



# Evaluation of Waste Anesthetic Gas Exposure and Miscarriages at a Veterinary Hospital

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## **Availability of Report**

Copies of this report have been sent to the employer and employees at the veterinary hospital. The state and local health department and the Occupational Safety and Health Administration Regional Office have also received a copy. This report is not copyrighted and may be freely reproduced.

## **Recommended Citation**

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# Table of Contents

## Main Report

Introduction .....	1
Our Approach .....	1
Our Key Findings.....	2
Our Recommendations .....	4

## Supporting Technical Information

Section A: Workplace Information.....	A-1
Building.....	A-1
Employee Information .....	A-1
History of Issue at Workplace .....	A-1
Process Description .....	A-3
Section B: Methods, Results, and Discussion .....	B-1
Methods: Work Practices .....	B-1
Results: Work Practices .....	B-1
Methods: Training and Policies on Workplace Hazards .....	B-3
Results: Training and Policies on Workplace Hazards .....	B-3
Methods: Exposure Assessment .....	B-4
Results: Exposure Assessment .....	B-5
Methods: Employee Health .....	B-8
Results: Employee Health .....	B-9
Discussion .....	B-10
Conclusions .....	B-13
Section C: Tables .....	C-1
Section D: Occupational Exposure Limits .....	D-1
Isoflurane.....	D-2
Section E: References .....	E-1

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# Introduction

## Request

In March 2017, employees of a veterinary hospital requested a health hazard evaluation because they were concerned that waste anesthetic gas exposures were causing reproductive health effects among employees. The veterinary hospital used two types of anesthetic gas, isoflurane and sevoflurane. Isoflurane was the primary anesthetic gas used during surgery.

## Workplace

Animal surgeries involved the following steps:

- Sedating the animal with propofol
- Intubating and anesthetizing the animal with isoflurane or sevoflurane
- Shaving, cleaning, and preparing the animal for surgery
- Conducting the surgery
- Recovering the animal until consciousness is regained

Departments in this veterinary hospital included administration, avian/exotics, emergency, internal medicine, inventory, oncology, and surgery. When we visited, 53 people worked at the veterinary hospital, including 6 people who worked in the surgery department. The hospital operated 8- and 10-hour shifts with staggered start times. Scheduled surgeries were conducted during the day shift on weekdays by employees in the surgery department. Emergency surgeries were conducted as needed by the on-call veterinary surgical staff.

Active scavenging systems for waste anesthetic gas were located in both operating rooms and areas of the recovery area/intensive care unit where nonsurgical procedures were conducted. A passive scavenging system was used in the knockdown side of the recovery area/intensive care unit.

**To learn more about the workplace, go to [Section A in the Supporting Technical Information](#)**

## Our Approach

We spent two days in the veterinary hospital in September 2017. On this visit, our primary objectives were to gather information about

- Work practices
- Ventilation
- Operation and maintenance of scavenging systems for recovery of waste anesthetic gases
- Employee exposures to isoflurane
- Area isoflurane concentrations in the air throughout the veterinary hospital
- Employee health

**To learn more about our methods, go to [Section B in the Supporting Technical Information](#)**

## Our Key Findings

### One employee was exposed to isoflurane levels in the air that were over an occupational exposure limit for waste anesthetic gas.

The overexposure to isoflurane happened while a veterinary technician was recovering a dog after surgery in the recovery area/intensive care unit (Figure 1). After surgery, anesthetic gas remains in the animal's exhaled breath. When veterinary technicians recovered animals after surgery, their faces were usually close to the animal's face to assess the animal's level of alertness.



Figure 1. Recovery area and intensive care unit of the veterinary hospital. Animal patients were kept in kennels along the wall before and after care. An active scavenging system (circled) used for nonsurgical procedures is visible by one of the tables. Photo by NIOSH.

None of the other 35 employee exposure measurements (measured on 6 employees) were above the National Institute for Occupational Safety and Health (NIOSH) recommended exposure limit for halogenated waste anesthetic gas of 2 parts per million in a 60-minute time period. This occupational exposure limit was recommended by NIOSH for the type of anesthetic gas to which isoflurane belongs, but before isoflurane came into use. We collected personal isoflurane measurements from initial isoflurane introduction until recovery. Full-shift area concentrations of isoflurane measured inside the veterinary hospital were low, ranging from not detected to just above the minimum detectable concentration.

Instantaneous isoflurane area measurements found higher concentrations of isoflurane:

- Near the mouth of the animal before, during, and after surgery (Figure 2)
- At the vacuum exhaust in the back of the building during surgery (Figure 3)

Of the 17 interviewed employees who worked in the operating room, only 7 (41%) reported receiving training about the potential health effects of anesthetic gases from the veterinary hospital.



Figure 2. A NIOSH investigator taking a direct-reading measurement for isoflurane concentrations using the Thermo Scientific™ MIRAN SapphIRE XL portable ambient analyzer. This photo was taken before surgery. Photo by NIOSH.



Figure 3. A NIOSH investigator taking measurements for isoflurane concentrations using a wand approximately 4 inches away from the exhaust pipe. The exhaust pipe for the hospital vacuum system was approximately 8 feet above the ground at the rear of the building. This area is accessible by staff and the public. Photo by NIOSH.

### **Seven employees reported 12 miscarriages while employed at the veterinary hospital. Our evaluation could not link the reported miscarriages to work at the veterinary hospital.**

What causes most miscarriages is not known. Some studies have found that anesthetic gases are associated with miscarriages, but those studies occurred before scavenging systems were in use and exposure levels were much higher than exposures found at the veterinary hospital. Scientists do not know how much anesthetic gas exposure is needed to increase the risk of miscarriage. We do know that miscarriages are common. Many factors have been linked to increased miscarriage, including maternal age, paternal age, and health conditions. However, we do not have enough information to evaluate whether the rate of miscarriage among employees of this veterinary hospital is substantially higher than would be expected given their health and reproductive history.

### **Other reproductive hazards present in the veterinary hospital should be evaluated for employee safety.**

Several employees have job tasks that might involve potential exposure to other reproductive hazards. Although these exposures were outside the scope of this evaluation, these job tasks included:

- Handling hazardous drugs associated with reproductive and developmental toxicity, including formalin, chemotherapy medications, prostaglandins, and other reproductive hormones.
- Being in the x-ray room while radiographs are being taken.
- Setting up the ethylene oxide sterilizer or being in the pack/prep area when the ethylene oxide sterilizer is on.

To learn more about our results, go to [Section B in the Supporting Technical Information](#)

## Our Recommendations

The Occupational Safety and Health Act requires employers to provide a safe workplace.

### Benefits of Improving Workplace Health and Safety:

- |  |  |
|--|--|
| ↑ Improved worker health and well-being    | ↑ Improved image and reputation            |
| ↑ Better workplace morale                  | ↑ Better products, processes, and services |
| ↑ Better employee recruiting and retention | ↑ Could increase overall cost savings      |

The recommendations below are based on the findings of our evaluation. For each recommendation, we list a series of actions you can take to address the issue at your workplace. The actions at the beginning of each list are preferable to the ones listed later. The list order is based on a well-accepted approach called the “hierarchy of controls.” The hierarchy of controls 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 personal protective equipment may be needed. Read more about the hierarchy of controls here: <https://www.cdc.gov/niosh/topics/hierarchy/>.



We encourage the company to use a health and safety committee to discuss our recommendations and develop an action plan. Both employee representatives and management representatives should be included on the committee. Helpful guidance can be found in *Recommended Practices for Safety and Health Programs* at: <https://www.osha.gov/shpguidelines/index.html>.

