Virbac Septicide Antiseptic Cream With Insecticide

Virbac (Australia) Pty Limited

Chemwatch: 8179-53
Version No: 5.1.1.1
Safety Data Sheet according to WHS and ADG requirements

SECTION 1 IDENTIFICATION OF THE SUBSTANCE / MIXTURE AND OF THE COMPANY / UNDERTAKING

Product Identifier

| Product name | Virbac Septicide Antiseptic Cream With Insecticide |
| Synonyms | APVMA No: 38896 |
| Proper shipping name | ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (contains alcohols C16-18 ethoxylated) |
| Other means of identification | Not Available |

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

| Relevant identified uses | For use in wounds on horses and dogs, especially where fly-strike is likely to occur. |

Details of the supplier of the safety data sheet

| Registered company name | Virbac (Australia) Pty Limited |
| Address | 361 Horsley Road Milperra NSW 2214 Australia |
| Telephone | 1800 242 100 |
| Fax | +61 2 9772 9773 |
| Website | www.virbac.com.au |
| Email | au_customerservice@virbac.com.au |

Emergency telephone number

| Association / Organisation | Poisons Information Centre |
| Emergency telephone numbers | 13 11 26 |
| Other emergency telephone numbers | Not Available |

SECTION 2 HAZARDS IDENTIFICATION

Classification of the substance or mixture

| Poisons Schedule | Not Applicable |
| Classification [1] | Skin Corrosion/Irritation Category 2, Serious Eye Damage Category 1, Skin Sensitizer Category 1, Acute Aquatic Hazard Category 1, Chronic Aquatic Hazard Category 1 |

Legend:


Label elements

| GHS label elements |

Continued...
Hazard statement(s)

H315 Causes skin irritation.
H318 Causes serious eye damage.
H317 May cause an allergic skin reaction.
H410 Very toxic to aquatic life with long lasting effects.

Precautionary statement(s)

Prevention

P280 Wear protective gloves/protective clothing/eye protection/face protection.
P261 Avoid breathing mist/vapours/spray.
P273 Avoid release to the environment.
P272 Contaminated work clothing should not be allowed out of the workplace.

Response

P305+P351+P338 IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P310 Immediately call a POISON CENTER or doctor/physician.
P362 Take off contaminated clothing and wash before reuse.
P333+P313 IF ON SKIN: Wash with plenty of soap and water.
P391 Collect spillage.

Storage

Not Applicable

Disposal

P501 Dispose of contents/container in accordance with local regulations.

SECTION 3 COMPOSITION / INFORMATION ON INGREDIENTS

Substances

See section below for composition of Mixtures

Mixtures

<table>
<thead>
<tr>
<th>CAS No</th>
<th>%[weight]</th>
<th>Name</th>
</tr>
</thead>
<tbody>
<tr>
<td>68439-49-6</td>
<td>10-25</td>
<td>alcohols C16-18 ethoxylated</td>
</tr>
<tr>
<td>134-62-3</td>
<td>1-5</td>
<td>N,N-diethyl-m-toluamide</td>
</tr>
<tr>
<td>113-48-4</td>
<td>1-5</td>
<td>2-ethylhexyl bicycloheptene dicarboximide</td>
</tr>
<tr>
<td>119-36-8</td>
<td>1-2</td>
<td>methyl salicylate</td>
</tr>
<tr>
<td>52645-53-1</td>
<td>0-1</td>
<td>permethrin</td>
</tr>
<tr>
<td>1811-28-5</td>
<td>0-1</td>
<td>proflavine hemisulfate dihydrate</td>
</tr>
<tr>
<td>Not Available</td>
<td>&gt;60</td>
<td>Ingredients determined not to be hazardous</td>
</tr>
</tbody>
</table>

SECTION 4 FIRST AID MEASURES

Description of first aid measures

Eye Contact

If this product comes in contact with the eyes:
- Immediately hold eyelids apart and flush the eye continuously with running water.
- 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.
- Continue flushing until advised to stop by the Poisons Information Centre or a doctor, or for at least 15 minutes.
- Transport to hospital or doctor without delay.
- Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

Skin Contact

If skin contact occurs:
- Immediately remove all contaminated clothing, including footwear.
- Flush skin and hair with running water (and soap if available).
- Seek medical attention in event of irritation.
Indication of any immediate medical attention and special treatment needed

for salicylate intoxication:

- Pending gastric lavage, use emetics such as syrup of ipecac or delay gastric emptying and absorption by swallowing a slurry of activated charcoal. **Do not give ipecac after charcoal.**
- Gastric lavage with water or perhaps sodium bicarbonate solution (3%-5%). Mild alkali delays salicylate absorption from the stomach and perhaps slightly from the duodenum.
- Saline catharsis with sodium or magnesium sulfate (15-30 gm in water).
- Take an immediate blood sample for an appraisal of the patient's acid-base status. A pH determination on an anaerobic sample of arterial blood is best. An analysis of the plasma salicylate concentration should be made at the same time. Laboratory controls are almost essential for the proper management of severe salicylism.
- In the presence of an established acidosis, alkali therapy is essential, but at least in an adult, alkali should be withheld until its need is demonstrated by chemical analysis. The intensity of treatment depends on the intensity of acidosis. In the presence of vomiting, intravenous sodium bicarbonate is the most satisfactory of all alkali therapy.
- Correct dehydration and hypoglycaemia (if present) by the intravenous administration of glucose in water or in isotonic saline. The administration of glucose may also serve to remedy ketosis which is often seen in poisoned children.
- Even in patients without hypoglycaemia, infusions of glucose adequate to produce distinct hyperglycaemia are recommended to prevent glucose depletion in the brain. This recommendation is based on impressive experimental data in animals.
- Renal function should be supported by correcting dehydration and incipient shock. Overhydration is not justified. An alkaline urine should be maintained by the administration of alkali if necessary with care to prevent a severe systemic alkalosis. As long as urine remains alkaline (pH above 7.5), administration of an osmotic diuretic such as mannitol or perhaps THAM is useful, but one must be careful to avoid hypokalaemia. Supplements of potassium chloride should be included in parenteral fluids.
- Small doses of barbiturates, diazepam, paraldehyde, or perhaps other sedatives (but probably not morphine) may be required to suppress extreme restlessness and convulsions.
- For hyperpyrexia, use sponge baths.

The presence of petechiae or other signs of haemorrhagic tendency calls for a large Vitamin K dose and perhaps ascorbic acid. Minor transfusions may be necessary since bleeding in salicylism is not always due to a prothrombin effect.
- Haemodialysis and haemoperfusion have proved useful in salicylate poisoning, as have peritoneal dialysis and exchange transfusions, but alkaline diuretic therapy is probably sufficient except in fulminating cases.

[GOsselin, et al.: *Clinical Toxicology of Commercial Products*]

The mechanism of the toxic effect involves metabolic acidosis, respiratory alkalosis, hypoglycaemia, and potassium depletion. Salicylate poisoning is characterised by extreme acid-base disturbances, electrolyte disturbances and decreased levels of consciousness. There are differences between acute and chronic toxicity and a varying clinical picture which is dependent on the age of the patient and their kidney function. The major feature of poisoning is metabolic acidosis due to "uncoupling of oxidative phosphorylation" which produces an increased metabolic rate, increased oxygen consumption, increased formation of carbon dioxide, increased heat production and increased utilisation of glucose. Direct stimulation of the respiratory centre leads to hyperventilation and respiratory alkalosis. This leads to compensatory increased renal excretion of bicarbonate which contributes to the metabolic acidosis which may coexist or develop subsequently. Hypoglycaemia may occur as a result of increased glucose demand, increased rates of tissue glycolysis, and impaired rate of glucose synthesis. **NOTE:** Tissue glucose levels may be lower than plasma levels. Hyperglycaemia may occur due to increased glycolysis. Potassium depletion occurs as a result of increased renal excretion as well as intracellular movement of potassium.

Salicylates competitively inhibit vitamin K dependent synthesis of factors II, VII, IX, X and in addition, may produce a mild dose dependent hepatitis. Salicylates are bound to albumin. The extent of protein binding is concentration dependent (and falls with higher blood levels). This, and the effects of acidosis, decreasing ionisation, means that the volume of distribution increases markedly in overdose as does CNS penetration. The extent of protein binding (50-80%) and the rate of metabolism are concentration dependent. Hepatic clearance has zero order kinetics and thus the therapeutic half-life of 2-4.5 hours but the half-life in overdose is 18-36 hours. Renal excretion is the most important route in overdose. Thus when the salicylate concentrations are in the toxic range there is increased tissue distribution and impaired clearance of the drug.

HyperTox 3.0 https://www.ozemail.com.au/-ouad/SALI0001.HTA

Treat symptomatically.

For chronic or short term repeated exposures to pyrethrum and synthetic pyrethroids:

- Mammalian toxicity of pyrethrum and synthetic pyrethroids is low, in part because of poor bioavailability and a large first pass extraction by the liver.
- The most common adverse reaction results from the potent sensitising effects of pyrethrins.
- Clinical manifestations of exposure include contact dermatitis (erythema, vesiculation, bullae); anaphylactoid reactions (pallor, tachycardia, diaphoresis)
and asthma. [Ellenhorn Barceloux]

In cases of skin contact, it has been reported that topical application of Vitamin E Acetate (alpha-tocopherol acetate) has been found to have high therapeutic value, eliminating almost all skin pain associated with exposure to synthetic pyrethroids. [Incitec]

SECTION 5 FIREFIGHTING MEASURES

Extinguishing media
The product contains a substantial proportion of water, therefore there are no restrictions on the type of extinguishing media which may be used. Choice of extinguishing media should take into account surrounding areas.

Though the material is non-combustible, evaporation of water from the mixture, caused by the heat of nearby fire, may produce floating layers of combustible substances.

In such an event consider:
- foam.
- dry chemical powder.
- carbon dioxide.

Special hazards arising from the substrate or mixture

| Fire Incompatibility | None known. |

Advice for firefighters

- Alert Fire Brigade and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves in the event of a fire.
- Prevent, by any means available, spillage from entering drains or water courses.
- Use fire fighting procedures suitable for surrounding area.
- 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.
- Equipment should be thoroughly decontaminated after use.

Fire/Explosion Hazard

The emulsion is not combustible under normal conditions. However, it will break down under fire conditions and the hydrocarbon component will burn.

