SECTION 1. IDENTIFICATION

Product name: Timolol 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
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWARD@merck.com

Recommended use of the chemical and restrictions on use
Recommended use: Pharmaceutical

SECTION 2. HAZARDS IDENTIFICATION

GHS classification in accordance with the OSHA Hazard Communication Standard (29 CFR 1910.1200)
Reproductive toxicity: Category 2
Specific target organ toxicity - repeated exposure: Category 1 (Cardio-vascular system, Lungs)

GHS label elements
Hazard pictograms:

Signal Word: Danger
Hazard Statements:
H361d Suspected of damaging the unborn child.
H372 Causes damage to organs (Cardio-vascular system, Lungs) through prolonged or repeated exposure.

Precautionary Statements:
Prevention:
P201 Obtain special instructions before use.
P202 Do not handle until all safety precautions have been read and understood.
P260 Do not breathe mist or vapors.
P264 Wash skin thoroughly after handling.
P270 Do not eat, drink or smoke when using this product.
P280 Wear protective gloves, protective clothing, eye protection and face protection.

Response:
P308 + P313 IF exposed or concerned: Get medical attention.

Storage:
P405 Store locked up.
SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Components</th>
</tr>
</thead>
<tbody>
<tr>
<td>(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate</td>
<td>Chemical name</td>
</tr>
<tr>
<td>26921-17-5</td>
<td>CAS-No.</td>
</tr>
<tr>
<td>&gt;= 0.1 - &lt; 1</td>
<td>Concentration (% w/w)</td>
</tr>
</tbody>
</table>

Actual concentration is withheld as a trade secret

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.

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
Suspected of damaging the unborn child. Causes damage to organs through prolonged or repeated exposure.

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.

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

Other hazards
None known.
SAFETY DATA SHEET

Timolol Formulation

<table>
<thead>
<tr>
<th>Version</th>
<th>SDS Number</th>
<th>Date of last issue</th>
<th>Date of first issue</th>
</tr>
</thead>
<tbody>
<tr>
<td>5.4</td>
<td>1598341-00010</td>
<td>03/23/2020</td>
<td>05/01/2017</td>
</tr>
</tbody>
</table>

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

Hazardous combustion products:
- Carbon oxides
- Metal oxides
- Phosphorus compounds

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.
- 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.

Local/Total ventilation:
- Use only with adequate ventilation.

Advice on safe handling:
- Do not breathe mist or vapors.
- Do not swallow.
- Avoid contact with eyes.
- Avoid prolonged or repeated contact with skin.
- Wash skin thoroughly after handling.
Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment.
Do not eat, drink or smoke when using this product. Take care to prevent spills, waste and minimize release to the environment.

Conditions for safe storage:
- Keep in properly labeled containers.
- 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
  - Gases

### 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>(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate</td>
<td>26921-17-5</td>
<td>TWA</td>
<td>10 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Further information: Eye, Skin
Wipe limit 100 µg/100 cm² Internal

#### Engineering measures
- Ensure adequate ventilation, especially in confined areas.
- Minimize workplace exposure concentrations.
- Dust formation may be relevant in the processing of this product. In addition to substance-specific OELs, general limitations of concentrations of particulates in the air at workplaces have to be considered in workplace risk assessment. Relevant limits include: OSHA PEL for Particulates Not Otherwise Regulated of 15 mg/m³ - total dust, 5 mg/m³ - respirable fraction; and ACGIH TWA for Particles (insoluble or poorly soluble) Not Otherwise Specified of 3 mg/m³ - respirable particles, 10 mg/m³ - inhalable particles.

#### 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 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

Remarks: Choose gloves to protect hands against chemicals depending on the concentration 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. Wash hands before breaks and at the end of workday.

Eye protection: Wear the following personal protective equipment:
Safety glasses

Skin and body protection: Select appropriate protective clothing based on chemical resistance data and an assessment of the local exposure potential. Skin contact must be avoided by using impervious protective clothing (gloves, aprons, boots, etc).

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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

Appearance: Aqueous solution

Color: Colorless to pale yellow

Odor: No data available

Odor Threshold: No data available

pH: No data available

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: soluble
Partition coefficient: n-octanol/water: No data available
Autoignition temperature: No data available
Decomposition temperature: No data available
Viscosity:
  Viscosity, kinematic: No data available
 Explosive properties: Not explosive
Oxidizing properties: The substance or mixture is not classified as oxidizing.
Molecular weight: Not applicable
Particle size: Not applicable

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.

Components:
(S)-3-[3-(tert-buty lamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Acute oral toxicity: LD50 (Rat): 1,000 mg/kg
LD50 (Mouse): 1,140 mg/kg

Acute toxicity (other routes of administration):
- LD50 (Mouse): 300 mg/kg (Application Route: Intraperitoneal)
- LD50 (Mouse): 800 mg/kg (Application Route: Subcutaneous)

**Skin corrosion/irritation**
Not classified based on available information.

**Components:**
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
- Species: Rabbit
- Method: Draize Test
- Result: No skin irritation

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

**Components:**
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
- Species: Rabbit
- Result: Mild eye irritation
- Species: Dog
- Result: No eye irritation

**Respiratory or skin sensitization**

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

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

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

**Components:**
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
- Genotoxicity in vitro: Test Type: Bacterial reverse mutation assay (AMES)
  Method: OECD Test Guideline 471
  Result: negative
- Genotoxicity in vivo: Test Type: In vivo micronucleus test
  Species: Mouse
  Method: OECD Test Guideline 474
  Result: negative
Carcinogenicity
Not classified based on available information.

