

Virbac Virbamec LV Pour-On Endectocide for Cattle

Virbac (Australia) Pty Limited

Chemwatch Hazard Alert Code: 3

Chemwatch: 6095685

Version No: 5.1.17.10

Safety Data Sheet according to WHS Regulations (Hazardous Chemicals) Amendment 2020 and ADG requirements

Issue Date: 08/20/2021

Print Date: 09/14/2021

L.GHS.AUS.EN

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

Product Identifier

Product name	Virbac Virbamec LV Pour-On Endectocide for Cattle
Chemical Name	Not Applicable
Synonyms	APVMA No: 56736
Chemical formula	Not Applicable
Other means of identification	Not Available

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

Relevant identified uses	<p>Drying oils are characterized by high levels of fatty acids One common measure of the siccative (drying) property of oils is iodine number. Oils with an iodine number greater than 130 are considered drying, those with an iodine number of 115-130 are semi-drying oils and those with an iodine number of less than 115 are non-drying oils</p> <p>The "drying", "hardening", or, more properly, "curing" of oils is the result of an exothermic reaction in the form of autoxidation Oxygen attacks the hydrocarbon chain, touching off a series of addition reactions. As a result, the oil, forms long, chain-like a vast polymer network molecules, resulting in a vast polymer network. Over time, this network may undergo further change. Certain functional groups in the networks become ionised and the network transitions from a system held together by nonpolar covalent bonds to one governed by the ionic forces between these functional groups and the metal ions present in the paint pigment.</p> <p>In oil autoxidation, oxygen attacks a hydrocarbon chain, often at the site of an allylic hydrogen (a hydrogen on a carbon atom adjacent to a double bond). This produces, a free radical a substance with an unpaired electron which makes it highly reactive. A series of addition reactions ensues. Each step produces additional free radicals, which then engage in further polymerization. The process finally terminates when free radicals collide, combining their unpaired electrons to form a new bond. The polymerisation stage occurs over a period of days to weeks, and renders the film dry to the touch.</p> <p>Use according to manufacturer's directions.</p>
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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	au.virbac.com
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

HAZARDOUS CHEMICAL. NON-DANGEROUS GOODS. According to the WHS Regulations and the ADG Code.

ChemWatch Hazard Ratings

	Min	Max	
Flammability	1	1	
Toxicity	0	0	0 = Minimum
Body Contact	2	2	1 = Low
Reactivity	1	1	2 = Moderate
Chronic	3	3	3 = High
			4 = Extreme

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Poisons Schedule	S5
Classification [1]	Skin Corrosion/Irritation Category 2, Sensitisation (Skin) Category 1, Serious Eye Damage/Eye Irritation Category 2A, Specific Target Organ Toxicity - Single Exposure (Respiratory Tract Irritation) Category 3, Specific Target Organ Toxicity - Single Exposure (Narcotic Effects) Category 3, Reproductive Toxicity Category 1B, Reproductive Toxicity Effects on or via Lactation, Hazardous to the Aquatic Environment Acute Hazard Category 3
Legend:	1. Classified by Chemwatch; 2. Classification drawn from HCIS; 3. Classification drawn from Regulation (EU) No 1272/2008 - Annex VI

Label elements

Hazard pictogram(s)	
Signal word	Danger

Hazard statement(s)

H315	Causes skin irritation.
H317	May cause an allergic skin reaction.
H319	Causes serious eye irritation.
H335	May cause respiratory irritation.
H336	May cause drowsiness or dizziness.
H360D	May damage the unborn child.
H362	May cause harm to breast-fed children.
H402	Harmful to aquatic life.

Precautionary statement(s) Prevention

P201	Obtain special instructions before use.
P260	Do not breathe mist/vapours/spray.
P263	Avoid contact during pregnancy and while nursing.
P271	Use only outdoors or in a well-ventilated area.
P280	Wear protective gloves, protective clothing, eye protection and face protection.
P270	Do not eat, drink or smoke when using this product.
P273	Avoid release to the environment.
P264	Wash all exposed external body areas thoroughly after handling.
P272	Contaminated work clothing should not be allowed out of the workplace.

Precautionary statement(s) Response

P308+P313	IF exposed or concerned: Get medical advice/ attention.
P302+P352	IF ON SKIN: Wash with plenty of water.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P312	Call a POISON CENTER/doctor/physician/first aider/if you feel unwell.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P337+P313	If eye irritation persists: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
P304+P340	IF INHALED: Remove person to fresh air and keep comfortable for breathing.

Precautionary statement(s) Storage

P405	Store locked up.
P403+P233	Store in a well-ventilated place. Keep container tightly closed.

Precautionary statement(s) Disposal

P501	Dispose of contents/container to authorised hazardous or special waste collection point in accordance with any local regulation.
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SECTION 3 Composition / information on ingredients

Substances

See section below for composition of Mixtures

Mixtures

CAS No	%[weight]	Name
70288-86-7	1	<u>ivermectin</u>
Not Available		(10g/L)
100-51-6	10-20	<u>benzyl alcohol</u>

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CAS No	%[weight]	Name
8001-22-7	>60	soybean oil
Legend: 1. Classified by Chemwatch; 2. Classification drawn from HCIS; 3. Classification drawn from Regulation (EU) No 1272/2008 - Annex VI; 4. Classification drawn from C&L; * EU IOELVs available		

SECTION 4 First aid measures

Description of first aid measures

Eye Contact	<p>If this product comes in contact with the eyes:</p> <ul style="list-style-type: none"> ▶ Wash out immediately with fresh 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. ▶ Seek medical attention without delay; if pain persists or recurs seek medical attention. ▶ Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.
Skin Contact	<p>If skin contact occurs:</p> <ul style="list-style-type: none"> ▶ 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.
Inhalation	<ul style="list-style-type: none"> ▶ If fumes or combustion products are inhaled remove from contaminated area. ▶ Lay patient down. Keep warm and rested. ▶ Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures. ▶ Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary. ▶ Transport to hospital, or doctor, without delay.
Ingestion	<ul style="list-style-type: none"> ▶ For advice, contact a Poisons Information Centre or a doctor at once. ▶ Urgent hospital treatment is likely to be needed. ▶ If swallowed do NOT induce vomiting. ▶ If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration. ▶ Observe the patient carefully. ▶ Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious. ▶ Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink. ▶ Transport to hospital or doctor without delay.

Indication of any immediate medical attention and special treatment needed

Treat symptomatically.

Clinical experience of benzyl alcohol poisoning is generally confined to premature neonates in receipt of preserved intravenous salines.

- ▶ Metabolic acidosis, bradycardia, skin breakdown, hypotonia, hepatorenal failure, hypotension and cardiovascular collapse are characteristic.
- ▶ High urine benzoate and hippuric acid as well as elevated serum benzoic acid levels are found.
- ▶ The so-called "gasping syndrome" describes the progressive neurological deterioration of poisoned neonates.
- ▶ Management is essentially supportive.

As in all cases of suspected poisoning, follow the ABCDEs of emergency medicine (airway, breathing, circulation, disability, exposure), then the ABCDEs of toxicology (antidotes, basics, change absorption, change distribution, change elimination).

For poisons (where specific treatment regime is absent):

BASIC TREATMENT

- ▶ Establish a patent airway with suction where necessary.
- ▶ Watch for signs of respiratory insufficiency and assist ventilation as necessary.
- ▶ Administer oxygen by non-rebreather mask at 10 to 15 L/min.
- ▶ Monitor and treat, where necessary, for pulmonary oedema.
- ▶ Monitor and treat, where necessary, for shock.
- ▶ Anticipate seizures.
- ▶ **DO NOT** use emetics. Where ingestion is suspected rinse mouth and give up to 200 ml water (5 ml/kg recommended) for dilution where patient is able to swallow, has a strong gag reflex and does not drool.

ADVANCED TREATMENT

- ▶ Consider orotracheal or nasotracheal intubation for airway control in unconscious patient or where respiratory arrest has occurred.
- ▶ Positive-pressure ventilation using a bag-valve mask might be of use.
- ▶ Monitor and treat, where necessary, for arrhythmias.
- ▶ Start an IV D5W TKO. If signs of hypovolaemia are present use lactated Ringers solution. Fluid overload might create complications.
- ▶ Drug therapy should be considered for pulmonary oedema.
- ▶ Hypotension with signs of hypovolaemia requires the cautious administration of fluids. Fluid overload might create complications.
- ▶ Treat seizures with diazepam.
- ▶ Proparacaine hydrochloride should be used to assist eye irrigation.

BRONSTEIN, A.C. and CURRANCE, P.L.

