectal and vaginal probes, endotracheal tubes, nebulizer cups, and nasal specula [Rideout 2005].

Glutaraldehyde (GTA) has been used for disinfecting heat-sensitive medical devices for more than 40 years. GTA is an eye and skin irritant, and has been reported to cause sensitization and occupational asthma [NIOSH 2001]. Detailed information about GTA can be found in Appendix B.

OPA was introduced to the U.S. market as a safer alternative to GTA in 1999. OPA was used for disinfection at the eight facilities that participated in our evaluation in two ways: manually and in automated endoscope reprocessors. Potential routes of exposure included dermal and inhalation. Exposure to OPA could occur during the following activities:

- Measuring and diluting concentrated OPA stock solution, and pouring OPA solution into or out of a cleaning container system (e.g., soaking basin in manual disinfecting operations and reservoir in automated processors)
- Opening the cleaning container system to immerse instruments to be disinfected
- Removing soaked instruments from the container system
- Rinsing the instruments containing residual OPA solution
- Disposing of used OPA solution to the sewer system
- Performing maintenance procedures, including filter or hose changes on automated processors that have not been pre-rinsed with water

The concentration of OPA was checked with test strips regularly by employees to ensure that the solution met the minimum effective concentration needed to provide disinfection. The OPA solution was reused for several days and changed according to the manufacturer's directions or if the minimum effective concentration level was not met. The time spent handling or working with OPA on the days it was used varied widely between facilities.

In 2004, the first report of allergic reaction to OPA was published [Sokol 2004]. Anaphylaxis (a rapidly progressing, potentially life-threatening allergic reaction) was seen in patients who had medical procedures with endoscopes disinfected with OPA. Subsequent immunological testing indicated that OPA was the inciting agent [Suzukawa et al. 2007; Cooper et al. 2008; Pala and Moscato 2013]. Following reports of patient sensitization, reports of adverse occupationally related health effects surfaced. For example, a nurse soaking endoscopes in OPA reported respiratory symptoms while using OPA about 100 minutes per day, 3 days per week [Franchi and Franco 2005]. Repeated skin exposure has been found to cause dryness and cracking of the skin and may lead to skin and respiratory sensitization [Metrex 2007; Advanced Sterilization Products 2010]. Additional information about OPA can be found in Appendix B.

Methods

The objectives of this evaluation were to gather information on potential health hazards associated with occupational exposure to OPA by: (1) assessing employee symptoms, health effects, and biological exposures; (2) observing and documenting OPA use; (3) evaluating OPA control methods; and (4) characterizing airborne exposures and surface levels of OPA.

We invited healthcare facilities to participate in this evaluation. The evaluation was announced in a presentation to the Greater Cincinnati Health Council, a posting on Epi-X (the Centers for Disease Control and Prevention web-based communication system for public health professionals), and a presentation at the 2008 American Industrial Hygiene Conference and Exposition. Eight healthcare facilities volunteered to participate. A 1-day site visit was made to each facility to get background information on OPA use and to identify and recruit participants. A second site visit lasting 3 days was made to each facility between July 2009 and April 2010 for medical testing and exposure monitoring.

Facility managers were asked to identify departments that used OPA during the 30 days prior to the scheduled days that medical testing was conducted. Employees in these departments were considered the exposed group. Employees from departments that reportedly did not use OPA during the 30 days prior to the testing days made up the comparison group. All employees over 18 years of age in the exposed and comparison departments were invited to participate in this evaluation. However, participants who reported previous history of anaphylaxis or who were or may have been pregnant were excluded from the puncture skin test component. Participation was voluntary, and informed consent was obtained. Employees were asked to participate in all 3 days if their work schedule permitted, although participation of 1 to 3 days was acceptable.

All participants completed a questionnaire about their personal characteristics, work history, medical history, and skin and respiratory symptoms during the 30 days prior to the evaluation. Symptoms were classified as work-related if they improved on days off work.

Since OPA stains proteins a gray-green color, we examined the forearms and hands of participants preshift and postshift daily for evidence of skin discoloration and irritation such as redness and cracking (Appendix C) [Rutala and Weber 2001; Streckenbach and Alston

2003]. We also administered a postshift survey about symptoms that began during that shift. The postshift symptom survey also asked about OPA use during the shift (yes or no) and how long they used it.

An allergist did a puncture skin test (PST) with two OPA concentrations (0.55 milligrams per milliliter [mg/mL] and 5.5 mg/mL) on each participant to identify if OPA might cause a skin reaction. The allergist also did a PST with a standard panel to check for atopy and two other PSTs using a histamine positive control and a saline negative control. Atopy is a genetic disposition to develop allergic diseases such as asthma, eczema, and rhinitis. A person who reacts to any of the tests on the standard panel is considered atopic. Details of the PST methodology and interpretation are included in Appendix C.

A physician or phlebotomist obtained a 10 milliliter (mL) blood sample from each participant. This sample was analyzed for OPA-specific immunoglobulin E (IgE) and immunoglobulin G (IgG) antibodies [Suzukawa et al. 2007] to assess past exposures to OPA. Details of the antibody analyses are included in Appendix C.

Using a draft NIOSH sampling and analytical method, we took personal breathing zone (PBZ) air samples for OPA using coated silica gel tubes as the sampling media. Details of the method can be found in Appendix C. The goal was to obtain a time-weighted average work shift concentration for each of the exposed participants. To maximize OPA recovery from the sample media the analytical chemist suggested that we limit sample times to 4 hours; subsequent analysis showed that recovery was not an issue for up to 6 hours of sampling [Streicher 2014]. We also took PBZ air samples for GTA because one facility reported still using GTA and it was possible that others may have had remaining supplies of GTA or GTA may have been unknowingly present in other cleaning or disinfectant products. These samples were analyzed according to NIOSH Method 2532 [NIOSH 2015]. PBZ sampling for OPA and GTA was also done on employees from the comparison group. Some employees did not participate in the air sampling portion of the study (three from the exposed group and eight from the comparison group).

We took wipe samples from surfaces such as tops of the OPA basins, countertops, floor, carts, and supply containers. Wipe samples were collected using Ghost™ wipes dampened with dimethyl sulfoxide and water to assess surface contamination with OPA. These samples were analyzed onsite with a portable fluorometer. Appendix C contains detailed information on the draft NIOSH sampling and analytical method.

Results and Discussion

Table 1 summarizes the method of OPA use, the estimated monthly volume, and the departments that used OPA by facility. Four facilities used only manual methods, three used automated washers and manual methods, and one used OPA in automated washers only, but used a basin filled with GTA for manual soaks. The volume of OPA used was higher at facilities with automated washers.

Table 1. Characteristics of OPA use, by facility

Facility	Method of use	Usage volume (gallons/month*)	Departments that used OPA
A	Manual	7	Endoscopy, ultrasound, cardiology, pulmonary function testing
B	Automated and manual	96	Central sterile processing, endoscopy
C	Manual	11	Endoscopy, ultrasound, cardiology, emergency
D	Manual	21–28	Anesthesiology, main operating room, surgery clinic; ears, nose, and throat
E	Manual	23	Cardiology, ultrasound, electroencephalography, respiratory therapy, operating suites
F	Automated	112	Gastroenterology
G	Automated and manual	60	Endoscopy, central sterile processing, labor and delivery†
H	Automated and manual	37	Endoscopy

*Estimated by facility managers

†We only performed air and surface wipe sampling in the endoscopy department since the other two departments used OPA rarely.

Questionnaire

The questionnaire was completed by 151 participants, 74 from the exposed group and 77 from the comparison group. Their basic demographic information is listed in Table 2.

Table 2. Demographics and medical history, by exposure group

	Exposed group n = 74 Frequency (%)	Comparison group n = 77 Frequency (%)
Mean age (range in years)	38 (19–62)	43 (19–66)
Mean duration of employment in current job (range in years)	7 (0.2–39)	7 (0.04–39)
Female	51 (69)	60 (78)
Smoking Status:		
Current smoker	5 (7)	3 (4)
Former smoker	11 (15)	19 (25)
Never smoked	58 (78)	55 (71)
Prior diagnosis of asthma	9 (12)	6 (8)
Prior allergic reaction to OPA during medical procedure	0 (0)	1 (1)
Prior history of eczema or atopic dermatitis	9 (12)	10 (13)

The most common job titles for the exposed group were endoscopy technician (27/74), ultrasound technician (8/74), respiratory technician/therapist (8/74), and healthcare assistant (7/74). The most common job titles for the comparison group were nurse (18/77), quality analyst (11/77), maintenance (10/77), management (9/77), and pharmacy technician (8/77). Patient access, registration staff, health care assistant, security guard, receptionist, and secretary job titles were also represented in this group.

The method, frequency, and duration of OPA use are summarized in Table 3. Most participants (78%) reported exclusive use of manual methods (using it by hand to disinfect equipment), 45% used it less than daily, and most (71%) used OPA for an hour or less on days they used it. Change outs were performed by draining the used solution then replacing it with unused solution. Six percent reported that OPA change outs were done after more than 14 days. The manufacturer recommends change out of OPA every 14 days or less.

