SAFETY DATA SHEET

Formoterol Formulation

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 the OSHA Hazard Communication Standard (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 doctor.

Storage:
P405 Store locked up.

Disposal:
P501 Dispose of contents and 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

Substance / Mixture: Mixture

<table>
<thead>
<tr>
<th>Components</th>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Formoterol</td>
<td></td>
<td>43229-80-7</td>
<td>&lt; 0.1</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 (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 breathe dust.
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.
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.
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 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**

**Material**: Chemical-resistant gloves

**Remarks**: 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**

**Material**: 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 : 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.
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.

**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
### Formoterol Formulation

<table>
<thead>
<tr>
<th>Application Route</th>
<th>Oral</th>
</tr>
</thead>
<tbody>
<tr>
<td>Exposure time</td>
<td>2 Years</td>
</tr>
<tr>
<td>LOAEL</td>
<td>0.5 mg/kg body weight</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Ovary</td>
</tr>
<tr>
<td>Remarks</td>
<td>The mechanism or mode of action may not be relevant in humans.</td>
</tr>
</tbody>
</table>

**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**  
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 (Cardio-vascular system, Central nervous system) if swallowed.  
Causes damage to organs (Cardio-vascular system, Central nervous system) if inhaled.

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

**Components:**
- **Formoterol:**  
  - **Routes of exposure:** Ingestion, inhalation (dust/mist/fume)  
  - **Target Organs:** Cardio-vascular 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:** $\geq 1.5$ mg/kg
Application Route: Inhalation
Exposure time: 13 Weeks
Target Organs: Heart
Species: Rat
NOAEL: 0.14 mg/kg
Application Route: Inhalation
Exposure time: 13 Weeks
Target Organs: Heart
Species: Dog
LOAEL: 0.003 mg/kg
Application Route: Oral
Exposure time: 1 y
Target Organs: Heart
Species: Rat
LOAEL: 0.3 mg/kg
Application Route: Oral
Exposure time: 1 y
Target Organs: Heart

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

SECTION 12. ECOLOGICAL INFORMATION

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

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:
HEALTH 0 1 0 1
PHYSICAL HAZARD 0 0 0 0
FLAMMABILITY 3 3 3 3
INSTABILITY 0 0 0 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 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 Sub-
<table>
<thead>
<tr>
<th>Source of Key Data Used to Compile the Material Safety Data Sheet</th>
<th>Details</th>
</tr>
</thead>
</table>

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.