Isoflurane

Standard Operating Procedure

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| PurposeThis standard operating procedure (SOP) presents an overview of the hazards and hazard control methods associated with isoflurane usage in animal research.This document describes basic prudent safety practice for handling this chemical in the laboratory and research setting. Scope This document applies to the storage, usage, and disposal of isoflurane at Penn State University. This includes the University Park campus and the Commonwealth campuses, but not the Penn State College of Medicine. Responsibilities Principal Investigators (PI) are responsible for:   * Obtaining the most current version of this SOP and ensuring that it is appropriate for the work being performed. * Verify that all individuals using isoflurane are approved on the appropriate IACUC protocol and listed for those procedures. * Providing hands-on laboratory and procedure specific training commensurate with the work being performed and maintaining a record of this training. This can be delegated, but the PI is ultimately responsible for ensuring that training has occurred. * Providing appropriate PPE for personnel and requiring its use performing activities. * Ensuring annual certification and leak testing for PI owned vaporizers, as per IACUC policy 9.   Personnel are responsible for:   * Following the provided SOP to perform their work. * Maintaining compliance with relevant IACUC, ARP, and EHS training. * Wearing PPE as required. * Referring to SDS prior to work involving isoflurane. This document is not a replacement for the SDS. |

# Potential Hazards

Penn State researchers must be aware of the potential risks and take appropriate precautions to reduce potential exposure to employees and students. Exposure can occur when isoflurane vapors leak into the surrounding room during research procedures.

The National Institute for Occupational Safety and Health (NIOSH) states that exposure to high concentrations of waste anesthetic gases- even for a short time - may cause the following health effects: headache, dizziness, lightheadedness, nausea, fatigue, and irritability. If any of these health effects are observed, see below section for reporting possible exposure.

Short term exposure to trace levels of isoflurane in the air is not considered dangerous. Higher levels will cause depression of the central nervous system leading to dizziness, confusion, headache, and potentially, loss of consciousness.

Chronic or repeated low-level exposure to isoflurane should be avoided. Long-term exposure to low concentrations of waste anesthetic gases has been linked to miscarriages, reproductive effects, central nervous system effects, genetic damage, and cancer. Women who are or may be pregnant should avoid areas where isoflurane is in use and consult with Occupational Medicine.

# Occupational Exposure Limits

The American Conference of Governmental Industrial Hygienist (ACGIH) has established a non-regulatory occupational exposure limit of 50 ppm over an 8-hour time weighted average. A safe human exposure concentration for any halogenated anesthetic agent is less than 2 parts per million (ppm) collected over a one-hour period. The isoflurane exposure limit is below the human odor detection threshold. If isoflurane can be smelled, the exposure level is too high. Contact EHS for assistance in performing an exposure assessment.

# Work Practice Controls

The following standard controls must be adhered to when using isoflurane:

* Each piece of equipment involved in the delivery and scavenging of anesthetic gases must be examined prior to each use.
* Anesthesia machines must be leak/output tested yearly as per Penn State IACUC Policy 9: Isoflurane Machine Certification.
* Induction chambers, nose cones, tubing, etc. must be in good condition and not damaged. Any compromised materials must be replaced before usage.
* Penn State personnel should not attempt to repair malfunctioning anesthetic machines. A certified contractor should perform routine maintenance to check for and fix leaking equipment and to ensure that ventilation requirements are met. If machines do not pass routine certification, the machine must be taken out of service until it can be fixed by a certified company. The Animal Resource Program can help facilitate annual certification and coordinate services with the third-party contractor.
* Charcoal filter usage must be documented in the logbook (start time, end time, and total usage). Filters must be replaced when total usage meets or exceeds the manufacturer’s recommended time limit. Time limits vary based on filter.