EMERGENCY CARE FOR HAZARDOUS MATERIALS EXPOSURE: 2nd Ed. 1994

Toxicity following accidental ingestion of ivermectin can be minimised by inducing vomiting within one half-hour of exposure. Since ivermectin is believed to bind to glutamate-gated chloride ion channels, it is probably wise to avoid drugs that also interact with other ligand-gated chloride channels including those that enhance GABA activity in patients with potentially toxic ivermectin exposure. [Mercke, Sharpe and Dohme]

SECTION 5 Firefighting measures

Extinguishing media

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

Special hazards arising from the substrate or mixture

Fire Incompatibility	<ul style="list-style-type: none"> ▶ Avoid contamination with oxidising agents i.e. nitrates, oxidising acids, chlorine bleaches, pool chlorine etc. as ignition may result
Advice for firefighters	
Fire Fighting	<ul style="list-style-type: none"> ▶ Alert Fire Brigade and tell them location and nature of hazard. ▶ Wear full body protective clothing with breathing apparatus. ▶ Prevent, by any means available, spillage from entering drains or water course. ▶ Use water delivered as a fine spray to control fire and cool adjacent area. ▶ Avoid spraying water onto liquid pools. ▶ DO NOT approach containers suspected to be hot. ▶ Cool fire exposed containers with water spray from a protected location. ▶ If safe to do so, remove containers from path of fire.
Fire/Explosion Hazard	<ul style="list-style-type: none"> ▶ Combustible. ▶ Slight fire hazard when exposed to heat or flame. ▶ Heating may cause expansion or decomposition leading to violent rupture of containers. ▶ On combustion, may emit toxic fumes of carbon monoxide (CO). ▶ May emit acrid smoke. ▶ Mists containing combustible materials may be explosive. <p>Combustion products include: carbon dioxide (CO₂) aldehydes acrolein other pyrolysis products typical of burning organic material. May emit poisonous fumes. May emit corrosive fumes.</p>
HAZCHEM	Not Applicable

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	<p>Environmental hazard - contain spillage. Slippery when spilt.</p> <ul style="list-style-type: none"> ▶ Remove all ignition sources. ▶ 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.
Major Spills	<p>Environmental hazard - contain spillage. CARE: Absorbent materials wetted with occluded oil must be moistened with water as they may auto-oxidize, become self heating and ignite. Some oils slowly oxidise when spread in a film and oil on cloths, mops, absorbents may autoxidise and generate heat, smoulder, ignite and burn. In the workplace oily rags should be collected and immersed in water. Slippery when spilt. Moderate hazard.</p> <ul style="list-style-type: none"> ▶ Clear area of personnel and move upwind. ▶ Alert Fire Brigade and tell them location and nature of hazard. ▶ Wear breathing apparatus plus protective gloves. ▶ Prevent, by any means available, spillage from entering drains or water course. ▶ No smoking, naked lights or ignition sources. ▶ Increase ventilation. ▶ Stop leak if safe to do so. ▶ Contain spill with sand, earth or vermiculite. ▶ Collect recoverable product into labelled containers for recycling. ▶ Absorb remaining product with sand, earth or vermiculite. ▶ Collect solid residues and seal in labelled drums for disposal. ▶ Wash area and prevent runoff into drains. ▶ If contamination of drains or waterways occurs, advise emergency services.

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

SECTION 7 Handling and storage

Precautions for safe handling

Safe handling	<ul style="list-style-type: none"> ▶ Avoid all personal contact, including inhalation. ▶ Wear protective clothing when risk of exposure occurs. ▶ Use in a well-ventilated area. ▶ Prevent concentration in hollows and sumps. ▶ DO NOT enter confined spaces until atmosphere has been checked. ▶ Avoid smoking, naked lights or ignition sources. ▶ Avoid contact with incompatible materials. ▶ When handling, DO NOT eat, drink or smoke. ▶ Keep containers securely sealed when not in use. ▶ Avoid physical damage to containers. ▶ Always wash hands with soap and water after handling.
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	<ul style="list-style-type: none"> ▶ Work clothes should be laundered separately. ▶ 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.
Other information	<ul style="list-style-type: none"> ▶ Store in original containers. ▶ Keep containers securely sealed. ▶ No smoking, naked lights or ignition sources. ▶ 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	<ul style="list-style-type: none"> ▶ Glass container is suitable for laboratory quantities ▶ DO NOT use aluminium or galvanised containers ▶ Metal can or drum ▶ Packaging as recommended by manufacturer. ▶ Check all containers are clearly labelled and free from leaks.
Storage incompatibility	<ul style="list-style-type: none"> ▶ Avoid reaction with oxidising agents

SECTION 8 Exposure controls / personal protection

Control parameters

Occupational Exposure Limits (OEL)

INGREDIENT DATA

Not Available

Emergency Limits

Ingredient	TEEL-1	TEEL-2	TEEL-3
benzyl alcohol	30 ppm	52 ppm	740 ppm

Ingredient	Original IDLH	Revised IDLH
ivermectin	Not Available	Not Available
benzyl alcohol	Not Available	Not Available
soybean oil	Not Available	Not Available

Occupational Exposure Banding

Ingredient	Occupational Exposure Band Rating	Occupational Exposure Band Limit
ivermectin	E	≤ 0.01 mg/m ³
benzyl alcohol	E	≤ 0.1 ppm
soybean oil	E	≤ 0.1 ppm

Notes: Occupational exposure banding is a process of assigning chemicals into specific categories or bands based on a chemical's potency and the adverse health outcomes associated with exposure. The output of this process is an occupational exposure band (OEB), which corresponds to a range of exposure concentrations that are expected to protect worker health.


MATERIAL DATA

Exposure controls

Appropriate engineering controls	Care: Atmospheres in bulk storages and even apparently empty tanks may be hazardous by oxygen depletion. Atmosphere must be checked before entry.	
	Requirements of State Authorities concerning conditions for tank entry must be met. Particularly with regard to training of crews for tank entry; work permits; sampling of atmosphere; provision of rescue harness and protective gear as needed	
	Engineering controls are used to remove a hazard or place a barrier between the worker and the hazard. Well-designed engineering controls can be highly effective in protecting workers and will typically be independent of worker interactions to provide this high level of protection. The basic types of engineering controls are:	
	Process controls which involve changing the way a job activity or process is done to reduce the risk.	
	Enclosure and/or isolation of emission source which keeps a selected hazard "physically" away from the worker and ventilation that strategically "adds" and "removes" air in the work environment. Ventilation can remove or dilute an air contaminant if designed properly. The design of a ventilation system must match the particular process and chemical or contaminant in use. Employers may need to use multiple types of controls to prevent employee overexposure.	
General exhaust is adequate under normal operating conditions. Local exhaust ventilation may be required in special circumstances. If risk of overexposure exists, wear approved respirator. Supplied-air type respirator may be required in special circumstances. Correct fit is essential to ensure adequate protection. Provide adequate ventilation in warehouses and enclosed storage areas. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.		
Type of Contaminant:		Air Speed:
solvent, vapours, degreasing etc., evaporating from tank (in still air).		0.25-0.5 m/s (50-100 f/min)
aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers, welding, spray drift, plating acid fumes, pickling (released at low velocity into zone of active generation)		0.5-1 m/s (100-200 f/min.)
direct spray, spray painting in shallow booths, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air motion)		1-2.5 m/s (200-500 f/min.)

Continued...

