SAFETY DATA SHEET

Doramectin Formulation

1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Doramectin Formulation

Manufacturer or supplier’s details
Company name of supplier: MSD
Address: Kumagaya, Saitama Prefecture, Xicheng 810 MSD Co., Ltd. Menuma factory
Telephone: 048-588-8411
E-mail address: EHSDATASTEWARD@msd.com
Emergency telephone number: +1-908-423-6000

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

2. HAZARDS IDENTIFICATION

GHS Classification
Effects on or via lactation

Short-term (acute) aquatic hazard: Category 1
Long-term (chronic) aquatic hazard: Category 1

GHS label elements
Hazard pictograms:

Signal word: Warning
Hazard statements: H362 May cause harm to breast-fed children.
H410 Very toxic to aquatic life with long lasting effects.
Precautionary statements:
Prevention:
P201 Obtain special instructions before use.
P263 Avoid contact during pregnancy/while nursing.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P273 Avoid release to the environment.
Response:
P308 + P313 IF exposed or concerned: Get medical advice/attention.
3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Mixture</th>
</tr>
</thead>
</table>

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
<th>ENCS No.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Doramectin</td>
<td>117704-25-3</td>
<td>&gt;= 1 - &lt; 2.5</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2,6-Di-tert-butyl-p-cresol</td>
<td>128-37-0</td>
<td>&gt;= 0.025 - &lt; 0.1</td>
<td>3-540, 9-1805</td>
</tr>
</tbody>
</table>

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.

In case of skin contact: In case of contact, immediately flush skin with soap and 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: Flush eyes with water as a precaution.
Get medical attention if irritation develops and persists.

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

Most important symptoms and effects, both acute and delayed: May cause harm to breast-fed children.

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.

5. FIREFIGHTING MEASURES

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

Unsuitable extinguishing media: None known.
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 dyking or other appropriate containment to keep material from spreading. If dyked 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.

7. HANDLING AND STORAGE

Handling

Technical measures

See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.

Local/Total ventilation

Use only with adequate ventilation.

Advice on safe handling

Avoid inhalation of vapour or mist. Do not swallow. Avoid contact with eyes. Avoid prolonged or repeated contact with skin. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure as-
Avoidance of contact:
Take care to prevent spills, waste and minimize release to the environment.

Hygiene measures:
- Oxidizing agents
- 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.

Storage
- Conditions for safe storage: Keep in properly labelled containers.
- Store in accordance with the particular national regulations.
- Materials to avoid: Do not store with the following product types:
  - Oxidizing solids
  - Oxidizing liquids

Packaging material: Unsuitable material: None known.

8. EXPOSURE CONTROLS/PERSOINAL PROTECTION

Threshold limit value and permissible exposure limits for each component in the work environment

<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>Doramectin</td>
<td>117704-25-3</td>
<td>TWA</td>
<td>OEB 3 (&gt;= 10 &lt; 100 µg/m3)</td>
<td>Internal</td>
</tr>
<tr>
<td>2,6-Di-tert-butyl-p-cresol</td>
<td>128-37-0</td>
<td>TWA (Inhalable fraction and vapor)</td>
<td>2 mg/m3</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Engineering measures:
- Use appropriate engineering controls and manufacturing technologies to control airborne concentrations (e.g., dripless quick connections).
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
- Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices).
- Minimize open handling.

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: Particulates type
Hand protection

Material : 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.

9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance : oily
Colour : light yellow
Odour : characteristic
Odour Threshold : No data available
pH : No data available
Melting point/freezing point : -7 °C
Initial boiling point and boiling range : 270 °C
Flash point : 215.7 °C

Evaporation rate : No data available
Flammability (solid, gas) : Not applicable
Flammability (liquids) : Not applicable
Upper explosion limit / Upper flammability limit : No data available
Lower explosion limit / Lower flammability limit : No data available
Vapour pressure : No data available
Relative vapour density : No data available
Relative density : 0.89 - 91
Density: No data available

Solubility(ies):
  Water solubility: practically insoluble

Partition coefficient: n-octanol/water: Not applicable

Auto-ignition temperature: No data available

Decomposition temperature: No data available

Viscosity:
  Viscosity, kinematic: 31.7 - 32.1 m2/s (25 °C)

Explosive properties: Not explosive

Oxidizing properties: The substance or mixture is not classified as oxidizing.

