ISOFLURANE SAFETY GUIDELINES

Isoflurane is a halogenated anesthetic gas commonly used in university animal research facilities and individual laboratories for inhalational anesthesia. The name for Isoflurane comes from its structural isomer of enflurane. It is a racemic mixture of (R) and (S) optical isomers. This document establishes procedures for the safe handling and use of 1-chloro-2,2,2-trifluoroethyl difluoromethyl ether, commonly known as Isoflurane.

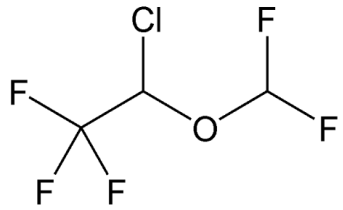
WARNING: Exposure to Isoflurane may occur during filling the anesthetic machine or from escape of waste anesthetic gases while administering the anesthetic. Exposure to Isoflurane may cause nausea, vomiting, headache, dizziness, and drowsiness. Acute effects of overexposure may cause anesthesia, respiratory depression and coughing. In the event of a large spill (*e.g.*, one bottle), lab users should not attempt to pick up the spill but should rather immediately evacuate the area.

1. Properties

Names: Isoflurane, 1-chloro-2,2,2-trifluoroethyl difluoromethyl ether, Forane®, Aerrane®, Isorrane®, Isovet®

Chemical Formula: $C_3H_2ClF_5O$

Chemical Structure:



CAS #: 26675-46-7

Physical aspect: Clear, colorless volatile liquid
Pungent, musty, mild ether-like odor
Soluble in organic solvents; slightly soluble in water (0.275% in water)

Physical and toxicological properties of isoflurane are summarized in **Table 1**.

Table 1. Physical and Toxicological Properties of Isoflurane

Molar Mass	184.5 g/mole
Boiling point	48.5°C
Melting point	Not available
Vapor pressure	238 mm Hg at 20°C
Density	1.3002 g/cm^3 at 20°C
pH	neutral
PEL (TWA)	50 ppm (383 mg/m^3) (UK)
STEL	150 ppm (1149 mg/m^3) (UK)

2. Hazard Classification

WHMIS (2015):

Eye irritation (Category 2B)
Specific target organ toxicity - single exposure (Category 3): central nervous system
Specific target organ toxicity - repeated exposure, Inhalation (Category 2): cardio- vascular system and central nervous system

NFPA 704:

Flammability: Non-Flammable
Health hazard: Moderate hazard – Material that could cause temporary incapacitation or possible residual injury.
Instability/Reactivity: Stable

3. Fire and Explosion Hazards

Isoflurane is a very volatile liquid at room temperature and pressure. Evaporation rate may increase with increasing temperature. Under normal conditions, Isoflurane is not flammable or combustible. However, hazardous decomposition products formed under fire conditions may include carbon oxides, hydrogen chloride gas or hydrogen fluoride. Suitable extinguishing media include water spray, alcohol-resistant foam, dry chemical, or carbon dioxide.

4. Health Hazards

Isoflurane is an anesthetic agent known to potentially cause central nervous system depression. Isoflurane is known to cause eye and skin irritation and human exposure to waste anesthetic gases (especially in certain situations frequently encountered when anesthetizing rodents) has been associated with reproductive effects.

Cardiovascular effects may include fluctuations in heart rate, changes in blood pressure and chest pain. Respiratory effects may include shortness of breath, bronchospasms, laryngospasms, and respiratory depression. Gastrointestinal effects may include nausea, upset stomach and loss of appetite. Nervous system effects may include ataxia, tremor, disturbance of speech, lethargy, headache, and dizziness.

The Federal Occupational Safety and Health Administration (OSHA) does not have a Permissible Exposure Limit (PEL) for Isoflurane. The National Institute of Occupational Safety and Health (NIOSH) have established a Recommended Exposure Limit (REL) of 2 ppm as a ceiling limit over a 1-hour time period for all halogenated anesthetic agents (1977). Isoflurane was developed later and considered to be safer. It is therefore not included in this standard setting process. However, some European countries have reported exposure limits for Isoflurane (**Table 2**):

Table 2. Exposure limits for isoflurane in some European countries

Country	STEL	TWA
United Kingdom	150 ppm (1149 mg/m^3)	50 ppm (383 mg/m^3)
Finland	20 ppm (150 mg/m^3)	10 ppm (77 mg/m^3)
Norway	4 ppm (22.5 mg/m^3)	2 ppm (15 mg/m^3)
Ireland	-----	50 ppm (380 mg/m^3)
Austria	20 ppm (160 mg/m^3)	10 ppm (80 mg/m^3) (MAK values)

Signs of acute (short-term) exposure include nausea, vomiting, nose/throat/respiratory irritation, headache, dizziness, drowsiness, and skin irritation. Signs of chronic (long-term) exposure include hypotension (low blood pressure), tachycardia (increased heart rate), respiratory depression and elevated blood glucose.

5. Safety Precautions for Isoflurane Use

5.1. Training

Students and employees who handle Isoflurane must have read the Safety Data Sheet (SDS) and receive training on the hazards of Isoflurane concerning:

- proper handling, use, storage and disposal of Isoflurane;
- the anesthesia procedures, including the use of the anesthetic machine, the waste anesthetic gas scavenging system;
- proper use of chemical fume hoods or other applicable local exhaust ventilation, and;
- spill clean-up and emergency response procedures.

