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Doxycycline Formulation

SECTION 1. IDENTIFICATION

Product name : Doxycycline Formulation

Manufacturer or supplier’s details
Company name of supplier : Merck & Co., Inc
Address : 2000 Galloping Hill Road
Kenilworth - New Jersey - U.S.A. 07033
Telephone : 908-740-4000
Emergency telephone : 1-908-423-6000
E-mail address : EHSDATASTEWARD@merck.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Combustible dust
Skin corrosion : Category 1
Serious eye damage : Category 1

GHS label elements
Hazard pictograms :

Signal Word : Danger

Hazard Statements : If small particles are generated during further processing, handling or by other means, may form combustible dust concentrations in air.
H314 Causes severe skin burns and eye damage.

Precautionary Statements :
Prevention:
P260 Do not breathe dust.
P264 Wash skin thoroughly after handling.
P280 Wear protective gloves, protective clothing, eye protection and face protection.

Response:
P301 + P330 + P331 + P310 IF SWALLOWED: Rinse mouth. Do NOT induce vomiting. Immediately call a POISON CENTER.
P303 + P361 + P353 + P310 IF ON SKIN (or hair): Take off immediately all contaminated clothing. Rinse skin with water.
Immediately call a POISON CENTER.
P304 + P340 + P310 IF INHALED: Remove person to fresh air and keep comfortable for breathing. Immediately call a POISON CENTER.
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P305 + P351 + P338 + P310 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing. Immediately call a POISON CENTER.

P363 Wash contaminated clothing before reuse.

Storage:
P405 Store locked up.

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

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Doxycycline Hyclate</td>
<td>24390-14-5</td>
<td>50</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.

If not breathing, give artificial respiration.

If breathing is difficult, give oxygen.

Get medical attention immediately.

In case of skin contact: In case of contact, immediately flush skin with plenty of water for at least 15 minutes while removing contaminated clothing and shoes.

Get medical attention immediately.

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 immediately.

If swallowed: If swallowed, DO NOT induce vomiting.

If vomiting occurs have person lean forward.

Call a physician or poison control center immediately.

Rinse mouth thoroughly with water.

Never give anything by mouth to an unconscious person.

Most important symptoms and effects, both acute and delayed:

- Causes serious eye damage.
- Causes severe burns.
- Causes digestive tract burns.

Protection of first-aiders: First Aid responders should pay attention to self-protection,
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: Avoid generating dust; fine dust dispersed in air in sufficient concentrations, and in the presence of an ignition source is a potential dust explosion hazard. 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 (see section 7) and personal protective equipment recommendations (see section 8).

Environmental precautions: Avoid release to the environment. Prevent further leakage or spillage if safe to do so. Retain and dispose of contaminated wash water. Local authorities should be advised if significant spills cannot be contained.

Methods and materials for containment and cleaning up: Sweep up or vacuum up spillage and collect in suitable container for disposal. Avoid dispersal of dust in the air (i.e., clearing dust surfaces with compressed air). Dust deposits should not be allowed to accumulate on surfaces, as these may form an explosive mixture if they are released into the atmosphere in sufficient concentration. 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: Static electricity may accumulate and ignite suspended dust causing an explosion. Provide adequate precautions, such as electrical grounding and bonding, or inert atmospheres.

Local/Total ventilation: If sufficient ventilation is unavailable, use with local exhaust ventilation.

Advice on safe handling: Do not get on skin or clothing. Do not breathe dust. Do not swallow. Do not get in eyes. Wash skin thoroughly after handling. Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. Keep container tightly closed. Minimize dust generation and accumulation. Keep container closed when not in use. Keep away from heat and sources of ignition. Take precautionary measures against static discharges. Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage: Keep in properly labeled containers. Store locked up. Keep tightly closed. Store in accordance with the particular national regulations.

Materials to avoid: Do not store with the following product types: Strong oxidizing agents Organic peroxides Explosives

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>Doxycycline Hyclate</td>
<td>24390-14-5</td>
<td>TWA</td>
<td>OEL = 100 µg/m3 (OEB 2)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures: Use feasible engineering controls to minimize exposure to compound. All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.

Personal protective equipment

Respiratory protection: General and local exhaust ventilation is recommended to maintain vapor exposures below recommended limits. Where concentrations are above recommended limits or are unknown, appropriate respiratory protection should be worn. Follow OSHA respirator regulations (29 CFR 1910.134) and
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use NIOSH/MSHA approved respirators. Protection provided by air purifying respirators against exposure to any hazardous chemical is limited. Use a positive pressure air supplied respirator if there is any potential for uncontrolled release, exposure levels are unknown, or any other circumstance where air purifying respirators may not provide adequate protection.