Table 3. Characteristics of OPA use among the exposed group

	Number (%)
Method of use	
Automated washers	8/74 (11%)
Manual (basins, cylinders, or tubes)	58/74 (78%)
Both methods	8/74 (11%)
Performed regular OPA change outs	52/74 (70%)
Frequency of OPA change outs*	
1 to 13 days	2/52 (4%)
Every 14 days	47/52 (90%)
15 to 90 days	3/52 (6%)
Frequency of handling OPA	
Daily (at least once a day)	40/73 (55%)
Weekly (at least once a week)	27/73 (37%)
Monthly (at least once a month)	6/73 (8%)
Average time spent handling or working with OPA on the days that OPA was handled	
Less than 0.5 hours	8/73 (11%)
0.5–1 hour	44/73 (60%)
> 1–6 hours	9/73 (12%)
> 6–10 hours	12/73 (16%)

*The manufacturer suggests changing OPA solution every 14 days or less.

There were no statistically significant differences in the prevalences of respiratory and skin symptoms reported in the past 30 days or "usually having a cough" between the exposed and comparison groups. The prevalences of symptoms were low overall (Table 4).

Table 4. Reported symptoms, by exposure group

Symptom	Exposed group n = 74		Comparison group n = 77	
	Frequency (%)	Work-related* (%)	Frequency (%)	Work-related (%)
Wheezing or whistling in chest in the past 30 days	2 (3)	0 (0)	1 (1)	0 (0)
Woken up with chest tightness in the past 30 days	2 (3)	0 (0)	3 (4)	1 (1)
Awakened by shortness of breath in the past 30 days	0 (0)	0 (0)	2 (3)	0 (0)
Usually have cough	4 (5)	2 (3)	2 (3)	1 (1)
Skin rash or discoloration on face, neck, hands, or arms in the past 30 days	3 (4)	2 (3)	4 (5)	0 (0)

*Symptoms were classified as work-related if they improved on days off work.

Postshift Symptom Surveys

Both exposure groups completed the survey about symptoms developed during that day's shift. On the first day 128 participants completed surveys, 120 on the second day, and 102 on the third day. Cough, stuffy nose, sneezing, and runny nose were reported by up to 6% of employees on a given day (Table 5). Wheezing, chest tightness, and unusual shortness of breath had prevalences less than 3%, and were reported only in the comparison group. In the exposed group, one participant with cough on Day 1 reported using OPA on Day 1; two participants with stuffy nose on Day 2 reported using OPA on Day 2; and one participant with cough, stuffy nose, and runny nose on Day 3 reported using OPA on Day 3. None of the participants in the comparison group who reported symptoms during the 3 days, reported using OPA the day symptoms were experienced.

Table 5. Reported postshift symptoms, by exposure group

Symptom	Day 1		Day 2		Day 3	
	Exposed group n = 60 Frequency (%)	Comparison group n = 68 Frequency (%)	Exposed group n = 60 Frequency (%)	Comparison group n = 60 Frequency (%)	Exposed group n = 51 Frequency (%)	Comparison group n = 51 Frequency (%)
Cough	1 (2%)	1 (1%)	0	0	2 (4%)	1 (2%)
Stuffy nose	1 (2%)	0	3 (5%)	0	1 (2%)	0
Sneezing	1 (2%)	2 (3%)	0	2 (3%)	0	3 (6%)
Runny nose	0	3 (4%)	0	3 (5%)	1 (2%)	0
Wheezing	0	1 (1%)	0	0	0	0
Chest Tightness	0	0	0	1 (2%)	0	0
Unusual shortness of breath	0	0	0	0	0	0

Preshift and Postshift Dermal Examinations of the Hands and Forearms

No participants from the exposed group had gray-green skin discoloration from direct skin contact with OPA. Three percent or fewer of the participants had more abnormalities on the postshift exam (such as redness and cracking) (Table 6). Most (> 88%) participants' hands and forearms were unchanged over the shift. For those who had more skin abnormalities at the end of the work shift, two of two participants in the exposed group reported using OPA during their work shift on the first day and one of two participants in the exposed group reported handling OPA during the second day. On Day 1, two participants with fewer skin problems at the end of the day reported handling OPA that day. On Day 2, three participants with fewer skin problems at the end of the day reported handling OPA that day.

Table 6. Summary of daily dermal examinations of hands and forearms pairs*

Skin Abnormalities	Day 1		Day 2		Day 3	
	Exposed group n = 60 Frequency (%)	Comparison group n = 67 Frequency (%)	Exposed group n = 60 Frequency (%)	Comparison group n = 60 Frequency (%)	Exposed group n = 51 Frequency (%)	Comparison group n = 51 Frequency (%)
More	2 (3%)	2 (3%)	2 (3%)	1 (2%)	0	1 (2%)
Unchanged	55 (92%)	63 (94%)	53 (88%)	58 (97%)	46 (90%)	48 (94%)
Fewer	3 (5%)	2 (3%)	5 (8%)	1 (2%)	5 (10%)	2 (4%)

*For each subject, we compared the number of skin abnormalities post shift to the number of skin abnormalities pre shift.

Symptom rates in this evaluation were lower than those reported in other studies of OPA exposed employees. In a Japanese study of 80 employees using automated washers and manual methods of OPA disinfection, 16% reported respiratory irritation, 10% skin irritation, 9% eye irritation, and 3% headache [Miyajima et al. 2010]. In that study, the manual disinfection employees processed from 1 to 14 endoscopes daily and the automated washer employees processed 8 to 37 endoscopes daily. Another study reported that 24% of 70 employees in an endoscopy unit using automated washers and manual methods of OPA disinfection reported at least one symptom of eye, respiratory, or skin irritation [Fujita et al. 2007]. There was no information included in the Fujita et al. paper about frequency of use. The frequency of use in these two studies may have varied from our evaluation.

We found no evidence of skin irritation, skin discoloration, or symptoms of unusual shortness of breath from exposure to OPA in this evaluation. One study of OPA use in an endoscopy unit found similar results to our evaluation [Cooke et al. 2003]. Another study reported that three employees developed contact dermatitis and another developed contact dermatitis and occupational asthma from workplace OPA exposure [Fujita et al. 2007]. A case report found that a nurse developed respiratory symptoms after exposure to OPA [Franchi and Franco 2005].

Puncture Skin Tests and Antibody Immunoassays

PSTs were performed on 129/151 participants. Five participants had a positive PST to the higher OPA concentration, and three of these had positive reactions to the lower OPA concentration (Table 7). Of the five participants with positive PSTs, four were in the comparison group. OPA-specific IgE or IgG antibodies were not found among the 150 participants from the exposed and comparison groups whose blood samples were analyzed. The prevalence of atopy in the groups was similar: 43% for the exposed group and 47% for the comparison group. Atopic employees were more likely to have a positive PST to OPA than nonatopic employees, but this was not a significant difference (7% vs. 1%, $P = 0.17$). These atopy prevalences were similar to the prevalence of 54% in the general U.S. population [Arbes et al. 2005].

Table 7. PST results, by exposure group

	Exposed group	Comparison group
Total number PSTs done	63/74 (85%)	66/77 (86%)
Positive to one or more sites on atopy panel	27/63 (43%)	31/66 (47%)
Positive to 0.55 mg/mL OPA solution	0/63 (0%)	3/66 (5%)
Positive to 5.5 mg/mL OPA solution	1/63 (2%)	4/66 (6%)

PST and serum IgE are methods of evaluating whether a person has developed substance-specific IgE antibodies. We were not able from our PST and OPA-specific IgE results to determine if either method was an accurate measure of OPA sensitization. A laboratory study in mice showed that dermal OPA exposure resulted in dermal irritation and potential sensitization [Anderson 2010]. Topical application of OPA to mice also resulted in significant increases in total IgE, OPA-specific IgE, and OPA-specific IgG_1 [Anderson et al. 2010].

OPA-specific IgG_1 antibodies were increased in a mouse inhalation study of OPA vapor [Johnson et al. 2011]. Four patients with anaphylactic reactions to cystoscopes cleaned with OPA had positive PSTs to an OPA solution of 5.5 mg/mL, but not to latex or GTA (alternative causes of the anaphylaxis) [Sokol 2004]. Total IgE was normal for three patients and slightly elevated for the fourth [Sokol 2004].

Personal Breathing Zone Air Samples

We took 270 PBZ air samples for OPA on 143 employees (75 in the exposed group and 68 in the comparison group). Three samples were excluded from analysis because of problems during sampling. Sampling times varied among participants because employees traveled between locations, sometimes to different buildings. Some employees worked with OPA only part of the day and asked to have their sampling pump removed after that work ended. Some of the comparison employees were willing to wear a sampling pump only for a portion of their work shift.

The geometric mean (GM) of the OPA air concentrations for exposed employees across all facilities was 0.34 micrograms per cubic meter ($\mu g/m^3$) compared to 0.14 $\mu g/m^3$ across all facilities for the comparison employees (Table 8). The two highest OPA concentrations measured were 35 $\mu g/m^3$ and 38 $\mu g/m^3$. Results of the PBZ air samples from the individual facilities are in Appendix A.