Molecular weight: No data available

Particle size: Not applicable

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.

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: > 2,000 mg/kg
  Method: Calculation method

Components:

Doramectin:
  Acute oral toxicity: LD50 (Rat, female): > 500 - 1,000 mg/kg
Acute dermal toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 402
Assessment: The substance or mixture has no acute dermal toxicity

2,6-Di-tert-butyl-p-cresol:
Acute oral toxicity: LD50 (Rat): > 6,000 mg/kg
Method: OECD Test Guideline 401

Acute dermal toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 402
Assessment: The substance or mixture has no acute dermal toxicity

Skin corrosion/irritation
Not classified based on available information.

Components:

Doramectin:
Species: Rabbit
Result: No skin irritation

2,6-Di-tert-butyl-p-cresol:
Species: Rabbit
Method: OECD Test Guideline 404
Result: No skin irritation
Remarks: Based on data from similar materials

Serious eye damage/eye irritation
Not classified based on available information.

Components:

Doramectin:
Species: Rabbit
Result: No eye irritation

2,6-Di-tert-butyl-p-cresol:
Species: Rabbit
Result: No eye irritation
Method: OECD Test Guideline 405
Remarks: Based on data from similar materials

Respiratory or skin sensitisation
Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.
Components:

Doramectin:
- **Test Type**: Local lymph node assay (LLNA)
- **Exposure routes**: Skin contact
- **Species**: Mouse
- **Method**: OECD Test Guideline 429
- **Result**: negative

2,6-Di-tert-butyl-p-cresol:
- **Test Type**: Human repeat insult patch test (HRIPT)
- **Exposure routes**: Skin contact
- **Species**: Humans
- **Result**: negative

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

Components:

Doramectin:
- **Genotoxicity in vitro**:
  - Test Type: Bacterial reverse mutation assay (AMES)
    - Result: negative
  - Test Type: In vitro mammalian cell gene mutation test
    - Result: negative
  - Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
    - Result: negative

- **Genotoxicity in vivo**:
  - Test Type: Mammalian erythrocyte micronucleus test (in vivo cytogenetic assay)
    - Species: Mouse
    - Application Route: Ingestion
    - Result: negative

2,6-Di-tert-butyl-p-cresol:
- **Genotoxicity in vitro**:
  - Test Type: Bacterial reverse mutation assay (AMES)
    - Result: negative
  - Test Type: In vitro mammalian cell gene mutation test
    - Result: negative
  - Test Type: Chromosome aberration test in vitro
    - Result: negative

- **Genotoxicity in vivo**:
  - Test Type: Mutagenicity (in vivo mammalian bone-marrow cytogenetic test, chromosomal analysis)
    - Species: Rat
    - Application Route: Ingestion
    - Result: negative
Carcinogenicity
Not classified based on available information.

Components:

2,6-Di-tert-butyl-p-cresol:

- Species: Rat
- Application Route: Ingestion
- Exposure time: 22 Months
- Result: negative

Reproductive toxicity
May cause harm to breast-fed children.

Components:

Doramectin:

- Effects on fertility: Test Type: Two-generation reproduction toxicity study
  Species: Rat
  Application Route: Ingestion
  Result: negative

- Effects on foetal development:
  Test Type: Fertility/early embryonic development
  Species: Rabbit
  Application Route: Ingestion
  Result: positive

- Reproductive toxicity - Assessment:
  Some evidence of adverse effects on development, based on animal experiments. Studies indicating a hazard to babies during the lactation period

2,6-Di-tert-butyl-p-cresol:

- Effects on fertility: Test Type: Two-generation reproduction toxicity study
  Species: Rat
  Application Route: Ingestion
  Result: negative

- Effects on foetal development:
  Test Type: Embryo-foetal development
  Species: Rat
  Application Route: Ingestion
  Result: negative

STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Not classified based on available information.

