# SAFETY DATA SHEETS

## This SDS packet was issued with item:

078947617

N/A

# SAFETY DATA SHEET

Revision Date 12/12/2023 (v 1.0)

## SECTION 1 Identification of the substance / mixture and of the company / undertaking

### Product Identifiers

| | |
|---|---|
| **Product name:** | Ethiqa XR (Buprenorphine extended-release injectable suspension) 1.3 mg/mL CIII |
| **Chemical Name:** | Buprenorphine extended-release injectable suspension |
| **Proper shipping name:** | Not Applicable |
| **Chemical formula:** | Not Applicable |
| **Other means of identification:** | Not Available |
| **CAS number:** | 52485-79-7 |

### Relevant identified uses of the substance or mixture and uses advised against

| | |
|---|---|
| **Relevant identified uses:** | Use according to manufacturer's directions.<br>Analgesic for the control of moderate to severe pain therapy in mice, rats, and ferrets. |

### Details of the supplier of the safety data sheet

| | |
|---|---|
| **Registered company name:** | Fidelis Animal Health, Inc. |
| **Address:** | 685 US Highway One, Suite 265<br>North Brunswick, NJ 08902 United States |
| **Telephone:** | +1-855-801-0888 |
| **Website:** | www.EthiqaXR.com |
| **Email:** | info@FidelisAH.com |

### Emergency telephone number

| | |
|---|---|
| **Association / Organization:** | Not Available |
| **Emergency telephone numbers:** | Not Available |
| **Other emergency telephone numbers:** | Not Available |

## SECTION 2 Hazards identification

### Classification of the substance or mixture


**Risk Phrases:** Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

**Safety advice:**

Do not empty into drains.

This material and its container must be disposed of in a safe way.

Dispose of this material and its container at hazardous or special waste collection point.

Use appropriate container to avoid environmental contamination.

### Other hazards

Ingestion may produce health damage*.

May produce skin discomfort*.

## SECTION 3 Composition / information on ingredients

### Substances

See section below for composition of Mixtures

### Mixtures

| CAS No | %[weight] | Name |
|---|---|---|
| 100-51-6 | 1.02 | BENZYL ALCOHOL |
| 53152-21-9 | <0.2 | BUPRENORPHINE HYDROCHLORIDE |
| | | other ingredients determined to be non hazardous |

## SECTION 4 First aid measures

### Description of first aid measures

**Eye Contact:**

If this product comes in contact with the eyes or other mucous membranes:

- Wash out immediately with fresh running water and contact a physician immediately.
- Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.
- Seek medical attention without delay; if pain persists or recurs seek medical attention.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel. If wearing contact lenses, flush the eye first and then remove the contact lens.

**Skin Contact:**

If skin contact occurs:

- Immediately remove all contaminated clothing, including footwear.
- Flush skin and hair with running water (and soap if available) and contact physician.
- Seek medical attention in event of irritation.

**Inhalation:**

- If fumes, aerosols or combustion products are inhaled, remove from contaminated area.
- Other measures are usually unnecessary.

**Ingestion:**

- If swallowed do **NOT** induce vomiting.
- If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.
- Observe the patient carefully.
- Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious.
- Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink.
- Seek medical advice.

### Indication of any immediate medical attention and special treatment needed

Treat symptomatically for a narcotic analgesic.
A vigorous program of symptomatic and supportive therapy has saved many victims of poisoning. The single most important element in therapy is the correction of anoxia by all available means: the maintenance of a patent airway, the administration of oxygen, the use of artificial respiration, and the injection of specific narcotic antagonists such as nalorphine, levallorphan or naloxone promptly antagonizes the respiratory depression, coma and hypotension from overdoses of morphine, codeine, all semi-synthetics and almost all synthetic narcotics.
GOSSELIN et al: Clinical Toxicology of Commercial Products.
In fully conscious patients, remove swallowed poison by thorough gastric lavage and emesis. The chances of removing a significant amount of the drug are better if treatment is started within the first two hours. If the patient is unconscious or depressed, emesis is contraindicated and the dangers of gastric lavage are not justified.
DREISBACH AND ROBERTSON: Handbook of Poisoning, Appleton & Lange
Treat symptomatically.

## SECTION 5 Firefighting measures

### Extinguishing media

- Foam.
- Dry chemical powder.
- BCF (where regulations permit).
- Carbon dioxide.
- Water spray or fog - Large fires only.