Table 8. Personal breathing zone air sampling results for OPA, by facility and exposure group

Facility	Exposed group				Comparison group			
	N*	Sampling time range (minutes)	Geometric mean† ($\mu g/m^3$)	Range ($\mu g/m^3$)	N*	Sampling time range (minutes)	Geometric mean† ($\mu g/m^3$)	Range ($\mu g/m^3$)
A	22	82–504	0.23	ND–0.96	310	233–500	0.13	ND–0.67
B	12	144–505	0.83	0.2–1.8	13	179–522	0.11	ND–0.53
C	24	147–609	0.17	ND–4.2	9	190–318	0.15	ND–0.48
D	43	151–562	0.16	ND–35	13	219–288	0.13	ND–0.23
E	32	127–514	0.34	ND–38	9	227–519	0.24‡	ND
F	12	403–535	1.6	0.47–13	4	177–252	0.18	0.07–0.49
G	15	258–569	1.0	0.15–7.9	19	222–283	0.11	ND–1.0
H	7	381–511	2.1	1.0–3.8	5	233–253	0.34	ND–0.63
Total	167		0.35		103		0.14	

ND = Not detected

*Number of personal samples collected on individuals over 3 days. Employees participated for 1 to 3 days. Some employees had two sequential samples collected on one day, which were combined for a single time-weighted concentration.

†For samples without detectable levels of OPA, the minimum detectable concentration divided by the root of square root of 2 was used to calculate geometric means.

‡None of the samples contained detectable concentrations of OPA; the limit of detection for this sample set was higher than those from the other facilities.

About half of the samples taken from participants in the comparison group had detectable OPA concentrations; the average concentrations were lower than the exposed group but some of the concentrations were higher than the exposed group. This finding was unexpected because these employees worked in departments where OPA reportedly was not used. It is possible that employees in the comparison group may have worked near or passed through areas where OPA was used, that there was cross contamination through shared ventilation systems, or that other chemicals used in the facility contained compounds such as other aldehydes or ketones that were detected as OPA by the draft NIOSH method [Tucker 2008].

Where possible, we calculated daily full-shift time-weighted average concentrations when a single sample or two sequential samples collected on the same individual during the same work shift covered at least 7 hours (Table 9) of an 8-hour work shift. Some of the ultrasound technicians at Facility C worked 10-hour shifts so full-shift samples were considered as those collected for at least 8 hours. Full-shift, time-weighted average OPA concentrations ranged from ND to 38 µg/m^3 in the exposed group (GM = 0.18–2.2 µg/m^3) and ND to 0.67 µg/m^3 (GM = ND–0.16 µg/m^3) in the comparison group. Only the comparison groups at Facilities A, B, and E had time-weighted average exposures that covered at least 7 hours. In the exposed group, 36% to 100% of the employees at a given facility reported using OPA during their work shift. None of the comparison group reported using OPA during their work shift.

Table 9. Full-shift personal breathing zone air sample results for OPA by facility*

Facility	Exposed group				Comparison group		
	N	GM (µg/m^3)	Range (µg/m^3)	Percentage reporting OPA usage	N	GM (µg/m^3)	Range (µg/m^3)
A	13	0.18	ND–1.3	62	16	0.16	ND–0.67
B	9	0.68	0.20–1.8	100	7	0.13	ND–0.49
C*	14	0.17	ND–4.2	71	NA	NA	NA
D	20	0.26	ND–35	55	NA	NA	NA
E	23	0.31	ND–38	68	4	ND	ND
F	11	1.6	0.47–13	36	NA	NA	NA
G	11	0.97	0.15–7.9	55	NA	NA	NA
H	6	2.2	1.0–3.8	83	NA	NA	NA
Total	105	0.42			27	0.15	

NA = Not applicable

*Single or sequential samples were collected for 7 hours or longer on 8-hour shifts and 8-hours or longer for 10-hour shifts.

NIOSH and the Occupational Safety and Health Administration (OSHA) have not established occupational exposure limits (OELs) for OPA. OPA is widely used in Japanese healthcare facilities, and Japanese researchers have developed a method similar to the draft NIOSH method for OPA in air using silica gel [Uchiyama et al. 2006]. One study with workplace monitoring reported time-weighted average concentrations of OPA in PBZ samples for

manual cleaning that ranged from 0.55 µg/m^3 to 7.8 µg/m^3 (median: 0.66 µg/m^3) and, for automated cleaning, from 0.99 µg/m^3 to 8.5 µg/m^3 (median: 0.06 µg/m^3) [Miyajima et al. 2010]. Fujita and associates collected seven short-term air samples (25 minutes or less) at four different locations. The highest concentration (11 µg/m^3) was found for the task of opening a bucket containing OPA while an endoscope washing machine was operating [Fujita et al. 2007]. A few of the concentrations we measured exceeded the highest measured concentrations in the two Japanese studies.

Table 10 shows the average number of hours handling or working with OPA on days it was handled by OPA method used. Participants who used automated washers, alone or with a manual method, reported an average of approximately 5 hours use on days they used OPA compared to an average of less than 2 hours for those who used manual methods only. Participants who used automated washers worked with OPA for longer periods than those who used manual methods, but had no evidence of adverse health effects attributed to OPA exposure. A recent national study of over 4,600 healthcare workers who use HLDs found that 63% of the employees surveyed used HLDs for less than 1 hour per day [Henn et al. 2015].

Table 10. Average hours handling or working with OPA on days it was handled by OPA method used

OPA method	N	Average reported hours [range]
Automated washers only	8	4.52 [0.2–10.0]
Manual methods only	58	1.53* [0.0–10.0]
Both methods	8	5.19 [1.0–10.0]

*n = 57 responses because of missing data on questionnaire

We took three task-based PBZ samples at Facility B while employees changed out the OPA solution from automated washers and used test strips to check OPA concentrations by dipping the test strips into the OPA reservoir. The process was similar for all facilities using automated washers. The times for the tasks were 11, 20, and 50 minutes, and the concentrations were 3.2, 32, and 6 µg/m^3. The employees used nitrile gloves, gowns, and eye protection during this procedure. These concentrations were similar to those reported by Miyajima and associates during OPA change outs where concentrations ranged up to 55 µg/m^3 (median: 14 µg/m^3) [Miyajima et al. 2010].

We collected 270 PBZ air samples for GTA on participants who had OPA PBZ air samples collected. GTA concentrations ranged from ND to 19 µg/m^3. There are no shift-based OEL's for GTA. The NIOSH ceiling limit for GTA is 800 µg/m^3 and the American Conference of Governmental Industrial Hygienists (ACGIH) ceiling limit is 205 µg/m^3. We did not calculate GMs for the GTA samples because 95% did not have quantifiable concentrations of GTA. Samples with quantifiable concentrations were found at Facilities D, F, G, and H. Facility D reported using GTA in the anesthesiology department and Facility F used GTA manually in the same room as OPA during the time of our site visit. Facilities G and H did not report

any known usage. The low concentrations of GTA that were found in Facilities B, C, and E (detectable but below quantification limits) may have resulted from its presence in other products used in the areas that we sampled or in departments we did not evaluate.

Surface Wipe Sampling Results

We collected 86 surface wipe samples (7–12 per facility) toward the end of each day shift from surfaces where OPA was used (i.e., countertops, sink areas) and high contact surfaces (i.e., keypads, basin covers, faucet handles, and trash can lids) (Table 11). Because we learned after the onsite evaluations that the fluorometer calibration curve drifted over time and the fluorometer had not been calibrated prior to each day's measurement, we are not reporting the measured surface concentrations of OPA; we only report whether the samples were positive or negative. All eight facilities had positive wipe samples. Areas within a facility with the highest relative surface contamination were usually around OPA basins and lids. Typically, the top of the OPA basin cover and other areas touched with potentially contaminated hands showed the highest surface concentration of OPA.

Table 11. Summary results for OPA on surfaces (countertops, sinks, keypads, basin covers, faucet handles, trash can lids)

Facility	N	Number of positive samples (%)	Location with highest concentration
A	11	8 (73)	Top of OPA basin cover
B	12	11 (92)	OPA soak tube transport cart
C	7	7 (100)	Decontamination room blue supply bin
D	12	11 (92)	Surgery clinic lid of OPA basin
E	12	12 (100)	Respiratory Therapy sink next to OPA basin
F	12	11 (92)	Radio top
G	8	7 (88)	Floor in front of automated washer
H	12	12 (100)	In front of sink

Ventilation

The type of engineering controls used to control OPA vapors varied by department. Some departments relied on general dilution ventilation, while other departments used general ventilation combined with vapor control systems. In large areas, increasing general ventilation to remove air contaminants may not be energy efficient because of the large amounts of air that must be moved, heated, and cooled; therefore, installing local exhaust ventilation (LEV) system may be more practical.

LEV should be located at the source of vapor release and pull vapors away from the employee(s) [ACGIH 2013]. LEV should be designed so that vapors from the top of the OPA container are captured and exhausted by a duct to the outdoors. The Facility Guidelines Institute recommends that HLDs be controlled at the source using ACGIH LEV design

principles [FGI 2014]. The American Industrial Hygiene Association recommends that an LEV have an average face velocity of 80 to 120 feet per minute [AIHA 1992]. If direct exhaust to the outdoors is not feasible, LEV systems can be designed so that the captured vapors are filtered and then recirculated back into the work area. Automated washers have built-in LEV that can be exhausted outdoors or through a charcoal filter. If the air is recirculated, maintenance and regular replacement of filters is essential in maintaining the effectiveness of the LEV.

Vapor control systems are designed to control OPA vapors from tubes that soak probes. Some departments used wall exhaust vents to pull air from the basins where OPA was kept, and some departments kept the tubs and basins in an enclosed fume hood. Some automated washers exhausted air from the washers directly outside; whereas other automated washers passed the air through a charcoal filter and released it back into the workroom.

