SAFETY DATA SHEET

Halofuginone Formulation

Version 3.9  Revision Date: 13.09.2019  SDS Number: 862857-00012  Date of last issue: 24.04.2019
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SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Halofuginone Formulation

Manufacturer or supplier’s details
Company: MSD
Address: Talcahuano 750, 6th floor, Ciudad Autonoma
Buenos Aires, Argentina  C1013AAP
Telephone: 908-740-4000
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@msd.com
Telefax: 908-735-1496

Recommended use of the chemical and restrictions on use
Recommended use: Veterinary product

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Skin irritation: Category 3
Eye irritation: Category 2A
Short-term (acute) aquatic hazard: Category 3
Long-term (chronic) aquatic hazard: Category 3

GHS label elements
Hazard pictograms:

Signal Word: Warning

Hazard Statements: H316 Causes mild skin irritation.
H319 Causes serious eye irritation.
H412 Harmful to aquatic life with long lasting effects.

Precautionary Statements: Prevention:
P264 Wash skin thoroughly after handling.
P273 Avoid release to the environment.
P280 Wear eye protection/ face protection.
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Response:
P305 + P351 + P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P332 + P313 If skin irritation occurs: Get medical advice/attention.
P337 + P313 If eye irritation persists: Get medical advice/attention.

Disposal:
P501 Dispose of contents/container to an approved waste disposal plant.

Other hazards which do not result in classification
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mixture</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactic acid</td>
<td>50-21-5</td>
<td>&gt;= 1 - &lt; 3</td>
</tr>
<tr>
<td>Halofuginone</td>
<td>82186-71-8</td>
<td>&gt;= 0,025 - &lt; 0,1</td>
</tr>
</tbody>
</table>

SECTION 4. FIRST AID MEASURES

General advice: In the case of accident or if you feel unwell, seek medical advice immediately. When symptoms persist or in all cases of doubt seek medical advice.

If inhaled: If inhaled, remove to fresh air. Get medical attention if symptoms occur.

In case of skin contact: In case of contact, immediately flush skin with plenty of water. Remove contaminated clothing and shoes. Get medical attention. Wash clothing before reuse. Thoroughly clean shoes before reuse.

In case of eye contact: In case of contact, immediately flush eyes with plenty of water for at least 15 minutes. If easy to do, remove contact lens, if worn. Get medical attention.

If swallowed: If swallowed, DO NOT induce vomiting. Get medical attention if symptoms occur. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed: Causes mild skin irritation. Causes serious eye irritation.

Protection of first-aiders: First Aid responders should pay attention to self-protection, and use the recommended personal protective equipment when the potential for exposure exists (see section 8).

Notes to physician: Treat symptomatically and supportively.
SECTION 5. FIRE-FIGHTING MEASURES

Suitable extinguishing media:
- Water spray
- Alcohol-resistant foam
- Carbon dioxide (CO2)
- Dry chemical

Unsuitable extinguishing media:
- None known.

Specific hazards during firefighting:
- Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
- Carbon oxides

Specific extinguishing methods:
- Use extinguishing measures that are appropriate to local circumstances and the surrounding environment.
- Use water spray to cool unopened containers.
- Remove undamaged containers from fire area if it is safe to do so.
- Evacuate area.

Special protective equipment for fire-fighters:
- In the event of fire, wear self-contained breathing apparatus.
- Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures:
- Use personal protective equipment.
- Follow safe handling advice and personal protective equipment recommendations.

Environmental precautions:
- Discharge into the environment must be avoided.
- Prevent further leakage or spillage if safe to do so.
- Prevent spreading over a wide area (e.g., by containment or oil barriers).
- Retain and dispose of contaminated wash water.
- Local authorities should be advised if significant spillages cannot be contained.

Methods and materials for containment and cleaning up:
- Soak up with inert absorbent material.
- For large spills, provide diking or other appropriate containment to keep material from spreading. If diked material can be pumped, store recovered material in appropriate container.
- Clean up remaining materials from spill with suitable absorbent.
- Local or national regulations may apply to releases and disposal of this material, as well as those materials and items employed in the cleanup of releases. You will need to determine which regulations are applicable.
- Sections 13 and 15 of this SDS provide information regarding certain local or national requirements.