Decomposes on heating and produces toxic fumes of:
- carbon dioxide (CO2)
- nitrogen oxides (NOx)
- sulfur oxides (SOx)
- other pyrolysis products typical of burning organic material.

HAZCHEM
- 3Z

SECTION 6 ACCIDENTAL RELEASE MEASURES

Personal precautions, protective equipment and emergency procedures
See section 8

Environmental precautions
See section 12

Methods and material for containment and cleaning up

| Minor Spills | Environmental hazard - contain spillage.
- Clean up all spills immediately.
- Avoid contact with skin and eyes.
- Wear impervious gloves and safety goggles.
- Trowel up/scrape up.
- Place spilled material in clean, dry, sealed container.
- Flush spill area with water.
- Clean up all spills immediately.
- Avoid breathing vapours 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.

Continued...
Major Spills

- 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.
- Stop leak if safe to do so.
- Contain spill with sand, earth or vermiculite.
- Collect recoverable product into labelled containers for recycling.
- Neutralise/decontaminate residue (see Section 13 for specific agent).
- Collect solid residues and seal in labelled drums for disposal.
- Wash area and prevent runoff into drains.
- After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using.
- If contamination of drains or waterways occurs, advise emergency services.

Environmental hazard - contain spillage.

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

SECTION 7 HANDLING AND STORAGE

Precautions for safe handling

- Overheating of ethoxylates/alkoxylates in air should be avoided. When some ethoxylates are heated vigorously in the presence of air or oxygen, at temperatures exceeding 160 C, they may undergo exothermic oxidative degeneration resulting in self-heating and autoignition.
- Nitrogen blanketing will minimise the potential for ethoxylate oxidation. Prolonged storage in the presence of air or oxygen may cause product degradation. Oxidation is not expected when stored under a nitrogen atmosphere. Inert gas blanket and breathing system needed to maintain color stability. Use dry inert gas having at least -40 C dew point.
- Trace quantities of ethylene oxide may be present in the material. Although these may accumulate in the headspace of storage and transport vessels, concentrations are not expected to exceed levels which might produce a flammability or worker exposure hazard.
- 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.
- DO NOT allow material to contact humans, exposed food or food utensils.
- 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. Launder contaminated clothing before re-use.
- Use good occupational work practice.
- Observe manufacturer's storage and handling recommendations contained within this SDS.
- Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.

Ethoxylates/alkoxylates react slowly with air or oxygen and may generate potentially sensitising intermediates (haptens). Storage under heated conditions in the presence of air or oxygen increases reaction rate. For example, after storing at 95 F/35 C for 30 days in the presence of air, there is measurable oxidation of the ethoxylate. Lower temperatures will allow for longer storage time and higher temperatures will shorten the storage time if stored under an air or oxygen atmosphere.

Other information

- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials and foodstuff containers.
- Protect containers against physical damage and check regularly for leaks.
- Observe manufacturer's storage and handling recommendations contained within this SDS.

Conditions for safe storage, including any incompatibilities

Suitable container

- Polyethylene or polypropylene container.
- Packing as recommended by manufacturer.
- Check all containers are clearly labelled and free from leaks.

Storage incompatibility

- Avoid reaction with oxidising agents
- 44acidabase

SECTION 8 EXPOSURE CONTROLS / PERSONAL PROTECTION

Control parameters
**OCCUPATIONAL EXPOSURE LIMITS (OEL)**

**INGREDIENT DATA**
Not Available

**EMERGENCY LIMITS**

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Material name</th>
<th>TEEL-1 (mg/m^3)</th>
<th>TEEL-2 (mg/m^3)</th>
<th>TEEL-3 (mg/m^3)</th>
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</thead>
<tbody>
<tr>
<td>alcohols C16-18 ethoxylated</td>
<td>Ethoxylated alcohols, C16-18; (Nonionic surfactant)</td>
<td>3.8</td>
<td>42</td>
<td>250</td>
</tr>
<tr>
<td>methyl salicylate</td>
<td>Methyl salicylate</td>
<td>2.3 ppm</td>
<td>25 ppm</td>
<td>150 ppm</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Original IDLH</th>
<th>Revised IDLH</th>
</tr>
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<tbody>
<tr>
<td>alcohols C16-18 ethoxylated</td>
<td>Not Available</td>
<td>Not Available</td>
</tr>
<tr>
<td>N,N-diethyl-m-toluamide</td>
<td>Not Available</td>
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</tr>
<tr>
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<td>Not Available</td>
<td>Not Available</td>
</tr>
<tr>
<td>Ingredients determined not to be hazardous</td>
<td>Not Available</td>
<td>Not Available</td>
</tr>
</tbody>
</table>

**MATERIAL DATA**

**Exposure 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.

Local exhaust ventilation usually required. If risk of overexposure exists, wear approved respirator. Correct fit is essential to obtain adequate protection. Supplied-air type respirator may be required in special circumstances. Correct fit is essential to ensure adequate protection.

An approved self contained breathing apparatus (SCBA) may be required in some situations.

Provide adequate ventilation in warehouse or closed storage area. 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.

<table>
<thead>
<tr>
<th>Type of Contaminant</th>
<th>Air Speed:</th>
</tr>
</thead>
<tbody>
<tr>
<td>solvent, vapours, degreasing etc., evaporating from tank (in still air).</td>
<td>0.25-0.5 m/s (50-100 f/min.)</td>
</tr>
<tr>
<td>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)</td>
<td>0.5-1 m/s (100-200 f/min.)</td>
</tr>
<tr>
<td>direct spray, spray painting in shallow booths, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)</td>
<td>1-2.5 m/s (200-500 f/min.)</td>
</tr>
<tr>
<td>grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion).</td>
<td>2.5-10 m/s (500-2000 f/min.)</td>
</tr>
</tbody>
</table>

Within each range the appropriate value depends on:

- Lower end of the range: Room air currents minimal or favourable to capture
- Upper end of the range: Disturbing room air currents
- 1: Contaminants of low toxicity or of nuisance value only.
- 2: Contaminants of high toxicity
- 3: Intermittent, low production.
- 3: High production, heavy use
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

- 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 lenses 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]

### 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 lenses 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

### Hands/feet protection

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

**NOTE:**

- The material may produce skin sensitisation in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.
- Contaminated leather items, such as shoes, belts and watch-bands should be removed and destroyed.

### Body protection

See Other protection below

### Other protection

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

### Thermal hazards

Not Available

### Recommended material(s)

#### GLOVE SELECTION INDEX

Glove selection is based on a modified presentation of the: "Forsberg Clothing Performance Index". The effect(s) of the following substance(s) are taken into account in the computer-generated selection:

**Virbac Septicide Antiseptic Cream With Insecticide**

<table>
<thead>
<tr>
<th>Material</th>
<th>CPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>BUTYL</td>
<td>C</td>
</tr>
<tr>
<td>NATURAL RUBBER</td>
<td>C</td>
</tr>
<tr>
<td>NEOPRENE</td>
<td>C</td>
</tr>
<tr>
<td>PVA</td>
<td>C</td>
</tr>
<tr>
<td>VITON</td>
<td>C</td>
</tr>
</tbody>
</table>

* CPI - Chemwatch Performance Index

A: Best Selection
B: Satisfactory; may degrade after 4 hours continuous immersion
C: Poor to Dangerous Choice for other than short term immersion

**NOTE:** As a series of factors will influence the actual performance of the glove, a final selection must be based on detailed observation. -

* Where the glove is to be used on a short term, casual or infrequent basis, factors such as "feel" or convenience (e.g. disposability), may dictate a choice of gloves which might otherwise be unsuitable following long-term or frequent use. A qualified practitioner should be consulted.

### Respiratory protection


Where the concentration of gas/particulates in the breathing zone, approaches or exceeds the "Exposure Standard" (or ES), respiratory protection is required. Degree of protection varies with both face-piece and Class of filter; the nature of protection varies with Type of filter.

<table>
<thead>
<tr>
<th>Required Minimum Protection Factor</th>
<th>Half-Face Respirator</th>
<th>Full-Face Respirator</th>
<th>Powered Air Respirator</th>
</tr>
</thead>
<tbody>
<tr>
<td>up to 10 x ES</td>
<td>A-AUS P2</td>
<td>-</td>
<td>A-PAPR-AUS / Class 1 P2</td>
</tr>
<tr>
<td>up to 50 x ES</td>
<td>-</td>
<td>A-AUS / Class 1 P2</td>
<td>-</td>
</tr>
<tr>
<td>up to 100 x ES</td>
<td>-</td>
<td>A-2 P2</td>
<td>A-PAPR-2 P2 ^</td>
</tr>
</tbody>
</table>

^ - Full-face

A(All classes) = Organic vapours, B AUS or B1 = Acid gasses, B2 = Acid gas or hydrogen cyanide(HCN), B3 = Acid gas or hydrogen cyanide(HCN), E = Sulfur dioxide(SO2), G = Agricultural chemicals, K = Ammonia(NH3), Hg = Mercury, NO = Oxides of nitrogen, MB = Methyl bromide, AX = Low boiling point organic compounds(below 65 degC)
### SECTION 9 PHYSICAL AND CHEMICAL PROPERTIES

Information on basic physical and chemical properties

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Appearance</td>
<td>Golden yellow viscous cream; mixes with water.</td>
</tr>
<tr>
<td>Physical state</td>
<td>Free-flowing Paste</td>
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<tr>
<td>Relative density (Water = 1)</td>
<td>0.901</td>
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<tr>
<td>Odour</td>
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<td>Odour threshold</td>
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<td>pH (as supplied)</td>
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<td>Melting point/freezing point (°C)</td>
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<td>Initial boiling point and boiling range (°C)</td>
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<td>Flash point (°C)</td>
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<tr>
<td>Evaporation rate</td>
<td>Not Available</td>
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<td>Flammability</td>
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<tr>
<td>Upper Explosive Limit (%)</td>
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<td>Lower Explosive Limit (%)</td>
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<tr>
<td>Vapour pressure (kPa)</td>
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<tr>
<td>Solubility in water (g/L)</td>
<td>Immiscible</td>
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<td>Vapour density (Air = 1)</td>
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<tr>
<td>Molecular weight (g/mol)</td>
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<tr>
<td>Auto-ignition temperature (°C)</td>
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<tr>
<td>Auto-ignition temperature</td>
<td>Not Available</td>
</tr>
<tr>
<td>Partition coefficient n-octanol/water</td>
<td>Not Available</td>
</tr>
<tr>
<td>Decomposition temperature</td>
<td>Not Available</td>
</tr>
<tr>
<td>Viscosity (cSt)</td>
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<tr>
<td>Taste</td>
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</tr>
<tr>
<td>Explosive properties</td>
<td>Not Available</td>
</tr>
<tr>
<td>Oxidising properties</td>
<td>Not Available</td>
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<tr>
<td>Surface Tension (dyn/cm or mN/m)</td>
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</tr>
<tr>
<td>Volatile Component (%vol)</td>
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</tr>
<tr>
<td>Gas group</td>
<td>Not Available</td>
</tr>
<tr>
<td>pH as a solution (1%)</td>
<td>Not Available</td>
</tr>
<tr>
<td>VOC g/L</td>
<td>Not Available</td>
</tr>
</tbody>
</table>

### SECTION 10 STABILITY AND REACTIVITY

Reactivity
See section 7

Chemical stability
- Unstable in the presence of incompatible materials.
- Product is considered stable.
- Hazardous polymerisation 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 respiratory irritation (as classified by EC Directives using animal models). Nevertheless inhalation, of the material, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.

