

Material Name: Flumazenil
Material Code: 17091
MSDS Number .: m-003747.asc

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Approved: 12/06/99

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MATERIAL SAFETY DATA SHEET

SECTION 1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

Material Name: Flumazenil
Inventory Code: 17091
RO #: 15-1788/000
CAS Number: 78755-81-4
Synonyms: 8-fluoro-5,6-dihydro-5-methyl-6-oxo-4H-imidazo[1,5-a]
[1,4]benzodiazepine-3-carboxylic acid ethyl ester
ethyl 8-fluoro-5,6-dihydro-5-methyl-6-oxo-4H-imidazo[1,
5-a][1,4]benzodiazepine-3-carboxylate
TSCA Status: FDA Exemption - Not on Inventory.
Chemical Family: Imidazobenzodiazepine
Therapeutic Category: Benzodiazepine antagonist
Formulations Used In: ROMAZICON(TM)

SECTION 2. COMPOSITION/INFORMATION ON INGREDIENTS

Ingredient Name	CAS Number	Concentration %
Flumazenil	78755-81-4	>=98

SECTION 3. HAZARDS IDENTIFICATION

EMERGENCY OVERVIEW

Physical State: Powder.
Color: White to off-white
Odor: Practically odorless

Severe dust explosion hazard.

POTENTIAL HEALTH EFFECTS

Relevant Routes of
Exposure: Inhalation, Skin Contact, Eye Contact, Ingestion.
Target Organs: Cardiovascular System, Gastrointestinal System, Central
Nervous System.

Acute Effects

General: May cause central nervous system effects such as
headache, dizziness, drowsiness, fatigue, and lack of
muscular coordination. May cause cardiovascular
effects such as increase or decrease in blood pressure,
irregular heartbeat, chest pain, and cardiac arrest.
May cause impairment of vision.

Chronic Effects: No adverse effects known.

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SECTION 3. HAZARDS IDENTIFICATION (Continued. . .)

Carcinogenicity : Not listed by NTP, IARC, or OSHA.

Reproductive

Toxicity : Since this material may affect the developing fetus, females planning to have a child and pregnant women should exercise caution regarding exposure. It is also advisable for nursing mothers to exercise caution regarding exposure.

Conditions

Aggravated : Hypersensitivity to this material and other materials in its chemical class.

Additional Health

Hazard Information : Individuals on benzodiazepine therapy should avoid exposure to this material. Individuals who are showing signs of serious cyclic antidepressant overdose should avoid exposure to this material.

SECTION 4. FIRST AID MEASURES

Inhalation : Remove to fresh air. Get medical attention. If not breathing, give artificial respiration. If breathing is difficult, administer oxygen by qualified personnel.

Skin Contact : Remove contaminated clothing and shoes. Wash skin with soap and plenty of water. If irritation occurs or persists, get medical attention. Wash clothing and shoes before reuse.

Eye Contact : Immediately flush eyes with plenty of water. If irritation occurs or persists, get medical attention.

Ingestion : If large quantities of this material are swallowed, get medical attention immediately. Do not induce vomiting unless directed by medical personnel. Never give anything by mouth to an unconscious person.

SECTION 5. FIRE FIGHTING MEASURES

Flash Point : Not Applicable

Extinguishing Media : Water, Carbon Dioxide, Dry Chemical, Foam.

Unusual Fire and

Explosion Hazards . . : Severe dust explosion hazard. Toxic emissions may be given off in a fire. See Decomposition Products in Section 10. Stability and Reactivity.

Fire Fighting

Instructions : Wear NIOSH/MSHA approved positive pressure, self contained breathing apparatus and full protective turn out gear. Use caution in approaching fire. Use water to keep fire exposed containers cool.

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SECTION 6. ACCIDENTAL RELEASE MEASURES

Spill Clean Up

Procedures: Use proper personal protective equipment and clothing specified in Section 8-Exposure Controls/Personal Protection. Shut off the source of the spill or leak if it is safe to do so. Shut off all electrical equipment if it is safe to do so. Eliminate possible ignition sources. Follow appropriate grounding procedures. Scoop or shovel spilled material into a suitable labeled open head drum. Secure the drum cover and move the container to a safe holding area. Wash spill area thoroughly with soapy water. Collect wash with a noncombustible absorbent material and transfer to labeled container for treatment and disposal. Check area for residual material and repeat clean up if detected.