SECTION 7. HANDLING AND STORAGE

Technical measures:
- See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.
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Local/Total ventilation : Use only with adequate ventilation.
Advice on safe handling : Do not get on skin or clothing.
                        : Avoid inhalation of vapor or mist.
                        : Do not swallow.
                        : Do not get in eyes.
                        : Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
                        : Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage : Keep in properly labeled containers.
Materials to avoid : Do not store with the following product types:
                        : Strong oxidizing agents

SECTION 8. EXPOSURE CONTROLS/PERSONAL PROTECTION

Ingredients with workplace control parameters

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters / Permissible concentration</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Halofuginone</td>
<td>82186-71-8</td>
<td>TWA</td>
<td>5 µg/m³ (OEB 4)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wipe limit 50 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Further information: DSEN, Skin

Engineering measures : All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment. Essentially no open handling permitted.
Use closed processing systems or containment technologies.
If handled in a laboratory, use a properly designed biosafety cabinet, fume hood, or other containment device if the potential exists for aerosolization. If this potential does not exist, handle over lined trays or benchtops.

Personal protective equipment

Respiratory protection : If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.
Filter type : Organic vapor Type
Hand protection : Chemical-resistant gloves

Remarks : Consider double gloving.
Eye protection : Wear safety glasses with side shields or goggles.
              : If the work environment or activity involves dusty conditions, mists or aerosols, wear the appropriate goggles.
              : Wear a faceshield or other full face protection if there is a potential for direct contact to the face with dusts, mists, or aerosols.

Skin and body protection : Work uniform or laboratory coat.
Additional body garments should be used based upon the task being performed (e.g., sleevelets, apron, gauntlets, disposable suits) to avoid exposed skin surfaces. Use appropriate degowning techniques to remove potentially contaminated clothing.

Hygiene measures: If exposure to chemical is likely during typical use, provide eye flushing systems and safety showers close to the working place. When using do not eat, drink or smoke. Wash contaminated clothing before re-use. The effective operation of a facility should include review of engineering controls, proper personal protective equipment, appropriate degowning and decontamination procedures, industrial hygiene monitoring, medical surveillance and the use of administrative controls.

### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

- **Appearance**: liquid
- **Color**: yellow
- **Odor**: odorless
- **Odor Threshold**: No data available
- **pH**: 2.1 - 3
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: No data available
- **Evaporation rate**: No data available
- **Flammability (solid, gas)**: Not applicable
- **Flammability (liquids)**: No data available
- **Upper explosion limit / Upper flammability limit**: No data available
- **Lower explosion limit / Lower flammability limit**: No data available
- **Vapor pressure**: No data available
- **Relative vapor density**: No data available
- **Density**: No data available
- **Solubility(ies)**: Water solubility: No data available
SECTION 10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions: Can react with strong oxidizing agents.
Conditions to avoid: None known.
Incompatible materials: Oxidizing agents.
Hazardous decomposition products: No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure:
- Inhalation
- Skin contact
- Ingestion
- Eye contact

Acute toxicity
Not classified based on available information.

Product:
Acute oral toxicity: Acute toxicity estimate: > 5,000 mg/kg
Method: Calculation method

Components:
Lactic acid:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
Remarks: Based on data from similar materials

Acute inhalation toxicity: LC50 (Rat): > 5 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist
Method: OECD Test Guideline 403
Remarks: Based on data from similar materials
Acute dermal toxicity: LD50 (Rabbit): > 2.000 mg/kg
Assessment: The substance or mixture has no acute dermal toxicity
Remarks: Based on data from similar materials

Halofuginone:
Acute oral toxicity: LD50 (Rat): 30 mg/kg
LD50 (Mouse): 5 mg/kg

Acute inhalation toxicity: LC50 (Rat): 0,053 mg/l
Test atmosphere: dust/mist

Acute dermal toxicity: LD50 (Rabbit): 16 mg/kg

Skin corrosion/irritation
Causes mild skin irritation.

Components:

Lactic acid:
Species: Rabbit
Result: Skin irritation
Remarks: Based on data from similar materials

Halofuginone:
Species: Rabbit
Result: Skin irritation

Serious eye damage/eye irritation
Causes serious eye irritation.