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	<p>grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion)</p> <p>2.5-10 m/s (500-2000 f/min.)</p> <p>Within each range the appropriate value depends on:</p> <table border="1"> <thead> <tr> <th>Lower end of the range</th> <th>Upper end of the range</th> </tr> </thead> <tbody> <tr> <td>1: Room air currents minimal or favourable to capture</td> <td>1: Disturbing room air currents</td> </tr> <tr> <td>2: Contaminants of low toxicity or of nuisance value only.</td> <td>2: Contaminants of high toxicity</td> </tr> <tr> <td>3: Intermittent, low production.</td> <td>3: High production, heavy use</td> </tr> <tr> <td>4: Large hood or large air mass in motion</td> <td>4: Small hood-local control only</td> </tr> </tbody> </table> <p>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.</p>	Lower end of the range	Upper end of the range	1: Room air currents minimal or favourable to capture	1: Disturbing room air currents	2: Contaminants of low toxicity or of nuisance value only.	2: Contaminants of high toxicity	3: Intermittent, low production.	3: High production, heavy use	4: Large hood or large air mass in motion	4: Small hood-local control only
Lower end of the range	Upper end of the range										
1: Room air currents minimal or favourable to capture	1: Disturbing room air currents										
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3: Intermittent, low production.	3: High production, heavy use										
4: Large hood or large air mass in motion	4: Small hood-local control only										
Personal protection											
Eye and face protection	<ul style="list-style-type: none"> ▶ 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	<ul style="list-style-type: none"> ▶ Wear chemical protective gloves, e.g. PVC. ▶ Wear safety footwear or safety gumboots, e.g. Rubber <p>NOTE:</p> <ul style="list-style-type: none"> ▶ 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. <p>The selection of suitable gloves does not only depend on the material, but also on further marks of quality which vary from manufacturer to manufacturer. Where the chemical is a preparation of several substances, the resistance of the glove material can not be calculated in advance and has therefore to be checked prior to the application.</p> <p>The exact break through time for substances has to be obtained from the manufacturer of the protective gloves and has to be observed when making a final choice.</p> <p>Personal hygiene is a key element of effective hand care. Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.</p> <p>Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include:</p> <ul style="list-style-type: none"> · frequency and duration of contact, · chemical resistance of glove material, · glove thickness and · dexterity <p>Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739, AS/NZS 2161.1 or national equivalent).</p> <ul style="list-style-type: none"> · When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended. · When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended. · Some glove polymer types are less affected by movement and this should be taken into account when considering gloves for long-term use. · Contaminated gloves should be replaced. <p>As defined in ASTM F-739-96 in any application, gloves are rated as:</p> <ul style="list-style-type: none"> · Excellent when breakthrough time > 480 min · Good when breakthrough time > 20 min · Fair when breakthrough time < 20 min · Poor when glove material degrades <p>For general applications, gloves with a thickness typically greater than 0.35 mm, are recommended.</p> <p>It should be emphasised that glove thickness is not necessarily a good predictor of glove resistance to a specific chemical, as the permeation efficiency of the glove will be dependent on the exact composition of the glove material. Therefore, glove selection should also be based on consideration of the task requirements and knowledge of breakthrough times.</p> <p>Glove thickness may also vary depending on the glove manufacturer, the glove type and the glove model. Therefore, the manufacturers' technical data should always be taken into account to ensure selection of the most appropriate glove for the task.</p> <p>Note: Depending on the activity being conducted, gloves of varying thickness may be required for specific tasks. For example:</p> <ul style="list-style-type: none"> · Thinner gloves (down to 0.1 mm or less) may be required where a high degree of manual dexterity is needed. However, these gloves are only likely to give short duration protection and would normally be just for single use applications, then disposed of. · Thicker gloves (up to 3 mm or more) may be required where there is a mechanical (as well as a chemical) risk i.e. where there is abrasion or puncture potential <p>Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.</p>										
Body protection	See Other protection below										
Other protection	<ul style="list-style-type: none"> ▶ Overalls. ▶ P.V.C apron. ▶ Barrier cream. ▶ Skin cleansing cream. ▶ Eye wash unit. 										

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:

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Material	CPI
BUTYL	A
VITON	A

* 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

Type A-P Filter of sufficient capacity. (AS/NZS 1716 & 1715, EN 143:2000 & 149:2001, ANSI Z88 or national equivalent)

Selection of the Class and Type of respirator will depend upon the level of breathing zone contaminant and the chemical nature of the contaminant. Protection Factors (defined as the ratio of contaminant outside and inside the mask) may also be important.

Required minimum protection factor	Maximum gas/vapour concentration present in air p.p.m. (by volume)	Half-face Respirator	Full-Face Respirator
up to 10	1000	A-AUS / Class1 P2	-
up to 50	1000	-	A-AUS / Class 1 P2
up to 50	5000	Airline *	-
up to 100	5000	-	A-2 P2
up to 100	10000	-	A-3 P2
100+			Airline**

* - Continuous Flow ** - Continuous-flow or positive pressure demand

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)

- ▶ Cartridge respirators should never be used for emergency ingress or in areas of unknown vapour concentrations or oxygen content.
- ▶ The wearer must be warned to leave the contaminated area immediately on detecting any odours through the respirator. The odour may indicate that the mask is not functioning properly, that the vapour concentration is too high, or that the mask is not properly fitted. Because of these limitations, only restricted use of cartridge respirators is considered appropriate.
- ▶ Cartridge performance is affected by humidity. Cartridges should be changed after 2 hr of continuous use unless it is determined that the humidity is less than 75%, in which case, cartridges can be used for 4 hr. Used cartridges should be discarded daily, regardless of the length of time used

SECTION 9 Physical and chemical properties**Information on basic physical and chemical properties**

Appearance	Liquid; does not mix water.		
Physical state	Liquid	Relative density (Water = 1)	Not Available
Odour	Not Available	Partition coefficient n-octanol / water	Not Available
Odour threshold	Not Available	Auto-ignition temperature (°C)	Not Available
pH (as supplied)	Not Available	Decomposition temperature	Not Available
Melting point / freezing point (°C)	Not Available	Viscosity (cSt)	Not Available
Initial boiling point and boiling range (°C)	Not Available	Molecular weight (g/mol)	Not Applicable
Flash point (°C)	Not Available	Taste	Not Available
Evaporation rate	Not Available	Explosive properties	Not Available
Flammability	Not Available	Oxidising properties	Not Available
Upper Explosive Limit (%)	Not Available	Surface Tension (dyn/cm or mN/m)	Not Available
Lower Explosive Limit (%)	Not Available	Volatile Component (%vol)	Not Available
Vapour pressure (kPa)	Not Available	Gas group	Not Available
Solubility in water	Not Available	pH as a solution (%)	Not Available
Vapour density (Air = 1)	Not Available	VOC g/L	208

SECTION 10 Stability and reactivity

Reactivity	See section 7
Chemical stability	<ul style="list-style-type: none"> ▶ 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

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Hazardous decomposition products

See section 5

SECTION 11 Toxicological information

Information on toxicological effects

Inhaled	<p>Evidence shows, or practical experience predicts, that the material produces irritation of the respiratory system, in a substantial number of individuals, following inhalation. In contrast to most organs, the lung is able to respond to a chemical insult by first removing or neutralising the irritant and then repairing the damage. The repair process, which initially evolved to protect mammalian lungs from foreign matter and antigens, may however, produce further lung damage resulting in the impairment of gas exchange, the primary function of the lungs. Respiratory tract irritation often results in an inflammatory response involving the recruitment and activation of many cell types, mainly derived from the vascular system.</p> <p>Inhalation of vapours may cause drowsiness and dizziness. This may be accompanied by narcosis, reduced alertness, loss of reflexes, lack of coordination and vertigo.</p> <p>The maximum attainable concentration of 5.11 mg/l ivermectin produced transient irritation of mucous membranes in rats but no deaths or other signs of toxicity after one hour exposure. An acute inhalation study showed a low order of toxicity in animals but this was attributed to the larger particle size of the sample used in the study.</p> <p>Inhalation hazard is increased at higher temperatures.</p> <p>Not normally a hazard due to non-volatile nature of product</p> <p>Inhalation of oil droplets/ aerosols may cause discomfort and may produce chemical pneumonitis.</p> <p>Fine mists generated from plant/ vegetable (or more rarely from animal) oils may be hazardous. Extreme heating for prolonged periods, at high temperatures, may generate breakdown products which include acrolein and acrolein-like substances.</p> <p>Inhalation of benzyl alcohol may affect respiration (paralysis of the respiratory center, respiratory depression, gasping respirations), cardiovascular system (hypotension)</p>
Ingestion	<p>Overexposure is unlikely in this form.</p> <p>Fatty acid esters are relatively non-toxic in rats. Large doses of 20-60 gm/kg are lethal in rats.</p> <p>JECFA established an acceptable daily intake (ADI) of 0-25 mg/kg bw for polyglyceryl esters of fatty acids having an average chain length of up to 3 glycerol units and an ADI of 0-7.5 mg/kg bw for polyglyceryl esters of interesterified ricinoleic acid.</p> <p>In the EU, the esters are listed as food additives at concentrations between 5000 and 10,000 mg/kg in certain foods, and up to 7% free glycerol/polyglycerol is allowed (i.e., 700 mg/kg).</p> <p>No major toxicity has been observed to date following ivermectin treatment of humans. Systemic reactions include fever, rash and lymph-node pain or swelling. Ocular reactions have been minimal.</p> <p>Acute rodent studies show that ivermectin is highly toxic; rodents may not however be a good model for humans, in this case, as they appear to be more sensitive to the effects of ivermectin. The dose-response curve for primates is relatively flat compared to rodents, suggesting that serious or life-threatening toxicity would only occur at higher multiples of the doses that cause clinical evidence of toxicity. Signs of toxicity reported in acute studies include ataxia (incoordination), bradypnea (slowed breathing), emesis (vomiting), mydriasis (dilated pupils), sedation and tremors. Similar signs indicative of central nervous system toxicity, were also observed in repeat dose studies at elevated dosages.</p> <p>Based on studies in animals and case of accidental ingestion in humans, overexposure to ivermectin may produce drowsiness, depressed motor activity, slowed breathing, dilation of the pupils, tremors, vomiting, anorexia and incoordination</p> <p>Use in food and as food additive, indicates high degree of tolerance</p> <p>Ingestion of large doses of benzyl alcohol may cause abdominal pain, nausea, vomiting, diarrhea. It may affect behavior/central nervous system and cause headache, somnolence, excitement, dizziness, ataxia, coma, convulsions, and other symptoms of central nervous system depression.</p> <p>Exposure to excessive amounts of benzyl alcohol has been associated with toxicity (hypotension, metabolic acidosis), particularly in neonates, and an increased incidence of kernicterus (a neurological condition that occurs in severe jaundice), particularly in small preterm infants. There have been rare reports of deaths, primarily in preterm infants, associated with exposure to excessive amounts of benzyl alcohol. The amount of benzyl alcohol from medications is usually considered negligible compared to that received in flush solutions containing benzyl alcohol.</p> <p>Administration of high dosages of medications containing this preservative must take into account the total amount of benzyl alcohol administered. The amount of benzyl alcohol at which toxicity may occur is not known. If the patient requires more than the recommended dosages or other medications containing this preservative, the practitioner must consider the daily metabolic load of benzyl alcohol from these combined sources.</p>
Skin Contact	<p>The material produces moderate skin irritation; evidence exists, or practical experience predicts, that the material either</p> <ul style="list-style-type: none"> ▶ produces moderate inflammation of the skin in a substantial number of individuals following direct contact, and/or ▶ produces significant, but moderate, inflammation when applied to the healthy intact skin of animals (for up to four hours), such inflammation being present twenty-four hours or more after the end of the exposure period. <p>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 spongy layer of the skin (spongiosis) and intracellular oedema of the epidermis.</p> <p>Skin contact with the material may damage the health of the individual; systemic effects may result following absorption.</p> <p>Tests with monkeys show that less than 1% of dermally applied ivermectin was absorbed into the bloodstream through the skin. Ivermectin does not cause allergic skin reactions</p> <p>Open cuts, abraded or irritated skin should not be exposed to this material</p> <p>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.</p>
Eye	<p>Limited evidence or practical experience suggests, that the material may cause eye irritation in a substantial number of individuals. Repeated or prolonged eye contact may cause inflammation characterised by temporary redness (similar to windburn) of the conjunctiva (conjunctivitis); temporary impairment of vision and/or other transient eye damage/ulceration may occur.</p>
Chronic	<p>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.</p> <p>Substances that can cause occupational asthma (also known as asthmagens and respiratory sensitisers) can induce a state of specific airway hyper-responsiveness via an immunological, irritant or other mechanism. Once the airways have become hyper-responsive, further exposure to the substance, sometimes even to tiny quantities, may cause respiratory symptoms. These symptoms can range in severity from a runny nose to asthma. Not all workers who are exposed to a sensitiser will become hyper-responsive and it is impossible to identify in advance who are likely to become hyper-responsive.</p> <p>Substances that can cause occupational asthma should be distinguished from substances which may trigger the symptoms of asthma in people with pre-existing air-way hyper-responsiveness. The latter substances are not classified as asthmagens or respiratory sensitisers</p> <p>Wherever it is reasonably practicable, exposure to substances that can cause occupational asthma should be prevented. Where this is not possible the primary aim is to apply adequate standards of control to prevent workers from becoming hyper-responsive.</p> <p>Activities giving rise to short-term peak concentrations should receive particular attention when risk management is being considered. Health surveillance is appropriate for all employees exposed or liable to be exposed to a substance which may cause occupational asthma and there should be appropriate consultation with an occupational health professional over the degree of risk and level of surveillance.</p> <p>There is sufficient evidence to provide a strong presumption that human exposure to the material may result in impaired fertility on the basis of: - clear evidence in animal studies of impaired fertility in the absence of toxic effects, or evidence of impaired fertility occurring at around the same</p>

