SAFETY DATA SHEET

Formoterol Formulation

Version 6.2 Revision Date: 09/13/2019 SDS Number: 525398-00011 Date of last issue: 04/24/2019 Date of first issue: 02/23/2016

SECTION 1. IDENTIFICATION

Product name: Formoterol 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 29 CFR 1910.1200
Combustible dust

Specific target organ toxicity - single exposure (Oral): Category 1 (Cardio-vascular system, Central nervous system)
Specific target organ toxicity - single exposure (Inhalation): Category 1 (Cardio-vascular system, Central nervous system)
Specific target organ toxicity - repeated exposure (Oral): Category 1 (Heart)
Specific target organ toxicity - repeated exposure (Inhalation): Category 1 (Heart)

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.
H370 Causes damage to organs (Cardio-vascular system, Central nervous system) if swallowed.
H370 Causes damage to organs (Cardio-vascular system, Central nervous system) if inhaled.
H372 Causes damage to organs (Heart) through prolonged or repeated exposure if swallowed.
H372 Causes damage to organs (Heart) through prolonged or repeated exposure if inhaled.
Precautionary Statements:

**Prevention:**
- P260 Do not breathe dust.
- P264 Wash skin thoroughly after handling.
- P270 Do not eat, drink or smoke when using this product.

**Response:**
- P307 + P311 IF exposed: Call a POISON CENTER or doctor/physician.

**Storage:**
- P405 Store locked up.

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

Other hazards:
Dust contact with the eyes can lead to mechanical irritation.
Contact with dust can cause mechanical irritation or drying of the skin.

### SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>Substance / Mixture</th>
<th>Mixture</th>
</tr>
</thead>
<tbody>
<tr>
<td>Components</td>
<td></td>
</tr>
<tr>
<td>Chemical name</td>
<td>CAS-No.</td>
</tr>
<tr>
<td>Formoterol</td>
<td>43229-80-7</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:**
Wash with water and soap.
Get medical attention if symptoms occur.

**In case of eye contact:**
If in eyes, rinse well with water.
Get medical attention if irritation develops and persists.

**If swallowed:**
If swallowed, DO NOT induce vomiting unless directed to do so by medical personnel.
Get medical attention.
Rinse mouth thoroughly with water.
Never give anything by mouth to an unconscious person.

**Most important symptoms and effects, both acute and delayed:**
Causes damage to organs if swallowed.
Causes damage to organs if inhaled.
Causes damage to organs through prolonged or repeated exposure if swallowed.
Causes damage to organs through prolonged or repeated exposure if inhaled.
Contact with dust can cause mechanical irritation or drying of the skin.
Dust contact with the eyes can lead to mechanical irritation.

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

Notes to physician:
Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES

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

Unsuitable extinguishing media:
None known.

Specific hazards during firefighting:
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 and personal protective equipment recommendations.

Environmental precautions:
Discharge into the environment must be avoided. 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 breathe dust.
- 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 assessment.
- 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.
- 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>Formoterol</td>
<td>43229-80-7</td>
<td>TWA</td>
<td>0.05 µg/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>0.5 µg/100 cm²</td>
<td>Internal</td>
</tr>
</tbody>
</table>

Engineering measures:
- Use closed processing systems or containment technologies to control at source (e.g., glove boxes/isolators) and to prevent leakage of compounds into the workplace.
- All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment.
- No open handling permitted.
- Totally enclosed processes and materials transport systems...
are required.
Operations require the use of appropriate containment technology designed to prevent leakage of compounds into the workplace.

**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**: Consider double gloving.

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

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

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

### SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

**Appearance**: powder

**Color**: No data available

**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 : Not applicable
Evaporation rate : Not applicable
Flammability (solid, gas) : May form explosive dust-air mixture during processing, handling or other means.
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 : 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
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.
Particle size : No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity : Not classified as a reactivity hazard.
Chemical stability : Stable under normal conditions.
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:

Formoterol:
Acute oral toxicity
LD50 (Rat): 3,130 mg/kg
LD50 (Mouse): 6,700 mg/kg

Acute inhalation toxicity
LC50 (Rat): 1.5 mg/l
Exposure time: 4 h
Test atmosphere: dust/mist

Acute dermal toxicity
Remarks: No data available

Acute toxicity (other routes of administration)
LD50 (Rat): 1,000 mg/kg
Application Route: Subcutaneous

LD50 (Mouse): 640 mg/kg
Application Route: Subcutaneous

Skin corrosion/irritation
Not classified based on available information.

Components:

Formoterol:
Species: Rabbit
Result: No skin irritation
Remarks: Slight irritation

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

Formoterol:
Species: Rabbit
Result: No eye irritation

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Formoterol:
Test Type: Maximization Test
Routes of exposure: Dermal
Species: Guinea pig
Result: Not a skin sensitizer.

Germ cell mutagenicity
Not classified based on available information.

Components:

Formoterol:
Genotoxicity in vitro: Test Type: In vitro mammalian cell gene mutation test
Result: negative

Test Type: Chromosomal aberration
Result: negative

Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Result: negative

Genotoxicity in vivo: Test Type: Micronucleus test
Species: Mouse
Application Route: Oral
Result: negative

Test Type: Micronucleus test
Species: Rat
Application Route: Oral
Result: negative

Carcinogenicity
Not classified based on available information.

