SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Estradiol Formulation

Version: 2.3  Revision Date: 09/13/2019  SDS Number: 2697998-00006  Date of last issue: 06.05.2019
Date of first issue: 12.04.2018

SECTION 1: Identification of the substance/mixture and of the company/undertaking

1.1 Product identifier
    Trade name : Estradiol Formulation

1.2 Relevant identified uses of the substance or mixture and uses advised against
    Use of the Substance/Mixture : Pharmaceutical

1.3 Details of the supplier of the safety data sheet
    Company : MSD
               Shotton Lane
               NE23 3JU  Cramlington NU - Great Britain
    Telephone : 44 1 670 59 30 00
    Telefax : 908-735-1496
    E-mail address of person responsible for the SDS : EHSDATASTEWARD@msd.com

1.4 Emergency telephone number
    1-908-423-6000

SECTION 2: Hazards identification

2.1 Classification of the substance or mixture
    Classification (REGULATION (EC) No 1272/2008)
    Flammable liquids, Category 2
    Eye irritation, Category 2
    Carcinogenicity, Category 1A
    Reproductive toxicity, Category 1A
    Specific target organ toxicity - repeated exposure, Category 1
    Long-term (chronic) aquatic hazard, Category 1
    H225: Highly flammable liquid and vapour.
    H319: Causes serious eye irritation.
    H350: May cause cancer.
    H360FD: May damage fertility. May damage the unborn child.
    H372: Causes damage to organs through prolonged or repeated exposure.
    H410: Very toxic to aquatic life with long lasting effects.

2.2 Label elements
    Labelling (REGULATION (EC) No 1272/2008)
    Hazard pictograms:
    Signal word : Danger
    Hazard statements : H225  Highly flammable liquid and vapour.
H319 Causes serious eye irritation.
H350 May cause cancer.
H360FD May damage fertility. May damage the unborn child.
H372 Causes damage to organs through prolonged or repeated exposure.
H410 Very toxic to aquatic life with long lasting effects.

Precautionary statements:
Prevention:
P201 Obtain special instructions before use.
P210 Keep away from heat, hot surfaces, sparks, open flames and other ignition sources. No smoking.
P273 Avoid release to the environment.
P280 Wear protective gloves/ protective clothing/ eye protection/ face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical advice/attention.
P391 Collect spillage.

Hazardous components which must be listed on the label:
Estradiol

2.3 Other hazards
Vapours may form explosive mixture with air.

SECTION 3: Composition/information on ingredients

3.2 Mixtures

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>EC-No.</th>
<th>Index-No.</th>
<th>Registration number</th>
<th>Classification</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>64-17-5</td>
<td>200-578-6</td>
<td>603-002-00-5</td>
<td>Flam. Liq. 2; H225 Eye Irrit. 2; H319</td>
<td>&gt;= 40 - &lt;= 50</td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td>50-28-2</td>
<td>200-023-8</td>
<td></td>
<td>Carc. 1A; H350 Repr. 1A; H360FD STOT RE 1; H372 Aquatic Chronic 1; H410</td>
<td>0.06</td>
<td></td>
</tr>
</tbody>
</table>

For explanation of abbreviations see section 16.
SECTION 4: First aid measures

4.1 Description of 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.

**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).

**If inhaled**: If inhaled, remove to fresh air. Get medical attention.

**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. Rinse mouth thoroughly with water.

4.2 Most important symptoms and effects, both acute and delayed

**Risks**: Causes serious eye irritation. May cause cancer. May damage fertility. May damage the unborn child. Causes damage to organs through prolonged or repeated exposure.

4.3 Indication of any immediate medical attention and special treatment needed

**Treatment**: Treat symptomatically and supportively.

SECTION 5: Firefighting measures

5.1 Extinguishing media

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

**Unsuitable extinguishing media**: High volume water jet
5.2 Special hazards arising from the substance or mixture

Specific hazards during firefighting:
- Do not use a solid water stream as it may scatter and spread fire.
- Flash back possible over considerable distance.
- Vapours may form explosive mixtures with air.
- Exposure to combustion products may be a hazard to health.