Inhalation of vapours may cause drowsiness and dizziness. This may be accompanied by narcosis, reduced alertness, loss of reflexes, lack of coordination and vertigo.

Inhalation of vapours or aerosols (mists, fumes), generated by the material during the course of normal handling, may be damaging to the health of the individual.

Inhalation of pyrethrins may produce nausea, vomiting, sneezing, serious nasal discharge, nasal stuffiness and asthma. High concentrations may produce hyperexcitability, incoordination, tremors, muscular paralysis and death (due to respiratory failure).

There have been some reports of transient facial tingling (paraesthesia) which lasts a few hours after exposure. In common with natural pyrethrins, the material may produce central nervous system stimulation with nausea, vomiting, gastroenteritis, diarrhoea, hypersensitivity, incoordination, tremors, muscle paralysis, convolution, coma, and respiratory...
failure. Synthetic pyrethroids are neuropoisons acting on the axons in the peripheral and central nervous systems by interacting with sodium channels in mammals and/or insects. A single dose produces toxic signs in mammals, such as tremors, hyperexcitability, salivation, choreoathetosis (a condition characterised by aimless muscle movements and involuntary motions), and paralysis. The signs disappear fairly rapidly, and the animals recover, generally within a week. At near-lethal dose levels, synthetic pyrethroids cause transient changes in the nervous system, such as axonal swelling and/or breaks and myelin degeneration in the sciatic nerves. They are not considered to cause delayed neurotoxicity of the kind induced by some organophosphorus compounds. Pyrethroids have at least two distinct actions- a short-term pharmacological effect at near-lethal dose levels and a more long-term neurotoxic effect that results in sparse axonal nerve damage.

This synthetic pyrethroid produces Type I poisoning syndrome (or "T" syndrome which is characteristic of those esters lacking an alpha-cyano substituent) and, in rats, causes such signs as sparring and aggressive behaviour, enhanced startle response, whole body tremor and prostration. Evidence indicates that Type I syndrome involves peripheral nerves in the mammal. Although this insecticide cannot be considered highly toxic in mammals its use indoors, in enclosed and poorly ventilated spaces may result in toxic effects in humans. Although natural pyrethroid produces allergic responses (rather than direct neurotoxicity) there is little evidence of allergic-type responses amongst humans exposed to the synthetic pyrethroid esters.

[ Cassaret & Doul's Toxicology: The Basic Science of Poisoning, 4th Ed.]

**Ingestion**

Nonionic surfactants may produce localised irritation of the oral or gastrointestinal mucosa and induce vomiting and mild diarrhoea.

Ingestion of pyrethrins may produce nausea, vomiting, headache and other central nervous system disturbances. Excitation, muscular tremors and a period of shock may be followed by death. Dogs fed 5000 ppm of pyrethrum, for 90 days, developed dyspnea, tremors, ataxia and excessive salivation. An estimated fatal human dose is thought to be 100 gms. for a typical 70 kg man (1430 mg/kg).

Large oral doses of salicylates may cause mild burning pain in the throat, stomach and usually prompt vomiting. Several hours may elapse before the development of deep and rapid breathing, lassitude, anorexia, nausea, vomiting, thirst and occasional diarrhoea. Common derivatives of salicylic acid produce substantially the same toxic syndrome, ("salicylism"). Major signs and symptoms arise from stimulation and terminal depression of the central nervous system. Stimulation produces vomiting, hyperpnea (abnormal increase in rate and depth of respiration), headache, tinnitus (ringing in the ears) confusion, bizarre behaviour or mania, generalised convulsions. Death is due to respiratory failure or cardiovascular collapse. Severe sensory disturbances such as deafness and dimness of vision are common. Less common features include sweating, skin eruptions, gastrointestinal and other hemorrhages, renal failure and pancreatitis. A tendency to bleed may be manifest by blood in the vomitus (haematemesis), bloody stools (melena) or purplish-red spots (petechiae) on the skin. Many of the toxic effects detailed here are due to or aggravated by severe disturbance of acid-base balance with the chief cause being prolonged hyperventilation from central stimulation. An assessment of acute salicylate intoxication based on dose suggests; 500 mg/kg: Potentially lethal

**Skin Contact**

The material produces mild skin irritation; evidence exists, or practical experience predicts, that the material either

- produces mild inflammation of the skin in a substantial number of individuals following direct contact, and/or
- produces significant, but mild, 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 characterised 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 spongylayer of the skin (spongiosis) and intracellular oedema of the epidermis.

The material may accentuate any pre-existing dermatitis condition.

Repeated exposure may cause skin cracking, flaking or drying following normal handling and use.

Skin contact with the material may damage the health of the individual; systemic effects may result following absorption. One of the mechanisms of skin irritation caused by surfactants is considered to be denaturation of the proteins of skin. It has also been established that there is a connection between the potential of surfactants to denature protein in vitro and their effect on the skin. Nonionic surfactants do not carry any net charge and, therefore, they can only form hydrophobic bonds with proteins. For this reason, proteins are not deactivated by nonionic surfactants, and proteins with poor solubility are not solubilized by nonionic surfactants.

Skin contact with natural pyrethrins may result in severe dermatitis and may also be associated with allergic rhinitis and asthma. Absorption through the skin may result in a toxic syndrome similar to that produced by inhalation. Systemic effects, following skin absorption, may include liver and kidney damage. Prolonged or repeated exposure may cause central nervous system effects and allergic skin reaction.

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**

When applied to the eye(s) of animals, the material produces severe ocular lesions which are present twenty-four hours or more after instillation.

Some nonionic surfactants may produce a localised anaesthetic effect on the cornea; this may effectively eliminate the warning discomfort produced by other substances and lead to corneal injury. Irritant effects range from minimal to severe dependent on the nature of the surfactant, its concentration and the duration of contact. Pain and corneal damage represent the most severe manifestation of irritation.

**Chronic**

Practical experience shows that skin contact with the material is capable either of inducing a sensitisation reaction in a substantial number of individuals, and/or of producing a positive response in experimental animals.

On the basis, primarily, of animal experiments, concern has been expressed by at least one classification body that the
material may produce carcinogenic or mutagenic effects; in respect of the available information, however, there presently exists inadequate data for making a satisfactory assessment.

Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

Exposure to the material may cause concerns for human fertility, on the basis that similar materials provide some evidence of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occurring at around the same dose levels as other toxic effects, but which are not a secondary non-specific consequence of other toxic effects.

Chronic poisoning by natural pyrethrins may result in convulsion, tetanic paralysis, rapid and uneven heart beat, liver and kidney damage, or death.

The natural pyrethrins may produce hypersensitivity, especially following previous sensitising exposure. In general, repeated exposures over 2 or 3 years are required to elicit a response and involve exposure to pyrethrum rather than its individual components (including pyrethrins). The sesquiterpene lactone (pyrethrin) and the pyrethrum glycoproteins account for the immediate and delayed hypersensitivity seen in guinea pigs following a single injection of ground chrysanthemum in Freud's adjuvant. Mild erythematous vesicular dermatitis (with papules), pruritus, localized oedema (particularly of the face, lips and eyelids), rhinitis, tachycardia, pallor and sweating are the most common syndromes. An initial skin sensitisation can progress to marked dermal oedema and skin cracking. Pyrethrum dermatitis appears to increase in hot weather or under conditions were heavy perspiration is produced. The active ingredients of pyrethrum (except pyrethrin II) are inactive in patch tests. Those patients allergic to ragweed pollen are particularly sensitive to pyrethrin.

Rats fed on a diet of pyrethrins for 5000 ppm for 2 years showed some signs of tissue damage including liver lesions, bile duct proliferation and focal necrosis of the liver cells. A no-effect level of 1000 ppm found in animal experiments correspond to a daily dose of 3600 mg/man.

Mild chronic salicylate intoxication, or "salicylism", may occur after repeated exposures to large doses. Symptoms include dizziness, tinnitus, deafness, sweating, nausea and vomiting, headache and mental confusion. Symptoms of more severe intoxication include hyperventilation, fever, restlessness, ketosis, and respiratory alkalosis and metabolic acidosis.

Depression of the central nervous system may lead to coma, cardiovascular collapse and respiratory failure.

Chronic exposure to the salicylates (o-hydroxybenzoates) may produce metabolic and central system disturbances or damage to the kidneys. Persons with pre-existing skin disorders, eye problems or impaired kidney function may be more susceptible to the effects of these substances. Certain individuals (atopics), notably asthmatics, exhibit significant hypersensitivity to salicyclic acid derivatives. Reactions include urticaria and other skin eruptions, rhinitis and severe (even fatal) bronchospasm and dyspnea. Chronic exposure to the p-hydroxybenzoates (parabens) is associated with hypersensitivity reactions following application of these to the skin. Hypersensitivity reactions have also been reported following parenteral or oral administration. Cross-sensitivity occurs between the p-hydroxybenzoates Hypersensitivity reactions may include by acute bronchospasm, hives (urticaria), deep dermal wheals (angioneurotic oedema), running nose (rhinitis) and blurred vision. Anaphylactic shock and skin rash (non-thrombocytopenic purpura) may also occur. Any individual may be predisposed to such anti-body mediated reaction if other chemical agents have caused prior sensitisation (cross-sensitivity).