### Special hazards arising from the substrate or mixture

**Fire Incompatibility:**

- Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result

### Advice for firefighters

**Fire Fighting:**

- Alert Fire Brigade and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.
- Prevent, by any means available, spillage from entering drains or water course.
- Use water delivered as a fine spray to control fire and cool adjacent area.
- Avoid spraying water onto liquid pools.
- **DO NOT** approach containers suspected to be hot.
- Cool fire exposed containers with water spray from a protected location.
- If safe to do so, remove containers from path of fire.

**Fire/Explosion Hazard:**

- Combustible.
- Slight fire hazard when exposed to heat or flame.
- Heating may cause expansion or decomposition leading to violent rupture of containers.
- On combustion, may emit toxic fumes of carbon monoxide (CO).
- May emit acrid smoke.
- Mists containing combustible materials may be explosive.

Combustion products include: carbon dioxide ($CO_2$) acrolein other pyrolysis products typical of burning organic material. May emit poisonous fumes. May emit corrosive fumes.
**CARE:** Water in contact with hot liquid may cause foaming and a steam explosion with wide scattering of hot oil and possible severe burns. Foaming may cause overflow of containers and may result in possible fire.

## SECTION 6 Accidental release measures

### Personal precautions, protective equipment and emergency procedures

**Minor Spills:**

Slippery when spilt.

- Remove all ignition sources.
- Clean up all spills immediately.
- Avoid breathing vapors and contact with skin and eyes.
- Control personal contact with the substance, by using protective equipment.
- Contain and absorb spill with sand, earth, inert material or vermiculite.
- Wipe up.
- Place in a suitable, labelled container for waste disposal.

**Major Spills:**

Slippery when spilt.
Moderate hazard.

- Clear area of personnel and move upwind.
- Alert Fire Brigade and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.
- Prevent, by any means available, spillage from entering drains or water course.
- No smoking, naked lights or ignition sources.
- Increase ventilation.
- Stop leak if safe to do so.
- Contain spill with sand, earth or vermiculite.
- Collect recoverable product into labelled containers for recycling.
- Absorb remaining product with sand, earth or vermiculite.
- Collect solid residues and seal in labelled drums for disposal.
- Wash area and prevent runoff into drains.
- If contamination of drains or waterways occurs, advise emergency services.

Personal Protective Equipment advice is contained in Section 8 of the MSDS.

## SECTION 7 Handling and storage

### Precautions for safe handling

**Safe handling:**

- Product should only be handled and administered by a veterinarian, veterinary technician, or laboratory staff trained in the handling of potent opioids.
- Avoid all personal contact, including inhalation.
- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- Prevent concentration in hollows and sumps.
- **DO NOT** enter confined spaces until atmosphere has been checked.
- Avoid smoking, naked lights or ignition sources
- Avoid contact with incompatible materials.
- When handling, **DO NOT** eat, drink or smoke.
- Keep containers securely sealed when not in use.
- Avoid physical damage to containers.
- Always wash hands with soap and water after handling.
- Work clothes should be laundered separately.

- Use good occupational work practice.
- Observe manufacturer's storage and handling recommendations contained within this MSDS.
- Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions.
- **DO NOT** allow clothing wet with material to stay in contact with skin

**Other information**

**NOTE:** Special security requirements may be mandated under Federal/State Regulation(s).

- Store in original containers.
- Store in vault fitted with warning devices or detectors recommended by various Federal/State authorities.
- Store in vault used only for the purpose of storage of drugs of addiction.
- Vault must be locked at all times except when the materials stored therein are required. Keep storage area free from debris, wastes and combustibles.
- Keep dry.
- Keep containers securely sealed.
- Protect containers against physical damage.
- Check regularly for spills and leaks.
- Use at room temperature under the supervision of Veterinarian or equivalent science personnel.

### Conditions for safe storage, including any incompatibilities

**Suitable container:**

5-10 ml glass vials with aluminum seals and rubber stoppers.

**Storage incompatibility:**

**NOTE**: Special security requirements may be mandated under Federal/State Regulation(s).

- Store in original containers.
- Store in vault fitted with warning devices or detectors recommended by various Federal/State authorities.
- Store in vault used only for the purpose of storage of drugs of addiction.
- Vault must be locked at all times except when the materials stored therein are required.
- Keep storage area free from debris, wastes and combustibles.
- Keep dry.
- Keep containers securely sealed.
- Protect containers against physical damage.
- Check regularly for spills and leaks.
- Avoid reaction with oxidizing agents

| | | | | | |
|---|---|---|---|---|---|
| + | + | + | + | X | + |

**X:** Must not be stored together
**0:** May be stored together with specific preventions
**+:** May be stored together

**Package Material Incompatibilities:**

## SECTION 8 Exposure controls / personal protection

### Control parameters

**Occupational Exposure Limits (OEL)**

**INGREDIENT DATA**

Not available.