Components:

Lactic acid:
Species: Chicken eye
Result: Irreversible effects on the eye
Remarks: Based on data from similar materials

Halofuginone:
Result: Severe irritation

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.
## Components:

### Lactic acid:
- **Test Type**: Buehler Test
- **Routes of exposure**: Skin contact
- **Species**: Guinea pig
- **Result**: negative
- **Remarks**: Based on data from similar materials

### Halofuginone:
- **Routes of exposure**: Dermal
- **Species**: Guinea pig
- **Result**: Sensitizer

### Germ cell mutagenicity
Not classified based on available information.

## Components:

### Lactic acid:
- **Genotoxicity in vitro**:
  - **Test Type**: Bacterial reverse mutation assay (AMES)
  - **Method**: OECD Test Guideline 471
  - **Result**: negative
  - **Remarks**: Based on data from similar materials
  - **Test Type**: In vitro mammalian cell gene mutation test
  - **Method**: OECD Test Guideline 476
  - **Result**: negative
  - **Remarks**: Based on data from similar materials
  - **Test Type**: Chromosome aberration test in vitro
  - **Method**: OECD Test Guideline 473
  - **Result**: negative
  - **Remarks**: Based on data from similar materials

### Halofuginone:
- **Genotoxicity in vitro**:
  - **Test Type**: Ames test
  - **Result**: positive
  - **Test Type**: Mouse Lymphoma
    - **Result**: negative
  - **Test Type**: Chromosomal aberration
    - **Test system**: human lymphoblastoid cells
    - **Result**: negative
  - **Test Type**: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
    - **Result**: negative

### Genotoxicity in vivo:
- **Test Type**: Micronucleus test
  - **Species**: Mouse
  - **Cell type**: Bone marrow
Application Route: Oral
Result: negative

Test Type: Cytogenetic assay
Species: Rat
Application Route: Oral
Result: negative

Test Type: DNA Repair
Species: Mouse
Application Route: Oral
Result: negative

Carcinogenicity
Not classified based on available information.

Components:

Lactic acid:
Species: Rat
Application Route: Ingestion
Exposure time: 2 Years
Result: negative
Remarks: Based on data from similar materials

Halofuginone:
Species: Mouse
Application Route: Oral
NOAEL: 0,24 mg/kg body weight
Result: negative

Species: Rat
Application Route: Oral
Exposure time: 63 weeks
NOAEL: 0,36 mg/kg body weight
Result: negative

Species: Rat
Application Route: Oral
Exposure time: 26 Months
NOAEL: 0,09 - 0,18 mg/kg body weight
Result: negative

Reproductive toxicity
Not classified based on available information.

Components:

Lactic acid:
Effects on fetal development: Test Type: Embryo-fetal development
Species: Mouse
Application Route: Ingestion
Result: negative
Halofuginone:

**Effects on fertility**
- **Test Type:** Fertility
- **Species:** Mouse
- **Application Route:** Oral
- **Fertility:** NOAEL: 0.126 mg/kg body weight
- **Result:** No effects on fertility.

**Test Type:** Fertility
- **Species:** Dog
- **Application Route:** Oral
- **Fertility:** LOAEL: 0.067 mg/kg body weight
- **Result:** Effects on fertility.

**Test Type:** Three-generation reproduction toxicity study
- **Species:** Mouse
- **Application Route:** Oral
- **General Toxicity F1:** LOAEL: 0.063 mg/kg body weight
- **Symptoms:** Reduced body weight
- **Result:** No effects on fertility and early embryonic development were detected.

**Effects on fetal development**
- **Test Type:** Embryo-fetal development
- **Species:** Rat
- **Application Route:** Oral
- **General Toxicity Maternal:** LOAEL: 0.34 mg/kg body weight
  - **Embryo-fetal toxicity:** NOAEL: 0.67 mg/kg body weight
  - **Result:** No embryo-fetal toxicity., No teratogenic effects.

**Test Type:** Embryo-fetal development
- **Species:** Rabbit
- **Application Route:** Oral
- **General Toxicity Maternal:** NOAEL: 0.025 mg/kg body weight
  - **Embryo-fetal toxicity:** NOAEL: 0.076 mg/kg body weight
  - **Result:** No embryo-fetal toxicity., No teratogenic effects.

**Reproductive toxicity - Assessment**
- Some evidence of adverse effects on sexual function and fertility, based on animal experiments.

**STOT - single exposure**
Not classified based on available information.

**STOT - repeated exposure**
Not classified based on available information.

**Components:**

**Halofuginone:**
- **Target Organs**
  - **Assessment:** Blood
  - Causes damage to organs through prolonged or repeated exposure.
Repeated dose toxicity

**Components:**

**Lactic acid:**
- **Species:** Rat
- **NOAEL:** > 100 mg/kg
- **Application Route:** Ingestion
- **Exposure time:** 13 Weeks
- **Remarks:** Based on data from similar materials

- **Species:** Rat
- **LOAEL:** 886 mg/kg
- **Application Route:** Skin contact
- **Exposure time:** 13 Weeks