### Recommendation 1: Reduce employees' exposure to waste anesthetic gas.

Why? Exposure to high concentrations of waste anesthetic gas may cause headache, irritability, fatigue, nausea, drowsiness, difficulties with judgment and coordination, and liver and kidney disease. Long-term exposure to lower concentrations of waste anesthetic gas have been linked to miscarriages, genetic damage, and cancer in some studies.

We found the highest concentrations of isoflurane near the animal's head after intubation and anesthetization with isoflurane. Isoflurane was detectable near the animal's head throughout the surgery and during postoperative x-rays and recovery.

**How? At your workplace, we recommend these specific actions:**



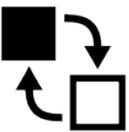
**Replace the passive scavenging systems with active scavenging systems.**

- Use an active scavenging system to reduce waste anesthetic gas concentrations when recovering animals.
- Use an active scavenging system when anesthetic gases are being used in the avian/exotics exam room.



**Consult with a ventilation engineer to ensure that the hospital ventilation system prevents exposure to waste anesthetic gas.**

- Operating rooms should have at least 15 air changes per hour with a minimum of 3 air changes of fresh air per hour.
- The recovery area/intensive care unit should have at least 6 air changes per hour, with a minimum of 2 air changes of fresh air per hour.



**Replace modified containers used to anesthetize birds and other small animals with induction chambers designed for this purpose. Use the building's existing vacuum system to remove waste anesthetic gas from induction chambers after use.**



**Properly maintain existing anesthesia machines and waste anesthetic gas scavenging systems to minimize leaks.**



**Move the vacuum exhaust away from areas accessible to pedestrians to reduce potential for exposure to exhausted waste anesthetic gas.**



**Avoid being near an animal's head before and during surgery, and while recovering after surgery.**



**Educate employees at least annually on procedures for reducing exposures to waste anesthetic gas.**

- Educate employees about waste anesthetic gas exposure, signs and symptoms of exposure, and methods to control this exposure, at hire and at least annually thereafter.
- Train employees on how to inspect the anesthetic delivery system and the scavenging equipment to ensure connections are correct before each use, and at hire and at least annually thereafter.

- More information on occupational exposures to waste anesthetic gases in hospitals is available at: <https://www.cdc.gov/niosh/docs/2007-151/>.



### **Improve the hazard communication program.**

- Label gas cylinders containing anesthetic gases.
- Make safety data sheets readily available.
- Train all employees as required by the Occupational Safety and Health Administration (OSHA) hazard communication standard.

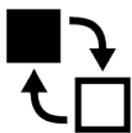
## **Recommendation 2: Evaluate other reproductive hazards in the workplace.**

Why? A workplace can have multiple health hazards that cause worker illness or injury. Similar to the ones identified above, these hazards can potentially cause serious health symptoms, lower morale and quality of life for your employees, and increase costs to your business. Although we only specifically evaluated anesthetic gas exposure in this workplace, we noticed the following potential issues at your workplace:

- Misoprostol, which should not be handled by pregnant women, was stored with other medications. The warning label was not completely visible and not directly below containers with misoprostol (Figure 4).
- Some employees whose job tasks involve potential exposure to other reproductive hazards reported that they were not trained on how to handle them or their potential health effects.
- Pouring formalin into large pathology specimen containers has the potential for splashes to the face and other skin exposure.
- Ethylene oxide, which has been linked to miscarriage, is used in sterilizing instruments.

Although they were not the focus of our evaluation, these hazards could cause harm to your workers' health and safety and should be evaluated and addressed as needed.

### ***How? At your workplace, we recommend these specific actions:***



### **Consider alternatives to ethylene oxide sterilization.**

- More information about different sterilization methods is available at: <https://www.cdc.gov/infectioncontrol/pdf/guidelines/disinfection-guidelines.pdf>.



**Do not store misoprostol and other drugs that pregnant women should not handle with other drugs.**



**Properly label hazardous drugs.**

- More information on the safe handling of hazardous drugs for veterinary healthcare workers is available at: <https://www.cdc.gov/niosh/docs/wp-solutions/2010-150/pdfs/2010-150.pdf>.



**Train employees whose job tasks involve potential exposure to other reproductive hazards on how to handle them or their potential health effects upon hire and at least annually afterwards.**

- Resources about reproductive hazards in veterinary practice can be found at: <https://www.cdc.gov/niosh/topics/veterinary/other.html>.
- Information on reproductive health and the workplace is available at: <https://www.cdc.gov/niosh/topics/repro/default.html>.
- Information on protecting employees from veterinary infections can be found at: <http://www.nasphv.org/Documents/VeterinaryStandardPrecautions.pdf>.



**Provide gloves appropriate for protecting against hazards associated with specific job tasks.**

- Latex gloves are not recommended for handling formalin. Nitrile gloves, which are already being used at the veterinary hospital, are recommended because they offer adequate protection against formalin.



**Provide eye and face protection for employees to use when there is a potential for splashes.**



Figure 4. Misoprostol, which should not be handled by pregnant women, was stored with other drugs and away from a partially visible warning about medications that pregnant women should not handle. Photo by NIOSH.

# Supporting Technical Information

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## Section A: Workplace Information

### Building

Building areas (Figure 5):

- Operating rooms: 2 (soft tissue and orthopedic). Each had an active scavenging system.
- Recovery area/intensive care unit (ICU): area where animals recover from surgery and animals receiving other treatments were kept. Animals were anesthetized for surgery in half of the room (Figure 1). This area had a passive scavenging system. An active scavenging system was used in this area for nonsurgical procedures requiring anesthesia.
- Pack/prep area: where staff prepare for surgery. Area had an ethylene oxide sterilizer.
- Avian/exotics exam room: area also contains office space and document storage for the avian/exotics department.
- Break room
- Reception area
- Office space
- General exam rooms

### Employee Information

- Total employees: 53
- Number of employees working at time of evaluation: 36
- Length of shift: varies, ranges from 5–10 hours
- Median age at time of the site visit: 32.5 years (range: 21–60 years)
- Median job tenure: 23 months (range: 2 weeks–15 years)
- Sex: 95% female
- Departments: 7

### History of Issue at Workplace

In February 2017, a veterinary technician discovered that the closed interface active scavenging systems used to remove waste anesthetic gas from the air (Figure 6) were incorrectly connected in each of the two operating rooms. Passive scavenging systems rely on the passive flow of gases out of the anesthesia machine and through either an activated charcoal canister or another method to ventilate waste anesthetic gas out of the workplace. Active scavenging systems actively pull anesthetic gases away and exhaust them using a vacuum system or a fume hood. Active scavenging is the preferred method, and generally results in lower exposures to waste anesthetic gas. The scavenging systems in the operating rooms were incorrectly connected in different ways. Due to their incorrect connections, employees were concerned that the scavenging systems were not working properly and thus not removing waste anesthetic gas from the operating rooms. This could have resulted in unnecessary and potentially excess waste anesthetic gas exposure to employees.