Most facilities used OPA in a dirty/soiled utility room, central sterile processing room, or dedicated cleaning room. Closed cylinders used to disinfect ultrasound probes were often located in patient rooms. OPA used for endoscopy disinfection usually had dedicated rooms for this purpose. In some cases, the instruments came into a dirty room and were disinfected then moved to a separate but adjoining clean area. ASHRAE recommends that areas where HLD is performed be designated for that use and be separate from the cleaning/decontamination area.

We observed that at some facilities, the doors between the dirty and clean rooms were left open. Negative pressure is established by exhausting more air out of the room than is supplied. Negative pressure relative to the surrounding areas is desired in the room where OPA is used. To maintain the needed pressure differential to contain OPA and other contaminants, doors, windows, and any other openings should have a reasonably close fit and seal. When doors are left open, the pressure differential is reduced, and a natural interchange of air takes place between the areas [ASHRAE 2011]. In many of the facilities we visited, the door to the room that contained OPA was left open. In some cases, there was a doorway, but no door between the room where OPA was used and the adjoining room. Also, partitions, such as a pass-through window separating the room that contained OPA and other areas were observed to be open. At one facility, OPA was not kept in a room, but in a hallway where negative pressure could not be maintained.

General ventilation guidelines recommend that soiled workrooms be under negative pressure in relation to surrounding areas and have a minimum of 10 air changes per hour (ACH). All air should be exhausted directly outdoors, and no air should be recirculated [ASHRAE 2013; FGI 2014]. ASHRAE also recommends that endoscope cleaning rooms have a minimum of two outdoor ACH [ASHRAE 2011; ANSI/ASHRAE/ASHE 2013; ASHRAE 2013]. At most facilities in this evaluation we were told that the ventilation systems for rooms that contained OPA were designed to provide a minimum of 10 ACH with no recirculation. In some cases, ventilation information was unavailable. We reviewed the test and balance reports provided for two facilities (C and G). Minimum air change recommendations were met for some departments. LEV was used in some departments of five facilities (A, B, D, F, and G).

Training

Most (89%) of the participants in the exposed group reported receiving formal training about safe handling procedures for OPA from their employer. About half (51%) [37/73] reported having a single training session, 30% (22/73) reported having two to four training sessions, and 8% (6/73) reported having five or more OPA training sessions. A variety of training materials were used across the facilities we visited; training materials sometimes varied by department within the same facility.

Some departments had written policies and procedures in place for using OPA, while others did not. Some departments used the manufacturer's training material. Other facilities created their own training curriculum with slides and quizzes. Three facilities that had departments where OPA was used more frequently required employees to have classroom and hands-on training with an experienced employee overseeing the newer employee.

Some of the training material on OPA handling we reviewed was incorrect or not specific. For example, one facility had training materials that stated OPA was not a potential problem in the workplace since there was no OSHA PEL or specific airflow recommendations for its use. Another facility used the same training material that was used for GTA because there were similarities in disinfectant principles and personal protective equipment use.

Personal Protective Equipment

Most departments had written policies for personal protective equipment use by employees who handled OPA. OPA manufacturer guidelines recommend gloves, eye protection, and protective clothing whenever OPA is used. All facilities required gloves and eye protection, and some required protective clothing. None required respirator use.

Most participants (65/74, 88%) reported always wearing gloves while working with OPA. Four participants (5%) reported usually wearing gloves; one participant (1%) reported sometimes using gloves; and four participants (5%) reported never using gloves. The two most common types of gloves used were nitrile gloves (45/70, 64%) and latex gloves (25/70, 36%).

According to self reports, employees did not always follow manufacturer's recommendations [Advanced Sterilization Products 2010] and facility training materials on glove use and eye protection use; 12% of participants in the exposed group reported not always wearing gloves and 33% reported not using eye protection (face shield, safety glasses, or safety goggles) when handling OPA. Thirty-six percent of participants in the exposed group reported using either disposable gowns or suits when working with OPA (Table 13).

Respirator use was uncommon, with 95% (70/73) of participants reporting they never wore one while working with OPA. This finding was not unexpected because respirator use was not required at any of the facilities. Two participants reported using an N95 filtering facepiece respirator when working with OPA, and that they had been fit tested for this respirator. The N95 filtering facepiece respirator is not recommended for OPA exposure since the respirator does not protect the wearer from gas or vapor exposures, only particulates. One participant was not sure what type of respirator s/he wore and had not been fit tested for it. Other types

of personal protective equipment worn are listed in Table 12. Sixty-seven percent (49/73) reported use of either safety goggles/glasses or face shields when handling OPA.

Table 12. Personal protective equipment (use other than gloves or respirators) when handling OPA

Equipment	Worn by itself or in combination with another item on this list*
Safety goggles/glasses	41/73 (56%)
Disposable suit	15/73 (21%)
Disposable gown	12/73 (16%)
Face shield	8/73 (11%)

*One participant did not answer this question so the denominator is 73 instead of 74.

Limitations

Many of the methods used in this investigation were experimental. This investigation was the first to use the draft NIOSH analytical methods for OPA in air and on surfaces. Because of instrument drift between calibrations, we report only the qualitative data from the surface wipe samples. The personal air samples for OPA did not always capture the full shift. For samples that were collected only for a partial shift, we may have missed the time that employees used OPA given the low frequency of OPA use overall. Finally, OPA was detected in the majority of the personal air samples in the comparison group, so the comparison employees had some exposure to OPA. The OPA-specific IgE and IgG are newly developed, experimental assays and were used for scientific investigation. They have not been approved by the U.S. Food and Drug Administration for use in diagnosis of allergy.

Conclusions

We did not find evidence of adverse health effects associated with exposure to OPA. In addition, few symptoms were reported by employees who used OPA. The majority of participants in the exposed group used OPA in basins or containers, rather than in automated systems. About half of the participants in the exposed group reported using OPA every day. Airborne OPA concentrations were similar or higher than those reported in other healthcare facilities, though the data are limited. The ventilation systems for the areas where OPA was used, employee training, and personal protective equipment use varied among the eight facilities. Some facilities did not have effective separation between the disinfection area and surrounding areas.

Recommendations

On the basis of our overall findings, we recommend the actions listed below. We encourage all companies to use a labor-management health and safety committee or working group to discuss the recommendations in this report and develop an action plan. Those involved in the work can best set priorities and assess the feasibility of our recommendations for the specific situation at any facility that uses OPA as an HLD. Our recommendations are based on the hierarchy of controls approach (Appendix B). This approach groups actions by their likely effectiveness in reducing or removing hazards. In most cases, the preferred approach is to eliminate hazardous materials or processes and install engineering controls to reduce exposure or shield employees. Until such controls are in place, or if they are not effective or feasible, administrative measures and/or personal protective equipment may be needed.

Elimination and Substitution

Eliminating or substituting hazardous processes or materials reduces hazards and protects employees more effectively than other approaches. Prevention through design, considering elimination or substitution when designing or developing a project, reduces the need for additional controls in the future. Elimination and substitution have been used for HLD, where GTA was substituted for ethylene oxide and OPA was substituted for GTA. As the substituted compounds became widely used, health hazards emerged. There is limited toxicological data available for OPA and it has not been well studied in the workplace. Caution must be used when substituting a known hazard with a potentially unknown hazard.

Engineering Controls

Engineering controls reduce employees' exposures by removing the hazard from the process or by placing a barrier between the hazard and the employee. Engineering controls protect employees effectively without placing primary responsibility of implementation on the employee.

1. Use OPA in a dedicated room where ventilation standards and guidelines can be followed. Restrict entry into designated areas to properly trained employees.
    a. Provide a minimum of 10 ACH to rooms where OPA is used with a minimum of 2 outdoor air changes per hour [ASHRAE 2013].
    b. Locate supply diffusers and return grills so that supply air reaches room occupants without "short circuiting," i.e., flowing directly from supply diffusers to return ducts without ventilating the occupied space.
    c. Completely exhaust air serving the room containing OPA to the outdoors with no recirculation.
    d. Keep rooms containing OPA under negative pressure relative to surrounding areas to prevent airborne OPA from moving into the surrounding work areas. Airflow should follow the best practice of moving from clean to dirty areas.
2. Install LEV to control OPA vapors at the source using industrial ventilation design principles available from ACGIH [ACGIH 2013; FGI 2014].

Administrative Controls

The term "administrative controls" refers to employer-dictated work practices and policies to reduce or prevent hazardous exposures. Their effectiveness depends on employer commitment and employee acceptance. Regular monitoring and reinforcement are necessary to ensure that policies and procedures are followed consistently.

1. Provide training and supervisory oversight to ensure policies and procedures for handling OPA are followed.
2. Preventive maintenance
    a. Test and balance ventilation systems and monitor the pressure differential between the disinfection area and surrounding areas regularly, and ensure that corrective action takes place when needed to maintain the minimum ventilation requirements.
    b. Include LEV, such as vapor control systems, and automated reprocessors in a preventive maintenance program so that they are regularly inspected to ensure they are functioning as designed.
    c. Ensure that filters are checked and replaced regularly as recommended by the manufacturer.
    d. Maintain a preventive maintenance plan to ensure that automated washers and associated LEV are properly exhausting vapors outside the building.
    e. Keep rooms separated by closing doors and partitions when not in use. When doors and partitions are closed, they should create a reasonably close fit and seal separating that area from adjacent areas.
    f. Ensure that the LEV systems in place are used when working with OPA.
3. Training and education
    a. Update training materials and design them specifically for OPA. Training requirements should be consistent across all departments for employees performing similar job tasks. These job tasks should be evaluated according to employees' potential risk for exposure (e.g., job hazard analysis) to determine the level of training and personal protective equipment required.
    b. Make employees aware of potential health effects of OPA exposure by providing information from the medical literature of severe allergic reactions and skin irritation in employees working with OPA. This education may help reinforce the need for adhering to proper work practices and personal protective equipment use.
    c. Hold refresher training periodically, at least annually.
    d. Inform employees that the lack of a permissible exposure limit does not imply that a potential health hazard does not exist.

