Standard Operating Procedure
For

ISOFLURANE

PURPOSE:
Isoflurane is a halogenated anesthetic gas commonly used in University animal research facilities and individual laboratories. This document establishes procedures for the safe handling and use of 1-chloro-2,2,2-trifluoroethyl difluoromethyl ether (CAS# 26675-46-7), commonly known as isoflurane or Forane®.

HEALTH EFFECTS:
Isoflurane is a halogenated hydrocarbon that is a clear, colorless volatile liquid at standard temperature and pressure with a mild ether-like odor. It is known to cause serious eye irritation and human exposure to waste anesthetic gases has been associated with reproductive effects.

Signs of acute exposure: nausea, vomiting, nose/throat/respiratory irritation, headache, dizziness, drowsiness, skin irritation.

Signs of chronic exposure: hypotension (low blood pressure), tachycardia (increased heart rate), respiratory depression, elevated blood glucose.

REGULATORY LIMITS: The Federal Occupational Safety and Health Administration (OSHA) do 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 was not included in this standard setting process so its applicability is questionable. However, based on potential risks it is recommended that no worker should be exposed to greater than 2 ppm of any halogenated anesthetic agent including isoflurane.
Air Monitoring:
- **Area** monitoring can be requested to assess potential exposures in the general laboratory work area. The monitoring is performed using a direct read instrument to give concentrations in room during surgeries or other procedures.
- **Personal** monitoring can be requested to determine potential exposures for individual employees who work with isoflurane. The monitoring is performed using a passive dosimeter that the employee wears in their breathing zone to quantify potential exposure.
- Air monitoring can be requested by contacting Environment, Health & Safety (EHS) at 919-962-5507.

Requirements:
Based on the risk associated with the use of waste anesthetic gases the safety procedures outlined below are required by all research staff when working with isoflurane.

Administrative Controls:
- IACUC protocols that include isoflurane should reference this SOP to verify that the standard operating procedures are being followed.
- Anyone who handles isoflurane is required to review this SOP and the attached Safety Data Sheet (SDS) prior to work.

Engineering Controls:
- Isoflurane must be used in a well-ventilated room from which there is no recirculation of exhaust air.
- **Active scavenging** is optimal for scavenging waste gas and can include any of the following:
  - Delivery of anesthetic inside a certified chemical fume hood or ducted biological safety cabinet (BSC). *Use of the “drop method” should always be done using this method unless air monitoring has verified exposure levels below REL.*
  - Connection of vaporizer and/or induction box exhaust hose into a certified chemical fume hood or ducted BSC.
  - Connection of vaporizer and/or induction box exhaust hose to house vacuum.
- **Passive scavenging** can be used safely if specific procedures are followed. Passive scavenging relies on the positive pressure from the anesthetic gas delivery system and/or the exhalation effort of the animal to drive contaminated exhaled air through a specially designed activated carbon charcoal filter (such as F/AIR). The charcoal canister will adsorb and remove the waste gas before being discharged back into the room. Charcoal canisters have a finite effective life span, which can be monitored by weight.
  - The weight of each new canister should be recorded before its first use.
  - Before each subsequent use, the weight should be checked and recorded. If the total increase is close to 50 g, it should be replaced, or monitored closely during use (weigh between animals).
To function appropriately, the carbon canister must be at a level below that of the vaporizer, to assist passive scavenging.

To function appropriately, the carbon canister must be in an upright/vertical position.

To function appropriately with adequate air flow, the holes on the bottom of the carbon canister must not be blocked.

**Personal Protective Equipment (PPE):**
- Nitrile gloves, a lab coat, and safety glasses.
- When in rodent barrier facilities, PPE use must be consistent with the facility policy.

**Waste Disposal:**
- Unused solutions of isoflurane will be disposed of as a hazardous material through EHS ([https://s4.its.unc.edu/HazMat_Pickup/](https://s4.its.unc.edu/HazMat_Pickup/))

**Accidents or Injuries:**
- If isoflurane is splashed on an individual or in eyes flush for 15 minutes with copious quantities of water and contact the University Employee Occupational Health Clinic (919-966-9119).
- Spill procedures:
  - Do not attempt to clean-up if you feel unsure of your ability to do so or if you perceive the risk to be greater than normal laboratory operations.
  - Small volumes of isoflurane evaporate readily at normal room temperatures, and may dissipate before any attempts to clean up or collect the liquid are initiated. If a small spill occurs rapidly absorb any liquid with absorbent pads or paper towels and place in chemical fume hood for safe evaporation.
  - If a large spill occurs notify others in the area and evacuate room immediately. Contact EHS (919-962-5507) during working hours and 911 if after hours.
1. PRODUCT AND COMPANY IDENTIFICATION

Product Identifier: Isoflurane, USP
Product Name: Isoflurane

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

Contains Isoflurane

Relevant identified uses of the substance or mixture and uses advised against

Product Use: Anesthetic.
Product Type: Regulated Prescription Drug
Uses advised against: No information available.