dose levels as other toxic effects but which is not a secondary non-specific consequence of other toxic effects.

There is sufficient evidence to provide a strong presumption that human exposure to the material may result in developmental toxicity, generally on the basis of:

- clear results in appropriate animal studies where effects have been observed in the absence of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not secondary non-specific consequences of the other toxic effects.

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

Allergic reactions to benzoic acid have been reported. Of 100 patients with asthma undergoing provocation tests with benzoic acid, 47 showed positive reactions. In another study, of 75 patients with recurrent urticaria (skin eruptions) and angio-oedema (a deep dermal condition characterised by large wheals) of more than 4 months duration, 44 were found to be sensitive to sodium benzoate or p-hydroxybenzoic acid (paraben), alone or in conjunction with aspirin or azo- dyes, or both. In a further work there was no significant objective or subjective skin response to two 500-mg daily doses of benzoic acid or lactic acid in a double blind study of 150 dermatological patients

Glyceryl triesters (triglycerides), following ingestion, are metabolised to monoglycerides, free fatty acids and glycerol, all of which are absorbed in the intestinal mucosa and undergo further metabolism. Medium chain triglycerides (C8-C10) appear to have relatively rapid metabolism and elimination from blood and tissues compared to long chain triglycerides (C16-C18). Little or no acute, subchronic or chronic oral toxicity was seen in animal studies unless levels approached a significant percentage of calorific intake. Subcutaneous injections of tricaprylin in rats over a five-week period caused granulomatous reaction characterised by oil deposits surrounded by macrophages. Diets containing substantial levels of tributyrin produced gastric lesions in rats fed for 3-35 weeks; the irritative effect of the substance was thought to be the cause of tissue damage. Dermal application was not associated with significant irritation in rabbit skin; ocular exposures were, at most, mildly irritating to rabbit eyes. No evidence of sensitisation or photosensitisation was seen in a guinea pig maximisation test. Most of the genotoxicity test systems were negative. Tricaprylin, trioctanoin and triolein have been used, historically, as vehicles in carcinogenicity testing of other chemicals. In one study, subcutaneous injection of tricaprylin, in newborn mice, produced more tumours in lymphoid tissue than were seen in untreated animals whereas, in another study, subcutaneous or intraperitoneal injection in 4- to 6-week old female mice produced no tumours. Trioctanoin injected subcutaneously in hamster produced no tumours; when injected intraperitoneally in pregnant rats there was an increase in mammary tumours among the off-spring but similar studies in pregnant hamsters and rabbits showed no tumours in the off-spring.

The National Toxicological Program conducted a 2-year study in rats given tricaprylin by gavage. The treatment was associated with a statistically significant dose-related increase in pancreatic acinar cell hyperplasia and adenoma but there were no acinar carcinomas.

Tricaprylin is not teratogenic to mice or rats but some reproductive effects were seen in rabbits. A low level of foetal eye abnormalities and a small percentage of abnormal sperm were reported in mice injected with trioctanoin.

Trioctanoin was also used as a vehicle control in a sperm abnormality test. Ten male control mice received an intraperitoneal injection of 0.25 ml trioctanoin 0.05 g/kg of benz[a]pyrene (known reproductive toxicant and mutagen) daily for 5 days and sperm from caudae epididymides analysed. Based on these studies there is no sufficient evidence to classify the trioctanoin as reproductive toxicant.

In the human body, high levels of triglycerides in the bloodstream have been linked to atherosclerosis, heart disease and stroke. However, the relative negative impact of raised levels of triglycerides compared to that of LDL:HDL ratios is as yet unknown. The risk can be partly accounted for by a strong inverse relationship between triglyceride level and HDL-cholesterol level. But the risk is also due to high triglyceride levels increasing the quantity of small, dense LDL particles

In dogs treated with ivermectin for 3 months or in monkeys treated for 2-weeks, there were no gross or histological changes. In rats treated for 3 months, there were changes in spleen, bone marrow and kidneys. Signs of toxicity reported in these repeat-dose studies were similar to those following acute over-exposure. The lowest no-effect-level reported was 0.4 mg/kg/day.

In animal studies ivermectin was found to be neither teratogenic or foetotoxic in rats and rabbits, but produced cleft palate in the foetuses of mice and occasional unexplained maternal deaths. Suckling neonatal rats exhibited enhanced sensitivity to the toxic effects of ivermectin due to exposure via maternal milk, after birth, when the blood-brain barrier is incomplete. Ivermectin produced developmental toxicity in animals only at or near dose levels that were maternally toxic. No evidence of genotoxicity was found in a battery of assays.

alpha-Linolenic acid (ALA) is metabolized to eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA). EPA is a precursor of the series-3 prostaglandins, the series-5 leukotrienes and the series-3 thromboxanes. These eicosanoids have anti-inflammatory and anti-atherogenic properties. The incorporation of metabolites of ALA in cell membranes may play a role in anti-inflammatory activity, inhibition of platelet aggregation and possibly in anti-proliferative actions of ALA-laden triacylglycerols (TAGs) (also known as triglycerides), following ingestion, undergo hydrolysis via lipases to form monoglycerides and free fatty acids. Once formed, the monoglycerides and the free fatty acids are absorbed by the enterocytes. In the enterocytes, reacylation takes place reforming TAGs, which are then reassembled with phospholipids, cholesterol and apolipoproteins into chylomicrons. The chylomicrons are released into the lymphatics from whence they are transported to the systemic circulation. In the circulation, the chylomicrons are degraded by lipoprotein lipase, and the fatty acids, including ALA, are taken up in part by the endothelial cells where ALA is metabolized to phospholipids. ALA is transported via the circulation to various tissues in the body where it is metabolized to EPA, DHA and series-3 prostaglandins, series-5 leukotrienes and series-3 thromboxanes. Most of this metabolism occurs in cell membrane phospholipids.