Treatment and

Disposal: Decontaminate equipment. Dispose of protective clothing with the spilled material. Dispose of in accordance with recommendations in Section 13 Disposal Considerations.

Reporting

Requirements: The United States Environmental Protection Agency (USEPA) has not established a Reportable Quantity (RQ) for releases of this material. In New Jersey, report all releases which are likely to endanger the public health, harm the environment or cause a complaint to the NJDEPE Hotline (1-609-292-5560) and to local officials. State and local regulations vary and may impose additional reporting requirements.

SECTION 7. HANDLING AND STORAGE

Storage Temperature

(min/max): 15 to 30 degrees C

Shelf Life: 24 months

Special Sensitivity : Heat. Do not heat above 160 degrees C.

Handling & Storage

Precautions: Do not generate dust or expose to ignition sources.
Ground and bond all transfer equipment.
Milling/mixing/drying should be performed in devices equipped with explosion relief or suppression systems or under inert conditions.
Avoid contact with eyes, skin and clothing.
Avoid breathing dust.
Use with adequate ventilation.
When handling, use proper personal protective equipment specified in section 8.
Wash thoroughly after handling.
Keep container tightly closed when not in use.
Store in a dry area at room temperature.

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SECTION 8. EXPOSURE CONTROLS / PERSONAL PROTECTION

ENGINEERING CONTROLS

Ventilation: Local ventilation is required when using this material.
Use in a lab hood.

PERSONAL PROTECTION

Respirator Type(s) .: Negative Pressure Air Purifying, Half Face, Toxic
Dust/Mist/Fume High Efficiency Filter.
Conditions for Use .: Respiratory protection is recommended for dusty
operations. In the laboratory, use of the above
mentioned respirator is required. For production
operations, a supplied-air full facepiece respirator or
supplied-air hood is required. OSHA considers
effective engineering controls to be the primary means
to control worker exposure. Respiratory protection
should not substitute for feasible engineering
controls. Whenever respiratory protection is used, a
complete respirator program should be developed in
accordance with OSHA Subpart I (29CFR1910.134)
requirements.
Glove Materials: Any plastic or rubber glove.
Conditions for Use .: Gloves are required if there is a potential for skin
contact.
Skin Protection: Use protective clothing (lab coats, disposable
coveralls, etc.) in both production and laboratory
areas. Consult the protective clothing manufacturer,
supplier and/or industrial hygienist.
Eye Protection: Safety Glasses Required, Safety Goggles Recommended.

OTHER CONTROL MEASURES

Administrative

Controls: Post the work area and limit access to authorized
personnel only.

Additional

Protective Measures : Work clothing should be removed in a changeroom on site
and laundered professionally. Employees should shower
and change into street clothes before leaving the
facility. Provide safety showers and eyewash stations
in the work area. Prevent the accumulation of dust in
the work area by thorough periodic cleaning of the
area.

EXPOSURE LIMITS

Flumazenil

Roche IOEL: 0.100 mg/m³ 8 Hr. Time Weighted Average.
Roche IOEL: 0.200 mg/m³ Short Term Exposure Limit.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Physical State: Powder.
Color: White to off-white
Odor: Practically odorless
Molecular Weight: 303.30

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SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES (Continued. . .)

Chemical Formula . . . : C15H14FN3O3
Pure/Mixture : Pure.
Melting Point : 198-202 C
H2O Solubility : Insoluble.
Solubility - Other .: Chloroform, methanol

SECTION 10. STABILITY AND REACTIVITY

Stability : Normally stable but may become unstable at elevated temperatures or reacts with water, releasing some energy but not violently.
Conditions to Avoid : Temperatures >100C
Dust Accumulation
Airborne Dust
Sources of Ignition
Incompatibility -
Materials to Avoid .: Strong acids, Strong bases.
Decomposition
Products : Carbon monoxide, carbon dioxide, hydrogen fluoride, oxides of nitrogen
Polymerization : No
Conditions of
Polymerization : Will not occur.