Details of the supplier of the safety data sheet
BAXTER HEALTHCARE CORPORATION
DEERFIELD, ILLINOIS 60015
(800) 422-9837 or (224) 948-4770

E-mail Address
onebaxter@baxter.com

Emergency telephone number
Carechem24 International
+44 (0) 1235 239 670

2. HAZARDS IDENTIFICATION

Label Elements
Signal Word
Warning

Hazard Statements
H319 - Causes serious eye irritation H361 - Suspected of damaging fertility or the unborn child H373 - May cause damage to organs through prolonged or repeated exposure

Serious Eye Damage/Eye Irritation
P264 - Wash face, hands and any exposed skin thoroughly after handling
P280 - Wear protective gloves/protective clothing/eye protection/face protection
P305 + P351 + P338 - IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing
P337 + P313 - If eye irritation persists: Get medical advice/attention
P260 - Do not breathe dust/fume/gas/mist/vapors/spray
P314 - Get medical attention/advice if you feel unwell
P501 - Dispose of contents/container to an approved waste disposal plant

Obligatory Precautionary Statements
P281 - Use personal protective equipment as required
Other Hazards

Indication of Danger: Xi - Irritant.

Risk Phrases:
R36 - Irritating to eyes.
R63 - Possible risk of harm to the unborn child.
R33 - Danger of cumulative effects.

### 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Component</th>
<th>EINECS-No.</th>
<th>CAS-No</th>
<th>Weight %</th>
<th>Classification</th>
<th>EU - GHS Substance Classification</th>
<th>REACH No.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>247-897-7</td>
<td>26675-46-7</td>
<td>100</td>
<td>Repro. Cat. 3; R63</td>
<td>Repr. 2 (H361) Eye Irrit. 2 (H319) STOT RE 2 (H373)</td>
<td>No data available</td>
</tr>
</tbody>
</table>

For the full text of the R-phrases mentioned in this Section, see Section 16

### 4. FIRST AID MEASURES

**Description of first aid measures**

**General Advice:** Treat symptomatically and supportively.

**Eye contact:** In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. Get medical attention if irritation develops.

**Skin contact:** In case of contact, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention if irritation develops.

**Ingestion:** Do NOT induce vomiting unless directed to do so by medical personnel. Never give anything by mouth to an unconscious person. If large quantities of this material are swallowed, call a physician immediately.

**Inhalation:** If inhaled, remove to fresh air. If not breathing, give artificial respiration. If breathing is difficult, give oxygen. Get medical attention.

**Most important symptoms and effects, both acute and delayed**
A dose less than that needed to produce anesthesia (approximately 1%) may result in symptoms such as dizziness. May cause allergic reactions. See patient package insert in shipping carton for complete information.

**Indication of any immediate medical attention and special treatment needed**
Treat symptomatically. See patient package insert in shipping carton for complete information.

### 5. FIRE-FIGHTING MEASURES

**Extinguishing media**
**Suitable extinguishing media:** Use extinguishing media suitable for surrounding materials.

**Extinguishing media which must not be used for safety reasons:**
No information available.
Special hazards arising from the substance or mixture
No information available.

Advice for fire-fighters
Fire fighters should wear positive pressure self-contained breathing apparatus (SCBA) and full turnout gear.

6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures
Depending on local ventilation, clean-up crews may need to wear a chemical cartridge respirator, with a cartridge for organic vapors. Self-contained breathing apparatus may be needed in extreme circumstances. Use suitable protective equipment (Section 8). Follow all fire fighting procedures (Section 5).

Environmental precautions
Do not allow material to contaminate ground water system.

Methods and material for containment and cleaning up

Methods for Containment:
Small volumes of liquid anesthetic agents may evaporate readily at normal room temperatures, and may dissipate before any clean up attempts are initiated. For large spills, one or more bottles break, ensure adequate ventilation or evacuate area. Large volumes of anesthetic agents may cause sedative effects.

Methods for cleaning up:
Large spills should be absorbed using a sorbent that is designed for clean up of organic chemicals. Spill pillows, vermiculite, and carbon-based sorbents are some suitable materials. Keep in suitable, closed containers for disposal.