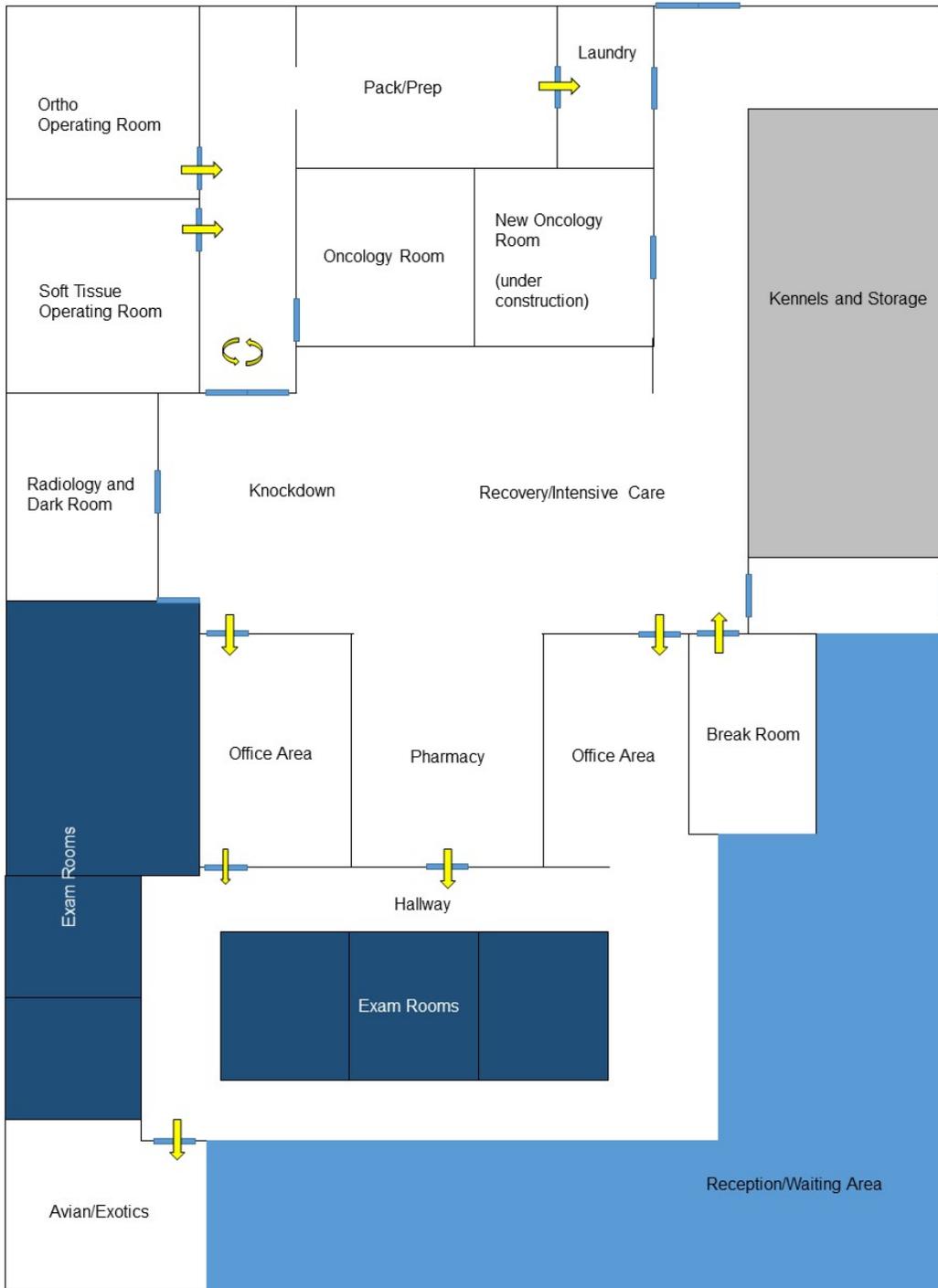


Figure 5. Diagram of the veterinary hospital. The lighter blue rectangles depict doors. The yellow arrows depict the direction of airflow and pressurization of the rooms.

The veterinary hospital has a contractor who maintains the anesthesia machines and the scavenging systems. During the two visits prior to the identification of the incorrect connections (April and May 2016), the contractors did not note abnormalities in the scavenging system setup. It is unknown how long the scavenging systems were connected incorrectly. The anesthesia maintenance contractor was brought in 2 days after the discovery to re-evaluate the anesthesia and scavenging systems. At that time, veterinary hospital staff had already fixed the scavenging system connections. The anesthesia maintenance contractor did not note any abnormalities during their follow-up visit in April 2017.

## Process Description

### Sedation and Intubation

At the time of our evaluation, two veterinary technicians sedated the animal with propofol in the knockdown area of the recovery area/ICU. One technician intubated the animal, anesthetized the animal with isoflurane, and monitored the animal's vital signs and level of isoflurane. The other technician shaved and cleaned the animal in preparation for surgery. There was a passive scavenging system in the recovery area/ICU. Once the animal was ready for surgery, preoperative x-rays were taken if needed. The animal was then brought into an operating room for surgery.

### Surgery

A veterinarian, veterinary intern, and veterinary technician or assistant participated in the surgeries. Surgeries varied in length, ranging from 60 to 90 minutes on the days of the site visit. The veterinarian and veterinary intern conducted the surgery, with the veterinary technician or assistant helping and monitoring the animal's vital signs, isoflurane level, and equipment. Each operating room had an active scavenging system.

### Postsurgery and Recovery

Postoperative x-rays may be taken in the radiology room to confirm the success of the surgery. When the surgery was completed, the animal was taken out of the operating room and brought back into the recovery area/ICU. The animal was then placed in a kennel. A veterinary technician watched the animal and attempted to wake the animal up. The veterinary technician monitored the animal until it woke up.



Figure 6. The anesthesia machine, ventilator, and active scavenging system in the soft tissue operating room. Photo by NIOSH.

## Section B: Methods, Results, and Discussion

The objectives of our evaluation were to

- Determine if the scavenging systems and building ventilation system were effectively removing waste anesthetic gas
- Assess employee exposures to isoflurane
- Determine the prevalence of employee symptoms and learn more about reproductive health concerns and outcomes among employees

### Methods: Work Practices

We gathered information about work practices through (1) confidential employee interviews and (2) observations.

We conducted confidential interviews with all 36 veterinary hospital employees who were working during the site visit. We reviewed an employee roster provided by the veterinary hospital to determine each employee's department. During the interviews, we interviewed employees about these topics:

- Work history
- Job tasks
- Work areas
- Personal protective equipment (PPE) use

We observed work practices before, during, and after surgery. We also observed PPE use.

### Results: Work Practices

#### Interviews

The 36 interviewed employees reported working for a median of 40 hours per week (range: 5–75 hours per week). Job categories included veterinarian (n = 12), veterinary technician (n = 10), veterinary assistant (n = 7), receptionist (n = 5), and other (n = 2). According to the roster provided by the hospital, employees worked in the surgery (n = 6), avian/exotics (n = 2), internal medicine (n = 4), emergency medicine (n = 15), oncology (n = 2), and administrative (n = 7) departments. The single employee in the inventory department was not working on the day of our site visit.

We asked employees whether they worked in various work areas or performed various job tasks.

Twenty-one (58%) interviewed employees reported ever working in operating rooms at this veterinary hospital for a median of 2 years (range: 1 week–15 years). Roles in the operating room included primary surgeon or assistant surgeon (n = 7), anesthesia monitor (n = 5), surgical technician (n = 5), and surgical technician and monitoring anesthesia (n = 4).

We asked the 17 (47%) employees who reported working in the operating rooms in the 3 months prior to the interview more about their operating room experience. All 17 reported working in the soft tissue operating room, and 8 reported working in the orthopedic operating room. All 17 reported using isoflurane in the operating room, while 2 of 17 also reported using sevoflurane in the operating room. Fourteen of the 17 reported that the endotracheal cuff was inflated for at least some surgeries. Of these

14 employees, 12 reported that the endotracheal tube cuff was inflated before isoflurane was turned on. Thirteen of the 17 employees who worked in the operating rooms reported filling isoflurane vaporizers. Most interviewed employees (n = 28, 78%) reported working in the recovery area/ICU in the 3 months prior to the interview. Of the 13 (36%) employees who reported working in the pack/prep area in the 3 months prior to the interview, 8 reported being in the area while the ethylene oxide sterilizer was being used. Three employees reported using the ethylene oxide sterilizer.