Hazardous combustion products:
- Carbon oxides
- Nitrogen oxides (NOx)

5.3 Advice for firefighters

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

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.

SECTION 6: Accidental release measures

6.1 Personal precautions, protective equipment and emergency procedures

Personal precautions:
- Remove all sources of ignition.
- Ventilate the area.
- Use personal protective equipment.
- Follow safe handling advice and personal protective equipment recommendations.

6.2 Environmental precautions

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.

6.3 Methods and material for containment and cleaning up

Methods for cleaning up:
- Non-sparking tools should be used.
- Soak up with inert absorbent material.
- Suppress (knock down) gases/vapours/mists with a water spray jet.
- 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.

6.4 Reference to other sections
See sections: 7, 8, 11, 12 and 13.

SECTION 7: Handling and storage

7.1 Precautions for safe handling

<table>
<thead>
<tr>
<th>Technical measures</th>
<th>See Engineering measures under EXPOSURE CONTROLS/PERSONAL PROTECTION section.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Local/Total ventilation</td>
<td>If sufficient ventilation is unavailable, use with local exhaust ventilation.</td>
</tr>
<tr>
<td></td>
<td>If advised by assessment of the local exposure potential, use only in an area equipped with explosion-proof exhaust ventilation.</td>
</tr>
<tr>
<td>Advice on safe handling</td>
<td>Do not get on skin or clothing.</td>
</tr>
<tr>
<td></td>
<td>Do not breathe vapours or spray mist.</td>
</tr>
<tr>
<td></td>
<td>Do not swallow.</td>
</tr>
<tr>
<td></td>
<td>Do not get in eyes.</td>
</tr>
<tr>
<td></td>
<td>Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.</td>
</tr>
<tr>
<td></td>
<td>Non-sparking tools should be used.</td>
</tr>
<tr>
<td></td>
<td>Keep container tightly closed.</td>
</tr>
<tr>
<td></td>
<td>Keep away from heat and sources of ignition.</td>
</tr>
<tr>
<td></td>
<td>Take precautionary measures against static discharges.</td>
</tr>
<tr>
<td></td>
<td>Take care to prevent spills, waste and minimize release to the environment.</td>
</tr>
<tr>
<td>Hygiene measures</td>
<td>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.</td>
</tr>
</tbody>
</table>

7.2 Conditions for safe storage, including any incompatibilities

| Requirements for storage areas and containers | Keep in properly labelled containers. Store locked up. Keep tightly closed. Keep in a cool, well-ventilated place. Store in accordance with the particular national regulations. Keep away from heat and sources of ignition. |
|#####################################################|
| Advice on common storage                        | Do not store with the following product types:                                 |
|                                               | Strong oxidizing agents                                                        |
|                                               | Organic peroxides                                                              |
|                                               | Flammable solids                                                               |
|                                               | Pyrophoric liquids                                                             |
|                                               | Pyrophoric solids                                                              |
|                                               | Self-heating substances and mixtures                                           |
|                                               | Substances and mixtures, which in contact with water, emit flammable gases     |
Explosives

Gases

7.3 Specific end use(s)
Specific use(s): No data available

SECTION 8: Exposure controls/personal protection

8.1 Control parameters

**Occupational Exposure Limits**

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Value type (Form of exposure)</th>
<th>Control parameters</th>
<th>Basis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>64-17-5</td>
<td>TWA</td>
<td>1,000 ppm</td>
<td>GB EH40</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>1,920 mg/m³</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Further information</td>
<td>Where no specific short-term exposure limit is listed, a figure three times the long-term exposure limit should be used.</td>
<td></td>
</tr>
<tr>
<td>Estradiol</td>
<td>50-28-2</td>
<td>TWA</td>
<td>0.05 µg/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Further information</td>
<td>Skin</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>0.5 µg/100 cm²</td>
</tr>
</tbody>
</table>