Components:

Formoterol:
Species: Rat
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<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>
</thead>
<tbody>
<tr>
<td>6.2</td>
<td>09/13/2019</td>
<td>525398-00011</td>
<td>04/24/2019</td>
<td>02/23/2016</td>
</tr>
</tbody>
</table>

**Application Route**: Oral  
**Exposure time**: 2 Years  
**LOAEL**: 0.5 mg/kg body weight  
**Target Organs**: Ovary  
**Remarks**: The mechanism or mode of action may not be relevant in humans.

**Species**: Mouse  
**Application Route**: Oral  
**Exposure time**: 18 month(s)  
**LOAEL**: 2 mg/kg body weight  
**Target Organs**: Adrenal gland, Liver, Uterus (including cervix)  
**Remarks**: The mechanism or mode of action may not be relevant in humans.

**Carcinogenicity - Assessment**  
**IARC**: Limited evidence of carcinogenicity in animal studies.  
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:**

**Formoterol:**

**Effects on fertility**  
Test Type: Fertility/early embryonic development  
Species: Rat  
Application Route: Oral  
Fertility: NOAEL: 3 mg/kg body weight  
Result: No effects on fertility.

**Effects on fetal development**  
Test Type: Embryo-fetal development  
Species: Rat  
Application Route: Oral  
Developmental Toxicity: LOAEL: 0.2 mg/kg body weight  
Result: Embryo-fetal toxicity., No malformations were observed.

Test Type: Embryo-fetal development  
Species: Rat  
Application Route: Oral  
Developmental Toxicity: LOAEL: 3 mg/kg body weight  
Result: Malformations were observed.

Test Type: Embryo-fetal development  
Species: Rat  
Application Route: inhalation (dust/mist/fume)  
Developmental Toxicity: NOAEL: 1.2 mg/kg body weight
Result: No embryo-fetal toxicity.

Test Type: Embryo-fetal development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: LOAEL: 60 mg/kg body weight
Result: Embryo-fetal toxicity., No malformations were observed.

Reproductive toxicity - Assessment:
- Some evidence of adverse effects on development, based on animal experiments.

**STOT-single exposure**
Causes damage to organs (Cardiovascular system, Central nervous system) if swallowed.
Causes damage to organs (Cardiovascular system, Central nervous system) if inhaled.

**Product:**
- **Routes of exposure:** Ingestion, Inhalation
- **Target Organs:** Cardiovascular system, Central nervous system
- **Assessment:** Causes damage to organs.

**Components:**
- **Formoterol:**
  - **Routes of exposure:** Ingestion, Inhalation (dust/mist/fume)
  - **Target Organs:** Cardiovascular system, Central nervous system
  - **Assessment:** Causes damage to organs.

**STOT-repeated exposure**
Causes damage to organs (Heart) through prolonged or repeated exposure if swallowed.
Causes damage to organs (Heart) through prolonged or repeated exposure if inhaled.

**Product:**
- **Routes of exposure:** Inhalation, Ingestion
- **Target Organs:** Heart
- **Assessment:** Causes damage to organs through prolonged or repeated exposure.

**Components:**
- **Formoterol:**
  - **Routes of exposure:** Ingestion, inhalation (dust/mist/fume)
  - **Target Organs:** Heart
  - **Assessment:** Causes damage to organs through prolonged or repeated exposure.

**Repeated dose toxicity**

**Components:**
- **Formoterol:**
  - **Species:** Dog
  - **LOAEL:** >= 1.5 mg/kg
## Application Route
- **Inhalation**

## Exposure time
- **13 Weeks**

## Target Organs
- **Heart**

<table>
<thead>
<tr>
<th>Species</th>
<th>NOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Target Organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>0.14 mg/kg</td>
<td>Inhalation</td>
<td>13 Weeks</td>
<td>Heart</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>LOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Target Organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dog</td>
<td>0.003 mg/kg</td>
<td>Oral</td>
<td>1 y</td>
<td>Heart</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Species</th>
<th>LOAEL</th>
<th>Application Route</th>
<th>Exposure time</th>
<th>Target Organs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Rat</td>
<td>0.3 mg/kg</td>
<td>Oral</td>
<td>1 y</td>
<td>Heart</td>
</tr>
</tbody>
</table>

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

**Experience with human exposure**

**Components:**

**Formoterol:**
- **Inhalation**
  - Target Organs: Heart
  - Symptoms: Palpitation, Tremors, Dizziness, Headache, dry mouth, Nausea, Fatigue

###Ecotoxicity

**Components:**

**Formoterol:**
- **Toxicity to fish**
  - LC50 (Oncorhynchus mykiss (rainbow trout)): > 120 mg/l
  - Exposure time: 96 h
  - Method: OECD Test Guideline 203

- **Toxicity to daphnia and other aquatic invertebrates**
  - EC50 (Daphnia magna (Water flea)): > 114 mg/l
  - Exposure time: 48 h
  - Method: OECD Test Guideline 202

- **Toxicity to algae/aquatic plants**
  - EC50 (Pseudokirchneriella subcapitata (green algae)): 94 mg/l
  - Exposure time: 72 h
  - Method: OECD Test Guideline 201
  - NOEC (Pseudokirchneriella subcapitata (green algae)): 30 mg/l
Persistence and degradability
No data available

Bioaccumulative potential

Components:
Formoterol:
Partition coefficient: n-octanol/water: log Pow: 0.41

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

EPCRA - Emergency Planning and Community Right-to-Know

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
- 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

Lactose 63-42-3

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

HMIS® IV:
- HEALTH: * 4
- FLAMMABILITY: 3
- PHYSICAL HAZARD: 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

AICS - Australian Inventory of Chemical Substances; 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 Sub-
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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