Twenty-seven (75%) of 36 interviewed employees reported being in the room while radiographs were being taken in the past 3 months; all reported always wearing lead shielding. Six (22%) of these 27 employees reported never wearing a dosimeter to measure radiation exposure. Of the remaining 21 employees who reported always or sometimes wearing a dosimeter, none reported ever having exceeded exposure limits.

Of the chemicals that we asked about, formalin was the most commonly handled chemical; 17 (47%) employees reported handling formalin in the past 3 months, either through opening a pre-filled specimen jar and placing a tissue specimen inside or pouring formalin into a container with a larger specimen. Pouring formalin has the potential for splashes to the face. While handling formalin, 13 (76%) employees reported always wearing gloves. The remaining four employees reported sometimes wearing gloves while handling formalin. Thirteen (76%) employees reported wearing nitrile gloves, which are generally recommended. Three employees reported wearing nitrile or latex gloves (18%) and one employee (6%) reported wearing latex gloves; latex gloves are not recommended because they do not offer adequate protection against formalin. Four employees reported always or sometimes wearing safety glasses while handling formalin. None reported using a face shield while handling formalin.

## Observations

We observed four surgeries on the first day, including two tibial-plateau-leveling osteotomy surgeries (orthopedic), one mass removal surgery (soft tissue), and one skin flap surgery (soft tissue). We observed one surgery on the second day, a thyroidectomy (soft tissue). Surgeries ranged from 60 to 90 minutes in length.

During surgical procedures, the veterinary surgeon and intern were observed wearing surgical caps, gowns, surgical masks, sterile gloves, and booties. Protective eyewear was also worn during some procedures. Veterinary technicians wore surgical caps and booties. No PPE was required in the recovery area/ICU or pack/prep areas. We did not observe any employees in these areas wearing PPE.

We observed employees (1) turning on the oxygen supply before turning on the isoflurane following intubation, and (2) employees inflating the endotracheal cuff before the isoflurane was turned on.

In the pharmacy area, we observed medications arranged on open shelves in alphabetical order. Misoprostol, which can cause miscarriages, was stored with other drugs and away from a partially visible shelf label warning that pregnant women should not handle it (Figure 4).

## Methods: Training and Policies on Workplace Hazards

We gathered information about training and policies through (1) document review and (2) interviews.

We reviewed the following documents:

- Internal guidelines on potential exposures of concern to employees
- Policies for pregnant employees provided to us in September 2017
- Training records for 2017

During interviews, if any of the 36 interviewed employees answered “yes” to performing various job tasks or working in various areas, we asked additional questions about training. We asked if employees had received training on (1) how to perform various job tasks and (2) potential health effects of various exposures. Regarding the potential health effects of anesthetic gases, we asked employees who reported working in the operating room in the past 3 months whether they had received training about potential health effects from the veterinary hospital.

## Results: Training and Policies on Workplace Hazards

### Document Review

The veterinary hospital’s internal guidelines on potential exposures of concern to employees were as follows:

- Chemical: formalin, anesthetic gases, dimethyl sulfoxide, bone cement
- Physical: long work hours, “being pushed, pulled, or kicked or otherwise put in physically harmful situations,” “unruly animals”
- Infectious agents
- Radiation

According to records provided by management, 25 employees acknowledged receiving information about these workplace hazards in October 2017, after our site visit. On the same day, 22 employees attended a hazard communication awareness training course provided by a third party, according to training attendance records provided by management.

The veterinary hospital has internal guidelines for pregnant employees that describe risks including radiation, “toxic drugs,” anesthetic gases, zoonotic diseases, and physical exposures. Specific substances mentioned included formalin, dimethyl sulfoxide, and bone cement. The veterinary hospital has a form where employees can voluntarily declare their pregnancy in writing.

Hospital policy “strongly discourages” pregnant employees from participating in boxing or masking a patient. It also instructs employees to maintain the patient on oxygen after the anesthetic gas has been turned off and avoid face-to-face or close contact with animals during recovery from anesthesia. In addition, an employee who declares pregnancy to the employer can choose to opt out of assisting in taking radiographs. If an employee chooses to participate in taking radiographs during pregnancy, hospital policy dictates wearing a fetal dosimeter at waist level in addition to a full gown, thyroid shield, and gloves. The choice to participate in radiography is documented on the declaration of pregnancy form, which is forwarded to the Radiation Safety Officer.

## Interviews

Table C1 shows the proportion of employees who reported receiving training on how to perform various job tasks. Among employees who reported performing various job task involving various reproductive hazards within the past 3 months, 71%–100% of employees reported having received training for the job task.

Table C2 shows the proportion of employees who reported receiving training on the potential health effects of various exposures. The percentage of employees who reported handling a chemical or being in the room with the exposure and receiving training on the potential health effects ranged from 25% for ethylene oxide to 100% for prostaglandins. Of the 17 interviewed employees who worked in operating rooms in the past 3 months, 7 employees (41%) reported being trained by the veterinary hospital on the potential health effects of anesthetic gases.

## Methods: Exposure Assessment

We gathered information about workers' exposure to isoflurane through (1) document review, (2) 60-minute active sampling for isoflurane in the air on employees from isoflurane introduction until recovery, (3) full-shift passive sampling for isoflurane in the air in areas and on employees, and (4) taking direct air measurements for isoflurane. We gathered information about the veterinary hospital's ventilation system and scavenging systems through (1) document review, (2) observation, and (3) informal discussions with employees.

We reviewed the following documents:

- Air sampling reports from an accredited laboratory
- Anesthesia machine maintenance reports
- Safety data sheets (SDSs) for chemicals used in the ORs and recovery area/ICU
- Photographs of the incorrect scavenging system configurations

We collected active 60-minute personal air samples for isoflurane:

- Number collected: 36
- Who: Veterinary technicians, veterinary surgeon, veterinary surgeon intern
- Method: OSHA 103 [OSHA 1994] using Anasorb 747 tubes

We collected full-shift passive personal air samples for isoflurane:

- Number collected: 10
- Who: Veterinary technicians, veterinary surgeon, veterinary surgeon intern
- Method: OSHA 103 using SKC 575-002 passive monitors

We collected full-shift passive area air samples for isoflurane:

- Number collected: 14
- Where: recovery area/ICU, both operating rooms, pack/prep area, reception desk, break room, office areas
- Method: OSHA 103 using SKC 575-002 passive monitors

We took direct measurements of isoflurane in the air:

- Where: recovery area/ICU, soft tissue operating room, pack/prep area, exhaust for hospital's vacuum system
- Method: Thermo Scientific™ MIRAN SapphIRE XL portable ambient analyzer calibrated to measure isoflurane (limit of detection 0.04–0.7 parts per million [ppm], high range limit 100 ppm)

We observed:

- Ventilation system performance and building pressurizations
- Scavenging system use

## Results: Exposure Assessment

### Document Review

After the discovery of the incorrect connections for the scavenging systems in both operating rooms in February 2017, an industrial hygiene contractor conducted personal sampling on employees using passive monitoring badges (reporting limit of 0.04 ppm for an 8-hour period). Sample times were longer (180–210 minutes) than the 60-minute interval that is specified for comparison to the NIOSH recommended exposure limit (REL) of a 60-minute ceiling limit (a concentration that should never be exceeded at any time in the workday) for waste anesthetic gas. The average concentration for the five personal sampling results collected from four employees ranged from 1.1–2.1 ppm.