Hand protection
Material : Chemical-resistant gloves

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

Hygiene measures : Work uniform or laboratory coat.
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 : powder

Color : light yellow

Odor : No data available

Odor Threshold : No data available

pH : 1.5 - 3.5

Melting point/freezing point : No data available

Initial boiling point and boiling range : No data available

Flash point : Not applicable

Evaporation rate : Not applicable

Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.

Flammability (liquids) : Not applicable

Upper explosion limit / Upper : No data available
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flammability limit

Lower explosion limit / Lower flammability limit: No data available

Vapor pressure: Not applicable

Relative vapor density: Not applicable

Relative density: No data available

Density: No data available

Solubility(ies)

Water solubility: No data available

Partition coefficient: n-octanol/water: Not applicable

Autoignition temperature: No data available

Decomposition temperature: No data available

Viscosity

Viscosity, kinematic: Not applicable

Explosive properties: Not explosive

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

Molecular weight: No data available

Particle size: 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

May form explosive dust-air mixture during processing, handling or other means.

Can react with strong oxidizing agents.

Conditions to avoid: Heat, flames and sparks.

Avoid dust formation.

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: 4,000 mg/kg
Method: Calculation method

**Components:**

**Doxycycline Hyclate:**
Acute oral toxicity: LD50 (Rat): 2,000 mg/kg
LD50 (Mouse): 1,870 mg/kg
LD50 (Dog): 500 mg/kg

Acute toxicity (other routes of administration): LD50 (Rat): 222 mg/kg
Application Route: Intravenous

**Skin corrosion/irritation**
Causes severe burns.

**Components:**

**Doxycycline Hyclate:**
Remarks: No data available
May irritate skin.

**Serious eye damage/eye irritation**
Causes serious eye damage.

**Components:**

**Doxycycline Hyclate:**
Remarks: No data available
May irritate eyes.

**Respiratory or skin sensitization**

**Skin sensitization**
Not classified based on available information.

**Respiratory sensitization**
Not classified based on available information.

**Components:**

**Doxycycline Hyclate:**
Remarks: No data available
May cause sensitization by skin contact.
May cause sensitization of susceptible persons by skin.
contact or by inhalation of dust.

Germ cell mutagenicity
Not classified based on available information.

Components:

Doxycycline Hyclate:
Genotoxicity in vitro : Test Type: Chromosome aberration test in vitro
Test system: Chinese hamster cells
Result: Weakly positive
Remarks: Based on data from similar materials

Test Type: In vitro mammalian cell gene mutation test
Test system: Chinese hamster cells
Result: negative
Remarks: Based on data from similar materials

Genotoxicity in vivo : Test Type: In vivo micronucleus test
Species: Mouse
Application Route: Oral
Result: negative
Remarks: Based on data from similar materials

Carcinogenicity
Not classified based on available information.

Components:

Doxycycline Hyclate:
Species : Rat
Application Route : Oral
Exposure time : 2 Years
: 200 mg/kg body weight
Symptoms : females
Target Organs : Uterus (including cervix)
Remarks : Benign tumor(s)

IARC No ingredient of this product present at levels greater than or equal to 0.1% is identified as probable, possible or confirmed human carcinogen by IARC.

OSHA No component of this product present at levels greater than or equal to 0.1% is on OSHA’s list of regulated carcinogens.

NTP No ingredient of this product present at levels greater than or equal to 0.1% is identified as a known or anticipated carcinogen by NTP.

Reproductive toxicity
Not classified based on available information.

Components:

Doxycycline Hyclate:
Effects on fetal development : Test Type: Fertility/early embryonic development
Species: Rat, females
Application Route: Oral
General Toxicity Maternal: NOAEL: 250 mg/kg body weight
Result: No adverse effects.

Test Type: Fertility/early embryonic development
Species: Rat, male
Application Route: Oral
General Toxicity Maternal: NOAEL: 50 mg/kg body weight
Symptoms: male reproductive effects
Remarks: Fertility and developmental toxicity tests did not reveal any effect on reproduction.

STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
Not classified based on available information.

Repeated dose toxicity

Components:

Doxycycline Hyclate:
Species: Rat
NOAEL: 25 mg/kg
Application Route: Oral
Exposure time: 28 d
Symptoms: Thyroid effects

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Doxycycline Hyclate:
General Information: May cause
Target Organs: Teeth
Symptoms: Gastrointestinal disturbance
Skin contact: Remarks: May cause photosensitization.