**Derived No Effect Level (DNEL) according to Regulation (EC) No. 1907/2006:**

<table>
<thead>
<tr>
<th>Substance name</th>
<th>End Use</th>
<th>Exposure routes</th>
<th>Potential health effects</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>Workers</td>
<td>Inhalation</td>
<td>Acute local effects</td>
<td>1900 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Workers</td>
<td>Skin contact</td>
<td>Long-term systemic effects</td>
<td>343 mg/kg bw/day</td>
</tr>
<tr>
<td></td>
<td>Workers</td>
<td>Inhalation</td>
<td>Long-term systemic effects</td>
<td>950 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Inhalation</td>
<td>Acute local effects</td>
<td>950 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Skin contact</td>
<td>Long-term systemic effects</td>
<td>206 mg/kg bw/day</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Inhalation</td>
<td>Long-term systemic effects</td>
<td>114 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Ingestion</td>
<td>Long-term systemic effects</td>
<td>87 mg/kg bw/day</td>
</tr>
<tr>
<td>2,2',2''-Nitritriethanol</td>
<td>Workers</td>
<td>Skin contact</td>
<td>Long-term systemic effects</td>
<td>6.3 mg/kg bw/day</td>
</tr>
<tr>
<td></td>
<td>Workers</td>
<td>Inhalation</td>
<td>Long-term local effects</td>
<td>5 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Workers</td>
<td>Inhalation</td>
<td>Long-term systemic effects</td>
<td>5 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Ingestion</td>
<td>Long-term systemic effects</td>
<td>13 mg/kg bw/day</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Skin contact</td>
<td>Long-term systemic effects</td>
<td>3.1 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Inhalation</td>
<td>Long-term local effects</td>
<td>1.25 mg/m³</td>
</tr>
<tr>
<td></td>
<td>Consumers</td>
<td>Inhalation</td>
<td>Long-term systemic effects</td>
<td>1.25 mg/m³</td>
</tr>
</tbody>
</table>
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Predicted No Effect Concentration (PNEC) according to Regulation (EC) No. 1907/2006:

<table>
<thead>
<tr>
<th>Substance name</th>
<th>Environmental Compartment</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ethanol</td>
<td>Fresh water</td>
<td>0.96 mg/l</td>
</tr>
<tr>
<td></td>
<td>Marine water</td>
<td>0.79 mg/l</td>
</tr>
<tr>
<td></td>
<td>Intermittent use/release</td>
<td>2.75 mg/l</td>
</tr>
<tr>
<td></td>
<td>Sewage treatment plant</td>
<td>580 mg/l</td>
</tr>
<tr>
<td></td>
<td>Fresh water sediment</td>
<td>3.6 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Marine sediment</td>
<td>2.9 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Soil</td>
<td>0.63 mg/kg</td>
</tr>
<tr>
<td></td>
<td>Oral (Secondary Poisoning)</td>
<td>720 mg/kg food</td>
</tr>
<tr>
<td>2,2',2''-Nitrilotriethanol</td>
<td>Fresh water</td>
<td>0.32 mg/l</td>
</tr>
<tr>
<td></td>
<td>Marine water</td>
<td>0.032 mg/l</td>
</tr>
<tr>
<td></td>
<td>Intermittent use/release</td>
<td>5.12 mg/l</td>
</tr>
<tr>
<td></td>
<td>Sewage treatment plant</td>
<td>10 mg/l</td>
</tr>
<tr>
<td></td>
<td>Fresh water sediment</td>
<td>1.7 mg/kg dry weight (d.w.)</td>
</tr>
<tr>
<td></td>
<td>Marine sediment</td>
<td>0.17 mg/kg dry weight (d.w.)</td>
</tr>
<tr>
<td></td>
<td>Soil</td>
<td>0.151 mg/kg dry weight (d.w.)</td>
</tr>
</tbody>
</table>

8.2 Exposure controls

Engineering measures
Minimize workplace exposure concentrations.
If sufficient ventilation is unavailable, use with local exhaust ventilation.
If advised by assessment of the local exposure potential, use only in an area equipped with explosion-proof exhaust ventilation.

