SAFETY DATA SHEET

Suvorexant Formulation

Version 5.2  Revision Date: 09/13/2019  SDS Number: 21544-00015  Date of last issue: 24.04.2019  Date of first issue: 14.10.2014

SECTION 1. PRODUCT AND COMPANY IDENTIFICATION

Product name: Suvorexant Formulation

Manufacturer or supplier's details
Company name of supplier: MSD
Address: Avenida 16 de Septiembre No. 301
Xaltocan - Xochimilco Mexico 16090
Telephone: 52 55 57284444
Telefax: 908-735-1496
Emergency telephone: 1-908-423-6000
E-mail address: EHSDATASTEWAR@msd.com

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

SECTION 2. HAZARDS IDENTIFICATION

GHS Classification
Specific target organ toxicity - repeated exposure (Oral): Category 2 (Central nervous system)

GHS label elements
Hazard pictograms:

Signal Word: Warning
Hazard Statements: H373 May cause damage to organs (Central nervous system) through prolonged or repeated exposure if swallowed.
Response: P314 Get medical advice/ attention if you feel unwell.
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.
May form explosive dust-air mixture during processing, handling or other means.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture
Components

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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 if symptoms occur.

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. Get medical attention if symptoms occur. Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed: May cause damage to organs through prolonged or repeated exposure if swallowed. 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 fire fighting: 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
Metal 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 spillages 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:
- Use only with adequate 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.

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.

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

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>Suvorexant</td>
<td>1030377-33-3</td>
<td>TWA</td>
<td>20 µg/m³ (OEB 3)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>200 µg/100 cm²</td>
<td>Internal</td>
</tr>
<tr>
<td>Magnesium stearate</td>
<td>557-04-0</td>
<td>VLE-PPT</td>
<td>10 mg/m³</td>
<td>NOM-010-STPS-2014</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Inhalable fraction)</td>
<td>10 mg/m³</td>
<td>ACGIH</td>
</tr>
<tr>
<td></td>
<td></td>
<td>TWA (Respirable fraction)</td>
<td>3 mg/m³</td>
<td>ACGIH</td>
</tr>
</tbody>
</table>

Engineering measures: All engineering controls should be implemented by facility design and operated in accordance with GMP principles to protect products, workers, and the environment. Containment technologies suitable for controlling compounds are required to control at source and to prevent migration of the compound to uncontrolled areas (e.g., open-face containment devices). Minimize open handling.

Personal protective equipment

Respiratory protection: If adequate local exhaust ventilation is not available or exposure assessment demonstrates exposures outside the recommended guidelines, use respiratory protection.

Filter type: Particulates type

Hand protection: 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.

SECTION 9. PHYSICAL AND CHEMICAL PROPERTIES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>powder</td>
</tr>
<tr>
<td>Color</td>
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<tr>
<td>Odor</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>No data available</td>
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<tr>
<td>pH</td>
<td>No data available</td>
</tr>
<tr>
<td>Melting point/freezing point</td>
<td>No data available</td>
</tr>
<tr>
<td>Initial boiling point and boiling range</td>
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</tr>
<tr>
<td>Flash point</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>May form explosive dust-air mixture during processing, handling or other means.</td>
</tr>
<tr>
<td>Flammability (liquids)</td>
<td>No data available</td>
</tr>
<tr>
<td>Upper explosion limit / Upper flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Lower explosion limit / Lower flammability limit</td>
<td>No data available</td>
</tr>
<tr>
<td>Vapor pressure</td>
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<tr>
<td>Relative vapor density</td>
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</tr>
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<td>Relative density</td>
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<tr>
<td>Density</td>
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<tr>
<td>Solubility(ies)</td>
<td>Water solubility</td>
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<td></td>
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</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
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<td>Autoignition temperature</td>
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</tr>
<tr>
<td>Decomposition temperature</td>
<td>No data available</td>
</tr>
<tr>
<td>Viscosity</td>
<td>Viscosity, kinematic</td>
</tr>
<tr>
<td></td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
Explosive properties: Not explosive

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

Molecular weight: No data available

Particle size: No data available

SECTION 10. STABILITY AND REACTIVITY

Reactivity: Not classified as a reactivity hazard.
Chemical stability: Stable under normal conditions.
Possibility of hazardous reactions: May form explosive dust-air mixture during processing, handling or other means. Can react with strong oxidizing agents.

