SECTION 1. IDENTIFICATION

Product name: Buprenorphine Liquid 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
Not a hazardous substance or mixture.

GHS label elements
Not a hazardous substance or mixture.

Other hazards
None known.

SECTION 3. COMPOSITION/INFORMATION ON INGREDIENTS

Substance / Mixture: Mixture

Components

<table>
<thead>
<tr>
<th>Chemical name</th>
<th>CAS-No.</th>
<th>Concentration (% w/w)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Buprenorphine Hydrochloride</td>
<td>53152-21-9</td>
<td>&lt; 0.1</td>
</tr>
</tbody>
</table>

Actual concentration is withheld as a trade secret

SECTION 4. FIRST AID MEASURES

If inhaled:
If inhaled, remove to fresh air.
Get medical attention if symptoms occur.

In case of skin contact:
Wash with water and soap as a precaution.
Get medical attention if symptoms occur.

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 if symptoms occur.
Rinse mouth thoroughly with water.

Most important symptoms and effects, both acute and delayed:
None known.

Protection of first-aiders:
No special precautions are necessary for first aid responders.

Notes to physician:
Treat symptomatically and supportively.

SECTION 5. FIRE-FIGHTING MEASURES
SAFETY DATA SHEET

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

Unsuitable extinguishing media: None known.

Specific hazards during firefighting: 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: Wear self-contained breathing apparatus for firefighting if necessary. Use personal protective equipment.

SECTION 6. ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures: 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. 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: Handle in accordance with good industrial hygiene and safety practice, based on the results of the workplace exposure assessment. 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.

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>Buprenorphine Hydrochloride</td>
<td>53152-21-9</td>
<td>TWA</td>
<td>0.2 µg/m³ (OEB 5)</td>
<td>Internal</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Wipe limit</td>
<td>2 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: No personal respiratory protective equipment normally required.

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

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>liquid</td>
</tr>
<tr>
<td>Color</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor</td>
<td>No data available</td>
</tr>
<tr>
<td>Odor Threshold</td>
<td>No data available</td>
</tr>
<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>
<td>No data available</td>
</tr>
<tr>
<td>Flash point</td>
<td>No data available</td>
</tr>
<tr>
<td>Evaporation rate</td>
<td>No data available</td>
</tr>
<tr>
<td>Flammability (solid, gas)</td>
<td>Not applicable</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>
<td>No data available</td>
</tr>
<tr>
<td>Relative vapor density</td>
<td>No data available</td>
</tr>
<tr>
<td>Relative density</td>
<td>No data available</td>
</tr>
<tr>
<td>Density</td>
<td>No data available</td>
</tr>
<tr>
<td>Solubility(ies)</td>
<td>No data available</td>
</tr>
<tr>
<td>Water solubility</td>
<td>No data available</td>
</tr>
<tr>
<td>Partition coefficient: n-octanol/water</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>
SAFETY DATA SHEET

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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.
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:

Buprenorphine Hydrochloride:
Acute oral toxicity : LD50 (Mouse): 261 mg/kg
LD50 (Rat): 600 mg/kg
Acute inhalation toxicity : Remarks: No data available
Acute dermal toxicity : Remarks: No data available
Acute toxicity (other routes of administration) : LD50 (Rat): 31 mg/kg
Application Route: Intravenous
LD50 (Mouse): 24 mg/kg
Application Route: Intravenous
Skin corrosion/irritation
Not classified based on available information.

Components:
Buprenorphine Hydrochloride:
Remarks : No data available

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

Components:
Buprenorphine Hydrochloride:
Remarks : No data available

Respiratory or skin sensitization

Skin sensitization
Not classified based on available information.

Respiratory sensitization
Not classified based on available information.

Components:
Buprenorphine Hydrochloride:
Remarks : No data available

Germ cell mutagenicity
Not classified based on available information.

Components:
Buprenorphine Hydrochloride:
Genotoxicity in vitro : Test Type: Bacterial reverse mutation assay (AMES)
Result: equivocal
Test Type: Chromosomal aberration
Result: negative
Test Type: DNA damage and repair, unscheduled DNA synthesis in mammalian cells (in vitro)
Result: positive

Germ cell mutagenicity - Assessment : Weight of evidence does not support classification as a germ cell mutagen.

Carcinogenicity
Not classified based on available information.
## Components:

### Buprenorphine Hydrochloride:

<table>
<thead>
<tr>
<th>Species</th>
<th>Rat</th>
</tr>
</thead>
<tbody>
<tr>
<td>Application Route</td>
<td>Oral</td>
</tr>
<tr>
<td>Exposure time</td>
<td>27 Months</td>
</tr>
<tr>
<td>LOAEL</td>
<td>56 mg/kg body weight</td>
</tr>
<tr>
<td>Result</td>
<td>positive</td>
</tr>
<tr>
<td>Target Organs</td>
<td>Testes</td>
</tr>
<tr>
<td>Remarks</td>
<td>The significance of these findings for humans is not certain.</td>
</tr>
</tbody>
</table>

Species : Mouse  
Application Route : Oral  
Exposure time : 86 weeks  
NOAEL : 100 mg/kg body weight  
Result : negative  

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

Not classified based on available information.

## Components:

### Buprenorphine Hydrochloride:

#### Effects on fertility:

Test Type: Fertility  
Species: Rat  
Application Route: Oral  
Fertility: NOAEL: 80 mg/kg body weight  
Result: No effects on fertility.

Test Type: Fertility  
Species: Rabbit  
Application Route: Oral  
Fertility: LOAEL: 1 mg/kg body weight  
Result: Preimplantation loss.