Personal protective equipment

Eye protection: Wear the following personal protective equipment:
- Safety goggles
- Equipment should conform to BS EN 166

Hand protection

Material: Chemical-resistant gloves

Remarks: Choose gloves to protect hands against chemicals depending on the concentration and quantity of the hazardous substance and specific to place of work. Breakthrough time is not determined for the product. Change gloves often! For special applications, we recommend clarifying the resistance to chemicals of the aforementioned protective gloves with the glove manufacturer. Take note that the product is flammable, which may impact the selection of hand protection. Wash hands before breaks and at the end of workday.

Skin and body protection: Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential.
- Wear the following personal protective equipment:
  - If assessment demonstrates that there is a risk of explosive atmospheres or flash fires, use flame retardant antistatic protective clothing.
  - Skin contact must be avoided by using impervious protective clothing.
Respiratory protection: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Combined particulates and organic vapour type (A-P)

SECTION 9: Physical and chemical properties

9.1 Information on basic physical and chemical properties

- **Appearance**: gel
- **Colour**: clear, colourless
- **Odour**: No data available
- **Odour Threshold**: No data available
- **pH**: 6.6 - 6.8
- **Melting point/freezing point**: No data available
- **Initial boiling point and boiling range**: No data available
- **Flash point**: 13 °C
- **Evaporation rate**: No data available
- **Flammability (solid, gas)**: No data available
- **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**: No data available
- **Density**: No data available
- **Solubility(ies)**
  - **Water solubility**: No data available
- **Partition coefficient: n-octanol/water**: No data available
- **Auto-ignition temperature**: No data available
- **Decomposition temperature**: No data available
- **Viscosity**
  - **Viscosity, kinematic**: 60000 - 85000 mm²/s
- **Explosive properties**: Not explosive
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Oxidizing properties: The substance or mixture is not classified as oxidizing.

SECTION 10: Stability and reactivity

10.1 Reactivity
Not classified as a reactivity hazard.

10.2 Chemical stability
Stable under normal conditions.

10.3 Possibility of hazardous reactions
Hazardous reactions: Highly flammable liquid and vapour. Vapours may form explosive mixture with air. Can react with strong oxidizing agents.

10.4 Conditions to avoid
Conditions to avoid: Heat, flames and sparks.

10.5 Incompatible materials
Materials to avoid: Oxidizing agents

10.6 Hazardous decomposition products
No hazardous decomposition products are known.

SECTION 11: Toxicological information

11.1 Information on toxicological effects
Information on likely routes of exposure: Inhalation, Skin contact, Ingestion, Eye contact

Acute toxicity
Not classified based on available information.

Components:

Ethanol:
Acute oral toxicity: LD50 (Rat): > 5,000 mg/kg
Method: OECD Test Guideline 401

Acute inhalation toxicity: LC50 (Rat): 124.7 mg/l
Exposure time: 4 h
Test atmosphere: vapour
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Estradiol:
Acute oral toxicity : LD50 (Rat): > 2,000 mg/kg
Acute toxicity (other routes of administration) : LD50 (Rat): > 300 mg/kg
Application Route: Subcutaneous

Skin corrosion/irritation
Not classified based on available information.

Components:
Ethanol:
Species : Rabbit
Method : OECD Test Guideline 404
Result : No skin irritation

Serious eye damage/eye irritation
Causes serious eye irritation.

Components:
Ethanol:
Species : Rabbit
Method : OECD Test Guideline 405
Result : Irritation to eyes, reversing within 21 days

Estradiol:
Result : No eye irritation

Respiratory or skin sensitisation

Skin sensitisation
Not classified based on available information.