Principal routes of exposure are usually by inhalation of mists or vapours from heated material and skin contact/absorption. A 5 year old girl sprayed with Deet nightly for 3 months, developed headaches and slurred speech, progressing to athetosis (ceaseless slow, writhing motions especially of the hands), shaking, screaming and convulsion. She died 24 days after hospitalisation; autopsy revealed generalised oedema of the brain with intense congestion of the meninges. The effect was thought to represent sensitisation to the substance.

Repeated application to human skin resulted in slight irritation and dryness of the face, desquamation around the nose and a slight tingling sensation. Incidences of sporadic allergy (anaphylaxis) and scarring dermatitis have been reported. Some individuals repeatedly exposed to the substance have shown encephalopathy and neurological symptoms (muscle cramp, urinary hesitation, insomnia, abnormal sweating, irritability, depression, paranoia, episodes of confusion, and aggressive behaviour).

An increased incidence sperm head abnormalities and period nausea, vomiting and nasal exudate were observed in animals following chronic exposure.

Prolonged or repeated skin contact may cause degreasing with drying, cracking and dermatitis following.

### Toxicity and irritation data

<table>
<thead>
<tr>
<th>Compound</th>
<th>Toxicity</th>
<th>Irritation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Virbac Septicide Antiseptic Cream With Insecticide</strong></td>
<td>Not Available</td>
<td>Not Available</td>
</tr>
<tr>
<td><strong>alcohols C16-18 ethoxylated</strong></td>
<td>Toxicity: Oral (rat) LD50: 1260 mg/kg[^2]</td>
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<td></td>
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<tr>
<td><strong>2-ethylhexyl bicycloheptene dicarboximide</strong></td>
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</tr>
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<td>IRRITATION</td>
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<tr>
<td>----------------------------</td>
<td>--------------------------------</td>
<td>---------------------------</td>
</tr>
<tr>
<td>methyl salicylate</td>
<td>dermal (rat) LD50: &gt;=2500 mg/kg</td>
<td>Eye (rabbit): 500 mg/24 h - mild</td>
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<tr>
<td></td>
<td>Oral (rat) LD50: 887 mg/kg</td>
<td>Skin (rabbit): 500 mg/24 h - moderate</td>
</tr>
<tr>
<td>permethrin</td>
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<td></td>
<td>Oral (rat) LD50: 383 mg/kg</td>
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<tr>
<td>proflavine hemisulfate dihydrate</td>
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</table>

**Legend:**
1. Value obtained from Europe ECHA Registered Substances - Acute toxicity 2.* Value obtained from manufacturer's SDS.

### Toxicity and Irritation

Human beings have regular contact with alcohol ethoxylates through a variety of industrial and consumer products such as soaps, detergents, and other cleaning products. Exposure to these chemicals can occur through ingestion, inhalation, or contact with the skin or eyes. Studies of acute toxicity show that volumes well above a reasonable intake level would have to occur to produce any toxic response. Moreover, no fatal case of poisoning with alcohol ethoxylates has ever been reported. Multiple studies investigating the acute toxicity of alcohol ethoxylates have shown that the use of these compounds is of low concern in terms of oral and dermal toxicity.

Clinical animal studies indicate these chemicals may produce gastrointestinal irritation such as ulcerations of the stomach, pilo-erection, diarrhea, and lethargy. Similarly, slight to severe irritation of the skin or eye was generated when undiluted alcohol ethoxylates were applied to the skin and eyes of rabbits and rats. The chemical shows no indication of being a genotoxin, carcinogen, or mutagen (HERA 2007). No information was available on levels at which these effects might occur, though toxicity is thought to be substantially lower than that of nonylphenol ethoxylates.

Polyethers, for example, ethoxylated surfactants and polyethylene glycols, are highly susceptible towards air oxidation as the ether oxygens will stabilize intermediary radicals involved. Investigations of a chemically well-defined alcohol (pentaethyleneglycol monoo-n-dodecyl ether) ethoxylate, showed that polyethers form complex mixtures of oxidation products when exposed to air.

Sensitization studies in guinea pigs revealed that the pure nonoxidized surfactant itself is nonsensitizing but that many of the investigated oxidation products are sensitizers. Two hydroperoxides were identified in the oxidation mixture, but only one (16-hydroperoxy-3,6,9,12,15-pentaaxaheptacosan-1-ol) was stable enough to be isolated. It was found to be a strong sensitizer in LLNA (local lymph node assay for detection of sensitization capacity). The formation of other hydroperoxides was indicated by the detection of their corresponding aldehydes in the oxidation mixture.

On the basis of the lower irritancy, nonionic surfactants are often preferred to ionic surfactants in topical products. However, their susceptibility towards autoxidation also increases the irritation. Because of their irritating effect, it is difficult to diagnose ACD to these compounds by patch testing.

Alcohol ethoxylates are according to CESIO (2000) classified as Irritant or Harmful depending on the number of EO-units:

- EO < 5 gives irritant (Xi) with R38 (Irritating to skin) and R41 (Risk of serious damage to eyes)
- EO > 5-15 gives Harmful (Xn) with R22-41
- EO > 15-20 gives Harmful (Xn) with R22-41
- EO > 20 is not classified (CESIO 2000)

Oxo-AE, C13 EO10 and C12 EO15, are irritating (Xi) with R38/38 (Irritating to eyes and skin).

### ALCOHOLS C16-18 ETHOXYLATED

In general, alcohol ethoxylates (AE) are readily absorbed through the skin of guinea pigs and rats and through the gastrointestinal mucosa of rats. AE are quickly eliminated from the body through the urine, faeces, and expired air (CO2). Orally dosed AE was absorbed rapidly and extensively in rats, and more than 75% of the dose was absorbed. When applied to the skin of humans, the doses were absorbed slowly and incompletely (50% absorbed in 72 hours). Half of the absorbed surfactant was excreted promptly in the urine and smaller amounts of AE appeared in the faeces and expired air (CO2). The metabolism of C12 AE yields PEG, carboxylic acids, and CO2 as metabolites. The LD50 values after oral administration to rats range from about 1-15 g/kg body weight indicating a low to moderate acute toxicity.

The ability of nonionic surfactants to cause a swelling of the stratum corneum of guinea pig skin has been studied. The swelling mechanism of the skin involves a combination of ionic binding of the hydrophilic group as well as hydrophobic interactions of the alkyl chain with the substrate. One of the mechanisms of skin irritation caused by surfactants is considered to be denaturation of the proteins of skin. It has also been established that there is a connection between the potential of surfactants to denature protein in vitro and their effect on the skin. Nonionic surfactants do not carry any net charge and, therefore, they can only form hydrophobic bonds with proteins. For this reason, proteins are not deactivated by nonionic surfactants, and proteins with poor solubility are not solubilized by nonionic surfactants. A substantial amount of toxicological data and information in vivo and in vitro demonstrates that there is no evidence for alcohol ethoxylates (AEs) being genotoxic, mutagenic or carcinogenic. No adverse reproductive or developmental effects were observed. The majority of available toxicity studies revealed NOAELs in excess of 100 mg/kg bw/d but the lowest NOAEL for an individual AE was established to be 50 mg/kg bw/day. This value was subsequently considered as a conservative, representative value in the risk assessment of AE. The effects were restricted to changes in organ weights with no histopathological organ changes with the exception of liver hypertrophy (indicative of an adaptive response to metabolism rather than a toxic effect). It is noteworthy that there was practically no difference in the NOAEL in oral studies of 90-day or 2 years of duration in rats. A comparison of the aggregate consumer exposure and the systemic NOAEL (taking into account an oral absorption value of
75%) results in a Margin of Exposure of 5,800. Taking into account the conservatism in the exposure assessment and the assigned systemic NOAEL, this margin of exposure is considered more than adequate to account for the inherent uncertainty and variability of the hazard database and inter and intra-species extrapolations.

AEs are not contact sensitisers. Neat AE are irritating to eyes and skin. The irritation potential of aqueous solutions of AEs depends on concentrations. Local dermal effects due to direct or indirect skin contact in certain use scenarios where the products are diluted are not of concern as AEs are not expected to be irritating to the skin in in-use concentrations. Potential irritation of the respiratory tract is not a concern given the very low levels of airborne AE generated as a consequence of spray cleaner aerosols or laundry powder detergent dust.

In summary, the human health risk assessment has demonstrated that the use of AE in household laundry and cleaning detergents is safe and does not cause concern with regard to consumer use. Remarks: Patch test on human volunteers did not demonstrate sensitization properties. * Cognis MSDS for Ceteraeth -20

For N,N-diethyl-m-toluamide (Deet)

**Acute toxicity:** Different preparations of Deet with different proportions of the m-isomer produced different oral LD50s. Rats killed by dosages in the LD50 range showed lacrimation, chromatocorony, depression, prostration, tremors, and asphyxial convulsions. Respiratory failure usually preceded cardiac failure. In rabbits, an intravenous dosage of 75 mg/kg was rapidly fatal, but 50 mg/kg was not. Five doses at the rate of 25 mg/kg/day produced no cumulative effect, except for injury of the intima of some veins used for injection. Single dermal applications to rabbits at rates of 2 or 4 ml/kg produced no systemic effect, but did produce mild to moderate erythema. Repeated dermal application of 50% solutions for 13 weeks at the rate of 2 ml/kg/day produced no evidence of systemic toxicity but did produce desquamation, coriaceousness, dryness, and fissuring in the same species. Except for some scarring, these lesions cleared within 3 weeks. Installation of Deet into the eyes of rabbits produced mild to moderate edema of the nictitating membrane, lacrimation, conjunctivitis, and some corneal injury, as revealed by fluorescein staining. After 5 days, all eyes appeared normal. No sensitisation was seen in guinea pigs.

Animals topically exposed to Deet have developed dermal and ocular reactions. Dermal effects including erythema, desquamation and scarring in rabbits and profuse sweating, irritation and exfoliation in horses have been reported following repeated applications of Deet at concentrations of 50 percent or greater. Direct ocular application of either diluted (30 or 40 percent Deet) or undiluted Deet in rabbits has produced edema, tearing, conjunctivitis, pus and clouding in the eyes.