Test Type: Fertility  
Species: Rabbit
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Application Route: Intravenous
Fertility: LOAEL: 0.2 mg/kg body weight
Result: Postimplantation loss.

Effects on fetal development:
Test Type: Development
Species: Rat
Application Route: Subcutaneous
Developmental Toxicity: LOAEL: 5 mg/kg body weight
Result: Embryo-fetal toxicity., No teratogenic effects., Skeletal malformations.

Test Type: Development
Species: Rat
Application Route: Oral
Developmental Toxicity: NOAEL: 160 mg/kg body weight
Result: No effects on fetal development.

Test Type: Development
Species: Rat
Application Route: Subcutaneous
Developmental Toxicity: LOAEL: 0.1 mg/kg body weight
Result: Effects on newborn.

Test Type: Development
Species: Rabbit
Application Route: Intramuscular
Developmental Toxicity: LOAEL: 5 mg/kg body weight
Result: Embryo-fetal toxicity., Skeletal malformations.

Test Type: Development
Species: Rabbit
Application Route: Oral
Developmental Toxicity: LOAEL: 1 mg/kg body weight
Result: Embryo-fetal toxicity., Skeletal malformations.

Reproductive toxicity - Assessment: May damage the unborn child. Suspected of damaging fertility.

STOT-single exposure
Not classified based on available information.

Components:

Buprenorphine Hydrochloride:
Assessment: May cause drowsiness or dizziness.

STOT-repeated exposure
Not classified based on available information.

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

Components:

**Buprenorphine Hydrochloride:**

**Inhalation**

- **Target Organs:** Central nervous system
- **Symptoms:** Drowsiness, sedation, Headache, Nausea, Vomiting, Dizziness, Vertigo, Sweating, constipation, insomnia, Pain, respiratory depression, constriction of pupils, decrease in heart rate, Lowered blood pressure
- **Remarks:** May cause neonatal withdrawal

SECTION 12. ECOLOGICAL INFORMATION

**Ecotoxicity**

Components:

**Buprenorphine Hydrochloride:**

**Toxicity to algae/aquatic plants**

- **EC50 (Pseudokirchneriella subcapitata (green algae)):** 6.25 mg/l
- **Exposure time:** 72 h
- **Method:** OECD Test Guideline 201
- **NOEC (Pseudokirchneriella subcapitata (green algae)):** 0.319 mg/l
- **Exposure time:** 72 h
- **Method:** OECD Test Guideline 201

**Toxicity to fish (Chronic toxicity)**

- **NOEC (Pimephales promelas (fathead minnow)):** 0.137 mg/l
- **Exposure time:** 28 d
- **Method:** OECD Test Guideline 210

**Toxicity to daphnia and other aquatic invertebrates (Chronic toxicity)**

- **NOEC (Daphnia magna (Water flea)):** 0.883 mg/l
- **Exposure time:** 21 d
- **Method:** OECD Test Guideline 211

- **LOEC (Daphnia magna (Water flea)):** 1.95 mg/l
- **Exposure time:** 21 d
- **Method:** OECD Test Guideline 211

**Toxicity to microorganisms**

- **EC50:** 588 mg/l
- **Exposure time:** 3 h
- **Test Type:** Respiration inhibition
- **Method:** OECD Test Guideline 209

- **NOEC:** 135 mg/l
- **Exposure time:** 3 h
- **Test Type:** Respiration inhibition
- **Method:** OECD Test Guideline 209
Persistence and degradability

Components:

Buprenorphine Hydrochloride:
Biodegradability: Result: Not readily biodegradable.

Bioaccumulative potential

Components:

Buprenorphine Hydrochloride:
Bioaccumulation: Species: Oncorhynchus mykiss (rainbow trout)
Bioconcentration factor (BCF): 0.4
Method: OECD Test Guideline 305

Partition coefficient: n-octanol/water: log Pow: 3.11

Mobility in soil

Components:

Buprenorphine Hydrochloride:
Distribution among environmental compartments: log Koc: 4.11

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
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Not regulated as a dangerous good

SECTION 15. REGULATORY INFORMATION

EPCRA - Emergency Planning and Community Right-to-Know

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>Hydrochloric acid</td>
<td>7647-01-0</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: No SARA Hazards

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
Glucose 50-99-7

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
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NFPA 704:

Flammability

Health

1

0

Instability

Special hazard

HMIS® IV:

HEALTH

/ 0

FLAMMABILITY

1

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 Substances List (Canada); ECx - Concentration associated with x% response; EHS - Extremely Hazardous Substance; 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; HMIS - Hazardous Materials Identification System; 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 Chemicals 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 to 50% of a test population (Median Lethal Dose); MARPOL - International Convention for the Prevention of Pollution from Ships; MSHA - Mine Safety and Health Administration; n.o.s. - Not Otherwise Specified; NFPA - National Fire Protection Association; NO(A)EC - No Observed (Adverse) Effect Concentration; NO(A)EL - No Observed (Adverse) Effect Level; NOELR - No Observable Effect Loading Rate; NTP - National Toxicology Program; NZIoC - New Zealand Inventory of Chemicals; 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; RCRA - Resource Conservation and Recovery Act; REACH - Regulation (EC) No 1907/2006 of the European Parliament and of the Council concerning the Registration, Evaluation, Authorisation and Restriction of Chemicals; RO - Reportable Quantity; SADT - Self-Accelerating Decomposition Temperature; SARA - Superfund Amendments and Reauthorization Act; SDS - Safety Data Sheet; TCSI - Taiwan Chemical Substance Inventory; 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
Sources of key data used to compile the Material Safety Data Sheet:

Revision Date: 03/23/2020

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.