An intake of from 3 to 4 grams daily of ALA is estimated to be equivalent to an intake of 0.3 grams daily of EPA, which one would get from a diet rich in fish.

Interactions may occur between ALA and aspirin, other NSAIDs or herbs, such as *Allium sativum* (garlic) and *Ginkgo biloba* (ginkgo). Such interactions, if they were to occur, might be manifested by nosebleeds and increased susceptibility to bruising. If this does occur, consideration should be given to lowering or stopping intake.

Repeated ingestion of linoleic acid, by man produces changes in platelet function tests. Animals tests show weight loss, progressive secondary anaemia, leukopenia and damage to erythrocyte and platelet membranes

Prolonged or repeated exposure to benzyl alcohol may cause allergic contact dermatitis.

Prolonged or repeated ingestion may affect behavior/central nervous system with symptoms similar to acute ingestion. It may also affect the liver, kidneys, cardiovascular system, and metabolism (weight loss).

Animal studies have shown this compound to cause lung, liver, kidney and CNS disorders. Studies in animals have shown evidence of teratogenicity in the chick embryo. The significance of the information for humans is unknown.

Benzyl alcohol showed no evidence of carcinogenic activity in long-term toxicology and carcinogenesis study.

Virbac Virbamec LV Pour-On Endectocide for Cattle	TOXICITY	IRRITATION
	Not Available	Not Available
ivermectin	TOXICITY	IRRITATION
	Dermal (rabbit) LD50: 406 mg/kg ^[2] Oral(Rat) LD50; 2 mg/kg ^[2]	Eye (rabbit): slight ** Skin (rabbit): non-irritating **
benzyl alcohol	TOXICITY	IRRITATION
	Dermal (rabbit) LD50: >2000 mg/kg ^[1]	Eye (rabbit): 0.75 mg open SEVERE
	Inhalation(Rat) LC50; >4.178 mg/L4h ^[1]	Eye: adverse effect observed (irritating) ^[1]
	Oral(Rabbit) LD50; 1040 mg/kg ^[2]	Skin (man): 16 mg/48h-mild Skin (rabbit):10 mg/24h open-mild Skin: no adverse effect observed (not irritating) ^[1]

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soybean oil	TOXICITY	IRRITATION
	Not Available	Not Available
Legend: 1. Value obtained from Europe ECHA Registered Substances - Acute toxicity 2. * Value obtained from manufacturer's SDS. Unless otherwise specified data extracted from RTECS - Register of Toxic Effect of chemical Substances		

IVERMECTIN	<p>The material may produce respiratory tract irritation. Symptoms of pulmonary irritation may include coughing, wheezing, laryngitis, shortness of breath, headache, nausea, and a burning sensation.</p> <p>Unlike most organs, the lung can respond to a chemical insult or a chemical agent, by first removing or neutralising the irritant and then repairing the damage (inflammation of the lungs may be a consequence).</p> <p>The repair process (which initially developed to protect mammalian lungs from foreign matter and antigens) may, however, cause further damage to the lungs (fibrosis for example) when activated by hazardous chemicals. Often, this results in an impairment of gas exchange, the primary function of the lungs. Therefore prolonged exposure to respiratory irritants may cause sustained breathing difficulties.</p> <p>For ivermectin:</p> <p>Therapeutic doses of 0.2 mg/kg do not produce signs of toxicity in a variety of species including humans.</p> <p>There were no gross or histological changes seen in dogs treated with ivermectin for 3 months (no-observed-adverse-effect-level (NOAEL) =0.5 mg/kg/day) or in monkeys treated for 2 weeks (NOAEL = 1.2 mg/kg/day).</p> <p>Changes in the spleen, bone marrow and kidneys were reported in rats treated for 3 months (NOAEL = 0.4 mg/kg/day). Ivermectin produced developmental toxicity in mice, rats and rabbits at or near dosage levels that were maternally toxic (NOAEL = 0.1 mg/kg/day in mice, the most sensitive species). Neonatal rats are about 20 times more susceptible to ivermectin than adult rats because the blood brain barrier is not fully developed until after birth. There has been no evidence of teratogenicity in controlled studies in pregnant cattle, swine and dogs at up to three times the clinical dose nor has breeding performance been affected in various species.</p> <p>Reproductive effects: Rats given 0.40 mg/kg/day of ivermectin had increased stillbirths, decreased pup viability, decreased lactation, and decreased pup weights. These data suggest that ivermectin may have the potential to cause reproductive effects at high enough doses.</p> <p>Teratogenic effects: Ivermectin produced cleft palate in the offspring of treated mice and rabbits, but only at doses that were also toxic to the mothers. There were no birth defects in the offspring of rats given up to 1 mg/kg/day. Ivermectin is unlikely to cause teratogenic effects except at doses toxic to the mother.</p> <p>The targeted clinical dosage of 0.15-0.2 mg/kg and doses in the range of 3 to 12 mg are given according to body weight. Higher dosages (0.4 mg/kg) have been given to patients with lymphatic filariasis. For treatment of onchocerciasis caused by <i>Onchocerca volvulus</i>, a leading cause of river blindness in tropical areas), the drug is given only once every six or twelve months. Ivermectin is metabolised in the liver and excreted almost exclusively in the faeces over a period of twelve days. The plasma half-life in man is about 10-12 hours for ivermectin and 3 days for its metabolites. Side-effects are not considered to be due to the toxicity of ivermectin as such, but are attributed to hypersensitivity reactions resulting from the death of the microfilariae. In cases of accidental overdose with ivermectin, there have been no fatalities reported; however symptoms resemble those in animal studies.</p> <p>Mutagenic effects: Ivermectin does not appear to be mutagenic. Mutagenicity tests in live rats and mice were negative. Ivermectin was shown to be nonmutagenic in the Ames test.</p> <p>Carcinogenic effects: Ivermectin is not carcinogenic in rats or mice. The rats were fed dietary doses of up to 2 mg/kg/day for 24 months, and the mice were up to 8 mg/kg/day for 22 months. These represent the maximum tolerated doses</p> <p>Oral (Rat) LD50: 2-3 mg/kg ** ADI: 0.8 mg/day ** * [Mercke] ** [Mercke, Sharpe and Dohme]</p>
	BENZYL ALCOHOL

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

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 conjugal 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 isoamyl 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 the quality of life of 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 axillary (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 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 Myroxylon pereirae are well recognised causes of contact urticaria, but others, including menthol, vanillin and benzaldehyde have also been reported. The reactions to Myroxylon pereirae may be due to cinnamates. 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 nonimmunological basis for the reactions seen.

Pigmentary anomalies: The term "pigmented cosmetic dermatitis" was introduced in 1973 for what had previously been known as melanosis 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 Musk ambrette produced a considerable number of allergic photocontact reactions (in which UV-light is required) in the 1970s and was later banned from use in the EU. Nowadays, photoallergic 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 furocoumarins 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 haptens, 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 prohaptens 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 prohaptens 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 prehaptens or as a prohaptens, 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.

Prohaptens

Compounds that are bioactivated in the skin and thereby form haptens are referred to as prohaptens.

In the case of prohaptens, 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.

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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 monooxygenases 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=C-CO- (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 prohaptenes) is more complex compared to that of compounds that act as direct haptens without any activation. The autoxidation patterns can differ due to differences in the stability of the intermediates formed, e.g. it has been shown that autoxidation of the structural isomers linalool and geraniol results in different major haptens/allergens. Moreover, the complexity of the prediction increases further for those compounds that can act both as pre- and prohaptenes. In such cases, the impact on the sensitisation potency depends on the degree of abiotic activation (e.g. autoxidation) in relation to the metabolic activation.

A member or analogue of a group of 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 substances in this group:

- contain a benzene ring substituted with a reactive primary oxygenated functional group or can be hydrolysed to such a functional group
- the major pathway of metabolic detoxification involves hydrolysis and oxidation to yield the corresponding benzoic acid derivative which is excreted either as the free acid or the glycine conjugate
- they show a consistent pattern of toxicity in both short- and long- term studies and
- they exhibit no evidence of genotoxicity in standardised batteries of in vitro and in vivo assays.

The benzyl derivatives are rapidly absorbed through the gut, metabolised primarily in the liver, and excreted in the urine as glycine conjugates of benzoic acid derivatives.

In general, aromatic esters are hydrolysed in vivo through the catalytic activity of carboxylesterases, the most important of which are the A-esterases. Hydrolysis of benzyl and benzoate esters to yield corresponding alcohols and carboxylic acids and hydrolysis of acetals to yield benzaldehyde and simple alcohols have been reported in several experiments.