**Halofuginone:**
- **Species:** Mouse
- **NOAEL:** 0.07 mg/kg
- **LOAEL:** 0.16 mg/kg
- **Application Route:** Oral
- **Exposure time:** 4 Weeks
- **Target Organs:** Blood

- **Species:** Rat
- **NOAEL:** 0.13 mg/kg
- **LOAEL:** 0.88 mg/kg
- **Application Route:** Oral
- **Exposure time:** 13 Weeks
- **Target Organs:** Liver

- **Species:** Dog
- **NOAEL:** 0.067 mg/kg
- **LOAEL:** 0.134 mg/kg
- **Application Route:** Oral
- **Exposure time:** 13 Weeks
- **Target Organs:** Blood

- **Species:** Dog
- **NOAEL:** 0.075 mg/kg
- **LOAEL:** 0.16 mg/kg
- **Application Route:** Oral
- **Exposure time:** 26 Weeks
- **Target Organs:** Blood

**Aspiration toxicity**
Not classified based on available information.

**Experience with human exposure**

**Components:**

**Halofuginone:**
- **General Information:** No human information is available.
Inhalation: Remarks: May cause irritation of respiratory tract.
Skin contact: Remarks: May cause skin irritation and/or dermatitis. May cause sensitization by skin contact. Can be absorbed through skin.
Eye contact: Remarks: May irritate eyes.

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Lactic acid:
Toxicity to fish: LC50 (Danio rerio (zebra fish)): > 100 mg/l
Exposure time: 96 h
Method: OECD Test Guideline 203
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): > 100 mg/l
Exposure time: 48 h
Method: OECD Test Guideline 202
Remarks: Based on data from similar materials

Toxicity to algae/aquatic plants: ErC50 (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

NOEC (Pseudokirchneriella subcapitata (green algae)): > 100 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

Toxicity to microorganisms: EC50: > 10 - 100 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209
Remarks: Based on data from similar materials

Halofuginone:
Toxicity to fish: LC50 (Oncorhynchus mykiss (rainbow trout)): 1,8 mg/l
Exposure time: 96 h
Remarks: Based on data from similar materials

LC50 (Cyprinus carpio (Carp)): 0,3 mg/l
Exposure time: 72 h
Remarks: Based on data from similar materials

LC50 (Lepomis macrochirus (Bluegill sunfish)): 0,12 mg/l
Exposure time: 96 h
Remarks: Based on data from similar materials

Toxicity to daphnia and other: EC50 (Daphnia magna (Water flea)): 0,02 mg/l
aquatic invertebrates: Exposure time: 48 h
Remarks: Based on data from similar materials

Toxicity to algae/aquatic plants
EC50 (Chlorella pyrenoidosa): 46 mg/l
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

M-Factor (Acute aquatic toxicity): 10
M-Factor (Chronic aquatic toxicity): 10

Persistence and degradability

Components:

Lactic acid:
Biodegradability: Result: Not readily biodegradable.
Remarks: Based on data from similar materials

Halofuginone:
Biodegradability: Result: Not readily biodegradable.

Bioaccumulative potential

Components:

Lactic acid:
Partition coefficient: n-octanol/water: log Pow: -0.62

Halofuginone:
Partition coefficient: n-octanol/water: log Pow: 1.18

Mobility in soil

Components:

Halofuginone:
Distribution among environmental compartments: log Koc: 3.87
Method: FDA 3.08

Other adverse effects
No data available

SECTION 13. DISPOSAL CONSIDERATIONS

Disposal methods
Waste from residues: Dispose of in accordance with local regulations.
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. If not otherwise specified: Dispose of as unused product.
SECTION 14. TRANSPORT INFORMATION

International Regulations

UNRTDG
Not regulated as a dangerous good

IATA-DGR
Not regulated as a dangerous good

IMDG-Code
Not regulated as a dangerous good

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code
Not applicable for product as supplied.

SECTION 15. REGULATORY INFORMATION

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

Argentina. Carcinogenic Substances and Agents Registry: Not applicable

Control of precursors and essential chemicals for the preparation of drugs: Not applicable

International Regulations

The ingredients of this product are reported in the following inventories:

AICS: not determined

DSL: not determined

IECSC: not determined

SECTION 16. OTHER INFORMATION

Further information


Full text of other abbreviations

AICS - Australian Inventory of Chemical Substances; ANTT - National Agency for Transport by Land of Brazil; ASTM - American Society for the Testing of Materials; bw - Body weight; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; ELx - Loading rate associated with x% response; EmS - Emergency Schedule;
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