SECTION 11. TOXICOLOGICAL INFORMATION

Flumazenil

Acute Oral, Rat: 4200 mg/kg

Summary: Acute oral LD50 (rat) of 4200 mg/kg body weight classifies this material as slightly toxic orally under the study conditions utilized.

Signs of toxicity include decrease motor activity, catatonia (schizophrenia), profuse salivation, and tremors.

Chronic Oral, Dog

Summary: No significant treatment related changes in histopathological or anatomical parameters were noted in one-year feeding study in dogs at doses of 5, 25, and 125 mg/kg/day. The clinical signs were dose-related and include sedation, decreased motor activity, and lethargy; tremors were noted in dogs at the high dose groups and elevated serum glyceride levels in female dogs in the high dose groups were also observed under the the study conditions utilized.

Chronic Oral, Rat

Summary: No significant treatment related changes in clinical, anatomical or histopathological parameters were noted in a one-year feeding study in rats at doses of 6, 20, and 125 mg/kg/day except for a reversible increase in thyroid weight in male rats under the study conditions utilized.

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SECTION 11. TOXICOLOGICAL INFORMATION (Continued. . .)

Reproductive Oral, Rat

Summary: In a Segment I study, there was no evidence of any impairment of fertility and reproductive capabilities of male and female rats at oral doses of 15, 45, and 125 mg/kg/day under the study conditions utilized. In another study, pregnant female rats given oral doses of 5, 25, and 125 mg/kg/day from day 15 of gestation through day 22 of lactation showed slight increases in liver weights and delays in incisor eruption and ear opening in the pups in the high dose groups.

Teratogenicity Oral, Rat

Summary: No evidence of teratogenic effects in rats when this material was administered orally at doses of 15, 50, 150 mg/kg/day from day 6 through day 15 of gestation, under the study conditions utilized.

Teratogenicity Oral, Rabbit

Summary: No evidence of teratogenic effects in rabbits when this material was administered orally at doses of 15, 50, and 150 mg/kg/day from day 6 through day 19 of gestation, under the study conditions utilized.

Mutagenicity

Summary: No evidence of mutagenicity was observed in the following in vitro assays: Ames test, "treat and plate" assay, HGPRT assay, chromosomal aberrations in human lymphocytes assay under the study conditions utilized. A positive response in the unscheduled DNA synthesis assay is not considered to be toxicologically relevant since this occurred at concentrations that were cytotoxic under the study conditions utilized and since there are negative results in other assays that measure DNA repair.

Mutagenicity Mouse

Summary: No evidence of mutagenicity was observed in the following in vivo assays: mouse micronucleus assay and the DNA repair assay in male mouse germ cells under the study conditions utilized.

SECTION 12. ECOLOGICAL INFORMATION

Flumazenil

Environmental Concentration Lethal to 50%, 48 Hour, Daphnia : >518 mg/L
Summary: The EC50 is greater than 518 mg/l which classifies this material as practically non-toxic to Daphnia under the study conditions utilized. The No Observed Effect Concentration (NOEC) is 65.6 mg/l.

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal

Recommendations: This material is suitable for incineration. These recommendations are based on the product as shipped. Use, processing, alteration or contamination may affect these disposal recommendations. State, local or site restrictions affecting the available proper disposal options may vary.

RCRA Waste #: Not regulated under RCRA

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SECTION 13. DISPOSAL CONSIDERATIONS (Continued. . .)

Empty Containers . . . : Empty containers must be triple rinsed prior to disposal, recycling, or reuse.

SECTION 14. TRANSPORTATION INFORMATION

Enforcement Agency .: US Dept. of Transportation
Country/Community .: USA
Proper Ship. Name .: Non-regulated

Enforcement Agency .: International Air Transport Association
Country/Community .: International
Proper Ship. Name .: Non-regulated

SECTION 15. REGULATORY INFORMATION

No regulatory information available on this material.

SECTION 16. OTHER INFORMATION

APPROVAL INFORMATION

Preparer : Annette Bucca-Janacek
Approver : Corporate Environmental & Safety Affairs
Approval Date : 12/06/99
Previous Approval
Date : 01/09/98
Reason For Issue . . . : Revision - Addition of IOEL

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