Respiratory sensitisation
Not classified based on available information.

Components:
Ethanol:
Test Type : Local lymph node assay (LLNA)
Exposure routes : Skin contact
Species : Mouse
Result : negative

Estradiol:
Exposure routes : Skin contact
Species : Guinea pig
Assessment : Does not cause skin sensitisation.
Result : negative
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Germ cell mutagenicity
Not classified based on available information.

**Components:**

**Ethanol:**
Genotoxicity in vitro: Test Type: In vitro mammalian cell gene mutation test  
Result: negative
Test Type: Bacterial reverse mutation assay (AMES)  
Result: negative

Genotoxicity in vivo: Test Type: Rodent dominant lethal test (germ cell) (in vivo)  
Species: Mouse  
Application Route: Ingestion  
Result: equivocal

**Estradiol:**
Genotoxicity in vitro: Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)  
Test system: mammalian cells  
Result: positive
Test Type: Chromosome aberration test in vitro  
Test system: mammalian cells  
Result: positive
Test Type: Chromosomal aberration  
Test system: mammalian cells  
Result: positive

Genotoxicity in vivo: Test Type: Chromosomal aberration  
Species: Rat  
Cell type: Bone marrow  
Result: negative
Test Type: Chromosomal aberration  
Species: Mouse  
Cell type: Bone marrow  
Result: negative

**Carcinogenicity**
May cause cancer.

**Components:**

**Estradiol:**
Species: Mouse  
Application Route: Ingestion  
Exposure time: 24 Months  
LOAEL: 100 µg/kg  
Result: positive
Target Organs: female reproductive organs

Species: Rat
Application Route: Subcutaneous
Exposure time: 13 weeks
LOAEL: 20 mg/kg body weight
Result: positive
Target Organs: Endocrine system

Carcinogenicity - Assessment: Positive evidence from human epidemiological studies

Reproductive toxicity
May damage fertility. May damage the unborn child.

Components:

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

Estradiol:
Effects on fertility: Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Ingestion
Fertility: LOAEL: 0.5 mg/kg body weight
Result: Effects on fertility

Test Type: One-generation reproduction toxicity study
Species: Rat
Duration of Single Treatment: 90 d
Fertility: LOAEL: 0.69 mg/kg body weight
Result: Effects on fertility

Test Type: Two-generation study
Species: Mouse
Application Route: Oral
Fertility: LOAEL: 0.1 mg/kg body weight
Result: Effects on fertility

Effects on foetal development: Test Type: Embryo-foetal development
Species: Mouse, female
Application Route: Subcutaneous
Teratogenicity: LOAEL: 4 mg/kg body weight
Symptoms: Malformations were observed.
Result: positive, Teratogenic effects

Test Type: One-generation reproduction toxicity study
Species: Rat
Application Route: Subcutaneous
Teratogenicity: LOAEL: 2.5 µg/kg body weight
Symptoms: Reduced body weight
Result: positive, Embryotoxic effects and adverse effects on the offspring were detected.

Test Type: Embryo-foetal development
Species: Rat
Application Route: Subcutaneous
Developmental Toxicity: LOAEL: 0.2 mg/kg body weight
Symptoms: Early Resorptions / resorption rate, Reduced number of viable fetuses, Reduced body weight
Result: Embryotoxic effects and adverse effects on the offspring were detected only at high maternally toxic doses

Reproductive toxicity - Assessment
STOT - single exposure
Not classified based on available information.

STOT - repeated exposure
Causes damage to organs through prolonged or repeated exposure.