Two employees, one veterinary technician during prep and surgery and one veterinary surgeon during surgery, had time-weighted average (TWA) exposures to isoflurane of 2 ppm or higher. The remainder of the personal sampling results had TWA exposures to isoflurane under 2 ppm. As the sample duration for these samples exceeded 60 minutes, these measurements are not directly comparable to the NIOSH REL of 2 ppm for a 60-minute time period. It is possible that even though some employees had TWA sample results below 2 ppm, they could have been exposed to concentrations above the NIOSH REL for a shorter duration of time.

Anesthesia machine maintenance was reportedly performed annually by a contractor. In April 2016, eight vaporizers (six for isoflurane and two for sevoflurane) were tested for pressure and calibrated. The valves and discs were checked, and no system leaks were detected. The extent of the inspection of the scavenging systems was unclear based on the documentation provided by the hospital, and there were no notes or tests on the performance of the scavenging systems. The specific vaporizer that was connected to the incorrectly connected scavenging system passed all tests: the contractor detected no system leaks and all machine components worked properly. Following the discovery of the incorrect connection in February 2017, the anesthesia contractor disassembled and cleaned the vaporizer, and replaced all O-rings. There were no notes about the scavenging systems and setup.

We reviewed the SDSs for chemicals used in the operating rooms and recovery area/ICU. These included chemicals used during medical procedures and for general cleaning and equipment disinfection. The hospital uses ethylene oxide, a reproductive hazard associated with greater incidences of miscarriages. It is also a carcinogen. The hospital also uses Nolvasan®, a disinfectant solution associated with maternal toxicity in rats at high concentrations. Speed-Clean, used at the hospital as an

autoclave cleaner, contains 2-butoxyethanol (< 3%), which may cause reproductive problems and birth defects in animals at high doses.

## **Isoflurane Exposures**

### **Personal Air Sampling for Isoflurane**

#### ***60-minute, active***

Personal air sampling results for isoflurane are shown in Table C3. For the veterinary surgeons, 60-minute concentrations for isoflurane ranged from 0.27–0.56 ppm. Personal air sample results were collected before, during, and after surgeries, including when surgeries were back-to-back. These surgeries included tibial-plateau-leveling osteotomy, mass removal surgery, skin flap surgery, and thyroidectomy. The veterinary surgeon intern had 60-minute concentrations in a similar range of 0.30–0.65 ppm. Veterinary technicians had measured 60-minute concentrations ranging from 0.28–4.4 ppm. One veterinary technician was exposed to isoflurane concentrations above the NIOSH REL of 2 ppm for a 60-minute ceiling. The tasks with higher isoflurane exposure were taking postoperative x-rays (1.7 ppm) and recovering a dog after surgery (1.0–4.4 ppm). Veterinary technicians are more likely to meet or exceed the NIOSH REL for waste anesthetic gas during these tasks.

#### ***Full-shift, passive***

One veterinary technician's full-shift personal air sample result for isoflurane on the first day of sampling was 0.076 ppm. This concentration was between the minimum detectable concentration of 0.076 ppm and the minimum quantifiable concentration of 0.23 ppm, meaning that there is more uncertainty associated with this result. The remainder of the full-shift personal air samples did not detect isoflurane (minimum detectable concentration: 0.076–0.10 ppm).

### **Area Air Sampling for Isoflurane**

Full-shift passive area air samples for isoflurane collected throughout the veterinary hospital did not detect isoflurane (minimum detectable concentration: 0.078–0.095 ppm).

### **Isoflurane Measurements Using the MIRAN SapphIRe**

Instantaneous measurements of isoflurane indicated that higher concentrations of isoflurane were found near the mouth of the animal before (2.6 ppm), during (2–5 ppm) and after surgery (5–70 ppm). Isoflurane concentrations were highest directly under the vacuum exhaust at the back of the hospital building (4–75 ppm). Background concentrations taken in various areas of the operating room during surgery (0.2 ppm), the pack/prep area during surgery (0.25 ppm), and the recovery area/ICU (0.1–0.25 ppm) were low.

### **Ventilation**

For infection control purposes, surgical suites are generally designed to be under positive pressure relative to the surrounding hallways and areas, so that air flows from operating rooms into the hallway. While this may not be ideal for waste anesthetic gas containment, a functioning active scavenging system should capture most or all waste anesthetic gas. An effective heating, ventilation, and air-conditioning system in the veterinary hospital will dilute and remove any waste anesthetic gas not collected by the active or passive scavenging systems. Four air handling units were located on the roof. Filters in these air handling units were reportedly changed every other month.

We used ventilation smoke tubes to observe the pressurization in different areas of the hospital. The observed pressurizations in the hospital are shown in Figure 5. Both operating rooms were positively pressured compared to the hallway, although the pressurization was neutral at the swinging door between the hallway and the recovery area/ICU. This neutral pressurization could have been due to a return vent located above the door. The avian/exotics office was negatively pressured compared to the hallway, meaning that air and potentially waste anesthetic gas would flow from the hallway into the avian/exotics office. Ideally, air would flow from the avian/exotics office into the hallway.

The avian/exotics office was a converted conference room. Avian/exotics staff noted that it often felt warmer and “muggy” in the office compared to other areas of the veterinary hospital. It is unknown if the heating, ventilation, and air-conditioning system was modified to accommodate the change in function of the space and when other renovations in the veterinary hospital occurred.

### **Scavenging Systems**

Active scavenging systems were used in both operating rooms and in the recovery area/ICU during non-surgical procedures requiring anesthetic gas. Employees and management reported that the activated charcoal canisters for the passive scavenging systems were weighed daily before surgeries and procedures and discarded when they reached a weight increase of 50 grams. The anesthetic gas scavenging systems were cleaned every week by hospital staff. Maintenance was performed annually by the anesthesia contractor.

Waste anesthetic gas collected by the active scavenging systems exhausted through the hospital’s central vacuum system. The vacuum system was exhausted at the back of the hospital approximately 8 feet above the ground. It was not located near the building’s air intakes and entrances (Figure 3). Pedestrians on the sidewalk path directly under the exhaust opening could potentially be exposed to waste anesthetic gas and other vacuum exhaust contents. Ideally, the vacuum system should exhaust away from locations where people could come into contact with the contents and away from air intakes and building entrances.

### **Evaluation of Past Connections**

Employees reported that when the active scavenging system in the orthopedic operating room was incorrectly configured, the bottom ports on the scavenging interface were not covered by a cap or a reservoir bag. These bottom ports are for the connection of one or two reservoir bags that are necessary to compensate for any increased volumes of excess anesthetic gas that may exceed the removal capacity of the connected building vacuum system. With caps and reservoir bags removed from the interface, there was no buffer for when the flow rate of the waste anesthetic gas exceeded the flow rate of the vacuum system. In these instances, the gas would escape out of the open interface ports and there would be higher employee exposure to waste anesthetic gas than if the interface was connected correctly. This configuration was reportedly corrected by placing a reservoir bag on one of the bottom ports, and a cap on the other port. When the scavenging system was connected properly, we observed that the reservoir bag was distended in each operating room. This means that the bag contains some waste anesthetic gas, which would have not been contained without the presence of the reservoir bag.

Employees also reported that the active scavenging system in the soft tissue operating room had been incorrectly configured, but in a different way than the other system. In the soft tissue operating room,

the bottom ports on the scavenging interface were both covered by caps. The interface has both positive and negative pressure relief valves to compensate for the lack of a buffer when no reservoir bags are attached to the interface. Employees could have been exposed to higher amounts of waste anesthetic gas if the flow rate of the waste anesthetic gas exceeded the flow rate of the vacuum system, causing the positive pressure relief valve to relieve the excess pressure back into the room.