The SDS must always be kept the immediate vicinity of the working area along with any Standard Operating Procedure (SOP) developed by the student/employee's department.

5.2. Engineering Controls

- Under no circumstances shall Isoflurane be used without the benefit of a scavenging/ventilation mechanism that eliminates inhalation exposure to the user. These mechanisms are:
  - a certified chemical fume hood when not using a precision.
  - vaporizer such as when using a bell jar.
- Connection of the exhaust hose must be to:
  - a certified chemical fume hood (preferred)
  - another appropriate exhaust device if a chemical fume hood is not available.
- In cases where the "open- drop" method is used the jar must be placed inside a properly functioning fume hood with the sash as far down as possible.
- Regarding the Isoflurane anesthetic machines, always follow recommended machine calibration times indicated by the manufacturer's manual or guidelines.

5.3. Eye Protection

Safety glasses, goggles or face shield if potential exists for direct exposure to aerosols or splashes.

5.4. Gloves

Use chemical resistant gloves, such as nitrile gloves.

5.5. Protection Clothing

Long pants, closed toed shoes and a lab coat (or work uniform) should be worn. Other body garments should be used based upon the task being performed (*e.g.*, sleeve lets, apron, gauntlets, disposable suits).

6. Storage, Spill and Waste Issues

6.1. Storage

Store Isoflurane bottles in a cool well-ventilated area, between 15-30°C, as indicated in the SDS. Do not store large quantities of Isoflurane. Ensure bottles are tightly closed and returned to storage location immediately after use. No special restrictions on storage with other products.

6.2. Spills

6.2.1. Small spill (a few milliliters).

Isoflurane is a highly volatile liquid. Therefore, any attempt to clean or collect liquid of small spills may not be successful as the liquid may dissipate quickly. If any residual liquid is to be picked-up, lab users must be aware of current spill procedures. They must:

- wear appropriate personal protective equipment (PPE);
- review cleaning/spill procedures found in SDS;
- absorb any residual solution with absorbent (spill pads, paper towels…);

- dispose of absorbent along with other chemical waste following Concordia University chemical waste procedures;
- clean spill area with soap and water.

6.2.2. Large spill (1-2 stock bottles)

In the event of a large spill, lab users should immediately:

1. Advise and warn co-workers;
2. Evacuate the area immediately;
3. Restrict the access to the area;
4. Notify Campus Safety and Prevention Services (CSPS) at ext. **3717** or **514 848-3717**, providing them with the following information:
    a. Location of the spill;
    b. Name of hazardous material;
    c. Quantity involved;
    d. Related health risks and precautions to be taken;
5. Provide Safety Data Sheet (SDS) or appropriate documentation.

6.3. Waste Handling

Isoflurane should be disposed of as a chemical hazardous waste only. Bottles of Isoflurane should not be discarded into biohazardous waste containers or broken glass boxes. Isoflurane bottle containing any residual liquid can be directly picked-up by EHS. For more information concerning hazardous waste, please contact EHS at hazardouswaste@concordia.ca.

7. Emergency Procedures

7.1. Skin Contact

1. Immediately rinse the affected area thoroughly with large amounts of water for at least 15 minutes.
2. Remove all contaminated clothing while continuing to flush with water.
3. While the victim is rinsing the affected area, someone should call CSPS at ext. **3717** and ask for medical assistance.

7.2. Eye Contact

1. Immediately flush the eyes with plenty of water for at least 15 minutes.
2. While the victim is rinsing the affected area, someone should call CSPS at ext. **3717** for emergency medical assistance.

7.3. Inhalation

1. Immediately move the victim to fresh air.
2. Call CSPS at ext. **3717** and ask for medical assistance.
3. Provide oxygen if victim has problems breathing.

7.4. Ingestion.

1. Call CSPS at ext. **3717** and ask for medical assistance.
2. Never induce vomiting unless directed to do so by medical personnel.

After any over exposure to anesthetic gases, such as Isoflurane, via skin, eye contact, inhalation or ingestion, the victim should immediately seek medical attention. In all cases of exposures, a copy of the Safety Data Sheet (SDS) must be brought to the emergency room as the treating physician might be unaware of the treatment measures for Isoflurane. All Isoflurane incidents and exposures must be reported to your supervisor and to Environmental Health & Safety (EHS). An Injury/Near-miss Report must be filled for any incident involving Isoflurane spill or exposure.

If you have any concerns about the use of Isoflurane at Concordia University, please contact EHS at **ehs@concordia.ca**.

Prepared in April 2014

Revision dates: August 2016, July 2024.

References:

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- Isoflurane, Occupational Safety and Health Administration – Consulted in July 2024.
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- University of California, Riverside EHS: Isoflurane Anesthetic Gas Safety Guidelines – Consulted in July 2024.
- The University of Iowa EHS: Isoflurane Anesthetic Gas Guidelines – Consulted in July 2024.
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- California Department of Public Health: Isoflurane may harm veterinary worker health – Consulted in July 2024.
- Princeton University, EHS – Safe Use of Isoflurane in Animal Research – Consulted in July 2024.
- Chandra, T.; Zebrowski, J. P.; McClain, R.; Lenertz, L. Y. Generating Standard Operating Procedures for the manipulation of hazardous chemicals in academic laboratories. *ACS Chem. Health Saf.* **2021**, *28*, 19-24. https://dx.doi.org/10.1021/acs.chas.0c00092.