**Emergency Limits**

| Ingredient | TEEL-0 | TEEL-1 | TEEL-2 | TEEL-3 |
|---|---|---|---|---|
| Benzyl alcohol | 10 (ppm) | **60 (ppm)** | **150 (ppm)** | **150 (ppm)** |

| Ingredient | Original IDLH | Revised IDLH |
|---|---|---|
| Ethiqa XR (1.3 mg/mL) | Not available | Not available |

### Exposure controls

**Appropriate engineering controls:**

Engineering controls are used to remove a hazard or place a barrier between the worker and the hazard. Well-designed engineering controls can be highly effective in protecting workers and will typically be independent of worker interactions to provide this high level of protection.

The basic types of engineering controls are:

- Process controls which involve changing the way a job activity or process is done to reduce the risk.
- Enclosure and/or isolation of emission source which keeps a selected hazard "physically" away from the worker and ventilation that strategically "adds" and "removes" air in the work environment.
- Ventilation can remove or dilute an air contaminant if designed properly. The design of a ventilation system must match the particular process and chemical or contaminant in use.

Employers may need to use multiple types of controls to prevent employee overexposure.
General exhaust is adequate under normal operating conditions. If risk of overexposure exists, wear SAA approved respirator. Correct fit is essential to obtain adequate protection.
Provide adequate ventilation in warehouse or closed storage areas. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.

| Type of Contaminant: | Air Speed: |
|---|---|
| solvent, vapors, degreasing etc., evaporating from tank (in still air) | 0.25-0.5 m/s (50-100 f/min) |
| aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers, welding, spray drift, plating acid fumes, pickling (released at low velocity into zone of active generation) | 0.5-1 m/s (100-200 f/min.) |
| direct spray, spray painting in shallow booths, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion) | 1-2.5 m/s (200-500 f/min) |
| grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion). | 2.5-10 m/s (500-2000 f/min.) |

Within each range the appropriate value depends on:

| Lower end of the range | Upper end of the range |
|---|---|
| 1: Room air currents minimal or favorable to capture | 1: Disturbing room air currents |
| 2: Contaminants of low toxicity or of nuisance value only | 2: Contaminants of high toxicity |
| 3: Intermittent, low production. | 3: High production, heavy use |
| 4: Large hood or large air mass in motion | 4: Small hood - local control only |

Simple theory shows that air velocity falls rapidly with distance away from the opening of a simple extraction pipe. Velocity generally decreases with the square of distance from the extraction point (in simple cases). Therefore, the air speed at the extraction point should be adjusted, accordingly, after reference to distance from the contaminating source. The air velocity at the extraction fan, for example, should be a minimum of 1-2 m/s (200-400 f/min.) for extraction of solvents generated in a tank 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.

**Personal protection:**

**Eye and face protection:**

- Safety glasses with side shields.
- Chemical goggles.
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59], [AS/NZS 1336 or national equivalent]

**Skin protection:**

See Hand protection below

**Hand protection:**

- Wear chemical protective gloves, e.g. PVC.
- Wear safety footwear or safety gumboots, e.g. Rubber

The selection of suitable gloves does not only depend on the material, but also on further marks of quality which vary from manufacturer to manufacturer. Where the chemical is a preparation of several substances, the resistance of the glove material can not be calculated in advance and has therefore to be checked prior to the application.
The exact break through time for substances has to be obtained from the manufacturer of the protective gloves and has to be observed when making a final choice. Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include:

- frequency and duration of contact, chemical resistance of glove material, glove thickness and
- dexterity

Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739, AS/NZS 2161.1 or national equivalent).

- When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended.
- Contaminated gloves should be replaced.

Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturizer is recommended.

**Body protection:**

See Other protection below

**Other protection:**

- Overalls.
- P.V.C. apron.
- Barrier cream.
- Skin cleansing cream.
- Eye wash unit.

**Thermal hazards:**

**Recommended material(s):**

PVC chemical resistant type.