Components:

Estradiol:
Target Organs: Liver, Bone, Blood, Endocrine system
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Ethanol:
Species: Rat
NOAEL: 1,280 mg/kg
LOAEL: 3,156 mg/kg
Application Route: Ingestion
Exposure time: 90 Days

Estradiol:
Species: Rat
LOAEL: >= 0.17 mg/kg
Application Route: Ingestion
Exposure time: 90 d
Target Organs: Mammary gland, Ovary, Uterus (including cervix), Liver, Bone, Endocrine system, Blood, Testis

Aspiration toxicity
Not classified based on available information.
Experience with human exposure

**Components:**

**Estradiol:**
- Inhalation: Symptoms: tingling, Nose bleeding
- Skin contact: Symptoms: Skin irritation, Redness, pruritis
- Ingestion: Symptoms: Headache, Gastrointestinal disturbance, Dizziness, Vomiting, Diarrhoea, water retention, liver function change, changes in libido, breast tenderness, menstrual irregularities

SECTION 12: Ecological information

12.1 Toxicity

**Components:**

**Ethanol:**
- Toxicity to fish: LC50 (Pimephales promelas (fathead minnow)): > 1,000 mg/l
  Exposure time: 96 h
- Toxicity to daphnia and other aquatic invertebrates: EC50 (Ceriodaphnia (water flea)): > 1,000 mg/l
  Exposure time: 48 h
- Toxicity to algae/aquatic plants: ErC50 (Chlorella vulgaris (Fresh water algae)): 275 mg/l
  Exposure time: 72 h
  EC10 (Chlorella vulgaris (Fresh water algae)): 11.5 mg/l
  Exposure time: 72 h
- Toxicity to microorganisms: EC50 (Pseudomonas putida): 6,500 mg/l
  Exposure time: 16 h
- Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 9.6 mg/l
  Exposure time: 9 d
  Species: Daphnia magna (Water flea)

**Estradiol:**
- Toxicity to fish: LC50 (Oryzias latipes (Japanese medaka)): 3.9 mg/l
  Exposure time: 96 h
- Toxicity to daphnia and other aquatic invertebrates: EC50 (Daphnia magna (Water flea)): 2.7 mg/l
  Exposure time: 48 h
- Toxicity to algae/aquatic plants: NOEC (Pseudokirchneriella subcapitata (green algae)): 1.7 mg/l
  Exposure time: 72 h
  Method: OECD Test Guideline 201
  EC50 (Pseudokirchneriella subcapitata (green algae)): > 1.7 mg/l
  Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to microorganisms: EC50: > 100 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

NOEC: 100 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Toxicity to fish (Chronic toxicity): NOEC: 0.000003 mg/l
Exposure time: 160 d
Species: Oryzias latipes (Japanese medaka)
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity): NOEC: 0.2 mg/l
Exposure time: 21 d
Species: Daphnia magna (Water flea)

M-Factor (Chronic aquatic toxicity): 1,000

12.2 Persistence and degradability

Components:

Ethanol:
Biodegradability: Result: Readily biodegradable.
Biodegradation: 84 %
Exposure time: 20 d

Estradiol:
Biodegradability: Result: rapidly degradable
Biodegradation: 84 %
Exposure time: 24 hrs

12.3 Bioaccumulative potential

Components:

Ethanol:
Partition coefficient: n-octanol/water: log Pow: -0.35

Estradiol:
Partition coefficient: n-octanol/water: log Pow: 4.01

12.4 Mobility in soil

Components:

Estradiol:
Distribution among environmental compartments: log Koc: 3.81

12.5 Results of PBT and vPvB assessment
Not relevant

12.6 Other adverse effects
No data available

SECTION 13: Disposal considerations

13.1 Waste treatment methods
Product: Dispose of in accordance with local regulations. According to the European Waste Catalogue, Waste Codes are not product specific, but application specific. Waste codes should be assigned by the user, preferably in discussion with the waste disposal authorities. 
Contaminated packaging: Empty containers should be taken to an approved waste handling site for recycling or disposal. Empty containers retain residue and can be dangerous. Do not pressurize, cut, weld, braze, solder, drill, grind, or expose such containers to heat, flame, sparks, or other sources of ignition. They may explode and cause injury and/or death. If not otherwise specified: Dispose of as unused product.