Repeated dermal application to horses produced hypersestotatis, an overactivity of the serous glands, when the solution of Deet was 15% or higher.

Dermal application in humans of insect repellents containing Deet can produce a variety of skin reactions in humans. Cases of localized skin irritation, large painful blisters and permanent scarring of skin at the crease of the elbow have been reported in soldiers who applied solutions of 50 percent or greater Deet. Results from questionnaire surveys conducted by the National Institute for Occupational Safety and Health (NIOSH) among Everglades National Park Employees indicated a variety of dermal reactions including rashes, irritation of skin and mucous membranes, and numb or burning sensations of the lips among park workers who were highly exposed to Deet-containing repellents. Urticaria or dermatitis, resulting from topical Deet exposure has been noted in both children and adults. In one instance involving only limited Deet exposure, the urticaria was accompanied by an anaphylactic reaction.

Controlled human exposure studies using 50 or 75 percent Deet have reproduced many of the dermal effects noted in field studies. The U.S. Army conducted an investigation in volunteers using 75 percent Deet applied to the upper arm and elbow's crease. Of the 77 volunteers, 37 (48%) had severe dermal reactions at the crease of the elbow. No dermal reactions were observed on the upper arm or in the control group of men tested with ethanol solvent alone. Several cases of toxic encephalopathy associated with the use of Deet in children have been reported in the medical literature. The first reported case involved a 3.5 year old girl whose body, bedclothes and bedding were sprayed each night for two weeks with an insect repellent containing 15 percent Deet. Since then, five additional cases of toxic encephalopathy have been temporally associated with the use of Deet products in children, all of whom were females. The toxic encephalopathy was characterised by agitation, weakness, disorientation, ataxia, seizures, coma and in three cases resulted in death. Autopsies conducted on two fatalities indicated oedema of the brain, with one case presenting necrotic lesions in the cerebellum and spinal cord and an enlarged liver accompanied by microscopic changes. One child was reported to be heterozygous for ornithine carbamoyl transferase deficiency (a sex linked enzyme deficiency which may produce effects similar to those reported above) and it has been hypothesised that children with this enzyme disorder may be at greater risk of adverse reactions to Deet. This enzyme deficiency which usually causes infant death in males is of variable severity in females. Accidental and deliberate ingestion of Deet-containing products has produced neurotoxic effects similar to those described following dermal exposure.

Generalised seizures have also been temporally associated with the use of Deet-containing insect repellent on skin. These cases differ from those described above in that they involved males (four boys aged 3-7 years and one 29-year-old adult), had few associated neurotoxic effects and resolved rapidly. Lower exposure to Deet in these males (four of five males had either one or two dermal applications) may have accounted for the effects being less severe than in females. That the majority of identified neurotoxic cases involved children raises concerns that this subpopulation is at greater risk of adverse reaction following exposure to Deet than are adults. Signs and symptoms of more subtle neurotoxicity have also been associated with extensive dermal application of Deet in adults. Questionnaire results indicate that Everglades National Park employees having extensive Deet exposure were more likely to have insomnia, mood disturbances and impaired cognitive function than were lesser exposed co-workers. A young male who repeatedly applied Deet to his skin prior to spending prolonged periods in a sauna was reported to develop acute manic psychosis characterized by aggressive behavior, delusions and hyperactivity. Either o-DET or p-DET, or both occur as impurities in commercial m-DET (Deet). A thorough study of the o-and p-isomers showed that the o-isomer is slightly more toxic than the other (oral LD50 1,210 mg/kg in rats). However, no alarming difference was found, and it was concluded that the presence of 5% of o-DET or p-DET as impurities in the

**Chronic toxicity:** When rats were fed Deet at a dietary level of 10,000 ppm for about 200 days, their growth rate was decreased without a decrease in food intake. There was a significant increase in the relative weight of the testes and liver in males, of the liver and spleen in females, and the kidneys of both males and females. Some of these changes were seen in...
lesser degree at a dietary level of 1,000 ppm. No gross or significant histological changes were seen at any dietary level and no changes of any kind were noted at 100 ppm or 500 ppm (about 25 mg/kg/day).

Essentially identical results were found in other subacute dermal and feeding studies each carried out on rats, rabbits, and dogs. In these oral studies, 2,000 ppm proved to be a no-effect-level. Oral administration of Deet to dogs at rates of 100 and 300 mg/kg/day caused tremor and hyperactivity and occasional vomiting, but no other effects. Blood studies (hemoglobin, haematocrit, sedimentation rate, platelet counts, total and differential white cell counts) on dogs receiving 300 mg/kg orally or dermally or on rabbits receiving 300 mg/kg dermally revealed no effect on the haematopoietic system. Gross and microscopic examination of the organs of all three species revealed only slight kidney damage in rabbits typical of that associated with burns of the skin. Thirteen other organs, including liver, spleen, and bone marrow, were normal in the three species.

No systemic toxicity was observed in rats exposed 8 hours/day, 5 days/week for 7 weeks to air saturated with Deet. No toxic effects were observed in rats exposed for 6 hours to an aerosol of Deet. No gross or significant histological changes were seen.

**Organ Toxicity:** Hypertrophy of the kidneys and liver and effects of mild central nervous system stimulation including tremors and hyperactivity were noted in animals following repeated exposure. Significant testicular hypertrophy was observed in male rats repeatedly fed a diet containing from 48 to 531 mg/kg/day of Deet.

**Reproductive Effects:** When Deet was applied to the skin of rats at the rate of 1,000 mg/kg/day throughout pregnancy, implantation was reduced significantly. Prenatal mortality was 34.1%, compared with 20.9% in the control. Mortality between birth and weaning was 44.0%, compared to 15.7% in the control. Injury was less (but probably significant) at a dosage of 100 mg/kg/day throughout pregnancy.

**Teratogenic Effects:** A dermal teratology study was conducted on rabbits. Groups of 20 pregnant rabbits received daily dermal applications of 0, 50, 100, 500, 1000, or 5000 mg Deet/kg/day in ethanol on shaved backs from day 0 through day 29 of gestation. There were no significant differences between control and treated animals with respect to the fertility index, number of implantations per animal, or number of fetuses per animal. In addition, treatment did not change fetal weight, fetal length or placental weights and no increases in the incidence of skeletal or soft tissue abnormalities were observed in treated groups when compared with untreated controls. This study demonstrated that Deet has no teratogenic or embryotoxic effects in rabbits exposed dermally to technical Deet. An additional supplementary teratology study was conducted on rats. Groups of 20 pregnant rats were daily administered 10 ml of peanut oil containing 0, 8, 20 or 80 mg/kg/Deet by gavage from day 5 through day 15 of gestation. No significant differences were reported between control and treated mothers with respect to fertility, fetuses per litter, foetal weight or fetal survival. However, the study did show decreases in number of implantation sites per dam and number of fetuses per animal.

In addition, a related increase was observed in the number of resorptions per dam.

**Carcinogenicity:** Researchers fed Deet to male and female rats in the diet for two years at doses of 10, 30, or 100 mg/kg/day, and 30, 100, or 400 mg/kg/day, respectively. Researchers fed mice 250, 500, or 1,000 mg/kg/day for 18 months, and dogs 30, 100, or 400 mg/kg/day. No specific target organ toxicity or oncogenicity was observed in any of the animals. Researchers often use studies designed to test for mutagenicity to screen chemicals for carcinogenicity. Sufficient evidence indicates that DEET does not have significant potential for mutagenicity.

**Fate in Humans and Animals:** Deet is absorbed promptly from the skin and distributed to all organs including the brain and the foetus. The compound is excreted in the milk but primarily in the urine.

The material may produce moderate eye irritation leading to inflammation. Repeated or prolonged exposure to irritants may produce conjunctivitis. Reproductive effector in rats.

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### For 2-ethylhexyl (or N-octyl) bicycloheptene dicarboximide (MGK-264)

**Dermal Absorption:** A study with human volunteers indicated that the dermal absorption factor for MGK-264 is approximately 10% based on the combination of radiolabeled material in the urine (about 1%) and unaccounted for radioactivity (about 9%, assumed to be retained in the body).

**Subchronic Inhalation Toxicity:** A 90-day rat inhalation toxicity study demonstrated that at the lowest dose tested, there were indications of metaplasia/hyperplasia and changes in the larynx. At higher doses, histopathology of the larynx revealed additional changes and more intense changes in the epithelium and throat. Thus, inhalation exposure is capable of causing alterations in the respiratory tract.

**Immunotoxicity and Neurotoxicity:** There were no indications of immunotoxicity or specific neurotoxicity.

**Subchronic and Chronic Oral Toxicity:** The liver is the target organ of MGK-264. Liver effects were noted in the adults in the rat chronic/oncogenicity study, the mouse chronic/oncogenicity study, the rat multi-generation reproduction study and subchronic and chronic dog studies. The dog appeared to be the most sensitive species for liver alterations but these alterations were limited to slight to moderate brown pigment and circulating enzyme changes. The dog study did not include histopathology of the liver to verify the presence of degenerative conditions. In the mouse, liver changes include bile duct histological changes including liver tumors, as well as kidney weight effects and brown pigment.

**Carcinogenicity:** MGK-264 has been identified as a possible human carcinogen based on statistically significant increases mainly in benign liver adenomas in both sexes of mice at doses approaching the limit dose and on increases in benign thyroid follicular tumors in male rats at doses considered to be adequate to assess carcinogenic potential.

**Developmental Toxicity:** The rat and rabbit developmental toxicology studies did not demonstrate developmental toxicity for MGK-264. Maternal toxicity consisted of body weight and food consumption decreases. However, at higher doses, abortions, resorptions, and deaths were noted.

**Reproductive Toxicity:** There were no effects on the reproductive performance of either males or females in the multi-generation reproduction study. Systemic effects were related to body weight decrease as well as histopathological changes in the liver similar to those seen in the rat chronic feeding study. However, offspring for all generations indicated decreased body weight during lactation at a lower dose than parental systemic effects. The effect was reversible after weaning as pups regained weight and their weights were comparable to control animal weights after weaning.