**Respiratory protection:**

## SECTION 9 Physical and chemical properties

### Information on basic physical and chemical properties

**Appearance:**

Off white color odorless oily suspension; very slightly miscible with water.

| | |
|---|---|
| **Physical state** | Liquid |
| **Odor** | Not Available |
| **Odor threshold** | Not Available |
| **pH (as supplied)** | Not Available |
| **Melting point / freezing point (°C)** | Not Available |
| **Initial boiling point and boiling range (°C)** | Not Available |
| **Flash point (°C)** | Not Available |
| **Evaporation rate** | Not Available |
| **Flammability** | Not Available |
| **Upper Explosive Limit (%)** | Not Available |
| **Lower Explosive Limit (%)** | Not Available |
| **Vapor pressure (kPa)** | Not Available |
| **Solubility in water (g/L)** | Partly Miscible |
| **Vapor density (Air = 1)** | Not Available |

| | |
|---|---|
| **Relative density (Water = 1)** | 0.96 |
| **Partition coefficient n-octanol / water** | Not Available |
| **Auto-ignition temperature (°C)** | Not Available |
| **Decomposition temperature** | Not Available |
| **Viscosity (cSt)** | Not Available |
| **Molecular weight (g/mol)** | Not Applicable |
| **Taste** | Not Available |
| **Explosive properties** | Not Available |
| **Oxidizing properties** | Not Available |
| **Surface Tension (dyn/cm or mN/m)** | Not Available |
| **Volatile Component (%vol)** | Not Available |
| **Gas group** | Not Available |
| **pH as a solution(1%)** | Not Available |

## SECTION 10 Stability and reactivity

**Reactivity:**

See section 7

**Chemical stability:**

- All components are compatible.
- Product is considered stable.
- Hazardous polymerization will not occur.

**Possibility of hazardous reactions:**

See section 7

**Conditions to avoid:**

See section 7

**Incompatible materials:**

See section 7

**Hazardous decomposition products:**

See section 5

## SECTION 11 Toxicological information

### Information on toxicological effects

**Inhaled:**

The material is not thought to produce either adverse health effects or irritation of the respiratory tract following inhalation (as classified by EC Directives using animal models). Nevertheless, adverse systemic effects have been produced following exposure of animals by at least one other route and good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting. Serious, life-threatening, or fatal respiratory depression may occur with accidental exposure to or with misuse or abuse of the product.
Not normally a hazard due to non-volatile nature of product Inhalation of oil droplets/ aerosols may cause discomfort and may produce chemical pneumonitis.

**Ingestion:**

Accidental ingestion of the material may be damaging to the health of the individual.
The commonest side-effects of narcotic analgesics (including morphine) are nausea, vomiting, constipation, drowsiness, and confusion. Urination may be difficult and there may be spasm of the gastrointestinal and biliary tracts. Other symptoms include dry mouth, pin-point pupils, sweating, flushing, vertigo, slow shallow respiration, weak pulse, cyanosis, palpitations, orthostatic hypotension, hypothermia, restlessness, and mood changes. Reports of acute toxicity have also included pulmonary oedema, spasticity, occur. Larger doses may produce respiratory depression and hypotension, with circulatory failure and deepening coma. Death may occur as a result of respiratory failure.
As analgesia wears off, there may be an increased sensitivity to pain. High doses may produce muscular rigidity and central nervous system depression may progress to stupor, sedation, unconsciousness, and coma. in which skeletal muscles become flaccid (although positive Babinski reflexes and muscle twitching may be present) and the pupils become breathing, apnea and cyanosis. Pulmonary oedema is relatively common. Other respiratory problems include bronchospasm and aspiration pneumonia. Peripheral vasodilation may result in flushing of the face, neck and upper thorax and fainting resulting from orthostatic hypotension. Serious effects deriving from cardiovascular system toxicity include hypertension, arrhythmias, shock, acute ventricular failure and cardiac arrest. Hypersensitivities may result from histamine-release and may produce rashes, pruritis and, on occasion, haemorrhagic urticaria. Gastrointestinal system effects produce decreased gastric motility, constipation, faecal impaction, cramping and increased muscle tone of the gastrointestinal and biliary tracts. Urinary retention and depressed urine formation have been recorded. Liver function tests may be abnormal and the liver may become enlarged and tender. Mild leukocytosis, lymophocytosis, acidosis and hypoglycaemia may also occur. Anaphylactic reactions to morphine and codeine, following injection, have been reported.

**Skin Contact:**

- The material may produce moderate skin irritation; limited evidence or practical experience suggests, that the material either: produces moderate inflammation of the skin in a substantial number of individuals following direct contact and/or
- produces significant, but moderate, inflammation when applied to the healthy intact skin of animals (for up to four hours), such inflammation being present twenty-four hours or more after the end of the exposure period.

Skin irritation may also be present after prolonged or repeated exposure; this may result in a form of contact dermatitis (nonallergic). The dermatitis is often characterized by skin redness (erythema) and swelling (oedema) which may progress to blistering (vesiculation), scaling and thickening of the epidermis. At the microscopic level there may be intercellular oedema of the spongy layer of the skin (spongiosis) and intracellular oedema of the epidermis.
Open cuts, abraded or irritated skin should not be exposed to this material
Entry into the blood-stream through, for example, cuts, abrasions, puncture wounds or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

**Eye:**

Although the liquid is not thought to be an irritant (as classified by EC Directives), direct contact with the eye may produce transient discomfort characterized by tearing or conjunctival redness (as with windburn).