4. Written policies/infection control

    a. Establish written policies for OPA handling and training. Requirements should be consistent across all departments for employees performing similar job tasks. These job tasks should be evaluated according to employees' potential risk for exposure based on a job hazard analysis to determine the level of training and personal protective equipment required.

5. Keep covers and lids to OPA basins and cylinders/jars closed whenever possible to reduce airborne exposure to OPA.
6. Clean areas around OPA basins, including the basin cover and other high contact areas regularly.
7. Rinse hands that have contacted OPA solution with water to remove the chemical from skin and to prevent cross contaminating surfaces with OPA. Wash hands after removing gloves.
8. Tell employees to stop work, leave the area, and seek immediate medical care if they develop any shortness of breath, wheezing, or chest tightness while handling OPA. Employees should report such an event to their supervisors once they are stable.
9. Tell employees to report skin rash or irritation from OPA to their supervisors.

Personal Protective Equipment

Personal protective equipment is the least effective means for controlling hazardous exposures. Proper use of personal protective equipment requires a comprehensive program and a high level of employee involvement and commitment. The right personal protective equipment must be chosen for each hazard. Supporting programs such as training, change-out schedules, and medical assessment may be needed. Personal protective equipment should not be the sole method for controlling hazardous exposures. Rather, personal protective equipment should be used until effective engineering and administrative controls are in place.

1. Enforce use of required personal protective equipment when working with OPA. Eye protection, such as goggles or face shields, should always be worn when directly handling OPA to prevent splashes from getting into eyes.
2. Ensure use of fluid repellant gown or apron to prevent OPA from getting on their clothes or skin.
3. Wear nitrile or butyl rubber gloves for routine OPA use. Latex gloves should not be used when handling OPA because natural rubber latex can break down after prolonged exposure to OPA. In addition, natural rubber latex can cause allergy. More detailed information on latex glove allergy in healthcare employees can be found at http://www.cdc.gov/niosh/docs/98-113/.
4. Do not provide N95 filtering facepiece respirators to reduce OPA exposures. This respirator provides only particulate filtration and does not remove chemical vapors.

Appendix A: Tables

Table A1. Facility A - personal breathing zone sampling results for OPA for employees in the exposed group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
GI lab tech	249	0.34	Yes	NA	NA	NA	NA	NA	NA
Endoscopy tech	NA	NA	NA	433	1.3	No	309	0.96	Yes
Echocardiology tech	254	0.28	No	504	0.25	No	369	0.5	No
Echocardiology tech	82	ND	No	479	[0.10]*	No	409	0.17	No
Ultrasound tech	455	[0.10]	Yes	443	ND	Yes	NA	NA	NA
Ultrasound tech	484	0.26	Yes	NA	NA	NA	463	0.45	Yes
Ultrasound tech	83	ND	No	504	0.29	Yes	434	ND	Yes
Ultrasound tech	242	0.52	Yes	NA	NA	NA	NA	NA	NA
Ultrasound tech	424	ND	Yes	149	ND	No	431	0.38	No
Respiratory tech	382	0.61	Yes	464	[0.11]	No	NA	NA	NA

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A2. Facility A - personal breathing zone sampling results for OPA for employees in the comparison group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Endoscopy nurse	NA	NA	NA	487	[0.08]*	No	404	ND	No
Nurse extern	484	[0.09]	No	500	[0.09]	No	485	[0.10]	No
Nurse extern	435	[0.09]	No	484	0.49	No	432	[0.10]	No
Patient access	452	0.29	No	447	0.67	No	476	0.55	No
Patient access	423	[0.17]	No	NA	NA	NA	384	[0.18]	No
Patient access	420	[0.23]	No	360	[0.27]	No	386	[0.21]	No
Secretary	342	ND	No	269	0.35	No	NA	NA	NA
Secretary	341	ND	No	266	[0.09]	No	223	[0.21]	No
Imaging nurse	486	[0.17]	No	496	[0.10]	No	445	[0.11]	No
Pre-operative nurse	290	[0.09]	No	257	ND	No	363	[0.08]	No
Nurse	415	ND	No	449	ND	No	416	ND	No
Receptionist	416	ND	No	NA	NA	NA	NA	NA	NA

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A3. Facility B - personal breathing zone sampling results for OPA for employees in the exposed group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Endoscopy technician	451	1.8	Yes	483	0.55	Yes	465	0.43	Yes
Endoscopy technician	501	0.71	Yes	505	0.31	Yes	461	0.20	Yes
Endoscopy technician	417	2.6	Yes	440	1.2	Yes	144	0.43	Yes
Endoscopy technician	439	1.8	Yes	378	3.0	Yes	471	0.82	Yes

Table A4. Facility B - personal breathing zone sampling results for OPA for employees in the comparison group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
OR nurse	224	ND	No	NA	NA	NA	463	ND	No
Maintenance staff	245	0.53	No	256	ND	No	NA	NA	NA
Maintenance staff	463	[0.08]*	No	520	[0.07]	No	513	0.49	No
Maintenance staff	481	ND	No	522	ND	No	393	0.33	No
Maintenance staff	NA	NA	NA	453	[0.12]	No	NA	NA	NA
Maintenance staff	179	ND	No	NA	NA	NA	350	[0.16]	No

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A5. Facility C - personal breathing zone sampling results for OPA for employees in the exposed group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Nurse	NA	NA	NA	NA	NA	NA	427	[0.11]*	No
Endoscopy technician	311	1.5	Yes	NA	NA	NA	461	[0.09]	Yes
Endoscopy technician	NA	NA	NA	483	ND	Yes	NA	NA	NA
Sterilization technician	275	[0.13]	Yes	464	ND	No	464	[0.08]	Yes
Sterilization technician	267	0.55	No	460	4.2	Yes	462	1.9	Yes
Sterilization technician	207	[0.11]	No	494	[0.13]	No	484	0.39	Yes
Sterilization technician	273	[0.16]	No	479	[0.11]	No	467	[0.11]	No
Ultrasound technician	NA	NA	NA	494	0.22	Yes	NA	NA	NA
Ultrasound technician	195	ND	Yes	147	ND	No	609	[0.08]	Yes
Ultrasound technician	NA	NA		431	[0.18]	Yes	265	[0.14]	Yes
Ultrasound technician	346	[0.08]	Yes	NA	NA		530	[0.08]	Yes

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A6. Facility C - personal breathing zone sampling results for OPA for employees in the comparison group using a draft NIOSH method

Job title	Day 1			Day 2		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Management	190	0.32	No	230	0.28	No
Management	NA	NA	NA	318	0.20	No
Quality analyst	NA	NA	NA	232	ND	No
Quality analyst	NA	NA	NA	258	[0.08]*	No
Quality analyst	NA	NA	NA	295	[0.13]	No
Quality analyst	NA	NA	NA	291	0.48	No
Quality analyst	NA	NA	NA	247	†	No
Quality analyst	NA	NA	NA	248	ND	No
Secretary	NA	NA	NA	207	[0.11]	No

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values associated with these values.

†Pre-calibration and post-calibration differences exceeded 50%.

Table A7. Facility D - personal breathing zone sampling results for OPA for employees in the exposed group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Medical assistant	489	[0.09]*	Yes	471	[0.09]	No	471	ND	No
Medical assistant	412	[0.09]	Yes	475	[0.18]	No	230	ND	No
Medical assistant	357	ND	Yes	475	[0.11]	Yes	448	[0.09]	Yes
Endoscopy technician	399	1.1	Yes	374	[0.13]	Yes	365	[0.11]	No
Endoscopy technician	562	[0.15]	No	219	ND	No	NA	NA	NA
Anesthesia technician	NA	NA	NA	422	[0.14]	Yes	NA	NA	NA
Anesthesia technician	227	[0.20]	Yes	NA	NA	NA	229	[0.18]	No
Anesthesia technician	478	[0.08]	Yes	NA	NA	NA	NA	NA	NA
Anesthesia technician	328	[0.18]	No	NA	NA	NA	NA	NA	NA
Anesthesia technician	180	[0.25]	No	NA	NA	NA	NA	NA	NA
Nurse	281	ND	Yes	395	[0.11]	Yes	249	ND	Yes
Registration staff	430	[0.14]	Yes	411	ND	Yes	233	ND	Yes
Health care assistant	NA	NA	NA	455	[0.08]	No	NA	NA	NA
Health care assistant	453	5.2	Yes	473	7.6	Yes	490	35	Yes
Health care assistant	482	[0.10]	No	520	[0.07]	No	NA	NA	NA
Health care assistant	226	ND	No	475	0.58	Yes	379	[0.10]	No
Health care assistant	371	[0.12]	Yes	476	[0.15]	No	452	0.62	No
Health care assistant	226	ND	No	NA	NA	NA	231	[0.12]	No
Health care assistant	151	ND	No	NA	NA	NA	NA	NA	NA
Health care assistant	242	ND	No	248	ND	Yes	NA	NA	NA