Components:

2,6-Di-tert-butyl-p-cresol:

- Assessment: No significant health effects observed in animals at concentrations of 100 mg/kg bw or less.
10. Repeated dose toxicity

Components:

2,6-Di-tert-butyl-p-cresol:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>NOAEL</td>
<td>25 mg/kg</td>
</tr>
<tr>
<td>Application Route</td>
<td>Ingestion</td>
</tr>
<tr>
<td>Exposure time</td>
<td>22 Months</td>
</tr>
</tbody>
</table>

11. Aspiration toxicity

Not classified based on available information.

12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Doramectin:

<table>
<thead>
<tr>
<th>Toxicity to fish</th>
<th>LC50 (Onchorhynchus mykiss (rainbow trout)): 0.005 mg/l Exposure time: 96 h</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity to daphnia and other aquatic invertebrates</td>
<td>EC50 (Daphnia magna (Water flea)): 0.1 µg/l Exposure time: 48 h</td>
</tr>
<tr>
<td>Toxicity to algae/aquatic plants</td>
<td>NOEC (Pseudokirchneriella subcapitata (green algae)): 0.026 mg/l Exposure time: 96 h</td>
</tr>
<tr>
<td>M-Factor (Acute aquatic toxicity)</td>
<td>10,000</td>
</tr>
<tr>
<td>M-Factor (Chronic aquatic toxicity)</td>
<td>10,000</td>
</tr>
</tbody>
</table>

2,6-Di-tert-butyl-p-cresol:

<table>
<thead>
<tr>
<th>Toxicity to fish</th>
<th>LC50 (Danio rerio (zebra fish)): &gt; 0.57 mg/l Exposure time: 96 h Method: Directive 67/548/EEC, Annex V, C.1.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Toxicity to daphnia and other aquatic invertebrates</td>
<td>EC50 (Daphnia magna (Water flea)): 0.48 mg/l Exposure time: 48 h Method: OECD Test Guideline 202</td>
</tr>
<tr>
<td>Toxicity to algae/aquatic plants</td>
<td>ErC50 (Pseudokirchneriella subcapitata (green algae)): &gt; 0.24 mg/l Exposure time: 72 h Method: OECD Test Guideline 201</td>
</tr>
<tr>
<td>NOEC (Pseudokirchneriella subcapitata (green algae)): 0.24 mg/l Exposure time: 72 h Method: OECD Test Guideline 201</td>
<td></td>
</tr>
<tr>
<td>M-Factor (Acute aquatic toxicity)</td>
<td>1</td>
</tr>
</tbody>
</table>

SAFETY DATA SHEET

Doramectin Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>Revision Date</th>
<th>SDS Number</th>
<th>Date of last issue</th>
<th>Date of first issue</th>
</tr>
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<tbody>
<tr>
<td>2.0</td>
<td>2019/11/26</td>
<td>5191216-00002</td>
<td>2019/10/22</td>
<td>2019/10/22</td>
</tr>
</tbody>
</table>

Toxicity

Toxicity to fish (Chronic toxicity): NOEC (Oryzias latipes (Japanese medaka)): 0.053 mg/l
Exposure time: 30 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC (Daphnia magna (Water flea)): 0.316 mg/l
Exposure time: 21 d

M-Factor (Chronic aquatic toxicity): 1

Toxicity to microorganisms: EC50: > 10,000 mg/l
Exposure time: 3 h
Method: OECD Test Guideline 209

Persistence and degradability

Components:

2,6-Di-tert-butyl-p-cresol:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 4.5%
Exposure time: 28 d
Method: OECD Test Guideline 301C

Bioaccumulative potential

Components:

Doramectin:
Partition coefficient: n-octanol/water: log Pow: 4.4

2,6-Di-tert-butyl-p-cresol:
Bioaccumulation: Species: Cyprinus carpio (Carp)
Bioconcentration factor (BCF): 330 - 1,800
Partition coefficient: n-octanol/water: log Pow: 5.1

Mobility in soil
No data available

Hazardous to the ozone layer
Not applicable

Other adverse effects
No data available

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.
14. TRANSPORT INFORMATION

International Regulations

UNRTDG
UN number : UN 3082
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (Doramectin)
Class : 9
Packing group : III
Labels : 9

IATA-DGR
UN/ID No. : UN 3082
Proper shipping name : Environmentally hazardous substance, liquid, n.o.s. (Doramectin)
Class : 9
Packing group : III
Labels : Miscellaneous
Packing instruction (cargo aircraft) : 964
Packing instruction (passenger aircraft) : 964
Environmentally hazardous : yes

IMDG-Code
UN number : UN 3082
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (Doramectin)
Class : 9
Packing group : III
Labels : 9
EmS Code : F-A, S-F
Marine pollutant : yes

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

National Regulations
Refer to section 15 for specific national regulation.