**Chronic:**

The symptoms of chronic poisoning or addiction may not be readily apparent. Pin-point pupils and rapid mood changes may be observed on occasion and the addict is usually not socially well integrated. Drug dependence of the morphine-type results from repeated administration and is characterized by an overwhelming need to continue taking the drug or one with similar properties and by a tendency to increase the dose owing to the development of tolerance, and by psychic or physiological and physical dependence on the drug. Physical dependence on morphine-like compounds has been reported in as little as two days whilst tolerance to morphine-like actions may occur over two to three weeks of moderate therapeutic doses. Prolonged therapy or abuse may produce abnormal pulmonary function, increased body temperature, myoglobinuria and renal failure. Some physiological values may not return to normal for several months following the acute withdrawal syndrome. Abrupt withdrawal of the opiates may produce yawning, mydriasis, lachrymation, rhinorrhea, sneezing, muscle tremor, headache, weakness, sweating, anxiety, irritability, disturbed sleep or insomnia, restlessness, orgasm, anorexia, anorexia, nausea, vomiting, loss of weight, diarrhoea, dehydration, leucocytosis, bone pain, abdominal and muscle cramps, increases in heart-rate, respiratory rate and blood pressure, rise in temperature and gooseflesh and vasomotor disturbance.
Glyceryl triesters (triglycerides), following ingestion, are metabolised to monoglycerides, free fatty acids and glycerol, all of which are absorbed in the intestinal mucosa and undergo further metabolism. Medium chain triglycerides (C8-C10) appear to have relatively rapid metabolism and elimination from blood and tissues compared to long chain triglycerides (C16-C18). Little or no acute, subchronic or chronic oral toxicity was seen in animal studies unless levels approached a significant percentage of calorific intake. Subcutaneous injections of tricaprylin in rats over a
five-week period caused granulomatous reaction characterized by oil deposits surrounded by macrophages. Diets containing substantial levels of tributyrin produced gastric lesions in rats fed for 3-35 weeks; the irritative effect of the substance was thought to be the cause of tissue damage.
Dermal application was not associated with significant irritation in rabbit skin; ocular exposures were, at most, mildly irritating to rabbit eyes. No evidence of sensitization or photosensitization was seen in a guinea pig maximization test. Most of the genotoxicity test systems were negative. Tricaprylin, trioctanoin and triolein have been used, historically, as vehicles in carcinogenicity testing of other chemicals. In one study, subcutaneous injection of tricaprylin, in newborn mice, produced more tumours in lymphoid tissue than were seen in untreated animals whereas, in another study, subcutaneous or intraperitoneal injection in 4- to 6-week old female mice produced no tumors. Trioctanoin injected subcutaneously in hamster produced no tumors; when injected intraperitoneally in pregnant rats there was an increase in mammary tumors among the off-spring but similar studies in pregnant hamsters and rabbits showed no tumors in the off-spring.
The National Toxicological Program conducted a 2-year study in rats given tricaprylin by gavage. The treatment was associated with a statistically significant dose-related increase in pancreatic acinar cell hyperplasia and adenoma but there were no acinar carcinomas.
Tricaprylin is not teratogenic to mice or rats but some reproductive effects were seen in rabbits. A low level of foetal eye abnormalities and a small percentage of abnormal sperm were reported in mice injected with trioctanoin.
Trioctanoin was also used as a vehicle control in a sperm abnormality test. Ten male control mice received an intraperitoneal
injection of 0.25 ml trioctanoin 0.05 g/kg of benz[a]pyrene (known reproductive toxicant and mutagen) daily for 5 days and sperm from caudae epididymides analysed. Based on these studies there is no sufficient evidence to classify the trioctanoin as reproductive toxicant.
|Buprenorphine appears to have similar adverse effects to morphine, with the possible exception of constipation. The most frequent side-effects of buprenorphine are drowsiness, nausea, vomiting, sweating and dizziness. Respiratory depression, euphoria, miosis, and dry mouth may occur.

| TOXICITY | IRRITATION |
|---|---|
| ***Ethiqa XR (buprenorphine extended-release injectable suspension) 1.3 mg/mL CIII*** | |
| Not Available | Not Available |
| ***benzyl alcohol*** | |
| Dermal (rabbit) LD50: 2000 mg/kg | Eye (rabbit): 0.75 mg open SEVERE |
| Inhalation (rat) LC50: >4178 mg/m3/4h | Skin (man): 16 mg/48h-mild |
| Inhalation (rat) LC50: 1000 ppm/8h | Skin (rabbit):10 mg/24h open-mild |
| Oral (rat) LD50: 1230 mg/kg | |
| Not Available | Not Available |
| ***buprenorphine hydrochloride*** | |
| Oral (mouse) LD50: 800 mg/kg | No data |
| Oral (rat) LD50: >1000 mg/kg | |
| Oral (rat) LD50: >600 mg/kg | |

Not available. Refer to individual constituents.