# Engineering Controls

Standard building ventilation systems cannot be relied upon to control waste anesthetic gas exposure. At least one of the following engineering controls must be used to minimize risk of unintended exposure:

* Class II Type B2 (hard-ducted) biosafety cabinet.
* Class II Type A2 Biosafety Cabinet with canopy connection to building exhaust to prevent recirculation.
* Chemical fume hood.
* Downdraft table with direct connection to building exhaust via 4” drop.
* Backdraft table with direct connection to building exhaust.
* Portable downdraft table with charcoal filter.
* Snorkel exhaust.
* Exposure Prevention System (EPS) with vacuum pump connected to a waste anesthetic gas filter or externally vented exhaust.

# Personal Protective Equipment

The SDS will indicate appropriate minimal PPE for individuals using this chemical. Chemical resistant gloves such as nitrile must be used while handling liquid isoflurane. Wear suitable protective clothing such as a lab coat. If eye contact is a possibility, safety glasses with side shield are required. An anti-spill adapter should be used to fill the vaporizer. When working with animals follow guidance on appropriate additional PPE based on the work being done.

# Transportation and Storage

Store in tightly closed original container in a dry, cool, and well-ventilated place. Protect the material from direct sunlight. Store below 30°C (86°F). Do not handle, store or open isoflurane containers near an open flame, sources of heat or sources of ignition.

# Waste Disposal

Do not allow anesthetic gas containers to evaporate in a chemical fume hood before disposal. Empty bottles, expired or unwanted anesthetic gas containers, and used charcoal canisters or filters must be disposed of as chemical waste.

Empty isoflurane containers may be disposed of according to [EHS Chemical Container Disposal/Recycling Guidelines](https://ehs.psu.edu/sites/ehs/files/recycling_chem_containers_ash_0.docx) if rinsing within a fume hood.

# Exposures/Unintended Contact

Exposure to isoflurane can occur in the following circumstances:

* While filling anesthetic vaporizers.
* Use of non-working or poorly functioning gas scavenging systems.
* Leaks from around an anesthesia mask or endotracheal tube.
  + Leaks in the anesthesia system, including tubing, seals, and gaskets.
  + Inadequate system flushing at the end of a procedure.
  + Opening the induction chamber without adequate scavenging.

Injuries and exposures must be reported following procedures outlined in SY03 Emergencies Involving Students and SY04 Employee Accidents-Reporting and Investigation.

If the employee needs emergency medical attention, call 911 immediately.

Exposure Response:

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| **INJURY TYPE** | **ACTION** | **NOTES** |
| Exposure-Eyes | 1. Flush with water for at least 15 minutes  2. Remove contact lenses if present and manageable.  3. Continue rinsing.  4. Seek medical attention if eye irritation persists. | Removal of contact lenses after an eye injury should only be undertaken by skilled personnel. |
| Exposure-Skin | 1. Remove contaminated clothing  2. Wash affected area with soap and water.  3. If irritation occurs, seek medical advice/attention. |  |
| Inhalation | 1. Remove patient from the contaminated area to fresh air and keep at rest in a position comfortable for breathing. |  |
| Ingestion | 1. If swallowed, refer for medical attention immediately. | Urgent hospital treatment is likely to be needed. |

# Spill Procedure

Isoflurane evaporates readily at normal room temperature and may dissipate before any attempts to clean up or collect the liquid are initiated. Do not attempt to wash any remaining liquid down the drain. Surfaces can be cleaned with water once liquid has been removed.

In the event of a **minor chemical spill**, use the following information for a safe spill response.

* + Alert people in immediate area of spill to evacuate. Restrict people from not wearing protective equipment from areas of spills or leaks until clean-up is complete.
  + Open outside windows and doors, if possible, to increase air flow in this area.
  + Wear protective equipment, including safety goggles, gloves, and a long-sleeved lab coat.
  + Avoid breathing vapors from spill.
  + Use absorbent material to contain the liquid. Collect the liquid spilled and the absorbent materials used to contain the spill in a glass or plastic container. Tightly cap and seal the container and remove it from the location. Label container clearly to indicate its contents.
  + Do not wash spill down the drain.
  + Clean spill area with water.
  + Report the spill to EHS.