Further information

Components:

Doxycycline Hyclate:
Remarks: Well tolerated in clinical use
SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Doxycycline Hyclate:
Toxicity to algae/aquatic plants: EC10 (Anabaena flos-aquae): 0.251 mg/l
End point: Growth rate
Exposure time: 72 h

Ecotoxicology Assessment
Acute aquatic toxicity: Very toxic to aquatic life.
Chronic aquatic toxicity: Toxic to aquatic life with long lasting effects.

Persistence and degradability
No data available

Bioaccumulative potential

Components:

Doxycycline Hyclate:
Partition coefficient: n-octanol/water
log Pow: 0.02

Mobility in soil
No data available

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
UN number: UN 3077
Proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Doxycycline Hyclate)

Class: 9
Packing group: III
Labels: 9
IATA-DGR
UN/ID No. : UN 3077
Proper shipping name : Environmentally hazardous substance, solid, n.o.s. (Doxycycline Hyclate)

IMDG-Code
UN number : UN 3077
Proper shipping name : ENVIRONMENTALLY HAZARDOUS SUBSTANCE, SOLID, N.O.S. (Doxycycline Hyclate)

Domestic regulation

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

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.

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity
This material does not contain any components with a CERCLA RQ.
SARA 304 Extremely Hazardous Substances Reportable Quantity
This material does not contain any components with a section 304 EHS RQ.

SARA 302 Extremely Hazardous Substances Threshold Planning Quantity
This material does not contain any components with a section 302 EHS TPQ.

SARA 311/312 Hazards
- Combustible dust
- Skin corrosion or irritation
- Serious eye damage or eye irritation

SARA 313
This material does not contain any chemical components with known CAS numbers that exceed the threshold (De Minimis) reporting levels established by SARA Title III, Section 313.

US State Regulations

Pennsylvania Right To Know
- Lactose 63-42-3
- Doxycycline Hyclate 24390-14-5

California Prop. 65
WARNING: This product can expose you to chemicals including Doxycycline Hyclate, which is/are known to the State of California to cause birth defects or other reproductive harm. For more information go to www.P65Warnings.ca.gov.

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
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NFPA 704:

HMIS® IV:

HMIS® ratings are based on a 0-4 rating scale, with 0 representing minimal hazards or risks, and 4 representing significant hazards or risks. The "*" represents a chronic hazard, while the "/" represents the absence of a chronic hazard.

Full text of other abbreviations

AIIIC - Australian Inventory of Industrial Chemicals; ASTM - American Society for the Testing of Materials; bw - Body weight; CERCLA - Comprehensive Environmental Response, Compensation, and Liability Act; CMR - Carcinogen, Mutagen or Reproductive Toxicant; DIN - Standard of the German Institute for Standardisation; DOT - Department of Transportation; DSL - Domestic Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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 System; GLP - Good Laboratory Practice; HMIS - Hazardous Materials Identification System; IARC - International Agency for Research on Cancer; IATA - International Air Transport Association; IBC - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk; IC50 - Half maximal inhibitory concentration; ICAO - International Civil Aviation Organization; IECSC - Inventory of Existing Chemical Substances in China; IMDG - International Maritime Dangerous Goods; IMO - International Maritime Organization; ISHL - Industrial Safety and Health Law (Japan); ISO - International Organisation for Standardization; KECI - Korea Existing Chemicals Inventory; LC50 - Lethal Concentration to 50 % of a test population; LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; OECD - Organization for Economic Co-operation and Development; OPPTS - Office of Chemical Safety and Pollution Prevention; PBT - Persistent, Bioaccumulative and Toxic substance; PICCS - Philippines Inventory of Chemicals and Chemical Substances; (Q)SAR - (Quantitative) Structure Activity Relationship; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RQ - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; TSCA - Toxic Substances Control Act (United States); UN - United Nations; UNRTDG - United Nations Recommendations on the Transport of Dangerous Goods; vPvB - Very Persistent and Very Bioaccumulative
<table>
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<tr>
<th>Version</th>
<th>Revision Date:</th>
<th>SDS Number:</th>
<th>Date of last issue:</th>
<th>Date of first issue:</th>
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<td>04/09/2021</td>
<td>6105695-00002</td>
<td>07/06/2020</td>
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Sources of key data used to compile the Material Safety Data Sheet:

Revision Date: 04/09/2021

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.

US / Z8