It is unknown how long the scavenging systems were improperly configured. Additionally, because no personal sampling measurements were collected during that time, employee exposures to waste anesthetic gas cannot be determined. Several factors could have affected the amount of waste anesthetic gas concentration in the operating room, including but not limited to fresh gas flow (a mixture of oxygen and anesthetic agent), building vacuum flow, ventilator settings, and anesthesia machine evacuation valve settings.

### **Avian/Exotics Department**

The avian/exotics office space was located in the same space as the exam room. This department focused on the care and treatment of birds and exotic species, which included small mammals, reptiles, and amphibians. Due to the varying sizes and shapes of these species, intubating these animals is difficult. Additionally, some avian and exotic animals must be anesthetized for short periods to avoid injuring the animal or staff during physical examinations. To do this, staff used induction chambers that had been modified from plastic storage containers of various sizes. Animals were placed in the container and the container closed, and then the inhalational anesthetic was introduced into the container until the animal became unconscious. Staff stated they then quickly removed the animal by opening the lid of the container and placed the container with waste anesthetic gas into the hallway outside of the avian/exotics office to dilute the anesthetic. This method is not ideal as it unnecessarily exposes avian/exotics staff to waste anesthetic gas when they remove the animal and handle the modified induction chamber, as well as other staff when the chamber is placed in the hallway.

Employee office space and documents were also kept in the exam room, which could result in unnecessary exposures to waste anesthetic gas.

### **Methods: Employee Health**

We gathered information about employee health through (1) review of OSHA Form 300 Logs of Workplace Injuries and Illnesses for 2013–2016 and (2) interviews.

During the confidential medical interviews with 36 employees, we also asked them about

- Demographic information
- Symptoms while at work
  - Within the past 3 months
  - Not from a cold or respiratory infection
  - Whether it improved when away from work on vacations or weekends
- Reproductive health history

We summarized descriptive statistics for demographic, work, and health information. We grouped employees in the surgical and avian/exotics departments together because both departments worked most directly with anesthetic gases. We defined a work-related symptom as a symptom experienced at

work that improved when away from work on vacations or weekends. We compared the prevalence of work-related symptoms of surgery and avian/exotics department employees to employees in other departments using a two-sided Fisher's exact test. Statistical significance was set at  $P < 0.05$ . We used R version 3.3.2 and EpiInfo 7 to perform statistical analyses.

## Results: Employee Health

### OSHA Logs

The OSHA Logs covering years 2013 through 2016 did not include any injuries or illnesses related to waste anesthetic gas exposure. Recorded injuries consisted of animal bites and scratches ( $n = 43$ ), sprains and strains ( $n = 3$ ), allergic reactions ( $n = 2$ ), falls ( $n = 1$ ), needlesticks ( $n = 1$ ), and other ( $n = 3$ ).

### Work-related Symptoms

Of the 36 interviewed employees, 15 (42%) employees reported experiencing at least one work-related symptom within the past 3 months. Work-related symptoms included headache ( $n = 12$ ), eye irritation ( $n = 6$ ), dizziness ( $n = 5$ ), nose irritation ( $n = 3$ ), and nausea ( $n = 3$ ). Of these 15 employees, 4 (27%) mentioned "isoflurane" or "gas" when asked to provide more details about when symptoms began; these symptoms consisted of headache ( $n = 2$ ), dizziness ( $n = 2$ ), nausea ( $n = 1$ ), and irritability ( $n = 1$ ). In addition to these four employees, one employee specifically mentioned symptoms beginning when inducing anesthesia with isoflurane via a box. Another employee reported that symptoms began when recovering patients. By department, a higher proportion of employees in the surgery and avian/exotics departments reported experiencing at least one work-related symptom (63%) compared with employees in other departments (36%), but this difference was not statistically significant ( $P = 0.23$ ).

### Reproductive Health

At the time of the interview, 28 (82%) of the 34 female employees interviewed were women of childbearing age, defined as 15–44 years [Centers for Disease Control and Prevention 2006]. This represented 78% of the 36 employees interviewed. All 36 interviewed employees were asked whether they had concerns about reproductive health related to their work at the veterinary hospital, and 8 (22%), all women of childbearing age, reported having these concerns. Of the 36 interviewed employees, 2 (6%) reported trying and not being able to become pregnant with their spouse or partner in the past year, which meets the screening definition of infertility [Crawford et al. 2015].

Among the 34 female employees interviewed, 9 employees reported 21 pregnancies while working at the veterinary hospital. This consisted of 6 pregnancies that resulted in live birth, 12 miscarriages, and 3 current pregnancies. Fourteen pregnancies were reported to the employer. During most disclosed pregnancies, the pregnant employee's work was modified. Work modifications were reported to be generally based on the guidance of the pregnant employee's personal physician. Examples included avoiding x-rays, induction or monitoring of anesthesia, handling dogs on misoprostol, or cleaning litter boxes; weight restrictions on lifting; and wearing a fetal dosimetry badge, which were generally consistent with the veterinary hospital's policies for pregnant employees.

Seven interviewed employees reported 12 miscarriages that occurred while working at the veterinary hospital. These seven employees worked at the veterinary hospital for a median of 4 years (range:

15 months–15 years). Six of the seven employees reported ever working in the operating room. Two employees each had three miscarriages, one employee had two miscarriages, and the remaining four employees each experienced one miscarriage during their employment.

Regarding maternal age at the time of miscarriage, age  $\geq 40$  years was the most common age group ( $n = 5$ ), followed by age 35–39 years ( $n = 3$ ). For one miscarriage, maternal age was not available. All miscarriages occurred during the first trimester (the first 13 weeks of pregnancy), which are considered early miscarriages.

## Discussion

Veterinary hospital employees were concerned about waste anesthetic gas exposures and reproductive health effects. Through our evaluation, we learned that seven employees reported 12 miscarriages while employed by the veterinary hospital. We evaluated this finding using an approach for investigating disease clusters. Scientists define a cluster as a greater than expected number of cases of a disease that occurs within a group of people in a geographic area over a defined period. A cluster also occurs when the disease is found among individuals of a different age group or sex than is usual. A statistically significant excess of cases may have a common cause, but it also can occur without a clear cause and by chance. This makes detecting whether the cases have a common cause difficult. It is common for the borders of the “cluster” to be drawn around where the cases are located, instead of defining the population and geographic area first. This often leads to a misleading appearance of a “cluster.”

To assess whether the miscarriages among employees could be related to waste anesthetic gas, we consider the number of miscarriages, their characteristics, and the likelihood of exposure to waste anesthetic gases and other substances. These issues are discussed below in a series of questions related to this evaluation at the veterinary hospital.

### **Do veterinary hospital employees have more miscarriages than women who do not work at the veterinary hospital?**

When several cases of a disease occur in a workplace, they may be part of a true cluster when the number is greater than we expect compared to other groups of people similar in age, sex, and race. Disease rates, however, are highly variable in small populations and rarely match the overall rate for a larger area, such as the state. As a result, for any given period, some populations have rates above the overall rate and others have rates below the overall rate. Even when a higher rate occurs, this may be completely consistent with the expected random variability. In addition, calculations like this make many assumptions that may not be appropriate for every workplace. Comparing rates without adjusting for age or other population characteristics assumes that the distribution of these characteristics are the same in the workplace as in the larger population, which may not be true.