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A8. Facility D - personal breathing zone sampling results for OPA for employees in the comparison group using a draft NIOSH method

Job title	Day 1		
	Time (min)	TWA	Used OPA
Nurse	228	ND	No
Nurse	231	[0.19]*	No
Nurse	231	[0.16]	No
Nurse	250	[0.11]	No
Nurse	272	[0.12]	No
Pharmacy technician	288	0.23	No
Pharmacy technician	261	[0.14]	No
Pharmacy technician	263	[0.15]	No
Pharmacy technician	255	[0.09]	No
Pharmacy technician	242	[0.16]	No
Pharmacy technician	263	[0.12]	No
Pharmacy technician	219	[0.14]	No
Health care assistant	235	0.14	No

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A9. Facility E - personal breathing zone sampling results for OPA for employees in the exposed group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Respiratory technician	NA	NA	NA	415	[0.67]*	Yes	NA	NA	NA
Respiratory technician	NA	NA	NA	409	ND	No	504	ND	Yes
Respiratory technician	468	ND	No	387	ND	No	NA	NA	NA
Respiratory technician	467	ND	No	NA	NA	NA	NA	NA	NA
EEG technician	486	ND	Yes	434	ND	Yes	486	ND	Yes
EEG technician	497	ND	Yes	476	ND	No	472	ND	No
EEG technician	493	ND	Yes	477	ND	Yes	NA	NA	NA
Ultrasound technician	475	ND	No	332	3.4	Yes	236	ND	No
Ultrasound technician	503	ND	Yes	NA	NA	NA	468	ND	Yes
Ultrasound technician	448	ND	Yes	127	ND	No	405	ND	Yes
Echocardiology technician	NA	NA	NA	432	ND	Yes	NA	NA	NA
Echocardiology technician	NA	NA	NA	439	ND	Yes	NA	NA	NA
Surgery technician	440	ND	Yes	195	ND	Yes	474	38	Yes
Respiratory technician	421	ND	Yes	514	ND	No	449	ND	Yes
Respiratory technician	NA	NA	NA	218	ND	Yes	NA	NA	NA
Respiratory technician	NA	NA	NA	439	ND	Yes	NA	NA	NA

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A10. Facility E - personal breathing zone sampling results for OPA for employees in the comparison group using a draft NIOSH method

Job title	Day 1			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Maintenance staff	236	ND	No	NA	NA	NA
Maintenance staff	227	ND	No	NA	NA	NA
Maintenance staff	245	ND	No	NA	NA	NA
Maintenance staff	257	ND	No	NA	NA	NA
Quality analyst	232	ND	No	NA	NA	NA
Quality analyst	495	ND	No	NA	NA	NA
Quality analyst	463	ND	No	NA	NA	NA
Management	499	ND	No	NA	NA	NA
Management	NA	NA	NA	519	ND	No

Table A11. Facility F - personal breathing zone sampling results for OPA for employees in the exposed group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Endoscopy technician	499	13	Yes	480	8.5	Yes	439	11	Yes
Endoscopy technician	535	0.47	Yes	488	0.67	No	474	0.66	No
Endoscopy technician	403	1.2	No	509	0.79	No	454	1.1	No
Endoscopy technician	433	1.7	No	466	0.78	Yes	452	1.1	No

Table A12. Facility F - personal breathing zone sampling results for OPA for employees in the comparison group using a draft NIOSH method

Job title	Day 1		
	Time (min)	TWA	Used OPA
Secretary	243	[0.16]*	No
Sterilization technician	243	0.07	No
Management	252	[0.16]	No
Management	177	0.50	No

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A13. Facility G - personal breathing zone sampling results for OPA for employees in the exposed group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Endoscopy technician	411	1.6	Yes	569	4.1	Yes	NA	NA	NA
Endoscopy technician	258	0.51	No	490	[0.15]*	No	508	0.24	No
Endoscopy technician	541	[0.19]	No	482	0.42	No	479	7.9	Yes
Endoscopy technician	385	2.8	Yes	NA	NA	NA	509	2.0	Yes
Endoscopy technician	532	2.8	Yes	433	0.33	No	NA	NA	NA
Endoscopy technician	466	1.2	Yes	415	0.86	Yes	NA	NA	NA
Endoscopy technician	484	3.5	Yes	NA	NA	NA	NA	NA	NA

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A14. Facility G - personal breathing zone sampling results for OPA for employees in the comparison group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Nurse	239	ND	No	242	ND	No	244	ND	No
Nurse	261	ND	No	243	0.14	No	NA	NA	NA
Nurse	264	1.0	No	237	[0.34]*	No	NA	NA	NA
Housekeeping/ Environmental Services	239	ND	No	232	ND	No	NA†	NA	No
Receptionist	231	ND	No	NA	NA	NA	237	ND	No
Management	267	ND	No	260	ND	No	244	[0.2]‡	No
Management	222	ND	No	NA	NA	NA	NA	NA	NA
Management	268	ND	No	NA	NA	NA	NA	NA	NA
Registration staff	230	ND	No	NA	NA	NA	NA	NA	NA
Registration staff	283	ND	No	NA	NA	NA	NA	NA	NA
Registration staff	267	ND	No	NA	NA	NA	NA	NA	NA

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Table A15. Facility H - personal breathing zone sampling results for OPA for employees in the exposed group using a draft NIOSH method

Job title	Day 1			Day 2			Day 3		
	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA	Time (min)	TWA	Used OPA
Endoscopy technician	480	2.6	No	446	3.8	Yes	381	1.8	Yes
Endoscopy technician	472	1.2	Yes	NA	NA	NA	NA	NA	NA
Endoscopy technician	472	2.9	Yes	502	2.5	Yes	511	1.5	Yes

Table A16. Facility H - personal breathing zone sampling results for OPA for employees in the comparison group using a draft NIOSH method

Job title	Day 1		
	Time (min)	TWA	Used OPA
Nurse	253	0.63	No
Nurse	240	0.46	No
Secretary	235	ND	No
Security staff	238	[0.30]*	No
Cashier	233	0.56	No

*Values in brackets indicate concentrations above the MDC but below the MQC. Brackets are used to indicate there is more uncertainty associated with these values.

Appendix B: Occupational Exposure Limits and Health Effects

NIOSH investigators refer to mandatory (legally enforceable) and recommended OELs for chemical, physical, and biological agents when evaluating workplace hazards. OELs have been developed by federal agencies and safety and health organizations to prevent adverse health effects from workplace exposures. Generally, OELs suggest levels of exposure that most employees may be exposed to for up to 10 hours per day, 40 hours per week, for a working lifetime, without experiencing adverse health effects. However, not all employees will be protected if their exposures are maintained below these levels. Some may have adverse health effects because of individual susceptibility, a pre-existing medical condition, or a hypersensitivity (allergy). In addition, some hazardous substances act in combination with other exposures, with the general environment, or with medications or personal habits of the employee to produce adverse health effects. Most OELs address airborne exposures, but some substances can be absorbed directly through the skin and mucous membranes.

Most OELs are expressed as a time-weighted average exposure. A time-weighted average refers to the average exposure during a normal 8- to 10-hour workday. Some chemical substances and physical agents have recommended short term exposure limit or ceiling values. Unless otherwise noted, the short term exposure limit is a 15-minute time-weighted average exposure. It should not be exceeded at any time during a workday. The ceiling limit should not be exceeded at any time.

In the United States, OELs have been established by federal agencies, professional organizations, state and local governments, and other entities. Some OELs are legally enforceable limits; others are recommendations.

- The U.S. Department of Labor OSHA permissible exposure limits (29 CFR 1910 [general industry]; 29 CFR 1926 [construction industry]; and 29 CFR 1917 [maritime industry]) are legal limits. These limits are enforceable in workplaces covered under the Occupational Safety and Health Act of 1970.
- NIOSH recommended exposure limits are recommendations based on a critical review of the scientific and technical information and the adequacy of methods to identify and control the hazard. NIOSH recommended exposure limits are published in the *NIOSH Pocket Guide to Chemical Hazards* [NIOSH 2010]. NIOSH also recommends risk management practices (e.g., engineering controls, safe work practices, employee education/training, personal protective equipment, and exposure and medical monitoring) to minimize the risk of exposure and adverse health effects.
- Other OELs commonly used and cited in the United States include the threshold limit values®, which are recommended by ACGIH, a professional organization, and the workplace environmental exposure levels™, which are recommended by the American Industrial Hygiene Association, another professional organization. The threshold limit values and the workplace environmental exposure levels™ are developed by committee members of these associations from a review of the published, peer-reviewed literature.

These OELs are not consensus standards. Threshold limit values are considered voluntary exposure guidelines for use by industrial hygienists and others trained in this discipline "to assist in the control of health hazards" [ACGIH 2015]. Workplace environmental exposure levels™ have been established for some chemicals "when no other legal or authoritative limits exist" [AIHA 2015].

Outside the United States, OELs have been established by various agencies and organizations and include legal and recommended limits. The Institut für Arbeitsschutz der Deutschen Gesetzlichen Unfallversicherung (Institute for Occupational Safety and Health of the German Social Accident Insurance) maintains a database of international OELs from European Union member states, Canada (Québec), Japan, Switzerland, and the United States. The database, available at http://www.dguv.de/ifa/Gefahrstoffdatenbanken/GESTIS-Internationale-Grenzwerte-für-chemische-Substanzen-limit-values-for-chemical-agents/index-2.jsp, contains international limits for more than 1,500 hazardous substances and is updated periodically.