**Mutagenicity:** Mutagenicity and genotoxicity were not evident in the Ames test for bacterial mutations, in the unscheduled DNA synthesis, or in a chromosome aberration studies. Although MGK-264 was considered weakly positive in the mouse lymphoma assay, there was a low concern for mutagenic or genetic toxicity.
Metabolism: The metabolism and pharmacokinetics data for MGK-264 in rats demonstrated that MGK-264 is absorbed and excreted with little retention of metabolites

Adverse reactions to fragrances in perfumes and in fragranced cosmetic products include allergic contact dermatitis, irritant contact dermatitis, photosensitivity, immediate contact reactions (contact urticaria), and pigmented contact dermatitis. Airborne and connubial contact dermatitis occur.

Intolerance to perfumes, by inhalation, may occur if the perfume contains a sensitising principal. Symptoms may vary from general illness, coughing, phlegm, wheezing, chest-tightness, headache, exertional dyspnoea, acute respiratory illness, hayfever, and other respiratory diseases (including asthma). Perfumes can induce hyper-reactivity of the respiratory tract without producing an IgE-mediated allergy or demonstrable respiratory obstruction. This was shown by placebo-controlled challenges of nine patients to "perfume mix". The same patients were also subject to perfume provocation, with or without a carbon filter mask, to ascertain whether breathing through a filter with active carbon would prevent symptoms. The patients breathed through the mouth, during the provocations, as a nose clamp was used to prevent nasal inhalation. The patient's earlier symptoms were verified; breathing through the carbon filter had no protective effect. The symptoms were not transmitted via the olfactory nerve but they may have been induced by trigeminal reflex via the respiratory tract or by the eyes.

Cases of occupational asthma induced by perfume substances such as isomyl acetate, limonene, cinnamaldehyde and benzaldehyde, tend to give persistent symptoms even though the exposure is below occupational exposure limits.

Inhalation intolerance has also been produced in animals. The emissions of five fragrance products, for one hour, produced various combinations of sensory irritation, pulmonary irritation, decreases in expiratory airflow velocity as well as alterations of the functional observational battery indicative of neurotoxicity in mice. Neurotoxicity was found to be more severe after mice were repeatedly exposed to the fragrance products, being four brands of cologne and one brand of toilet water.

Contact allergy to fragrances is relatively common, affecting 1 to 3% of the general population, based on limited testing with eight common fragrance allergens and about 16% of patients patch tested for suspected allergic contact dermatitis.

Contact allergy to fragrance ingredients occurs when an individual has been exposed, on the skin, to a sufficient degree of fragrance contact allergens. Contact allergy is a life-long, specifically altered reactivity in the immune system. This means that once contact allergy is developed, cells in the immune system will be present which can recognise and react towards the allergen. As a consequence, symptoms, i.e. allergic contact dermatitis, may occur upon re-exposure to the fragrance allergen(s) in question. Allergic contact dermatitis is an inflammatory skin disease characterised by erythema, swelling and vesicles in the acute phase. If exposure continues it may develop into a chronic condition with scaling and painful fissures of the skin. Allergic contact dermatitis to fragrance ingredients is most often caused by cosmetic products and usually involves the face and/or hands. It may affect fitness for work and is a quality of life issue for the individual. Fragrance contact allergy has long been recognised as a frequent and potentially disabling problem. Prevention is possible as it is an environmental disease and if the environment is modified (e.g. by reduced use concentrations of allergens), the disease frequency and severity will decrease. Fragrance contact allergy is mostly non-occupational and related to the personal use of cosmetic products. Allergic contact dermatitis can be severe and widespread, with a significant impairment of quality of life and potential consequences for fitness for work. Thus, prevention of contact sensitisation to fragrances, both in terms of primary prevention (avoiding sensitisation) and secondary prevention (avoiding relapses of allergic contact dermatitis in those already sensitised), is an important objective of public health risk management measure.

Hands: Contact sensitisation may be the primary cause of hand eczema, or may be a complication of irritant or atopic hand eczema. The number of positive patch tests has been reported to correlate with the duration of hand eczema, indicating that long-standing hand eczema may often be complicated by sensitisation. Fragrance allergy may be a relevant problem in patients with hand eczema; perfumes are present in consumer products to which their hands are exposed. A significant relationship between hand eczema and fragrance contact allergy has been found in some studies based on patients investigated for contact allergy. However, hand eczema is a multi-factorial disease and the clinical significance of fragrance contact allergy in (severe) chronic hand eczema may not be clear.

Axillae Bilateral auxillary (underarm) dermatitis may be caused by perfume in deodorants and, if the reaction is severe, it may spread down the arms and to other areas of the body. In individuals who consulted a dermatologist, a history of such first-time symptoms was significantly related to the later diagnosis of perfume allergy.

Face: Facial eczema is an important manifestation of fragrance allergy from the use of cosmetic products (16). In men, after-shave products can cause an eczematous eruption of the beard area and the adjacent part of the neck and men using wet shaving as opposed to dry have been shown to have an increased risk of of being fragrance allergic.

Irritant reactions (including contact urticaria): Irritant effects of some individual fragrance ingredients, e.g. citral are known. Irritant contact dermatitis from perfumes is believed to be common, but there are no existing investigations to substantiate this. Many more people complain about intolerance or rashes to perfumes/perfumed products than are shown to be allergic by testing. This may be due to irritant effects or inadequate diagnostic procedures. Fragrances may cause a dose-related contact urticaria of the non-immunological type (irritant contact urticaria). Cinnamal, cinnamic alcohol, and Myroxyylon pereirae are well recognised causes of contact urticaria, but others, including menthol, vanillin and benzaldehyde have also been reported. The reactions to Myroxyylon pereirae may be due to cineamates. A relationship to delayed contact hypersensitivity was suggested, but no significant difference was found between a fragrance-allergic group and a control group in the frequency of immediate reactions to fragrance ingredients in keeping with a non-immunological basis for the reactions seen.

Pigmentary anomalies: The term "pigmented cosmetic dermatitis" was introduced in 1973 for what had previously been known as melanosia faciei feminae when the mechanism (type IV allergy) and causative allergens were clarified. It refers to increased pigmentation, usually on the face/neck, often following sub-clinical contact dermatitis. Many cosmetic ingredients were patch tested at non-irritant concentrations and statistical evaluation showed that a number of fragrance ingredients were associated: jasmine absolute, ylang-ylang oil, cananga oil, benzyl salicylate, hydroxycitronellal, sandalwood oil, geraniol, geranium oil.

Photo-reactions: Musc ambrette produced a considerable number of allergic photoreactions (in which UV-light is required) in the 1970s and was later banned from use in the EU. Nowadays, phototoxic contact dermatitis is uncommon. Furocoumarins (psoralens) in some plant-derived fragrance ingredients caused phototoxic reactions with erythema followed by hyperpigmentation resulting in Berloque dermatitis. There are now limits for the amount of furcocumarin in fragrance
products. Phototoxic reactions still occur but are rare.

**General/respiratory:** Fragrances are volatile and therefore, in addition to skin exposure, a perfume also exposes the eyes and naso-respiratory tract. It is estimated that 2-4% of the adult population is affected by respiratory or eye symptoms by such an exposure. It is known that exposure to fragrances may exacerbate pre-existing asthma. Asthma-like symptoms can be provoked by sensory mechanisms. In an epidemiological investigation, a significant association was found between respiratory complaints related to fragrances and contact allergy to fragrance ingredients, in addition to hand eczema, which were independent risk factors in a multivariate analysis.

Fragrance allergens act as hapten, i.e. low molecular weight chemicals that are immunogenic only when attached to a carrier protein. However, not all sensitising fragrance chemicals are directly reactive, but require previous activation. A prehapten is a chemical that itself is non- or low-sensitising, but that is transformed into a hapten outside the skin by simple chemical transformation (air oxidation, photoactivation) and without the requirement of specific enzymatic systems. A prohapten is a chemical that itself is non- or low-sensitising but that is transformed into a hapten in the skin (bioactivation) usually via enzyme catalysis. It is not always possible to know whether a particular allergen that is not directly reactive acts as a prehapten or as a prohapten, or both, because air oxidation and bioactivation can often give the same product (geraniol is an example). Some chemicals might act by all three pathways.

**Prohapten**

Compounds that are bioactivated in the skin and thereby form haptenes are referred to as prohapten.

In the case of prohapten, the possibility to become activated is inherent to the molecule and activation cannot be avoided by extrinsic measures. Activation processes increase the risk for cross-reactivity between fragrance substances.

Crossreactivity has been shown for certain alcohols and their corresponding aldehydes, i.e. between geraniol and geranial (citral) and between cinnamyl alcohol and cinnamal.

The human skin expresses enzyme systems that are able to metabolise xenobiotics, modifying their chemical structure to increase hydrophilicity and allow elimination from the body. Xenobiotic metabolism can be divided into two phases: phase I and phase II. Phase I transformations are known as activation or functionalisation reactions, which normally introduce or unmask hydrophilic functional groups. If the metabolites are sufficiently polar at this point they will be eliminated. However, many phase I products have to undergo subsequent phase II transformations, i.e. conjugation to make them sufficiently water soluble to be eliminated. Although the purpose of xenobiotic metabolism is detoxification, it can also convert relatively harmless compounds into reactive species. Cutaneous enzymes that catalyse phase I transformations include the cytochrome P450 mixed-function oxidase system, alcohol and aldehyde dehydrogenases, monoamine oxidases, flavin-containing monoxygenases and hydrolytic enzymes. Acyltransferases, glutathione S-transferases, UDP-glucuronosyltransferases and sulfotransferases are examples of phase II enzymes that have been shown to be present in human skin. These enzymes are known to catalyse both activating and deactivating biotransformations, but the influence of the reactions on the allergenic activity of skin sensitisers has not been studied in detail. Skin sensitising prohaptenes can be recognised and grouped into chemical classes based on knowledge of xenobiotic bioactivation reactions, clinical observations and/or in vivo and in vitro studies of sensitisation potential and chemical reactivity.

**QSAR prediction:** The relationships between molecular structure and reactivity that form the basis for structural alerts are based on well established principles of mechanistic organic chemistry. Examples of structural alerts are aliphatic aldehydes (alerting to the possibility of sensitisation via a Schiff base reaction with protein amino groups), and alpha,beta-unsaturated carbonyl groups, C=O-C=O (alerting to the possibility of sensitisation via Michael addition of protein thiol groups). Prediction of the sensitisation potential of compounds that can act via abiotic or metabolic activation (pre- or prohapten) is more complex compared to that of compounds that act as direct haptenes without any activation. The autooxidation patterns can differ due to differences in the stability of the intermediates formed, e.g. it has been shown that autooxidation of the structural isomers linalool and geraniol results in different major haptenes/allergens. Moreover, the complexity of the prediction increases further for those compounds that can act both as pre- and prohapten. In such cases, the impact on the sensitisation potency depends on the degree of abiotic activation (e.g. autooxidation) in relation to the metabolic activation.