The alcohols and aldehydes are rapidly oxidised to benzoic acid while benzoate esters are hydrolysed to benzoic acid.

Flavor and Extract Manufacturers Association (FEMA)

The aryl alkyl alcohol (AAA) fragrance ingredients are a diverse group of chemical structures with similar metabolic and toxicity profiles.

The AAA fragrances demonstrate low acute and subchronic dermal and oral toxicity.

At concentrations likely to be encountered by consumers, AAA fragrance ingredients are non-irritating to the skin.

The potential for eye irritation is minimal.

With the exception of benzyl alcohol and to a lesser extent phenethyl and 2-phenoxyethyl AAA alcohols, human sensitization studies, diagnostic patch tests and human induction studies, indicate that AAA fragrance ingredients generally have no or low sensitization potential. Available data indicate that the potential for photosensitization is low.

NOAELs for maternal and developmental toxicity are far in excess of current human exposure levels.

No carcinogenicity in rats or mice was observed in 2-year chronic testing of benzyl alcohol or a-methylbenzyl alcohol; the latter did induce species and gender-specific renal adenomas in male rats at the high dose. There was no to little genotoxicity, mutagenicity, or clastogenicity in the mutagenicity in vitro bacterial assays, and in vitro mammalian cell assays. All in vivo micronucleus assays were negative.

It is concluded that these materials would not present a safety concern at current levels of use as fragrance ingredients

The Research Institute for Fragrance Materials (RIFM) Expert Panel

For omega 6 fatty acids and derivatives:

Some medical research suggests that excessive levels of certain omega-6 fatty acids relative to certain omega-3 fatty acids may increase the probability of a number of diseases.

Modern Western diets typically have ratios of omega-6 to omega-3 in excess of 10 to 1, some as high as 30 to 1; the average ratio of omega-6 to omega-3 in the Western diet is 15:1–16.7:1. Humans are thought to have evolved with a diet of a 1-to-1 ratio of omega-6 to omega-3 and the optimal ratio is thought to be 4 to 1 or lower although some sources suggest ratios as low as 1:1). A ratio of 2–3:1 omega 6 to omega 3 helped reduce inflammation in patients with rheumatoid arthritis. A ratio of 5:1 had a beneficial effect on patients with asthma but a 10:1 ratio had a negative effect. A ratio of 2.5:1 reduced rectal cell proliferation in patients with colorectal cancer, whereas a ratio of 4:1 had no effect.

Excess omega-6 fatty acids from vegetable oils interfere with the health benefits of omega-3 fats, in part because they compete for the same rate-limiting enzymes. A high proportion of omega-6 to omega-3 fat in the diet shifts the physiological state in the tissues toward the pathogenesis of many diseases: prothrombotic, proinflammatory and procontractive.

Chronic excessive production of omega-6 eicosanoids is correlated with arthritis, inflammation, and cancer. Many of the medications used to treat and manage these conditions work by blocking the effects of the COX-2 enzyme. Many steps in formation and action of omega-6 prostaglandins from omega-6 arachidonic acid proceed more vigorously than the corresponding competitive steps in formation and action of omega-3 hormones from omega-3 eicosapentaenoic acid. The COX-1 and COX-2 inhibitor medications, used to treat inflammation and pain, work by preventing the COX enzymes from turning arachidonic acid into inflammatory compounds. The LOX inhibitor medications often used to treat asthma work by preventing the LOX enzyme from converting arachidonic acid into the leukotrienes. Many of the anti-mania medications used to treat bipolar disorder work by targeting the arachidonic acid cascade in the brain.

A high consumption of oxidised polyunsaturated fatty acids (PUFAs), which are found in most types of vegetable oil, may increase the likelihood that postmenopausal women will develop breast cancer. Similar effect was observed on prostate cancer, but the study was performed on mice. Another "analysis suggested an inverse association between total polyunsaturated fatty acids and breast cancer risk, but individual polyunsaturated fatty acids behaved differently [from each other]. [...] a 20:2 derivative of linoleic acid [...] was inversely associated with the risk of breast cancer"

PUFAs are prone to spontaneous oxidation/ peroxidation. The feeding of lipid oxidation products and oxidised fats has been reported to cause adverse biological effects on laboratory animals, including growth retardation, teratogenicity, tissue damage and increased liver and kidney weights, as well as cellular damage to the testes and epididymes, increased peroxidation of membrane and tissue lipids and induction of cytochrome P450 activities in the colon and liver.

The propensity for PUFAs to oxidise leads to the generation of free radicals and eventually to rancidity.

Culinary oils, when heated, undergo important chemical reaction involving self-sustaining, free radical-mediated oxidative deterioration of PUFAs. Such by-products may be cytotoxic, mutagenic, reproductive toxins and may produce chronic disease. Samples of repeatedly used oils collected from fast-food retail outlets and restaurants have confirmed the production of aldehydic lipid oxidation products (LOPs) at levels exceeding 10 exp-2 moles per kilogram (mol/kg) during "on-site" frying episodes. Volatile emissions from heated culinary oils used in Chinese-style cooking are mutagenic; exposure to such indoor air pollution may render humans more susceptible to contracting lung or further cancers, together with rhinitis and diminished lung function. The high temperatures used in standard (especially Chinese) frying result in fumes that are rich in volatile LOPs, including acrolein.

The end products of lipid peroxidation are reactive aldehydes, such as malondialdehyde (MDA) and 4-hydroxynonenal (HNE), the second one being known also as "second messenger of free radicals" and major bioactive marker of lipid peroxidation, due to its numerous biological activities resembling activities of reactive oxygen species. end-products of lipid peroxidation may be mutagenic and carcinogenic

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malondialdehyde reacts with deoxyadenosine and deoxyguanosine in DNA, forming DNA adducts. Malondialdehyde produces mutagenic effects in several bioassays.

Side products of lipid peroxidation can also exert toxic effects, even at sites distant from the primary oxidation site. Such products (typically malondialdehyde and a large group of hydroxyalkenals - alpha-beta-unsaturated aldehydes) may interact with protein thiols (producing intermolecular cross-links) and, as a result produce functional impairment to enzyme systems, receptors and structural proteins. Aldehydes may also inhibit protein biosynthesis and increase osmotic fragility of lysosomes (releasing hydrolytic enzymes) and other subcellular organelles. They may also react with nucleic acids.

The toxicity of lipid hydroperoxides to animals is best illustrated by the lethal phenotype of glutathione peroxidase 4 (GPX4) knockout mice.

These animals do not survive past embryonic day 8, indicating that the removal of lipid hydroperoxides is essential for mammalian life.

Peroxidised linoleic acid applied to the shaved skin of guinea pigs, in a patch test experiment, produced necrosis and bleeding. When the abdominal skin of guinea pig was patched for 8 days with a cream containing 25 nmol (in terms of malondialdehyde) of lipid peroxides per gram, a thickening of the epidermis was found

Lipid peroxidation in cellular membranes may produce several morphological alterations resulting, for example, in membrane aggregation, deformation or breakage. This may result in the release of hydrolytic enzymes which in turn may degrade functional macromolecules and cause secondary damage. In addition membrane-bound enzyme systems may be disrupted.

Epoxidation of double bonds is a common bioactivation pathway for alkenes. The allylic epoxides, so formed, were found to possess sensitizing capacity in vivo and in vitro and to be chemically reactive towards a common hexapeptide containing the most common nucleophilic amino acids.

Further-more, a SAR study of potentially prohaptenic alkenes demonstrated that conjugated dienes in or in conjunction with a six-membered ring are prohaptenic, whereas related alkenes containing isolated double bonds or an acyclic conjugated diene were weak or nonsensitizing compounds. This difference in sensitizing capacity of conjugated dienes as compared to alkenes with isolated double bonds was found to be due to the high reactivity and sensitizing capacity of the allylic epoxides metabolically formed from conjugated dienes.

Allergic Contact Dermatitis—Formation, Structural Requirements, and Reactivity of Skin Sensitizers.