**BENZYL ALCOHOL**

The material may cause skin irritation after prolonged or repeated exposure and may produce a contact dermatitis (nonallergic). This form of dermatitis is often characterized by skin redness (erythema) and swelling the epidermis. Histologically there may be intercellular oedema of the spongy layer (spongiosis) and intracellular oedema of the epidermis.

**For benzyl alkyl alcohols**:
Unlike benzylic alcohols, the beta-hydroxyl group of the members of this cluster is unlikely to undergo phase II metabolic activation. Instead, the beta-hydroxyl group is expected to contribute to detoxification via oxidation to hydrophilic acid. Despite structural similarity to carcinogenic ethyl benzene, only a marginal concern has been assigned to phenethyl alcohol due to limited mechanistic analogy.
For benzoates:

**Acute toxicity:** Benzyl alcohol, benzoic acid and its sodium and potassium salt can be considered as a single category regarding human health, as they are all rapidly metabolized and excreted via a common pathway within 24 hrs. Systemic toxic effects of similar nature (e.g. liver, kidney) were observed. However, with benzoic acid and its salts toxic effects are seen at higher doses than with benzyl alcohol.
The compounds exhibit low acute toxicity as for the oral and dermal route. The LD50 values are > 2000 mg/kg bw except for benzyl alcohol which needs to be considered as harmful by the oral route in view of an oral LD50 of 1610 mg/kg bw. The 4 hrs inhalation exposure of benzyl alcohol or benzoic acid at 4 and 12 mg/l as aerosol/dust respectively gave no mortality, showing low acute toxicity by inhalation for these compounds.
Benzoic acid and benzyl alcohol are slightly irritating to the skin, while sodium benzoate was not skin irritating. No data are available for potassium benzoate but it is also expected not to be skin irritating. Benzoic acid and benzyl alcohol are irritating to the eye and sodium benzoate was only slightly irritating to the eye. No data are available for potassium benzoate but it is expected also to be only slightly irritating to the eye.

**Sensitization:** The available studies for benzoic acid gave no indication for a sensitizing effect in animals, however occasionally very low positive reactions were recorded with humans (dermatological patients) in patch tests. The same occurs for sodium benzoate. It has been suggested that the very low positive reactions are non-immunologic contact urticaria. Benzyl alcohol gave positive and negative results in animals. Benzyl alcohol also demonstrated a maximum incidence of sensitization of only 1% in human patch testing. Over several decades no sensitization with these compounds has been seen among workers.

**Repeat dose toxicity:** For benzoic acid repeated dose oral toxicity studies give a NOAEL of 800 mg/kg/day. For the salts values > 1000 mg/kg/day are obtained. At higher doses increased

mortality, reduced weight gain, liver and kidney effects were observed.
For benzyl alcohol the long-term studies indicate a NOAEL > 400 mg/kg bw/d for rats and > 200 mg/kg bw/d for mice. At higher doses effects on bodyweights, lesions in the brains, thymus, skeletal muscle and kidney were observed. It should be taken into account that administration in these studies was by gavage route, at which saturation of metabolic pathways is likely to occur.

**Mutagenicity:** All chemicals showed no mutagenic activity in in vitro Ames tests. Various results were obtained with other in vitro genotoxicity assays. Sodium benzoate and benzyl alcohol showed no genotoxicity in vivo. While some mixed and/or equivocal in vitro chromosomal/chromatid responses have been observed, no genotoxicity was observed in the in vivo cytogenetic, micronucleus, or other assays. The weight of the evidence of the in vitro and in vivo genotoxicity data indicates that these chemicals are not mutagenic or clastogenic. They also are not carcinogenic in long-term carcinogenicity studies.
In a 4-generation study with benzoic acid no effects on reproduction were seen (NOAEL: 750 mg/kg). No compound related effects on reproductive organs (gross and histopathology examination) could be found in the (sub) chronic studies in rats and mice with benzyl acetate, benzyl alcohol, benzaldehyde, sodium benzoate and supports a non-reprotoxic potential of these compounds. In addition, data from reprotoxicity studies on benzyl acetate (NOAEL >2000 mg/kg bw/d; rats and mice) and benzaldehyde (tested only up to 5 mg/kg bw; rats) support the non-reprotoxicity of benzyl alcohol and benzoic acid and its salts.