Miscarriage, defined as pregnancy loss before 20 weeks of gestation, is a common phenomenon. Early miscarriage, or early pregnancy loss, is defined by the American College of Obstetricians and Gynecologists as pregnancy loss occurring before 13 weeks of gestation. Approximately 10%–25% of all clinically recognized pregnancies end in early miscarriage [American College of Obstetricians and Gynecologists 2015; American Society for Reproductive Medicine 2012; Wang et al. 2003; Wilcox et al. 1988; Zinaman et al. 1996]. Employees reported 12 early miscarriages among 21 pregnancies during

employment at the veterinary hospital. All 12 miscarriages occurred during the first trimester, which is consistent with the finding that approximately 80%–90% of miscarriages occur during the first trimester.

Risks factors for early miscarriage include higher maternal age and prior miscarriages [Andersen et al. 2000; Cunningham et al. 2018; Feodor Nilsson et al. 2014]. Age  $\geq 30$  years was identified as a risk factor for early miscarriage. One large study found that the risk of miscarriage ranged from 9% at age 22 years to 84% by age  $\geq 48$  years [Andersen et al. 2000]. Regarding the age distribution, 83% of miscarriages during employment at the veterinary hospital were experienced by employees aged  $\geq 30$  years. Five miscarriages occurred in the age  $\geq 40$  group, which was more than in each of the other age groups (age 25–29, 30–34, and 35–39 years).

Recurrent miscarriage is classically defined as three or more consecutive miscarriages before 20 weeks of gestation. Based on this definition, it occurs in approximately 1% of women [Cunningham et al. 2018]. Two employees met the definition of having recurrent miscarriages, but given the small numbers of employees at this workplace, this apparent increase might still be within the expected random variability. The risk of another miscarriage increases as the number of prior miscarriages increases from zero to two, but having had three or more miscarriages does not increase the odds of another miscarriage further [Bhattacharya et al. 2010]. However, if an occupational exposure is causing miscarriages, recurrent miscarriages can be expected. In summary, we do not have enough information to conclude whether the rate of miscarriage among employees at this veterinary hospital is substantially higher than would be expected given their health and reproductive history.

### **Is exposure to a specific chemical or physical agent known or suspected of causing miscarriages occurring at the veterinary hospital?**

Possibly. Isoflurane and sevoflurane, which are used at the veterinary hospital, are halogenated anesthetic gases. Epidemiologic studies have shown that anesthetic gases in general are associated with an increased risk of miscarriages. Congenital abnormalities are also health effects of concern [NIOSH 1977; Teschke et al. 2011]. However, most studies about anesthetic gases and miscarriages were performed before scavenging systems were commonly in use and did not measure levels of anesthetic gases in air [Boivin 1997; Byhahn et al. 2001; Shirangi et al. 2008].

What causes most miscarriages is not known. Approximately half of early miscarriages are associated with chromosomal abnormalities in the fetus [Alijotas-Reig and Garrido-Gimenez 2013; American Society for Reproductive Medicine 2012; Cunningham et al. 2018]. Medical workup for early miscarriage is generally not recommended until a woman has experienced her second consecutive early miscarriage. Recurrent miscarriage remains unexplained despite a medical workup in approximately half of the cases, but recognized causes of recurrent miscarriage include chromosomal abnormalities in either parent, antiphospholipid syndrome, and some uterine abnormalities [Cunningham et al. 2018].

We found that one employee was exposed to levels of isoflurane over the NIOSH REL of 2 ppm over a 60-minute time period for waste anesthetic gas while recovering an animal. Currently, OSHA has no permissible exposure limits (PELs) regulating these agents. In 1977, NIOSH published a criteria document setting a REL of 2 ppm over a sampling period not to exceed 1 hour for any halogenated anesthetic agent. At the time, the REL was based on adverse reproductive health effects and congenital

abnormalities as the primary health effects of concern and the “lowest feasible” level for these agents. The agents included in this document were chloroform, trichloroethylene, halothane, methoxyflurane, enflurane, and fluroxene [NIOSH 1977]. Isoflurane was not included in this criteria document because it was not in clinical use at the time. Since publication of the NIOSH criteria document, other anesthetic agents (e.g., isoflurane, desflurane, sevoflurane) have become more commonly used because of their perceived low toxicity and because of rapid patient recovery from anesthesia. These newer halogenated anesthetics are often used as sole anesthetics and require much higher concentrations for induction of anesthesia. California OSHA and other health and safety entities have set occupational exposure limits (OELs) that are specific to isoflurane. Although not applicable to this worksite, all of our full-shift personal air sampling concentrations were below the California OSHA limit of 2 ppm. More information about isoflurane OELs can be found in Appendix D.

There was potential for higher employee exposures to isoflurane when the scavenging systems were in incorrect configurations compared with proper configurations. However, how long the scavenging systems were in incorrect configurations was not documented, and it was not possible to retrospectively assess the levels of exposure during the incorrect configurations. The incorrect configurations may have resulted in exposure to higher isoflurane concentrations than what would have been expected if the systems were configured properly.

Several employees reported work-related symptoms that they related to isoflurane. However, area air measurements were low during our site visit. Most employees who worked in the operating room in the past 3 months reported that the endotracheal cuff was inflated before the isoflurane was turned on, a practice that would decrease the leaking of isoflurane around the endotracheal tube. The available scientific evidence provides little information on the relationship between the level of exposure to anesthetic gases and the magnitude of risk for miscarriages, but it would be prudent to minimize or reduce exposure as much as possible through engineering controls and ventilation.

In general, veterinary practice can pose other reproductive health hazards. Other than anesthetic gases, exposures in veterinary practice that can result in an increased risk for miscarriages include ethylene oxide, formaldehyde, prostaglandins and other reproductive hormones, and zoonotic infections [Duong et al. 2011; Scheftel et al. 2017]. We learned through our site visit and document review that some employees at this veterinary hospital engage in job tasks with potential exposure to reproductive health hazards besides anesthetic gases. However, we did not specifically assess whether employees were exposed during the pregnancies that ended in miscarriage. Instead, we asked about recent conditions at the time of our site visit. In situations with multiple exposures, it is not possible to attribute the outcome (miscarriage) to just one of the exposures (for example, anesthetic gases). The veterinary hospital has identified some reproductive hazards and have policies in place to control those hazards. However, the training records and interview responses indicate that not all employees were trained on the potential reproductive health effects associated with their job tasks. Training all employees on the potential health effects of workplace exposures and safe work practices are important components of providing a safe workplace.

## Limitations of this Evaluation

One limitation of our evaluation is its cross-sectional design. Cross-sectional studies collect information on exposures and health outcomes at the same time, so a causal relationship between exposures and health outcomes cannot be proven. Industrial hygiene sampling can only document exposures on the days of sampling in the locations sampled. On the second day of the site visit, there was only one surgery performed, which may result in lower exposure measurements compared to days with more surgeries performed. We were unable to recreate past scenarios of exposure, for example, when the scavenging system was improperly configured or during employee pregnancies that resulted in miscarriage. In addition, responses from the interviews were based on self-report. For example, the veterinary hospital provided records for training that occurred after the interviews, so we were not able to verify responses to interview questions about training. Another limitation is the possibility of recall bias when employees responded to the interview questions.

## Conclusions

Veterinary hospital employees were concerned about waste anesthetic gas exposures causing adverse reproductive health effects. One isoflurane overexposure was measured for an employee who was recovering an animal after surgery. All other personal sampling results were below the lowest OEL. Twelve miscarriages were reported among 21 known pregnancies while employed at the veterinary hospital, but this may not be excessive after taking into account maternal age, reproductive history, and other non-occupational risk factors for miscarriage. The reported miscarriages could not be linked to waste anesthetic gas exposures. However, employees' exposures to waste anesthetic gas in the perioperative period and the avian/exotics department should be minimized through appropriate engineering controls and work practices. Several employees have job tasks that might involve potential exposure to other reproductive hazards. The workplace should be evaluated for other reproductive hazards; other reproductive hazards identified should be minimized through the appropriate use of engineering controls, work practices, and PPE.