Conditions to avoid: Heat, flames and sparks. Avoid dust formation.

Incompatible materials: Oxidizing agents

Hazardous decomposition products: No hazardous decomposition products are known.

SECTION 11. TOXICOLOGICAL INFORMATION

Information on likely routes of exposure

Inhalation
Skin contact
Ingestion
Eye contact

Acute toxicity
Not classified based on available information.

Components:

Suvorexant:
Acute oral toxicity: LD50 (Rat): > 1,200 mg/kg
LD50 (Dog): > 1,125 mg/kg
LDLo (Mouse): 2,000 mg/kg

Magnesium stearate:
Acute oral toxicity: LD50 (Rat): > 2,000 mg/kg
Method: OECD Test Guideline 423
Assessment: The substance or mixture has no acute oral toxicity
Remarks: Based on data from similar materials

Acute dermal toxicity: LD50 (Rabbit): > 2,000 mg/kg
Remarks: Based on data from similar materials
Skin corrosion/irritation
Not classified based on available information.

Components:

Suvorexant:
Species: Rabbit
Result: No skin irritation

Magnesium stearate:
Species: Rabbit
Result: No skin irritation
Remarks: Based on data from similar materials

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

Components:

Suvorexant:
Species: Bovine cornea
Result: Mild eye irritation
Method: Bovine cornea (BCOP)

Magnesium stearate:
Species: Rabbit
Result: No eye irritation
Remarks: Based on data from similar materials

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:

Suvorexant:
Test Type: Local lymph node assay (LLNA)
Species: Mouse
Assessment: Does not cause skin sensitization.
Result: negative

Magnesium stearate:
Test Type: Maximization Test
Routes of exposure: Skin contact
Species: Guinea pig
Method: OECD Test Guideline 406
Result: negative
Remarks: Based on data from similar materials
Germ cell mutagenicity
Not classified based on available information.

**Components:**

**Suvorexant:**
- Genotoxicity in vitro:
  - Test Type: Bacterial reverse mutation assay (AMES)
    Result: negative
  - Test Type: Alkaline elution assay
    Test system: rat hepatocytes
    Result: negative
  - Test Type: Chromosomal aberration
    Test system: Chinese hamster ovary cells
    Result: negative
- Genotoxicity in vivo:
  - Test Type: Micronucleus test
    Species: Mouse
    Result: negative
  - Test Type: Micronucleus test
    Species: Rat
    Result: negative

**Magnesium stearate:**
- Genotoxicity in vitro:
  - Test Type: In vitro mammalian cell gene mutation test
    Result: negative
    Remarks: Based on data from similar materials
  - Test Type: Chromosome aberration test in vitro
    Method: OECD Test Guideline 473
    Result: negative
    Remarks: Based on data from similar materials
  - Test Type: Bacterial reverse mutation assay (AMES)
    Result: negative
    Remarks: Based on data from similar materials

**Carcinogenicity**
Not classified based on available information.

**Components:**

**Suvorexant:**
- Species: Mouse
- Application Route: Oral
- Exposure time: 6 month(s)
- Result: negative
- Species: Rat
- Application Route: Oral
- Exposure time: 2 Years
- Result: negative
Reproductive toxicity
Not classified based on available information.

Components:

Suvorexant:
Effects on fertility: Test Type: Fertility/early embryonic development
Species: Rat, male and female
Application Route: Oral
General Toxicity Parent: NOAEL: >= 325 mg/kg body weight
Result: negative

Effects on fetal development: Test Type: Embryo-fetal development
Species: Rabbit, female
Application Route: Oral
Developmental Toxicity: NOAEL: 150 mg/kg body weight
Result: negative

Test Type: Embryo-fetal development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 80 mg/kg body weight
Result: negative

Magnesium stearate:
Effects on fertility: Test Type: Combined repeated dose toxicity study with the reproduction/developmental toxicity screening test
Species: Rat
Application Route: Ingestion
Method: OECD Test Guideline 422
Result: negative
Remarks: Based on data from similar materials

Effects on fetal development: Test Type: Embryo-fetal development
Species: Rat
Application Route: Ingestion
Result: negative
Remarks: Based on data from similar materials

STOT-single exposure
Not classified based on available information.