For certain benzyl derivatives:

All members of this group (benzyl, benzoate and 2-hydroxybenzoate (salicylate) esters) contain a benzene ring bonded directly to an oxygenated functional group (aldehyde or ester) that is hydrolysed and/or oxidised to a benzoic acid derivative. As a stable animal metabolite, benzoic acid derivatives are efficiently excreted primarily in the urine. These reaction pathways have been reported in both aquatic and terrestrial species. The similarity of their toxicologic properties is a reflection their participation in these common metabolic pathways.

In general, members of this group are rapidly absorbed through the gastrointestinal tract, metabolised primarily in the liver, and excreted in the urine either unchanged or as conjugates of benzoic acid derivatives. At high doses, conjugation pathways (e.g., glycine) may be saturated; in which case, free benzoic acid is excreted unchanged. Absorption, distribution and excretion studies have been conducted several members of this group and structural relatives. These substances exhibit remarkably similar patterns of pharmacokinetics and metabolism. The benzyl, benzoate, and 2-hydroxybenzoate (salicylate) esters which comprise this category are hydrolysed to the corresponding alcohols and carboxylic acids. The benzyl alcohol and benzaldehyde derivatives are oxidised to the corresponding benzoic acid derivatives that are subsequently excreted unchanged or as glycine or gluconuronic acid conjugates. If methoxy or phenolic functional groups are present on the benzene ring, additional minor metabolic options become available. O-demethylation yields the corresponding phenol that is subsequently excreted as the glucuronic acid or sulfate conjugates. At high dose levels, gut microflora may act to produce minor amounts of reduction metabolites.

**Acute toxicity:** Oral LD50 values ranged from 887 to greater than 5,000 mg/kg bw demonstrating the low to moderate toxicity of these compounds.

**Repeat dose toxicity:** Overall, numerous repeat-dose studies using various routes of exposure have been conducted in different animal species with members of this chemical category or their close structural relatives. It is important to note that all the benzyl derivatives in this category are eventually metabolised to a common metabolite, benzoic acid, and are rapidly excreted in the urine as benzoate, or glucuronate, or benzoic acid or as its glycine, sulfate, or glucuronate conjugate. For this reason, the repeat-dose studies currently available provide adequate support for the safety of the benzyl derivatives. Moreover, the levels at which no adverse effects were reported were sufficiently high to accommodate any potential differences among the members of the category.

**Reproductive toxicity:** Several reproductive toxicity studies have been conducted with representatives of this group and...
produced no evidence of reproductive toxicity. As with the repeat-dose studies, the benzyl derivatives generally follow the similar metabolic pathways and the studies conducted provide an adequate database for this endpoint. In addition, the dose levels tested provide margins of safety large enough to accommodate any differences among the group.

**Developmental toxicity:** Representative substances from this group were tested for developmental toxicity with uniform results, and indicated no teratogenic potential in the absence of maternal toxicity. Again, the representative substances undergo similar metabolism to the entire benzyl derivative group and therefore, provide an adequate representation for this endpoint.

**Genetic toxicity:** Overall, *in vitro* and *in vivo* genotoxicity studies have been conducted with substances representing the structural characteristics of the benzyl category. The results of these studies were predominantly negative demonstrating a low order of genotoxic potential. Limited positive and/or equivocal findings have been reported for 3 aldehydes and benzyl acetate, but, in most cases, other studies of the same endpoint with same test substance show no activity. Most importantly, *in vivo* studies on benzaldehyde derivatives and closely related benzyl esters have all yielded negative results. These negative *in vivo* genotoxicity assays are supported by the lack of tumorigenicity in chronic animal studies with representatives of this group.

Data available for more than 100 *in vitro* genotoxicity assays for 9 members of the category and five metabolic precursors or metabolites of benzyl derivatives indicate a low genotoxic potential for members of this chemical category. Equivocal results have been reported mainly for aromatic aldehydes in the MLA and ABS assays.

A member or analogue of a group of hydroxy and alkoxy-substituted benzyl derivatives generally regarded as safe (GRAS) based in part on their self-limiting properties as flavouring substances in food; their rapid absorption, metabolic detoxification, and excretion in humans and other animals, their low level of flavour use, the wide margin of safety between the conservative estimates of intake and the no-observed-adverse effect levels determined from chronic and subchronic studies and the lack of significant genotoxic and mutagenic potential. This evidence of safety is supported by the fact that the intake of benzyl derivatives as natural components of traditional foods is greater than the intake as intentionally added flavouring substances.

All members of this group are aromatic primary alcohols, aldehydes, carboxylic acids or their corresponding esters or acetals. The structural features common to all members of the group is a primary oxygenated functional group bonded directly to a benzene ring. The ring also contains hydroxy or alkoxy substituents. The hydroxy- and alkoxy-substituted benzyl derivatives are rapidly absorbed by the gastrointestinal tract, metabolised in the liver to yield benzoic acid derivatives and excreted primarily in the urine either unchanged or conjugated. It is expected than aromatic esters and acetals will be hydrolysed in vivo through the catalytic activity of carboxylesterases, (A-esterases), Acetals hydrolyse uncatysed in gastric juices and intestinal fluids to yield acetaldehydes. Substituted benzyl esters and benzoic acid derivatives are hydrolysed to the corresponding alcoholic alcohols and carboxylic acid.

In general hydroxy- and alkoxy-derivatives of benzaldehyde and benzyl alcohol are oxidised to the corresponding benzoic acid derivatives and, to a lesser extent reduced to corresponding benzyl alcohol derivatives. Following conjugation these are excreted in the urine. Benzyl alcohol derivatives may also be reduced in gut microflora to toluene derivatives.

**Flavor and Extract Manufacturers Association (FEMA)**

- The salicylates are well absorbed by the oral route, and oral bioavailability is assumed to be 100%. Absorption by the dermal route in humans is more limited with bioavailability in the range of 11.8-30.7%.
- The salicylates are expected to undergo extensive hydrolysis, primarily in the liver, to salicylic acid which is conjugated with either glycine or glucuronic acid and is excreted in the urine as salicylic acid and acyl and phenolic glucuronides. The hydrolyzed side chains are metabolized by common and well-characterized metabolic pathways leading to the formation of innocuous end products. The expected metabolism of the salicylates does not present toxicological concerns.
- The acute dermal toxicity of the salicylates is very low, with LD50 values in rabbits reported to be greater than 5000 mg/kg body weight. The acute oral toxicity of the salicylates is moderate, with toxicity generally decreasing with increasing size of the ester R-group and with LD50’s between 1000 and >5000 g/kg. In dermal subchronic toxicity studies, extreme doses of methyl salicylate (5 g/kg body weight/day) possibly were nephrotoxic but the data were minimal. The subchronic oral NOAEL is concluded to be 50 mg/kg body weight/day.
- Genetic toxicity data for methyl salicylate, a few other salicylates and for structurally related alkyl- and alkoxy-benzyl derivatives are negative for genotoxicity.
- Given the metabolism of salicylate and the evidence that they are non-genotoxic, it can be concluded that the salicylates are without carcinogenic potential.
- The reproductive and developmental toxicity data on methyl salicylate demonstrate that high, maternally toxic doses result in a pattern of embryotoxicity and teratogenesis similar to that characterized for salicylic acid.
- At concentrations likely to be encountered by humans through the use of the salicylates as fragrance ingredients, these chemicals are considered to be non-irritating to the skin.
- The salicylates (with the exception of benzyl salicylate) in general have no or very limited skin sensitization potential.
- The salicylates are non-phototoxic and have no photocarcinogenic activity.
- The use of the salicylates in fragrances produces low levels of exposure relative to doses that elicit adverse systemic effects in laboratory animals exposed by the dermal or oral route. Based on NOAEL values of 50 mg/kg body weight/day identified in the subchronic and the chronic toxicity studies, a margin of safety for systemic exposure of humans to the individual salicylates in cosmetic products, may be calculated to range from 125 to 2,500,000 (depending upon the assumption of either 12–30% or 100% bioavailability following dermal application) times the maximum daily exposure.

The acute dermal toxicity of the salicylates is very low. Rabbit dermal LD50 values have been reported to be >5000 mg/kg body weight for 15 of the 16 salicylates tested findings likely related to the limited degree of dermal absorption, the retention of salicylate in the skin, and the relatively moderate toxicity of salicylic acid itself upon systemic exposure (i.e., oral LD50 value of 891 mg/kg body weight in rats).

Overall, the acute oral toxicity of the salicylates is moderate, with toxicity generally decreasing with increasing size of the
The material may produce severe skin irritation after prolonged or repeated exposure, and may produce a contact dermatitis (nonallergic). This form of dermatitis is often characterised by skin redness (erythema) and swelling of the epidermis. Histologically there may be intercellular oedema of the spongy layer (spongiosis) and intracellular oedema of the epidermis. Prolonged contact is unlikely, given the severity of response, but repeated exposures may produce severe ulceration.

The Research Institute for Fragrance Materials (RIFM) Expert Panel
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The following information refers to contact allergens as a group and may not be specific to this product. Contact allergies quickly manifest themselves as contact eczema, more rarely as urticaria or Quincke’s oedema. The pathogenesis of contact eczema involves a cell-mediated (T lymphocytes) immune reaction of the delayed type. Other allergic skin reactions, e.g. contact urticaria, involve antibody-mediated immune reactions. The significance of the contact allergen is not simply determined by its sensitisation potential; the distribution of the substance and the opportunities for contact with it are equally important. A weakly sensitising substance which is widely distributed can be a more important allergen than one with stronger sensitising potential with which few individuals come into contact. From a clinical point of view, substances are noteworthy if they produce an allergic test reaction in more than 1% of the persons tested.