OSHA requires an employer to furnish employees a place of employment free from recognized hazards that cause or are likely to cause death or serious physical harm [Occupational Safety and Health Act of 1970 (Public Law 91–596, sec. 5(a)(1))]. This is true in the absence of a specific OEL. It also is important to keep in mind that OELs may not reflect current health-based information.

When multiple OELs exist for a substance or agent, NIOSH investigators generally encourage employers to use the lowest OEL when making risk assessment and risk management decisions. NIOSH investigators also encourage use of the hierarchy of controls approach to eliminate or minimize workplace hazards. This includes, in order of preference, the use of (1) substitution or elimination of the hazardous agent, (2) engineering controls (e.g., local exhaust ventilation, process enclosure, dilution ventilation), (3) administrative controls (e.g., limiting time of exposure, employee training, work practice changes, medical surveillance), and (4) personal protective equipment (e.g., respiratory protection, gloves, eye protection, hearing protection). Control banding, a qualitative risk assessment and risk management tool, is a complementary approach to protecting employee health. Control banding focuses on how broad categories of risk should be managed. Information on control banding is available at http://www.cdc.gov/niosh/topics/ctrlbanding/. This approach can be applied in situations where OELs have not been established or can be used to supplement existing OELs.

Glutaraldehyde

GTA is a colorless liquid with a pungent odor. Its dialdehyde structure imparts significant reactivity making it a highly effective disinfectant. It is used in a variety of industries, including healthcare for cleaning endoscopes and other heat sensitive equipment, cosmetics, paper manufacturing, water treatment, and agriculture. Airborne exposure to GTA can cause eye, skin, and respiratory tract irritation; allergic response; shortness of breath; and headache [Di Stefano et al. 1998, 1999; NIOSH 2001]. GTA has also been associated with the development of occupational asthma via sensitization, and cases of occupational asthma have occurred after exposure far below existing OELs [Gannon et al. 1995; Di Stefano et al. 1999;

Ong et al. 2004]. One study of healthcare workers who used GTA found that 7/24 employees reporting symptoms consistent with asthma had GTA-specific IgE, 8/24 had positive specific bronchial provocation testing [Di Stefano et al. 1999].

OSHA has no permissible exposure limit for GTA. The NIOSH recommended exposure limit for GTA is a ceiling limit of 0.2 parts per million or 800 $\mu g/m^3$, while the ACGIH threshold limit value for GTA is a ceiling limit of 0.05 parts per million or 205 $\mu g/m^3$ [NIOSH 2010; ACGIH 2015].

Ortho-phthalaldehyde

OPA is a dialdehyde that exhibits similar reactivity and effectiveness as a biocide as GTA. OPA has benzene ring or aromatic structure. OPA is a clear, light blue liquid and does not have a pungent odor. OPA has a lower vapor pressure (0.69 Pascal) [Integrated Laboratory Systems 2007] than GTA (80 Pascals), therefore, it has been marketed as a safer alternative. For disinfectant use, it is typically diluted to 0.55%–0.60% OPA in an aqueous base containing buffers, chelating agents, and a corrosion inhibitor. OPA does not require activation or dilution before use and is stable over a wide pH range (3–9). The solution can be reused for up to 14 days or when test strips indicate that the solution has fallen below the accepted concentration. Unopened, OPA has a shelf life of up to 2 years.

There are currently no OELs for OPA. The manufacturer of Cidex® OPA (Advanced Sterilization Products, Johnson & Johnson), states OPA can cause skin irritation, dryness, cracking, and staining after direct contact with the liquid form, and irritation of the eyes, nose, and respiratory tract from vapor. Other symptoms from inhalation of OPA may include chest and throat tightness, difficulty breathing, a stinging sensation in the nose and throat, tingling of the mouth and lips, headache, loss of smell, and dry mouth [Advanced Sterilization Products 2010]. Cases of anaphylaxis have been associated with OPA exposure after undergoing a procedure with devices cleaned with OPA that were not adequately rinsed to remove OPA residue [Sokol 2004; Suzukawa et al. 2007; Cooper et al. 2008].

Elicitation of irritant and allergic reactions in mice has been reported [Anderson et al. 2010; Morinaga et al. 2010]. More recently, other investigators have found that inhalation of OPA vapors in mice can trigger both respiratory and systemic sensitization. The respiratory sensitization can manifest as asthma-like symptoms [Johnson et al. 2011]. Morinaga and associates found that OPA induced the production of IgE and IgG in the sera, suggesting that OPA acts as a hapten [Morinaga et al. 2010].

Qualitative structure-activity relationship analysis has been used to determine if molecular structure could be used to predict the potential for respiratory sensitization when compared against other known sensitizers. Qualitative structure-activity relationship analysis produces an odds ratio of the hazard or risk for respiratory sensitization potential with 0 being the lowest risk and 1.00 denoting the highest risk. This method was used to compare the four most common HLDs: GTA, OPA, peracetic acid, and hydrogen peroxide. The results of the qualitative structure-activity relationship analysis indices were 0.82 for GTA, 0.72 for OPA, 0.03 for peracetic acid, and 0.01 for hydrogen peroxide [Rideout et al. 2005].

Appendix C: Methods

Recruitment of Health Hazard Evaluation Participants

Eight facilities throughout the United States agreed to participate in this study from 2006 through 2009. Participation in any or all aspects of the HHE was voluntary. Informed consent was obtained from participating employees. Participants who completed all elements of the HHE for all shifts worked were reimbursed $50. Participants were reimbursed $25 if they participated in the other elements of the HHE, but were unwilling or unable to provide either a blood sample or undergo allergy testing. If neither blood draw nor the PST was completed, then no compensation was given.

Participants were asked to participate in the HHE for all 3 days of the site visit if their work schedule permitted, although participation of 1–3 days was acceptable. We excluded from the PSTs anyone with a prior history of anaphylaxis, pregnant women, and women who might be pregnant. Employees with suppressed immune systems from illness (HIV/AIDS, genetic immune disorder, etc.) or medication (corticosteroids, posttransplant antirejection therapy, or chemotherapy) were excluded. Pregnancy status was reconfirmed at the return site visit.

Questionnaire

On the first day, participants completed a questionnaire about their personal characteristics, work history, medical history, cough, and skin and respiratory symptoms during the prior 30 days. Symptoms were considered work-related if they were better on days off work. This questionnaire also asked about OPA use, personal protection equipment use, and training about handling OPA.

Postshift Survey

We asked each participant about respiratory and mucous membrane symptoms at the end of their shift each day. Only symptoms that were not present prior to the shift were documented.

Puncture Skin Test

An allergist performed PSTs once on each participant with a bifurcated needle (Figure C1) using published methods [Sokol 2004]. The PSTs included an atopy panel, which included red cedar, meadow fescue (a type of grass), short ragweed, timothy grass, *Alternaria* mold, white oak, *Aspergillus fumigatus* fungus, maple mix, *Cladosporium* (a type of mold), American elm, dust mite mix, dog, and cat. The atopy panel also included a histamine positive control and a saline negative control. The positive control assured that the participant had an adequately functioning immune system that could produce a positive response, while the negative control identified those with dermatographia, a medical condition in which applied pressure on the skin produces a reaction similar to an actual positive response to a specific allergen. Two OPA solutions (0.55 mg/mL and 5.5 mg/mL) were developed (not U.S. Food and Drug Administration approved) for this hazard assessment. The allergist read the PSTs 15 minutes after placement of the final allergen.

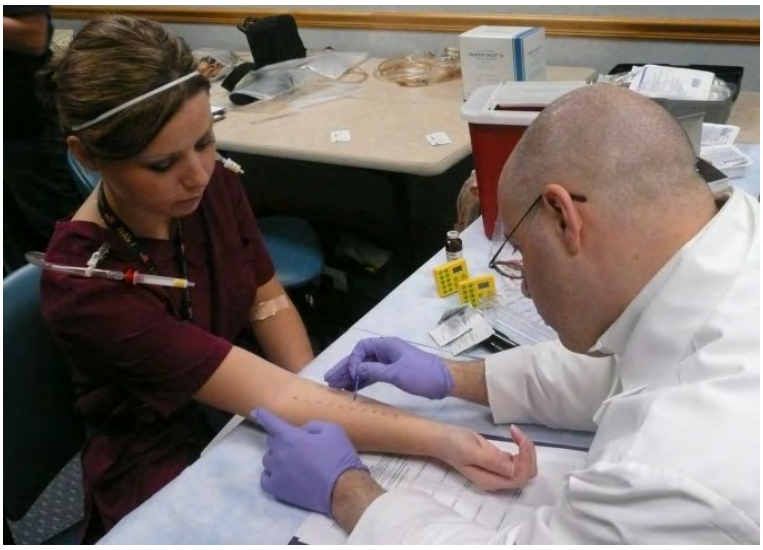

Figure C1. Allergist placing PST panel on a study participant. Photo by NIOSH.

We measured the diameters of the wheal (swelling caused by collection of fluid in the tissues under the skin caused by the gathering of inflammatory mediators) and flare (flat area of redness) of a positive reaction (Figure C2). The diameter of each wheal and flare was outlined with a marker, transferred off the skin with tape, placed on a data form, and measured in millimeters on a flat surface. It was possible to have a flare without wheal and vice versa. A positive test was 3 millimeters or greater.