SECTION 14: Transport information

14.1 UN number
ADN: UN 1170
ADR: UN 1170
RID: UN 1170
IMDG: UN 1170
IATA: UN 1170

14.2 UN proper shipping name
ADN: ETHANOL SOLUTION
ADR: ETHANOL SOLUTION
RID: ETHANOL SOLUTION
IMDG: ETHANOL SOLUTION
            (Estradiol)
IATA: Ethanol solution

14.3 Transport hazard class(es)
ADN: 3
ADR: 3
RID: 3
Estradiol Formulation

**IMDG**: 3
**IATA**: 3

### 14.4 Packing group

**ADN**
- Packing group: II
- Classification Code: F1
- Hazard Identification Number: 33
- Labels: 3

**ADR**
- Packing group: II
- Classification Code: F1
- Hazard Identification Number: 33
- Labels: 3
- Tunnel restriction code: (D/E)

**RID**
- Packing group: II
- Classification Code: F1
- Hazard Identification Number: 33
- Labels: 3

**IMDG**
- Packing group: II
- Labels: 3
- EmS Code: F-E, S-D

**IATA (Cargo)**
- Packing instruction (cargo aircraft): 364
- Packing instruction (LQ): Y341
- Packing group: II
- Labels: Flammable Liquids

**IATA (Passenger)**
- Packing instruction (passenger aircraft): 353
- Packing instruction (LQ): Y341
- Packing group: II
- Labels: Flammable Liquids

### 14.5 Environmental hazards

**ADN**
- Environmentally hazardous: yes

**ADR**
- Environmentally hazardous: yes

**RID**
- Environmentally hazardous: yes

**IMDG**
- Marine pollutant: yes
14.6 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.

14.7 Transport in bulk according to Annex II of Marpol and the IBC Code
Remarks: Not applicable for product as supplied.

SECTION 15: Regulatory information

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

REACH - Candidate List of Substances of Very High Concern for Authorisation (Article 59): Not applicable
REACH - List of substances subject to authorisation (Annex XIV): Not applicable
Regulation (EC) No 1005/2009 on substances that deplete the ozone layer: Not applicable
Regulation (EC) No 850/2004 on persistent organic pollutants: Not applicable
Regulation (EC) No 649/2012 of the European Parliament and the Council concerning the export and import of dangerous chemicals: Not applicable
REACH - Restrictions on the manufacture, placing on the market and use of certain dangerous substances, preparations and articles (Annex XVII): Conditions of restriction for the following entries should be considered: Number on list 3

<table>
<thead>
<tr>
<th>Entry</th>
<th>Environmental Hazards</th>
<th>Quantity 1</th>
<th>Quantity 2</th>
</tr>
</thead>
<tbody>
<tr>
<td>E1</td>
<td>ENVIRONMENTAL</td>
<td>100 t</td>
<td>200 t</td>
</tr>
<tr>
<td></td>
<td>FLAMMABLE LIQUIDS</td>
<td>5,000 t</td>
<td>50,000 t</td>
</tr>
</tbody>
</table>

Other regulations:
Take note of Directive 92/85/EEC regarding maternity protection or stricter national regulations, where applicable.
Take note of Directive 94/33/EC on the protection of young people at work or stricter national regulations, where applicable.

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

<table>
<thead>
<tr>
<th>Inventory</th>
<th>Not determined</th>
</tr>
</thead>
<tbody>
<tr>
<td>AICS</td>
<td></td>
</tr>
<tr>
<td>DSL</td>
<td></td>
</tr>
<tr>
<td>IECSC</td>
<td></td>
</tr>
</tbody>
</table>

15.2 Chemical safety assessment
A Chemical Safety Assessment has not been carried out.

SECTION 16: Other information
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Estradiol Formulation

Version 2.3
Revision Date: 09/13/2019
SDS Number: 2697998-00006
Date of last issue: 06.05.2019
Date of first issue: 12.04.2018

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

Full text of H-Statements
H225: Highly flammable liquid and vapour.
H319: Causes serious eye irritation.
H350: May cause cancer.
H360FD: May damage fertility. May damage the unborn child.
H372: Causes damage to organs through prolonged or repeated exposure.
H410: Very toxic to aquatic life with long lasting effects.