Ann-Therese Karlberg et al: Chem. Res. Toxicol. 2008, 21, pp 53–69

http://ftp.cdc.gov/pub/Documents/OEL/06.%20Dotson/References/Karlberg_2008.pdf

For Group E aliphatic esters (polyol esters):

According to a classification scheme described by the American Chemistry Council' Aliphatic Esters Panel, Group E substances are esters of monoacids, mainly common fatty acids, and trihydroxy or polyhydroxyalcohols or polyols, such as pentaerythritol (PE), 2-ethyl-2-(hydroxymethyl)-1,3-propanediol or trimethylolpropane (TMP), and dipentaerythritol (diPE). The Group E substances often are referred to as "polyol esters" The polyol esters are unique in their chemical characteristics since they lack beta-tertiary hydrogen atoms, thus leading to stability against oxidation and elimination. The fatty acids often range from C5-C10 to as high as C18 (e.g., oleic, stearic, isostearic, tall oil fatty acids) in carbon number and generally are derived from naturally occurring sources. Group E esters may have multiple ester linkages and may include mixed esters derived from different carbon-length fatty acid mixtures. The lack of beta-tertiary hydrogen atoms in the structure of the polyol esters makes them characteristically and chemically stable against oxidation and elimination in comparison to other ester classes or groups. For these reasons, trimethylolpropane (TMP) and pentaerythritol (PE) esters with fatty acids of C5 to C10 carbon-chain length have applications as synthetic lubricants for passenger car motor oil and military and civilian jet engines. TMP and PE esters of C18 acids (e.g., isostearic and oleic acids) also have found use in synthetic lubricant applications, including refrigeration lubricants and hydraulic fluids. Because of their higher thermal stability characteristics, they also find use in a variety of high temperature applications such as industrial oven chain oils, high temperature greases, fire resistant transformer coolants and turbine engines

Polyol esters that are extensively esterified also have greater polarity, less volatility and enhanced lubricity characteristics. **Acute toxicity:**

Depending on the degree of esterification, the polyol esters can be resistant or slow towards chemical or enzymatic hydrolysis (i.e., esterase or lipases) as a result of steric hindrance. PE and diPE esters that are capable of being enzymatically hydrolyzed will generate pentaerythritol or dipentaerythritol, and the corresponding fatty acids which, for most of the Group E esters, are comprised mainly of oleic, linoleic and stearic acids as well as the fatty acids in the C5-10 carbon-length. Similarly, TMP esters can undergo metabolism to yield trimethylolpropane (2-ethyl-2-hydroxymethyl-1,3-propanediol) and fatty acid constituents. Pentaerythritol and trimethylolpropane have been reported to have a low order of toxicity. The acute oral LD50 for these substances was greater than 2000 mg/kg indicating a relatively low order of toxicity. The similarity in the low order of toxicity for these substances is consistent with their similar chemical structure and physicochemical properties.

Metabolic studies of polyglyceryl esters indicated that these esters are hydrolyzed in the gastrointestinal (GI) tract, and utilization and digestibility studies supported the assumption that the fatty acid moiety is metabolized in the normal manner. Analytical studies have produced no evidence of accumulation of the polyglycerol moiety in body tissues.

In an acute dermal toxicity study in rats, the LD50 of 1,2,3-propanetriol, homopolymer, diisooctadecanoate was >5000 mg/kg. Low toxicity was reported in acute oral studies. In rats, the LD50 >2000 mg/kg for polyglyceryl-3 caprate, polyglyceryl-3 caprylate, polyglyceryl-4 caprate, diisostearoyl polyglyceryl-3 dimer dilinoleate, and the LD50 was >5000 mg/kg for polyglyceryl-3 iso-stearate, polyglyceryl-3-oleate, polyglyceryl-2 diisostearate and polyglyceryl-3 diisostearate.

The ability to enhance skin penetration was examined for several of the polyglyceryl fatty acid esters.

Repeat dose toxicity: Polyol esters are generally well tolerated by rats in 28-day oral toxicity studies. NOAEL for these substances was 1000 mg/kg/day in Sprague-Dawley rats. The TMP ester of heptanoic and octanoic acid did not produce signs of overt systemic toxicity at any dose levels tested (i.e., 100, 300, and 1000 mg/kg/day). There were no treatment-related clinical in-life, functional observation battery, or gross postmortem findings. There were no treatment related mortality, and no adverse effects on body weight, food consumption, clinical laboratory parameters, or organ weights. However, there were increased numbers of hyaline droplets in the proximal cortical tubular epithelium of the 300 and 1000 mg/kg/day in male rats. Based on these findings (hyaline droplets), the NOAEL for this polyol ester was established at 100 mg/kg/day for male rats. Hyaline droplet formation observed in the male kidneys is believed to be a sex/species condition specific to only male rats, which has little relevance to humans.

The results from these repeated dose dermal toxicity studies suggest that polyol esters exhibit a low order of toxicity following repeated application. This may be attributable to similarities in their chemical structures, physicochemical properties, and common metabolic pathways (i.e., esters can be enzymatically hydrolyzed to the corresponding polyalcohol and the corresponding fatty acids) The polyol, hexanedioic acid, mixed esters with decanoic acid, heptanoic acid, octanoic acid and PE, was applied to the skin of groups of 10 (male and female) rats for five days a week for four (4) weeks at dose levels of 0, 125, 500 and 2000 mg/kg/day. Treated animals exhibited no signs indicative of systemic toxicity. No visible signs of irritation were observed at treatment sites. Microscopically, treated skin (viz., greater than or equal to 500 mg/kg/day) exhibited a dose-related increased incidence and severity of hyperplasia and hyperkeratosis of the epidermis and sebaceous gland hyperplasia. These effects were reversible. None of the minor changes in haematology and serum chemistry parameters were considered biologically significant. High dose females (2000 mg/kg/day) exhibited a significant increase in relative adrenal and brain weights when compared to the controls. These differences were attributed to the lower final body weight of the female animals. The NOAEL in this study for systemic toxicity was established as 500 mg /kg/day and 125 mg/kg/day for skin irritation.

Two 28-day study conducted with fatty acids, C5-10, esters with pentaerythritol (CAS RN: 68424-31-7) and dipentaerythritol ester of n-C5/iso-C9 acids (CAS RN: 647028-25-9) showed no signs of overt toxicity. The 90-day study pentaerythritol ester of pentanoic acids and isononanoic acid (CAS RN: 146289-36-3) did not show any signs of overt toxicity. However, increased kidney and liver weights in the male animals was observed. In conclusion, since the effects observed are not considered to be systemic and relevant for humans, the NOAEL was found to exceed 1000 mg/kg bw for all substances based on the result from the 28 and 90-day studies.

Reproductive and developmental toxicity: Since metabolism of the polyol esters can occur, leading to the generation of the corresponding fatty acids and the polyol alcohol (such as pentaerythritol, trimethylolpropane, and dipentaerythritol), the issue of whether these metabolites may pose any potential reproductive/developmental toxicity concerns is important. However, the polyol alcohols such as pentaerythritol, trimethylolpropane, and dipentaerythritol, would be expected to undergo further metabolism, conjugation and excretion in the urine. Available evidence indicates that these ester hydrolysates (i.e., hydrolysis products), primarily fatty acids (e.g., heptanoic, octanoic, and decanoic acids) and secondarily the polyol alcohols should exhibit a low order of reproductive toxicity. It can be concluded that this group of high molecular weight polyol esters should not produce profound reproductive effects in rodents.

Genotoxicity: Polyols tested for genetic activity in the Salmonella assay, have been found to be inactive. Several polyol esters have been adequately tested for chromosomal mutation in the in vitro mammalian chromosome aberration assay, and all were inactive. Two TMP esters were also tested for in vivo chromosomal aberration in rats, and both demonstrated no activity. Thus, it is unlikely that these substances are

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chromosomal mutagens.

Carcinogenicity: In a 2-yr study, 28 male and 28 female rats were fed 5% polyglyceryl ester in the diet. No adverse effects on body weight, feed consumption, haematology values, or survival rate were noted. Liver function tests and renal function tests performed at 59 and 104 wks of the study were comparable between the test group and a control group fed 5% ground nut oil. The carcass fat contained no polyglycerol, and the levels of free fatty acid, unsaponifiable residue and fatty acid composition of carcass fat were not different from the controls. Organ weights, tumour incidence and tumour distribution were similar in control and test groups. A complete histological examination of major organs showed nothing remarkable

For polyunsaturated fatty acids and oils (triglycerides)

Studies on animals have shown a link between polyunsaturated fat and the incidence of tumours. In some of these studies the incidence of tumours increased with increasing intake of polyunsaturated fat, up to about 5% of total energy, near to the middle of the current dietary intake in humans.

The propensity for polyunsaturated fats to oxidise is another possible risk factor. This leads to the generation of free radicals and eventually to rancidity

Research evidence suggests that consuming high amounts of polyunsaturated fat may increase the risk of cancer spreading.

Researchers found that linoleic acid in polyunsaturated fats produced increasing membrane phase separation, and thereby increased adherence of circulating tumour cells to blood vessel walls and remote organs.

At least one study in mice has shown that consuming high amounts of polyunsaturated fat (but not monounsaturated fat) may increase the risk of metastasis in cancer.