Components:

Suvorexant:
Remarks: Based on human experience.

STOT-repeated exposure
May cause damage to organs (Central nervous system) through prolonged or repeated exposure if swallowed.
Components:

Suvorexant:

Routes of exposure : Ingestion
Target Organs : Central nervous system
Assessment : May cause damage to organs through prolonged or repeated exposure.

Repeated dose toxicity

Components:

Suvorexant:

Species : Rat
NOAEL : 325 mg/kg
LOAEL : 1,200 mg/kg
Application Route : Oral
Exposure time : 30 d
Target Organs : Blood, Pancreas

Species : Dog
NOAEL : 50 mg/kg
LOAEL : 125 mg/kg
Application Route : Oral
Exposure time : 30 d
Target Organs : Blood, Liver, Central nervous system

Species : Rat
NOAEL : 75 mg/kg
LOAEL : 300 mg/kg
Application Route : Oral
Exposure time : 180 d
Target Organs : Pancreas, Blood, Stomach

Species : Dog
NOAEL : 50 mg/kg
LOAEL : 125 mg/kg
Application Route : Oral
Exposure time : 270 d
Target Organs : Blood

Species : Rat
NOAEL : 40 mg/kg
LOAEL : 80 mg/kg
Application Route : Oral
Exposure time : 18 Months
Target Organs : Eye, Central nervous system

Magnesium stearate:

Species : Rat
NOAEL : > 100 mg/kg
Application Route : Ingestion
Exposure time : 90 Days
Remarks : Based on data from similar materials
Aspiration toxicity
Not classified based on available information.

Experience with human exposure

Components:

Suvorexant:
Ingestion:
Symptoms: Drowsiness, Headache, abnormal dreams, Fatigue, Dizziness, dry mouth, Nausea, liver function change, upper respiratory tract infection, urinary tract infection, Cough, Diarrhea, Palpitation, tachycardia

SECTION 12. ECOLOGICAL INFORMATION

Ecotoxicity

Components:

Suvorexant:
Toxicity to daphnia and other aquatic invertebrates:
EC50 (Mysidopsis bahia (opossum shrimp)): 0.56 mg/l
Exposure time: 96 h
Method: US-EPA OPPTS 850.1035

Toxicity to algae/aquatic plants:
EC50 (Pseudokirchneriella subcapitata (green algae)): > 5 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

NOEC (Pseudokirchneriella subcapitata (green algae)): 2.5 mg/l
Exposure time: 72 h
Method: OECD Test Guideline 201

Toxicity to fish (Chronic toxicity):
NOEC (Pimephales promelas (fathead minnow)): 0.14 mg/l
Exposure time: 32 d
Method: OECD Test Guideline 210

Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity):
NOEC (Daphnia magna (Water flea)): 0.5 mg/l
Exposure time: 21 d
Method: OECD Test Guideline 211

Toxicity to microorganisms:
EC50: > 1,000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

NOEC: 1,000 mg/l
Exposure time: 3 h
Test Type: Respiration inhibition
Method: OECD Test Guideline 209

Magnesium stearate:
Toxicity to fish:
LC50 (Leuciscus idus (Golden orfe)): > 100 mg/l
Exposure time: 48 h
Method: DIN 38412
Remarks: Based on data from similar materials

Toxicity to daphnia and other aquatic invertebrates:
EL50 (Daphnia magna (Water flea)): > 1 mg/l
Exposure time: 47 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials
No toxicity at the limit of solubility.

Toxicity to algae/aquatic plants:
EL50 (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials
No toxicity at the limit of solubility.