Full text of other abbreviations
Aquatic Chronic: Long-term (chronic) aquatic hazard
Carc.: Carcinogenicity
Eye Irrit.: Eye irritation
Flam. Liq.: Flammable liquids
Repr.: Reproductive toxicity
STOT RE: Specific target organ toxicity - repeated exposure
GB EH40: UK. EH40 WEL - Workplace Exposure Limits
GB EH40 / TWA: Long-term exposure limit (8-hour TWA reference period)

ADN - European Agreement concerning the International Carriage of Dangerous Goods by Inland Waterways;
ADR - European Agreement concerning the International Carriage of Dangerous Goods by Road;
AICS - Australian Inventory of Chemical Substances;
ASTM - American Society for the Testing of Materials;
bw - Body weight;
CLP - Classification Labelling Packaging Regulation;
EC-Number - European Community number;
EC50 - Half maximal inhibitory concentration;
ECHA - European Chemicals Agency;
ENCS - Existing and New Chemical Substances (Japan);
ERCoR - European Reference Values;
EU - European Union;
GB EH40 WEL - Workplace Exposure Limits;
GB EH40 / TWA - Long-term exposure limit (8-hour TWA reference period);
GBR - Great Britain;
GHS - Globally Harmonized System;
GLP - Good Laboratory Practice;
IARC - International Agency for Research on Cancer;
IATA - International Air Transport Association;
ICAO - International Civil Aviation Organization;
IECSC - Inventory of Existing Chemical Substances in China;
IMDG - International Maritime Dangerous Goods;
IMO - International Maritime Organization;
ISO - International Organization for Standardization;
KECI - Korea Existing Chemicals Inventory;
LD50 - Lethal Dose to 50% of a test population (Median Lethal Dose);
LC50 - Lethal Concentration to 50% of a test population;
MARPOL - International Convention for the Prevention of Pollution from Ships;
MRL - Maximum Residue Limit;
NO(A)EL - No Observed (Adverse) Effect Level;
NOELR - No Observable Effect Loading Rate;
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;
RID - Regulations concerning the International Carriage of Dangerous Goods by Rail;
SADT - Self-Accelerating Decomposition Temperature;
SDS - Safety Data Sheet;
SVHC - Substance of Very High Concern;
TCSI - Taiwan Chemical Substance Inventory;
TRGS - Technical Rule for Hazardous Substances;
TSCA - Toxic Substances Control Act.
SAFETY DATA SHEET
according to Regulation (EC) No. 1907/2006

Estradiol Formulation

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Date of first issue: 12.04.2018

stances Control Act (United States); UN - United Nations; vPvB - Very Persistent and Very Bioac-
cumulative

Further information
Sources of key data used to compile the Safety Data Sheet: Internal technical data, data from raw material SDSs, OECD

Classification of the mixture: Classification procedure:

| Flam. Liq. 2    | H225    | Based on product data or assessment |
| Eye Irrit. 2    | H319    | Calculation method                   |
| Carc. 1A        | H350    | Calculation method                   |
| Repr. 1A        | H360FD  | Calculation method                   |
| STOT RE 1       | H372    | Calculation method                   |
| Aquatic Chronic 1 | H410   | Calculation method                   |

The information provided in this Safety Data Sheet is correct to the best of our knowledge, inform-
ation 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 mate-
rial 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 ap-
propriateness of the SDS material in the user’s end product, if applicable.

GB / EN