Components:

**(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:**

- **Species:** Rat
- **Application Route:** Oral
- **Exposure time:** 2 Years
- **LOAEL:** 300 mg/kg body weight
- **Result:** negative
- **Target Organs:** Adrenal gland
- **Remarks:** The significance of these findings for humans is not certain.

Species: Mouse, female
Application Route: Oral
Exposure time: 18 Months
LOAEL: 500 mg/kg body weight
Result: negative
Target Organs: Lungs, Mammary gland, Uterus (including cervix)
Remarks: The significance of these findings for humans is not certain.

Carcinogenicity - Assessment: Weight of evidence does not support classification as a carcinogen

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
Suspected of damaging the unborn child.

Components:

**(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:**

- **Effects on fertility:** Test Type: Fertility/early embryonic development
  Species: Rat
  Application Route: Oral
  Fertility: NOAEL Mating/Fertility: 150 mg/kg body weight
  Early Embryonic Development: NOAEL F1: 150 mg/kg body weight

- **Effects on fetal development:** Test Type: Embryo-fetal development
  Species: Rabbit
  Developmental Toxicity: LOAEL F1: 50 mg/kg body weight
  Result: Some evidence of adverse effects on development, based on animal experiments.

Reproductive toxicity - Assessment: Some evidence of adverse effects on development, based on animal experiments.
STOT-single exposure
Not classified based on available information.

STOT-repeated exposure
Causes damage to organs (Cardio-vascular system, Lungs) through prolonged or repeated exposure.

Product:
Target Organs: Cardio-vascular system, Lungs
Assessment: Causes damage to organs through prolonged or repeated exposure.

Components:
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Target Organs: Lungs, Cardio-vascular system
Assessment: Causes damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Species: Rat
NOAEL: 25 mg/kg
Application Route: Oral
Exposure time: 67 Weeks

Species: Dog
NOAEL: 10 mg/kg
Application Route: Oral
Exposure time: 54 Weeks
Target Organs: Kidney

Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Product:
General Information: May cause Stomach/intestinal disorders, Respiratory disorders
Symptoms: Irregular cardiac activity, central nervous system effects
Eye contact: Symptoms: burning or stinging of the eye

Components:
(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:
Eye contact: Symptoms: burning or stinging of the eye, dryness of the eyes, Headache, Nausea, Dizziness, dry mouth, changes in
Ingestion:
Symptoms: Headache, Fatigue, Respiratory disorders, Gastrointestinal discomfort, Allergic reactions, Rash, hair loss, altered mental status, Dizziness, changes in libido

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

**Components:**

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:

**Toxicity to fish:**
- LC50 (Pimephales promelas (fathead minnow)): 411 mg/l
- Exposure time: 96 h

**Toxicity to daphnia and other aquatic invertebrates:**
- EC50 (Daphnia magna (Water flea)): 161 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202

**Toxicity to microorganisms:**
- EC50: > 1,000 mg/l
  - Exposure time: 3 h
  - Test Type: Respiration inhibition
  - EC50 (Photobacterium phosphoreum): > 1,800 mg/l

Persistence and degradability

**Components:**

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:

**Biodegradability:**
- Result: Not readily biodegradable.
- Biodegradation: 0%
- Exposure time: 30 d

**Stability in water:**
- Hydrolysis: 0% (61 d)
- Method: FDA 3.09

Bioaccumulative potential

**Components:**

(S)-3-[3-(tert-butylamino)-2-hydroxypropoxy]-4-morpholino-1,2,5-thiadiazole monomaleate:

**Partition coefficient:**
- n-octanol/water
- log Pow: 1.48

**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
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.

Domestic regulation

49 CFR
Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

CERCLA Reportable Quantity

<table>
<thead>
<tr>
<th>Components</th>
<th>CAS-No.</th>
<th>Component RQ (lbs)</th>
<th>Calculated product RQ (lbs)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disodium hydrogenorthophosphate</td>
<td>7558-79-4</td>
<td>5000</td>
<td>*</td>
</tr>
</tbody>
</table>

*: Calculated RQ exceeds reasonably attainable upper limit.

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
- Reproductive toxicity
- Specific target organ toxicity (single or repeated exposure)

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
Water 7732-18-5
Disodium hydrogenorthophosphate 7558-79-4

**California List of Hazardous Substances**

Disodium hydrogenorthophosphate 7558-79-4

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**

**NFPA 704:**

- **Health**: 0
- **Flammability**: 1
- **Instability**: 0

**HMIS® IV:**

- **Health**: *
- **Flammability**: 1
- **Physical Hazards**: 0

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**

- **AIIC**: 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
- **EN**: Existing and New Chemical Substances (Japan)
- **ERG**: Emergency Response Guide
- **GHS**: Globally Harmonized System
- **GLP**: Good Laboratory Practice
- **HMS**: Hazardous Materials Identification System
- **IC50**: Half maximal inhibitory concentration
- **ICAO**: International Civil Aviation Organization
- **IECSC**: Inventory of Existing Chemical Substances in China
- **ICSHL**: Industrial Safety and Health Law (Japan)
- **ISO**: International Organisation for Standardization
- **KECI**: Korea Existing Chemical...
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.