Special precautions for user
The transport classification(s) provided herein are for informational purposes only, and solely based upon the properties of the unpackaged material as it is described within this Safety Data Sheet. Transportation classifications may vary by mode of transportation, package sizes, and variations in regional or country regulations.

15. REGULATORY INFORMATION

Related Regulations

Fire Service Law
Group 4, Type 4 petroleums, (6000 litre), Hazardous rank III
Chemical Substance Control Law
Priority Assessment Chemical Substance

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>2,6-Di-tert-buty1-4-methylphenol</td>
<td>64</td>
</tr>
</tbody>
</table>

Industrial Safety and Health Law

Harmful Substances Prohibited from Manufacture
Not applicable

Harmful Substances Required Permission for Manufacture
Not applicable

Substances Prevented From Impairment of Health
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 2: Information on Existing Chemicals having Mutagenicity
Not applicable

Circular concerning Information on Chemicals having Mutagenicity - Annex 1: Information on Notified Substances having Mutagenicity
Not applicable

Substances Subject to be Notified Names
Not applicable

Substances Subject to be Indicated Names
Not applicable

Ordinance on Prevention of Hazards Due to Specified Chemical Substances
Not applicable

Ordinance on Prevention of Lead Poisoning
Not applicable

Ordinance on Prevention of Tetraalkyl Lead Poisoning
Not applicable

Ordinance on Prevention of Organic Solvent Poisoning
Not applicable

Enforcement Order of the Industrial Safety and Health Law - Attached table 1 (Dangerous Substances)
Not applicable

Poisonous and Deleterious Substances Control Law
Not applicable

Act on Confirmation, etc. of Release Amounts of Specific Chemical Substances in the Environment and Promotion of Improvements to the Management Thereof
Not applicable

High Pressure Gas Safety Act
Not applicable

Explosive Control Law
Not applicable
Vessel Safety Law
Miscellaneous dangerous substances and articles (Article 2 and 3 of rules on shipping and storage of dangerous goods and its Attached Table 1)

Aviation Law
Miscellaneous dangerous substances and articles (Article 194 of The Enforcement Rules of Aviation Law and its Attached Table 1)

Marine Pollution and Sea Disaster Prevention etc Law
Bulk transportation: Not classified as noxious liquid substance
Pack transportation: Classified as marine pollutant

Narcotics and Psychotropics Control Act
Narcotic or Psychotropic Raw Material (Export / Import Permission)
Not applicable
Specific Narcotic or Psychotropic Raw Material (Export / Import permission)
Not applicable

Waste Disposal and Public Cleansing Law
Industrial waste

The components of this product are reported in the following inventories:
AICS: not determined
DSL: not determined
IECSC: not determined

16. OTHER INFORMATION

Further information

Items where changes have been made to the previous version are highlighted in the body of this document by two vertical lines.

Date format: yyyy/mm/dd

Full text of other abbreviations
ACGIH: USA. ACGIH Threshold Limit Values (TLV)
ACGIH / TWA: 8-hour, time-weighted average

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; ENCS - Existing and New Chemical Substances (Japan); ErCx - Concentration associated with x% growth rate response; ERG - Emergency Response Guide; GHS - Globally Harmonized Sys-
The information provided in this Safety Data Sheet is correct to the best of our knowledge, information and belief at the date of its publication. The information is designed only as a guidance for safe handling, use, processing, storage, transportation, disposal and release and shall not be considered a warranty or quality specification of any type. The information provided relates only to the specific material identified at the top of this SDS and may not be valid when the SDS material is used in combination with any other materials or in any process, unless specified in the text. Material users should review the information and recommendations in the specific context of their intended manner of handling, use, processing and storage, including an assessment of the appropriateness of the SDS material in the user’s end product, if applicable.