The first two positions on the panel were reserved for the positive and negative controls (Figure C2). If a participant had a dermatographic reaction, we subtracted the response seen at the saline location from the responses at the other locations on the PST panel and recorded the difference.

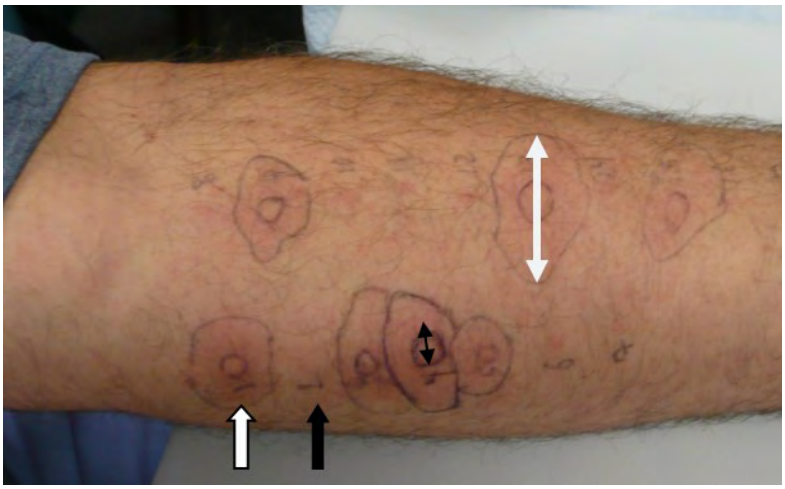

Figure C2 – A PST with wheal (double black arrow) and flare (double white arrow) marked. The positive histamine control is designated by the white arrow and the negative saline control by the black arrow. Photo by NIOSH

If any reaction other than itching at positive PST sites occurred, treatment was immediately provided by the allergist, and the participant was transferred to the nearest emergency department. No further skin testing was performed on any individual who showed evidence of a systemic reaction. The contract allergist provided us with a copy of each participant's results, an interpretation of skin test results, and results/recommendations for each participant.

Ortho-phthalaldehyde-specific Antibody Testing

A physician or a phlebotomist collected approximately 10 milliliters of whole blood from each participant following the universal precautions for working with blood and blood products specified by CDC [1998] and the OSHA bloodborne pathogen standard [29 CFR 1910.1030]. After venipuncture, we centrifuged the blood and transported the serum to the NIOSH laboratory for analysis.

We prepared OPA-human serum albumin (HSA) conjugates using a modification of existing methods [Tse and Pesce 1979]. We assayed OPA-specific IgE and IgG antibodies in triplicate by indirect enzyme-linked immunosorbent assay detection of the immunocomplexes with a labeled immunoglobulin as previously described [Biagini et al. 1990; Biagini et al. 1996; Crowther 2001]. We assayed specific IgE and IgG at 1:10 and 1:100 dilutions of test sera. We incubated plates at room temperature for 1 hour with 0.1 mL/well of test or control sera. We detected IgG immunocomplexes with goat anti-human IgG, γ-chain and species-specific, alkaline phosphatase labeled, 1:20,000 dilution, 0.1 mL/well (Product #3187, Sigma). We detected IgE immunocomplexes with unlabeled goat anti-human IgE, Fc-specific, affinity purified IgG, 100 nanograms/well, followed by rabbit anti-goat IgG, γ-chain specific, alkaline phosphatase labeled, 50 nanograms/well (KPL). For all enzyme-linked immunosorbent assay tests, substrate consisted of 1 mg/mL p-nitrophenyl phosphate in 10% weight by volume diethanolamine, 0.5 millimolar magnesium chloride, pH 9.8. For both specific IgE and IgG, a test was considered positive if the mean optical density 405 nm of test serum (1:10 dilution) triplicates was at least 0.1 and also > 3 standard deviations above the mean of eight negative reference sera, and if the serum tested negative for antibody to mock-conjugated HSA.

We performed competitive inhibition assays [Biagini et al. 1990; Christopoulos and Diamandis 1996] for all sera exhibiting positive binding to OPA-HSA antigen with an optical density of at least 0.2. We mixed aliquots of test sera, diluted 1:5, with equal volumes of blocking buffer (antibody control), 1, 10, 100, or 1000 micrograms per milliliter of OPA-HSA conjugate, and also 1, 10, 100, 1000 micrograms per milliliter of mock-conjugated HSA, and incubated them overnight on a rotary shaker at room temperature. We then added the inhibition mixtures to antigen-coated plates, and performed IgG or IgE specific enzyme-linked immunosorbent assay tests according to the protocols described above.

We calculated percent inhibition as:

$$\frac{(\text{Mean optical density uninhibited serum} - \text{Mean optical density inhibited serum}) \times 100}{\text{Mean optical density of uninhibited serum}}$$

We considered test results showing at least 50% inhibition by any OPA-HSA antigen concentration tested, without concomitant inhibition by HSA (< 50% inhibition at any HSA

concentration and consistently less than inhibition by antigen), indicative of serum specific antibody reactions.

Preshift and Postshift Dermal Examinations

We examined participants' hands and forearms before and after each shift for discoloration and for signs of skin irritation, such as redness and cracking. A dermal examination rating form was used to document findings and included a key for coding findings. If participants did not have a preshift and postshift set of dermal exams, they were not included in that day's analysis. Participants were categorized as unchanged if their preshift and postshift dermal examinations were unchanged, better if they had fewer findings on the postshift examination than the preshift examination, and worse if they had more findings on the postshift examination than on their preshift examination.

Statistical Analysis

We used the SAS Institute, SAS software Version 9.1.3 for statistical analysis. Fisher's exact tests were used analyze symptoms and to compare atopy and PST results for OPA. Values for the exposure measurements that were below the minimum detectable concentration were estimated by dividing the minimum detectable concentration by the square root of 2 [Hornung and Reed 1990]. GMs and maximum measures were used to report exposure concentrations. P values < 0.05 were considered statistically significant.

Air and Surface Sampling Measurements

We used a sampling pump that pulled air through a Supelco LpDNPH S10L tube that contained silica gel coated with 1 milligram of acidified 2,4-dinitrophenylhydrazine to take personal air samples for OPA. We filled sample cartridges with approximately 600 microliters (µL) of ethyl acetate using a syringe in the field. The samples stood at room temperature for 72 hours before being eluted with 3 mL of dimethyl sulfoxide. The eluent was analyzed by high performance liquid chromatography according to the NIOSH draft method SPT12 [Tucker 2008] for OPA in air samples.

To sample for GTA, a sampling pump pulled air through a Supelco LpDNPH S10L cartridge containing a double bed of silica gel coated with DNPH. Each bed was separated into individual vials, and 3.0 mL of acetonitrile were added. Vials were agitated for at least 2 hours and analyzed by high performance liquid chromatography according to NIOSH Method 2532 [NIOSH 2015].

Table C1 shows the limits of detection and quantitation obtained for air samples analyzed at each of the facilities we evaluated. Table C2 shows the minimum detectable concentrations and minimum quantifiable concentrations obtained for air samples analyzed at each of the facilities we evaluated.

Table C1. Limit of detection and limit of quantitation information

Location	OPA – Silica gel tube draft method		GTA	
	LOD (µg/sample)	LOQ (µg/sample)	LOD (µg/sample)	LOQ (µg/sample)
Facility A	0.02	0.06	0.2	0.65
Facility B	0.02	0.06	0.2	0.65
Facility C	0.02	0.06	0.2	0.65
Facility D	0.02	0.06	0.4	1.4
Facility E	0.08	0.27	0.2	0.79
Facility G	0.03	0.10	0.2	0.61
Facility H (Day 1)	0.03	0.10	0.2	0.61
Facility H (Day 2 and 3)	0.009	0.03	0.2	0.53
Facility F	0.01	0.05	0.2	0.77

LOD = Limit of detection

LOQ = Limit of quantitation

Table C2. Minimum detectable concentrations and minimum quantifiable concentrations

Location	OPA – silica gel tube draft method		GTA	
	MDC* ($\mu g/m^3$)	MQC* ($\mu g/m^3$)	MDC† ($\mu g/m^3$)	MQC† ($\mu g/m^3$)
Facility A	0.08	0.25	0.42	1.35
Facility B	0.08	0.25	0.42	1.35
Facility C	0.08	0.25	0.42	1.35
Facility D	0.08	0.25	0.83	2.92
Facility E	0.33	1.13	0.42	1.65
Facility G	0.13	0.42	0.42	1.27
Facility H Day 1	0.13	0.42	0.42	1.27
Facility H Day 2&3	0.04	0.13	0.42	1.10
Facility F	0.04	0.20	0.42	1.60

MDC = Minimum detectable concentration

MQC = Minimum quantifiable concentration

*Based on volume of 240 liters

†Based on volume of 480 liters

We collected wipe samples using extracted Ghost™ Wipes cut into three strips and dampened with 20 µL of 40:60 dimethyl sulfoxide and water solution. We wiped the same area of 50 to 100 square centimeters with each strip, and then immersed them in a vial containing 12 mL of dimethyl sulfoxide and shook it. We placed 3 mL of this dimethyl sulfoxide solution in a curvet then added 100 µL of an 11.1% N-acetyl-L-cysteine solution and 50 µL of a 4.4% ethylenediamine solution. We mixed the solutions and measured the fluorescence reading with a calibrated portable fluorometer. We determined the OPA concentration using a calibration curve constructed according to NIOSH draft method SPT14 [Tucker 2008].

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