Reference to other sections
See Section 12 for additional information.

7. HANDLING AND STORAGE

Precautions for Safe Handling
Technical measures/precautions: Wash thoroughly after handling.

Conditions for safe storage, including any incompatibilities
Technical measures/conditions: Keep containers tightly closed in a dry, cool and well-ventilated place. Store between 15-30°C (59 to 86°F).

Incompatible products:
No special restrictions on storage with other products.

Specific End Uses
Other Guidelines: None

8. EXPOSURE CONTROLS / PERSONAL PROTECTION

Control parameters
Exposure Limits:

<table>
<thead>
<tr>
<th>Component</th>
<th>European Union</th>
<th>United Kingdom</th>
<th>France</th>
<th>Spain</th>
<th>Germany</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>None</td>
<td>150 ppm STEL 1149 mg/m³ STEL 50 ppm TWA 383 mg/m³ TWA</td>
<td>None</td>
<td>50 ppm VLA-ED 383 mg/m³ VLA-ED</td>
<td>None</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Component</th>
<th>Italy</th>
<th>Portugal</th>
<th>Netherlands</th>
<th>Finland</th>
<th>Denmark</th>
</tr>
</thead>
</table>
## Exposure controls

### Engineering measures:
Use process enclosures, local exhaust ventilation, or other engineering controls to keep airborne levels below recommended exposure limits. Well designed and maintained scavenging system on the anesthesia equipment (combined with a good general room ventilation) is important in limiting the exposures of all personnel.

### Personal protective equipment

#### Eye protection:
Eye protection not required for normal final product use. Safety glasses with side-shields are recommended for laboratory and manufacturing use.

#### Hand protection:
Use chemical resistant, impervious gloves. Additional body garments should be used based upon the task being performed (e.g./ sleevelets, apron, gauntlets, disposable suits).

#### Respiratory protection:
Personal respiratory protection equipment not typically required if engineering controls are in place. If exposure levels may exceed regulatory limits, implement a respiratory protection program including respiratory protection that is in compliance with OSHA 29 CFR1910.134 (in the US) or equivalent regulation in other regions.

#### Skin and body protection:
Work uniform or laboratory coat.

### Environmental Exposure Controls:
Do not allow material to contaminate ground water system.

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## 9. PHYSICAL AND CHEMICAL PROPERTIES

### Information on basic physical and chemical properties

<table>
<thead>
<tr>
<th>Physical state:</th>
<th>Liquid</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance:</td>
<td>Aqueous solution</td>
</tr>
<tr>
<td>Color:</td>
<td>Clear, Colorless.</td>
</tr>
<tr>
<td>Odor Threshold:</td>
<td>No information available.</td>
</tr>
<tr>
<td>pH:</td>
<td>Not applicable.</td>
</tr>
<tr>
<td>Melting point/range:</td>
<td>No information available.</td>
</tr>
<tr>
<td>Boiling point/range:</td>
<td>48.5°C (119.3°F)</td>
</tr>
<tr>
<td>Flash point:</td>
<td>No information available.</td>
</tr>
<tr>
<td>Flammability (solid, gas):</td>
<td>No information available.</td>
</tr>
<tr>
<td>Evaporation rate:</td>
<td>No information available.</td>
</tr>
<tr>
<td>Flammable limits in air-upper (%):</td>
<td>No information available.</td>
</tr>
<tr>
<td>Flammable limits in air-lower (%):</td>
<td>No information available.</td>
</tr>
<tr>
<td>Vapor pressure:</td>
<td>238 mmHg at 20°C (68°F)</td>
</tr>
<tr>
<td>Vapor Density:</td>
<td>No information available.</td>
</tr>
<tr>
<td>Density:</td>
<td>1.3002 g/cm³ at 20°C (68°F)</td>
</tr>
</tbody>
</table>
Solubility: 0.275% in water.
Partition coefficient (n-octanol/water): No information available.
Autoignition temperature: No information available.
Decomposition Temperature: No information available.
Viscosity: No information available.
Explosive Properties: No information available.
Oxidizing Properties: No information available.

Other information
Molecular weight: 184.5 g/mole

10. STABILITY AND REACTIVITY

Reactivity
No data available

Chemical Stability
Stable under recommended storage conditions.

Possibility of Hazardous Reactions
Polymerization: Not applicable
Hazardous Reactions: No information available

Conditions to Avoid
Do not freeze.

Incompatible Materials
Peroxides.

Hazardous Decomposition Products
These products are halogenated compounds (hydrochloric and hydrofluoric acids). Phosgene.