## Section C: Tables

Table C1. Receipt of training on performing job tasks involving reproductive hazards\*

Job task	Received training Number (%)
Handling formalin (n = 17)	12 (71)
Handling chemotherapy medications (n = 8)	7 (88)
Handling reproductive hormones (n = 6)	5 (83)
Handling prostaglandins (n = 3)	3 (100)
Using ethylene oxide sterilizer (n = 3)	3 (100)

\*Based on responses of employees who reported performing the job task in the past 3 months.

Table C2. Receipt of training on potential health effects of various exposures\*

Exposure	Received training Number (%)
Ethylene oxide† (n = 8)	2 (25)
Anesthetic gases‡ (n = 17)	7 (41)
Formalin (n = 17)	11 (65)
Reproductive hormones (n = 6)	4 (67)
Chemotherapy medications (n = 8)	6 (75)
Radiation§ (n = 27)	26 (97)
Prostaglandins (n = 3)	3 (100)

\*Based on responses of employees who reported handling the chemical or being in the room with the exposure in the past 3 months.

†Being in the pack/prep area while the ethylene oxide sterilizer was in use.

‡Working in the operating room. Employees were asked if they had received training specifically from the veterinary hospital.

§Being in the room while x-rays were being taken.

Table C3. 60-minute personal air sample measurements for isoflurane

Job title	Day	Task	Sampling result (ppm)
Veterinary surgeon 1	1	Tibial-plateau-leveling osteotomy	0.27
		Tibial-plateau-leveling osteotomy	0.40
		Mass removal surgery	0.33
		In office, preparing for surgery	0.37
		Tibial-plateau-leveling osteotomy	0.45
		Tibial-plateau-leveling osteotomy	0.36
		Skin flap surgery	0.39
		Skin flap surgery	0.56
Veterinary surgeon 2	2	Thyroidectomy	0.41
Veterinary surgeon intern	1	Tibial-plateau-leveling osteotomy	0.30
		Mass removal surgery	0.38
		Mass removal surgery	0.65
		Tibial-plateau-leveling osteotomy	0.31
		Tibial-plateau-leveling osteotomy	0.53
		Skin flap surgery	0.35
		Skin flap surgery	Not detected*
	2	Thyroidectomy	0.39
Veterinary technician 1	2	Prepping for thyroidectomy	0.70
		Working in pack/prep room	0.28
		Recovering a dog after surgery	<b>4.4</b>
Veterinary technician 2	1	Sedation and x-rays of a dog	0.29
		Tibial-plateau-leveling osteotomy	[0.35]†
		Postoperative x-rays, prepping for surgery	0.75
		Sedation of a dog	0.45
		Preparing for tibial-plateau-leveling osteotomy	0.65
		Tibial-plateau-leveling osteotomy	0.51
		Postoperative x-rays	1.7
		Recovering a dog after surgery	1.0
Veterinary technician 3	1	Sedation of a dog	0.33
		Mass removal surgery and surgery preparation	0.59
		Mass removal surgery	0.44
		Preparation for skin flap surgery	0.56
		Preparation for skin flap surgery	0.42
		Skin flap surgery	0.40
	2	Preparation for thyroidectomy	0.57
Thyroidectomy	0.33		

NIOSH REL for waste anesthetic gas is 2 ppm for a 60-minute ceiling.

[ ] = Estimated concentration; this concentration was between the minimum detectable and minimum quantifiable concentration.

\*The minimum detectable concentration was 0.071 ppm for this sample.

†The sampling pump associated with this sample was off during sample retrieval, and only 10 minutes were sampled. The minimum quantifiable concentration was 0.66 ppm.

## Section D: Occupational Exposure Limits

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 preexisting 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 TWA exposure. A TWA refers to the average exposure during a normal 8- to 10-hour workday. Some chemical substances and physical agents have recommended short-term exposure limits ceiling values. Unless otherwise noted, the short-term exposure limit is a 15-minute TWA 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 RELs 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 RELs 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, PPE, exposure and medical monitoring) to minimize the risk of exposure and adverse health effects.
- Another set of OELs commonly used and cited in the United States is the American Conference of Governmental Industrial Hygienists (ACGIH) TLVs. The TLVs are developed by committee members of this professional organization from a review of the published, peer-reviewed literature. TLVs are not consensus standards. They 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 2019].

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/GESTIS/GESTIS-Internationale-Grenzwerte-für-chemische-Substanzen-limit-values-for-chemical-agents/index-2.jsp>, contains international limits for more than 2,000 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.

## Isoflurane

Isoflurane is a halogenated anesthetic gas introduced in the 1980s [OSHA 1999]. Other common halogenated anesthetic gases include halothane, enflurane, desflurane, and sevoflurane. Acute exposure to isoflurane has been associated with skin irritation, eye irritation, headache, drowsiness, and dizziness [ILO and WHO 2002]. There is limited data on the health effects of long-term isoflurane exposure to humans. Most studies concerned with anesthetic gas exposure to humans have focused on nitrous oxide. Additionally, anesthetic gases are often used together. Therefore, few studies have focused specifically on isoflurane exposure. Isoflurane has not been associated with negative reproductive outcomes in humans. The International Agency for Research on Cancer (IARC) considers the evidence for the human carcinogenicity of isoflurane to be inadequate [IARC 1987]. Limited human and animal data have been reported in the literature on the potential for reproductive or other adverse effects from exposure to enflurane, isoflurane, desflurane, and sevoflurane. The Health Council of the Netherlands reviewed the literature on enflurane and isoflurane in 2002 and concluded that there were insufficient data to assess the reproductive hazard for these anesthetic agents [Arbete och Halsa 2009].

Currently OSHA has no PELs regulating these halogenated anesthetic agents. In 1977, NIOSH published a criteria document that recommended an REL that no employee should be exposed to ceiling concentrations greater than 2 ppm of any halogenated anesthetic agent over a sampling period not to exceed one hour. At the time, the REL was based on the “lowest feasible” level. The agents included in this document were chloroform, trichloroethylene, halothane, methoxyflurane, enflurane, and fluroxene [NIOSH 1977]. Isoflurane was not included in this criteria document because it was not in clinical use at the time.

Since publication of the NIOSH criteria document, other anesthetic agents (e.g., isoflurane, desflurane, sevoflurane) have become more commonly used because of their perceived low toxicity and because of rapid patient recovery from anesthesia. These newer halogenated anesthetics are often used as the sole anesthetic, therefore requiring much higher concentrations for induction of anesthesia.

In research studies and clinical applications, the REL for halogenated gases has been applied to isoflurane and other newer halogenated ethers because of the lack of established OELs for these agents

and lack of research on chronic health effects. Isoflurane is currently listed as a chemical under study by ACGIH, meaning the process for establishment of a TLV might occur in the upcoming year [ACGIH 2018]. California OSHA and other health and safety entities have set OELs that are specific to isoflurane [Arbete och Halsa 2009; Cal/OSHA 2018].

Table D1. Selected isoflurane OELs

Agency/Country	Full-shift TWA (ppm)	15-minute TWA (ppm)
California OSHA	2	—
Finland	10	20
Sweden	10	20
Switzerland	10	80
United Kingdom	50	—
Spain	50	—

## Section E: References

### Health Effects of Anesthetic Gases

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