The substance is classified by IARC as Group 3: NOT classifiable as to its carcinogenicity to humans. Evidence of carcinogenicity may be inadequate or limited in animal testing.
SECTION 12 ECOLOGICAL INFORMATION

Toxicity

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Endpoint</th>
<th>Test Duration (hr)</th>
<th>Species</th>
<th>Value</th>
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Legend: Extracted from 1. IUCLID Toxicity Data 2. Europe ECHA Registered Substances - Ecotoxicological Information - Aquatic Toxicity 3. EPIWIN Suite V3.12 - Aquatic Toxicity Data (Estimated) 4. US EPA, Ecotox database - Aquatic Toxicity Data 5. ECETOC Aquatic Hazard Assessment Data 6. NITE (Japan) - Bioconcentration Data 7. METI (Japan) - Bioconcentration Data 8. Vendor Data

Very toxic to aquatic organisms, may cause long-term adverse effects in the aquatic environment.

DO NOT discharge into sewer or waterways.

Persistence and degradability

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<th>Persistence: Water/Soil</th>
<th>Persistence: Air</th>
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<tr>
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<td>HIGH</td>
</tr>
<tr>
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<td>LOW</td>
</tr>
<tr>
<td>permethrin</td>
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Bioaccumulative potential

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<tr>
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<tr>
<td>2-ethylhexyl bicycloheptene dicarboximide</td>
<td>LOW (LogKOW = 3.7)</td>
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<tr>
<td>methyl salicylate</td>
<td>LOW (LogKOW = 2.55)</td>
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<tr>
<td>permethrin</td>
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Mobility in soil

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<th>Mobility</th>
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SECTION 13 DISPOSAL CONSIDERATIONS

Waste treatment methods

- Containers may still present a chemical hazard/ danger when empty.
- Return to supplier for reuse/ recycling if possible.
- If container can not be cleaned sufficiently well to ensure that residuals do not remain or if the container cannot be used to store the same product, then puncture containers, to prevent re-use, and bury at an authorised landfill.
- Where possible retain label warnings and SDS and observe all notices pertaining to the product.
- 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.
- 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 authorised landfill.

SECTION 14 TRANSPORT INFORMATION

Labels Required

- Marine Pollutant
- HAZCHEM •3Z

Land transport (ADG)

- UN number: 3082
- UN proper shipping name: ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (contains alcohols C16-18 ethoxylated)
- Transport hazard class(es): Class 9
- Subrisk: Not Applicable
- Packing group: III
### Environmental hazard

<table>
<thead>
<tr>
<th>Special precautions for user</th>
</tr>
</thead>
<tbody>
<tr>
<td>Special provisions</td>
</tr>
<tr>
<td>Limited quantity</td>
</tr>
</tbody>
</table>

Environmentally Hazardous Substances meeting the descriptions of UN 3077 or UN 3082 are not subject to this Code when transported by road or rail in:
(a) packagings;
(b) IBCs; or
(c) any other receptacle not exceeding 500 kg(L).
- Australian Special Provisions (SP AU01) - ADG Code 7th Ed.

### Air transport (ICAO-IATA / DGR)

<table>
<thead>
<tr>
<th>UN number</th>
<th>3082</th>
</tr>
</thead>
<tbody>
<tr>
<td>UN proper shipping name</td>
<td>Environmentally hazardous substance, liquid, n.o.s. * (contains alcohols C16-18 ethoxylated)</td>
</tr>
<tr>
<td>Transport hazard class(es)</td>
<td>ICAO/IATA Class</td>
</tr>
<tr>
<td></td>
<td>ICAO / IATA Subrisk</td>
</tr>
<tr>
<td></td>
<td>ERG Code</td>
</tr>
<tr>
<td>Packing group</td>
<td>III</td>
</tr>
<tr>
<td>Environmental hazard</td>
<td>Not Applicable</td>
</tr>
</tbody>
</table>

#### Special precautions for user

<table>
<thead>
<tr>
<th>Special provisions</th>
<th>A97 A158 A197</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cargo Only Packing Instructions</td>
<td>964</td>
</tr>
<tr>
<td>Cargo Only Maximum Qty / Pack</td>
<td>450 L</td>
</tr>
<tr>
<td>Passenger and Cargo Packing Instructions</td>
<td>964</td>
</tr>
<tr>
<td>Passenger and Cargo Maximum Qty / Pack</td>
<td>450 L</td>
</tr>
<tr>
<td>Passenger and Cargo Limited Quantity Packing Instructions</td>
<td>Y964</td>
</tr>
<tr>
<td>Passenger and Cargo Limited Maximum Qty / Pack</td>
<td>30 kg G</td>
</tr>
</tbody>
</table>

### Sea transport (IMDG-Code / GGVSee)

<table>
<thead>
<tr>
<th>UN number</th>
<th>3082</th>
</tr>
</thead>
<tbody>
<tr>
<td>UN proper shipping name</td>
<td>ENVIRONMENTALLY HAZARDOUS SUBSTANCE, LIQUID, N.O.S. (contains alcohols C16-18 ethoxylated)</td>
</tr>
<tr>
<td>Transport hazard class(es)</td>
<td>IMDG Class</td>
</tr>
<tr>
<td></td>
<td>IMDG Subrisk</td>
</tr>
<tr>
<td>Packing group</td>
<td>III</td>
</tr>
<tr>
<td>Environmental hazard</td>
<td>Marine Pollutant</td>
</tr>
</tbody>
</table>

#### Special precautions for user

<table>
<thead>
<tr>
<th>EMS Number</th>
<th>F-A, S-F</th>
</tr>
</thead>
<tbody>
<tr>
<td>Special provisions</td>
<td>274 335 969</td>
</tr>
<tr>
<td>Limited Quantities</td>
<td>5 L</td>
</tr>
</tbody>
</table>

### Transport in bulk according to Annex II of MARPOL and the IBC code

Not Applicable

### SECTION 15 REGULATORY INFORMATION

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

| ALCOHOLS C16-18 ETHOXYLATED(68439-49-6) IS FOUND ON THE FOLLOWING REGULATORY LISTS |
| Australia Inventory of Chemical Substances (AICS) |

| N,N-DIETHYL-M-TOLUAMIDE(134-62-3) IS FOUND ON THE FOLLOWING REGULATORY LISTS |
| Australia Hazardous Substances Information System - Consolidated Lists |
| Australia Inventory of Chemical Substances (AICS) |

| 2-ETHYLHEXYL BICYCLOHEPTENE DICARBOXIMIDE(113-48-4) IS FOUND ON THE FOLLOWING REGULATORY LISTS |
| Continued... |
Australia Inventory of Chemical Substances (AICS)

METHYL SALICYLATE (119-36-8) IS FOUND ON THE FOLLOWING REGULATORY LISTS

Australia Inventory of Chemical Substances (AICS)

PERMETHRIN (52645-53-1) IS FOUND ON THE FOLLOWING REGULATORY LISTS

Australia Hazardous Substances Information System - Consolidated Lists
Australia Inventory of Chemical Substances (AICS)
International Agency for Research on Cancer (IARC) - Agents Classified by the IARC Monographs

PROFLAVINE HEMISULFATE DIHYDRATE (1811-28-5) IS FOUND ON THE FOLLOWING REGULATORY LISTS

Australia Inventory of Chemical Substances (AICS)
International Agency for Research on Cancer (IARC) - Agents Classified by the IARC Monographs

<table>
<thead>
<tr>
<th>National Inventory</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>Australia - AICS</td>
<td>Y</td>
</tr>
<tr>
<td>Canada - DSL</td>
<td>N (permethrin; proflavine hemisulfate dihydrate)</td>
</tr>
<tr>
<td>Canada - NDSL</td>
<td>N (N,N-diethyl-m-toluamide; 2-ethylhexyl bicycloheptene dicarboximide; methyl salicylate; alcohols C16-18 ethoxylated; permethrin)</td>
</tr>
<tr>
<td>China - IECSC</td>
<td>N (proflavine hemisulfate dihydrate)</td>
</tr>
<tr>
<td>Europe - EINEC / ELINCS / NLP</td>
<td>Y</td>
</tr>
<tr>
<td>Japan - ENCS</td>
<td>N (alcohols C16-18 ethoxylated; proflavine hemisulfate dihydrate)</td>
</tr>
<tr>
<td>Korea - KECI</td>
<td>N (2-ethylhexyl bicycloheptene dicarboximide; proflavine hemisulfate dihydrate)</td>
</tr>
<tr>
<td>New Zealand - NZIoC</td>
<td>N (proflavine hemisulfate dihydrate)</td>
</tr>
<tr>
<td>Philippines - PICCS</td>
<td>N (proflavine hemisulfate dihydrate)</td>
</tr>
<tr>
<td>USA - TSCA</td>
<td>N (2-ethylhexyl bicycloheptene dicarboximide; permethrin)</td>
</tr>
</tbody>
</table>

Legend: 
Y = All ingredients are on the inventory
N = Not determined or one or more ingredients are not on the inventory and are not exempt from listing (see specific ingredients in brackets)

SECTION 16 OTHER INFORMATION

Other information

Ingredients with multiple cas numbers

<table>
<thead>
<tr>
<th>Name</th>
<th>CAS No</th>
</tr>
</thead>
<tbody>
<tr>
<td>2-ethylhexyl bicycloheptene dicarboximide</td>
<td>113-48-4, 7786-80-3</td>
</tr>
<tr>
<td>methyl salicylate</td>
<td>119-36-8, 8024-54-2, 9041-28-5</td>
</tr>
<tr>
<td>permethrin</td>
<td>52645-53-1, 54774-45-7, 57608-04-5, 93388-66-0, 63364-00-1, 60018-94-2, 75497-64-2</td>
</tr>
</tbody>
</table>

Classification of the preparation and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references.

A list of reference resources used to assist the committee may be found at: www.chemwatch.net

The 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.

Definitions and abbreviations

PC—TWA: Permissible Concentration-Time Weighted Average
PC—STEL: Permissible Concentration-Short Term Exposure Limit
IARC: International Agency for Research on Cancer
ACGIH: American Conference of Governmental Industrial Hygienists
STEL: Short Term Exposure Limit
TEEL: Temporary Emergency Exposure Limit,
IDLH: Immediately Dangerous to Life or Health Concentrations
OSF: Odour Safety Factor
NOAEL: No Observed Adverse Effect Level
LOAEL: Lowest Observed Adverse Effect Level
TLV: Threshold Limit Value
LOD: Limit Of Detection

Continued...
OTV: Odour Threshold Value
BCF: BioConcentration Factors
BEI: Biological Exposure Index

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TEL (+61 3) 9572 4700.