A **major (large) chemical spill** of isoflurane, such as when one or more bottles of liquid break, necessitates specific cleaning and containment procedures, as well as appropriate disposal. The recommendations of the chemical manufacturer’s SDS that identify exposure reduction techniques for spills and emergencies should be followed. Workers should not attempt to clean up spills of large volumes of isoflurane and should notify EHS.

Report large spills in corridors or common areas, e.g., hallways, elevators, eating areas, rest rooms, offices, etc., to University Police at 911 and to EHS.

For additional information regarding spill response procedures, refer to the EHS Website.

# Procedure

**Precision Vaporizer Usage**

The usage of a precision vaporizer is the most frequent method for isoflurane administration. The following are recommended steps for reducing human exposure to isoflurane:

1. Check vaporizer for current certification.
2. Check tubing and fittings for proper connection.
3. If applicable, weigh the charcoal canister and check for any obstructions on the exhaust.
4. Turn on scavenging system if applicable. Verify appropriate flow.
5. Check the isoflurane level in the reservoir to ensure there is adequate liquid for the entire procedure.
6. Use an anti-spill adapter to refill machine reservoir from the isoflurane bottle.
7. If using an F/AIR Canister or charcoal filter: Weigh charcoal canister before first use and then after every use. Discard properly when it reaches the maximum limit listed on the specific product. Do not block canister exhaust holes (e.g., if holes located on flat end, place canister on side). Charcoal filter usage must be documented in the logbook (start time, end time, and total usage). Filters must be replaced when total usage meets or exceeds the manufacturer’s recommended time limit.

**Open Drop Anesthetic Usage**

The second method is referred to as open drop. There is a high risk of isoflurane exposure using the open drop method because there are no provisions for scavenging anesthetic waste gas. Proper procedure and anesthetic dose must be determined in consultation with ARP veterinary staff. The following are recommended steps for reducing human exposure:

1. Work should always be performed in a chemical fume hood or under local exhaust ventilation unless performed outdoors. It is also acceptable to use a Biosafety Cabinet that directly exhausts the air out of the building such as a B2 or A2 Biosafety Cabinet with a canopy connection.
2. The container must have a secure lid and be constructed of non-porous material that is sanitizable and allows for constant visualization of the animal.
3. Personnel must wear nitrile gloves.

If it is not feasible to use one of these controls, contact EHS to conduct a Risk Assessment. If working in the field, engineering controls might not be possible. There are additional steps that can be taken to reduce the users’ exposure when using open drop jar anesthesia in the field:

1. Use only for brief procedures lasting no longer than 1 minute.
2. Keep the container at arms-length when opening it.
3. Use the smallest amount of isoflurane needed to achieve the intended results.

# Training of Personnel

Personnel must be trained prior to working with isoflurane. Individuals are required to complete IACUC CITI training and EHS Lab and Research Safety Training online. They must also comply with ARP training requirements in order to have access to the vivarium. ARP veterinary staff offers hands on training in surgery and experimental procedures. Individuals must be familiar with their particular isoflurane machine and how their scavenging system operates prior to use.

# References

[Isoflurane SDS](https://northamerica.covetrus.com/Content/SDS/017579.pdf)

[OSHA Anesthetic Gases: Guidelines for Workplace Exposures](https://www.osha.gov/waste-anesthetic-gases/workplace-exposures-guidelines)

[Penn State IACUC Policy 9: Isoflurane Machine Certification](https://pennstateoffice365.sharepoint.com/:w:/s/VPR-ORP/Ebby_-bUVbxCpJ9x9QTYLpQBK2PPikfjHKOc8tc9wzlWfg)

[Penn State IACUC Guideline 8: Rodent Surgery Guidelines](https://pennstateoffice365.sharepoint.com/:w:/s/VPR-ORP/EcXzLBUvPCZOo22V8fUJgWQBrRIYruz-mKeObvucK-aCtg?e=WMCe0i)

[NIOSH Waste Anesthetic Gases- Occupational Hazards in Hospitals](https://www.cdc.gov/niosh/docs/2007-151/)