11. TOXICOLOGICAL INFORMATION

<table>
<thead>
<tr>
<th>Component</th>
<th>LC50 Inhalation</th>
<th>LD50 Dermal</th>
<th>LD50 Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>58.5 g/m³ (rat)</td>
<td>-</td>
<td>4770 µL/kg (rat)</td>
</tr>
<tr>
<td>26675-46-7</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Information on Toxicological Effects

Acute Toxicity

Irritation: Irritating to eyes. Mild skin irritation.
Corrosivity: None.

Inhalation: Practically non-toxic by inhalation. Cardiovascular effects (may include fluctuations in heart rate, changes in blood pressure, chest pain). Respiratory effects (may include shortness of breath, bronchospasms, laryngospasms, respiratory depression). Gastrointestinal effects (may include nausea, upset stomach, loss of appetite). Nervous System effects (may include ataxia, tremor, disturbance of speech, lethargy, headache, dizziness, blurred vision).

Eye contact: May cause eye irritation.
Skin contact: May cause skin irritation.
Ingestion: Practically non-toxic if swallowed. No specific hazards other than therapeutic effects.
1087151 - Isoflurane, USP

Revision Date: 09/17/2012

Sensitization: None known.
Mutagenic effects: No data is available on the product itself.
Carcinogenic effects: Not classified or listed by IARC, NTP, OSHA, EU and ACGIH. No drug related carcinogenic/tumorigenic effects based on animal data.
Reproductive toxicity: Contains a known or suspected reproductive toxin. Epidemiological studies suggest higher than normal incidences of problem pregnancies (particularly spontaneous abortions) among exposed personnel.

STOT - single exposure: None known.
STOT - repeated exposure: Liver.
Aspiration Hazard: No information available

12. ECOLOGICAL INFORMATION

<table>
<thead>
<tr>
<th>Component</th>
<th>Ecotoxicity - Water Flea Data</th>
<th>Fish Species Ecotoxicity</th>
<th>Ecotoxicity - Freshwater Algae Data</th>
<th>Ecotoxicity - Microtox Data</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isoflurane</td>
<td>None.</td>
<td>None.</td>
<td>None.</td>
<td>None.</td>
</tr>
<tr>
<td>26675-46-7</td>
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</tr>
</tbody>
</table>

Ecotoxicity Effects: No information available

Persistence and degradability
No information available.

Bioaccumulative potential
No information available.

Mobility in soil
No information available.

Results of PBT and vPvB assessment
This substance is not considered to be persistent, bioaccumulating nor toxic (PBT). This substance is not considered to be very persistent nor very bioaccumulating (vPvB).

Other adverse effects
Endocrine Disruptor Information: This product does not contain any known or suspected endocrine disruptors

13. DISPOSAL CONSIDERATIONS

Waste treatment methods
Waste from residues / unused products: In accordance with local and national regulations.
Contaminated Packaging: In accordance with local and national regulations.

14. TRANSPORT INFORMATION

IMDG/IMO Not regulated
RID

Not regulated

ICAO / IATA:

IATA Proper shipping name: Aviation regulated liquid n.o.s. (Isoflurane)
IATA UN Number: UN3334
IATA Primary Hazard: 9

15. REGULATORY INFORMATION

Safety, health and environmental regulations/legislation specific for the substance or mixture

International Inventories

EU EINECS List - This product complies with EINECS

Legend

EINECS/ELINCS - European Inventory of Existing Commercial Chemical Substances/EU List of Notified Chemical Substances

Chemical Safety Assessment

No

16. OTHER INFORMATION

Full text of R-phrases referred to under Section 3:

R36 - Irritating to eyes
R63 - Possible risk of harm to the unborn child
R33 - Danger of cumulative effects

Additional information:

Not Available.

Key literature references and sources for data:

www.ChemADVISOR.com/

Prepared by: Technology Resources, Baxter Healthcare Corporation
Revision Date: 09/17/2012

This data sheet contains changes from the previous version in section(s)?:

New GHS format. Changes to Section 1.

This safety data sheet complies with the requirements of Regulation (EC) No. 1907/2006

To the best of our knowledge, the information contained herein is accurate. However, neither the above named supplier nor any of its subsidiaries assumes any liability whatsoever for the accuracy or completeness of the information contained herein. Final determination of suitability of any material is the sole responsibility of the user. All materials may present unknown hazards and should be used with caution. Although certain hazards are described herein, we cannot guarantee that these are the only hazards that exist.

End of Safety Data Sheet