**Developmental toxicity:** In rats for sodium benzoate dosed via food during the entire gestation developmental effects occurred only in the presence of marked maternal toxicity (reduced food intake and decreased body weight) (NOAEL = 1400 mg/kg bw). For hamster (NOEL: 300 mg/kg bw), rabbit (NOEL: 250 mg/kg bw) and mice (CD-1 mice, NOEL: 175 mg/kg bw) no higher doses (all by gavage) were tested and no maternal toxicity was observed. For benzyl alcohol: NOAEL= 550 mg/kg bw (gavage; CD-1 mice). LOAEL = 750 mg/kg bw (gavage mice). In this study maternal toxicity was observed e.g. increased mortality, reduced body weight and clinical toxicology. Benzyl acetate: NOEL = 500 mg/kg bw (gavage rats). No maternal toxicity was observed.

***BUPRENORPHINE HYDROCHLORIDE***

**WARNING:** Abuse can lead to habituation. Subject to Federal and State Regulations. Narcotic Substance, Schedule I (UN).
Oral (mouse) LD50: 260-261 mg/kg [Tasmanian Alkaloids] (Behavioural effects) Reproductive effects:- (Effects on Newborn- viability, behavioural, physical)

| | | | |
|---|---|---|---|
| **Acute Toxicity:** | Not Applicable | **Carcinogenicity:** | Not Applicable |
| **Skin Irritation/Corrosion:** | Not Applicable | **Reproductivity:** | Not Applicable |
| **Serious Eye Damage/Irritation:** | Not Applicable | **STOT - Single Exposure:** | Not Applicable |
| **Respiratory or Skin sensitization:** | Not Applicable | **STOT - Repeated Exposure:** | Not Applicable |
| **Mutagenicity:** | Not Applicable | **Aspiration Hazard:** | Not Applicable |

**CMR STATUS**

## SECTION 12 Ecological information

### Toxicity

Harmful to aquatic organisms, may cause long-term adverse effects in the aquatic environment.
Do NOT allow product to come in contact with surface waters or to intertidal areas below the mean high water mark. Do not contaminate water when cleaning equipment or disposing of equipment wash-waters.
Wastes resulting from use of the product must be disposed of on site or at approved waste sites.
DO NOT discharge into sewer or waterways.

### Persistence and degradability

| Ingredient | Persistence: Water/Soil | Persistence: Air |
|---|---|---|
| Not Available | Not Available | Not Available |

### Bioaccumulative potential

| Ingredient | Bioaccumulation |
|---|---|
| Not Available | Not Available |

### Mobility in soil

| Ingredient | Mobility |
|---|---|
| Not Available | Not Available |

## SECTION 13 Disposal considerations

### Waste treatment methods

**Product / Packaging disposal:**

- **DO NOT** allow wash water from cleaning or process equipment to enter drains. It may be necessary to collect all wash water for treatment before disposal.
- In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first. Where in doubt contact the responsible authority.
  Valuable substance, hold all residues for recovery. Disposal of the material must be carried out in accordance with the requirements of the relevant Federal/State Act(s) or Code(s) regulating the disposal of Drugs of Addiction.
- Consult manufacturer/supplier for recycling options.
- Decontaminate empty containers with water; incinerate plastic bags.
- **DO NOT** reuse containers. Bury empty containers in an authorized landfill.
- Recycle wherever possible or consult manufacturer for recycling options.
- Consult State Land Waste Authority for disposal.
- Bury or incinerate residue at an approved site.
- Recycle containers if possible, or dispose of in an authorized landfill.

## SECTION 14 Transport information

**Labels Required:**

**Marine Pollutant: NO**

**Land transport (DOT): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS**

**Air transport (ICAO-IATA / DGR): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS**

**Sea transport (IMDG-Code / GGVSee): NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS**

**Transport in bulk according to Annex II of MARPOL 73 / 78 and the IBC code**

| Source | Ingredient | Pollution Category | Residual Concentration - Outside Special Area (% w/w) | Residual Concentration |
|---|---|---|---|---|
| IMO MARPOL 73/78 (Annex II) - List of Noxious Liquid Substances Carried in Bulk | benzyl alcohol | C | | |