NOELR (Pseudokirchneriella subcapitata (green algae)): > 1 mg/l
Exposure time: 72 h
Test substance: Water Accommodated Fraction
Method: OECD Test Guideline 201
Remarks: Based on data from similar materials

Toxicity to microorganisms:
EC10 (Pseudomonas putida): > 100 mg/l
Exposure time: 16 h
Test substance: Water Accommodated Fraction
Remarks: Based on data from similar materials

Persistence and degradability

Components:

Suvorexant:
Biodegradability: Result: Not readily biodegradable.
Biodegradation: 81 %
Exposure time: 28 d
Method: OECD Test Guideline 314

Stability in water: Hydrolysis: < 10 % (5 d)
Method: OECD Test Guideline 111

Magnesium stearate:
Biodegradability: Result: Not biodegradable.
Remarks: Based on data from similar materials
Bioaccumulation
Species: Lepomis macrochirus (Bluegill sunfish)
Bioconcentration factor (BCF): 358
Method: OECD Test Guideline 305

Partition coefficient: n-octanol/water
Log Pow: 4.04

Magnesium stearate:
Partition coefficient: n-octanol/water
Log Pow: > 4

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

NOM-002-SCT
Not regulated as a dangerous good

Special precautions for user
Not applicable

SECTION 15. REGULATORY INFORMATION

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

Federal Law for the control of chemical precursors, essential chemical products and machinery for producing capsules, tablets and pills.
Not applicable
The ingredients of this product are reported in the following inventories:

- **AICS**: not determined
- **DSL**: not determined
- **IECSC**: not determined

**SECTION 16. OTHER INFORMATION**

**Full text of other abbreviations**

- **ACGIH**: USA. ACGIH Threshold Limit Values (TLV)
- **NOM-010-STPS-2014**: Mexico. Norm NOM-010-STPS-2014 on Chemicals Polluting the Work Environment - Identification, Assessment and Control - Appendix 1 Occupational Exposure Limits
- **ACGIH / TWA**: 8-hour, time-weighted average
- **NOM-010-STPS-2014 / VLE- PPT**: Time weighted average limit value

- **AICS** - Australian Inventory of Chemical Substances
- **ANTT** - National Agency for Transport by Land of Brazil
- **ASTM** - American Society for the Testing of Materials
- **bw** - Body weight
- **CMR** - Carcinogen, Mutagen or Reproductive Toxicant
- **DIN** - Standard of the German Institute for Standardisation
- **DSL** - Domestic Substances List (Canada)
- **ECx** - Concentration associated with x% response
- **ELx** - Loading rate associated with x% response
- **EmS** - Emergency Schedule
- **ENCS** - Existing and New Chemical Substances (Japan)
- **ErCx** - Concentration associated with x% growth rate response
- **ERG** - Emergency Response Guide
- **GHS** - Globally Harmonized System
- **GLP** - Good Laboratory Practice
- **IARC** - International Agency for Research on Cancer
- **IATA** - International Air Transport Association
- **IBC** - International Code for the Construction and Equipment of Ships carrying Dangerous Chemicals in Bulk
- **IC50** - Half maximal inhibitory concentration
- **ICAO** - International Civil Aviation Organization
- **IECSC** - Inventory of Existing Chemical Substances in China
- **IMDG** - International Maritime Dangerous Goods
- **IMO** - International Maritime Organization
- **ISHL** - Industrial Safety and Health Law (Japan)
- **ISO** - International Organisation for Standardization
- **KECI** - Korea Existing Chemicals Inventory
- **LC50** - Lethal Concentration to 50 % of a test population
- **LD50** - Lethal Dose
- **MARPOL** - International Convention for the Prevention of Pollution from Ships
- **n.o.s.** - Not Otherwise Specified
- **Nch** - Chilean Norm
- **NO(A)EC** - No Observed (Adverse) Effect Concentration
- **NO(A)EL** - No Observed (Adverse) Effect Level
- **NOELR** - No Observable Effect Loading Rate
- **OECD** - Organisation 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
- **SADT** - Self-Accelerating Decomposition Temperature
- **SDS** - Safety Data Sheet
- **TCSI** - Taiwan Chemical Substance Inventory
- **TDG** - Transportation of Dangerous Goods
- **TSCA** - Toxic Substances Control Act (United States)
- **UN** - United Nations
- **UNRTDG** - United Nations Recommendations on the Transport of Dangerous Goods
- **vPvB** - Very Persistent and Very Bioaccumulative
- **WHMIS** - Workplace Hazardous Materials Information System

Sources of key data used to: Internal technical data, data from raw material SDSs, OECD
The information is considered as correct, but not exhaustive, and will be used only as a guide, which is based in the current knowledge of the substance or mixture, and is applicable to proper safety precautions for the product.

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