## SECTION 15 Regulatory information

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

**benzyl alcohol(100-51-6) is found on the following regulatory lists**

"US National Toxicology Program (NTP) Technical Reports Index","US Toxic Substances Control Act (TSCA) - Chemical Substance Inventory","US DOE Temporary Emergency Exposure Limits (TEELs)","US - Pennsylvania - Hazardous Substance List","Sigma-AldrichTransport Information","Acros Transport Information","US DOT Coast Guard Bulk Hazardous Materials - List of Flammable and Combustible Bulk Liquid Cargoes","US CAA (Clean Air Act) - HON Rule - Organic HAPs (Hazardous Air Pollutants)","US CAA (Clean Air Act) - HON Rule - Synthetic Organic Chemical Manufacturing Industry Chemicals","GESAMP/EHS Composite List - GESAMP Hazard Profiles","IMO IBC Code Chapter 17: Summary of minimum requirements","US Coast Guard, Department of Homeland Security Part 153: Ships Carrying Bulk Liquid, Liquefied gas or compressed gas hazardous materials. Table 1 to Part 153 --Summary of Minimum Requirements","International Fragrance Association IFRA Standards Annex I","US Cosmetic Ingredient Review (CIR) Cosmetic ingredients found safe as used","International Fragrance Association (IFRA) Survey: Transparency List","IOFI Global Reference List of Chemically Defined Substances","US FDA Indirect Food Additives - Substances for use as Components of Coatings - Resinous and polymeric coatings 21CFR 175-300","International Fragrance Association (IFRA) Standards Restricted","OECD List of High Production Volume (HPV) Chemicals","US American Cleaning Institute Cleaning Product Ingredient Inventory","International Numbering System for Food Additives","US FDA Indirect Food Additives: Adhesives and Components of Coatings - Substances for Use Only as Components of Adhesives - Adhesives","US RCRA (Resource Conservation & Recovery Act) - Appendix IX to Part 264 Ground-Water Monitoring List 1","US RCRA (Resource Conservation & Recovery Act) - List of Hazardous Inorganic and Organic Constituents","US NTP (National Toxicology Program) - Management Status Report","US - Massachusetts - Right To Know Listed Chemicals","IMO MARPOL 73/78 (Annex II) - List of Noxious Liquid Substances Carried in Bulk","US - Minnesota Hazardous Substance List","US FDA Everything Added to Food in the United States (EAFUS)","US EPA High Production Volume Program Chemical List","International Council of Chemical Associations (ICCA) - High Production Volume List","US FMA Air Freshener Fragrance Ingredient Survey Results","US AIHA Workplace Environmental Exposure Levels (WEELs)","US NFPA Fire Hazard Properties of Flammable Liquids, Gases, and Volatile Solids Table","International Maritime Dangerous Goods Requirements (IMDG Code) - Substance Index","Regulations concerning the International Carriage of Dangerous Goods by Rail - Table A: Dangerous Goods List - RID 2013 (English)","US Postal Service (USPS) Numerical Listing of Proper Shipping Names by Identification (ID) Number","US Department of Transportation (DOT), Hazardous Material Table","International Air Transport Association (IATA) Dangerous Goods Regulations","US Postal Service (USPS) Hazardous Materials Table: Postal Service Mailability Guide","International Maritime Dangerous Goods Requirements (IMDG Code)"

**buprenorphine hydrochloride(53152-21-9) is found on the following regulatory lists**

"Sigma-AldrichTransport Information","US FDA Maximum Recommended Therapeutic Dose (MRTD) Database","United Nations List of psychotropic substances under international control - Pure drug content of bases and salts","US - Connecticut - Schedules of Controlled Substances - Schedule III","US - Arizona Controlled Substances Schedule III","US - West Virginia Uniform Controlled Substances Act - Schedule V","US - Arkansas - Controlled Substances Schedule III","US - Alabama Controlled Substances List Schedule III","US - California Schedule V Controlled Substances","US Harmonized Tariff Schedule - Pharmaceutical Appendix","US FDA Controlled Substances Schedule III","US - Utah Secondary Drinking Water Standards - Inorganic Contaminants","US - Massachusetts Drinking Water - Secondary Contaminants Maximum Contaminant Levels (MCLs)","WHO Guidelines for Drinking-water Quality - Chemicals for which guideline values have not been established"

## SECTION 16 Other information

**Other information:**

The (M)SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.
This SDS applies only to the material as packaged. If this product is combined with other materials, deteriorates, or becomes contaminated, it may pose hazards not mentioned in this SDS. Fidelis Animal Health, Inc. assumes no responsibility for incidental or consequential damages, including lost profits, arising from the use of these data. It shall be the user's responsibility to develop proper methods of handling and personal protection based on the actual conditions of use. While this SDS is based on technical data judged to be reliable, Fidelis Animal Health, Inc. assumes no responsibility for the completeness or accuracy of the information contained herein.