Lipid peroxides with complex components can damage macromolecules, such as DNA, proteins, and membrane lipids. Some components of lipid peroxides, for example, 4,5(E)-epoxy-2(E)-heptenal (EH) can react with L-lysine and damage proteins. 4,5-epoxy-2-alkenals can react with phenylalanine and cause strecker-type degradation of amino acids. Autoxidized methyl linoleate can decrease DNA synthesis in thymocytes

Animals consuming oxidized lipids suffered a wide array of biological consequences, such as decreased feed utilization and performance, oxidative stress and tissue lipid oxidation and, most strikingly, adverse effects on redox indices and shelf life of meat. This manifested in malondialdehyde (MDA) content reduced activities of antioxidant enzymes and elevated transcript levels of oxidative stress-responsive genes

The intestinal mucosa is directly exposed to oxidized fatty acids of dietary origin and this tissue readily experiences redox imbalances and oxidative stress after the ingestion of large amounts of oxidized fat. As the first line of defense, the intestines with abundant gut-associated lymphoid tissues (GALTs) and lymphocytes play an important role in immune defense. The immune response in the intestinal tract is complex and is impaired by any damage to the mucosal barrier. When oxidative stress of the intestines caused by oxidized fat occurs, its immune competence and responsiveness may be compromised by the peroxides they contain

When body insulin levels are low, fatty acids flow from the fat cells into the bloodstream and are taken up by various cells and metabolised in a process called beta-oxidation. The end result of beta-oxidation is a molecule called acetyl-coA, and as more fatty acids are released and metabolised, acetyl-coA levels in the cells rise. Liver cells shunt excess acetyl-coA into "ketogenesis", or the making of ketone bodies. When the rate of synthesis of ketone bodies exceeds the rate of utilisation, their concentration in blood increases; this is known as ketonaemia. This is followed by ketonuria – excretion of ketone bodies in urine. The overall picture of ketonaemia and ketonuria is commonly referred as ketosis.

Smell of acetone in breath is a common feature in ketosis

For polyunsaturated fatty acids and oils (triglycerides), products of heating and recycling.*

Culinary oils, when heated, undergo important chemical reaction involving self-sustaining, free radical-mediated oxidative deterioration of polyunsaturated fatty acids (PUFAs). Such by-products may be cytotoxic, mutagenic, reproductive toxins and may produce chronic disease.

Saturated fatty acid (SFA)-rich fats also undergo such reactions but to a substantially lower degree.

Samples of repeatedly used oils collected from fast-food retail outlets and restaurants have confirmed the production of aldehydic lipid oxidation products (LOPs, active aldehydes) at levels exceeding 10 exp-2 moles per kilogram (mol/kg) during "on-site" frying episodes. Volatile emissions from heated culinary oils used in Chinese-style cooking are mutagenic; exposure to such indoor air pollution may render humans more susceptible to contracting lung or further cancers, together with rhinitis and diminished lung function. The high temperatures used in standard (especially Chinese) frying result in fumes that are rich in volatile LOPs, including acrolein.

Teratogenic actions. In principle, if aldehydic LOPs induce DNA and chromosomal damage during embryo development, foetal malformations may arise. A study was conducted to investigate the ability of the chain-breaking antioxidant α -tocopherol (α -TOH, vitamin E) to prevent the teratogenic effects of uncontrolled diabetes mellitus in rats (a study based on the hypothesis that diabetic animals have an elevated level of oxidative stress and therefore in vivo lipid peroxidation when expressed relative to that of healthy controls). It found that a PUFA-rich culinary oil (which served as a vehicle for oral administration of α -TOH) increased the rate of malformations and reabsorptions in both normal and diabetic pregnancies. Further investigations revealed that safflower oil subjected to thermal stressing episodes (according to standard frying practices for a period of 20 minutes) markedly enhanced its teratogenic effects. That is, the evidence indicates that the LOPs therein are primarily responsible for these actions.

Further adverse health effects of dietary LOPs. Further documented health effects of LOPs include their pro-inflammatory and gastropathic properties (for the latter, oral administration of the LOP, 4-hydroxy-trans-2-nonenal -HNE- to rats at a dose level of only 0.26 μ mol-dm-3, a level similar to that of healthy human blood plasma, induced peptic ulcers), and also a significant elevation in systolic blood pressure and an impaired vasorelaxation observed in rats fed pre-heated soy oil

Oxidative degradation process involving culinary oils, can generate extremely toxic conjugated lipid hydroperoxydienes (CHPDs). These are unstable at standard frying temperatures (ca. 180 degrees C) and are degraded to a broad range of secondary products, particularly saturated and unsaturated aldehydes, together with di- and epoxyaldehydes. Such aldehydic fragments also have toxicological properties in humans owing to their high reactivity with critical biomolecules in vivo (proteins such as low-density lipoprotein, amino acids, thiols such as glutathione, DNA, etc.). Despite their reactivities, high levels of CHPDs can remain in PUFA-rich oils which have been subjected to routine frying practices.

Thermally stressed PUFA-containing culinary oils contain high levels of alpha,beta-unsaturated aldehydes (including trans-2-alkenals, and cis,trans- and trans,trans-alka-2,4-dienals, the latter including the mutagen trans,trans-2,4-decadienal), and n-alkanals, together with their CHPD and hydroxydiene precursors.

Toxicological and pathogenic properties of dietary LOPS

Potential influence of dietary LOPS on metabolic pathways. As a consequence of their absorption from the gut into the systemic circulation, LOPs may penetrate cellular membranes, allowing their entry into particular intracellular sites/organelles where many critical metabolic processes occur. Literature evidence indicates that feeding thermally stressed or repeatedly used culinary oils to experimental animals induces significant modifications to key liver microsomal pathways and to the mitochondrial respiratory chain, for example. These effects are likely to occur via reactions of LOPs with key enzymes (and more especially their active sites), for example, the oxidation of active methioninyl and cysteinyl residues by CHPDs, or alteration of critical side-chain amino acid amine or thiol groups with aldehydes via Schiff base or Michael addition reactions.

Atherosclerosis. Investigations have revealed that dietary derived LOPs can accelerate all three stages of the development of atherosclerosis (i.e., endothelial injury, accumulation of plaque, and thrombosis). Animal studies have shown that diets containing thermally stressed, PUFA-laden (and hence LOP-rich) oils exhibit a greater atherogenicity than those containing unheated ones. Because cytotoxic aldehydes can be absorbed, they have the capacity to attack and structurally alter the apolipoprotein B component of low density lipoproteins (LDLs). This mechanism can engender uptake of lipid-loaded LDLs by macrophages, which, in turn, transforms them to foam cells, the accumulation of which is responsible for the development of aortic fatty streaks, a hallmark of the aetiology of atherosclerosis and its pathological sequelae. More recently, our co-investigators found that aldehydic LOPs elevated the expression of the CD36 scavenger receptor of macrophages, a phenomenon that also promotes this process.

Mutagenic and carcinogenic properties. Since they are powerful electrophilic alkylating agents, alpha,beta-unsaturated aldehydes can covalently modify DNA base units via a mechanistically complex process that may involve their prior epoxidation in vivo. Such chemically altered bases may therefore be of mutagenic potential. Additionally, these LOPs can inactivate DNA replicating systems, a process that can, at least in principle, elevate the extent of DNA damage. Hence, following cellular uptake, such aldehydes have the potential to cause both DNA and chromosomal damage.

Malondialdehyde (MDA) is also generated by thermally stressing culinary oils, although at concentrations much lower than those of the more reactive alpha,beta-unsaturated aldehydes. MDA and other aldehydes arising from lipid peroxidation (especially acrolein) present a serious carcinogenic hazard. Indeed, adenomas and carcinomas of the thyroid gland, together with adenomas of the pancreatic islet cells, were induced

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in rats by MDA in a prolonged gavage study; nasal and laryngeal cancers arose in rats and hamsters, respectively, during long-term acetaldehyde inhalation experiments. Hence, both these aldehydes satisfied the NIOSH criteria for classification as carcinogens, and therefore it has set exacting limits for their occupational exposure.

The most obvious solution to the generation of LOPs in culinary oils during frying is to avoid consuming foods fried in PUFA-rich oils as much as possible. Indeed, consumers, together with those involved in the fast-food sector, could employ culinary oils of only a low PUFA content, or mono-unsaturated fatty acids (MUFA) such as canola (a variety of rape seed oil), olive oil, (both oils are rich in oleic acid) selected palm oils (rich in palmitic acid), or coconut oils (an SFA alternative rich in lauric and myristic acids) - for frying MUFAs such as oleoylglycerol adducts are much more resistant to peroxidative degradation than are PUFAs, and hence markedly lower levels of only selected classes of aldehydes are generated during frying.

Previous studies that investigated the prospective health effects or benefits of dietary PUFAs (i.e., those involving feeding trials with humans or animals or, alternatively, related epidemiological ones) should be scrutinized. With hindsight, it seems to us that many of these experimental investigations were flawed since, in addition to some major design faults, they failed to take into account or even consider the nature and concentrations of any cytotoxic LOPs present in the oils or diets involved. Similarly, corresponding epidemiological (or meta-analysis-based) investigations incorporated only the (estimated) total dietary intake of selected PUFAs and further fatty acids, and ignored any LOPs derived or derivable from frying/cooking. Even if PUFA containing culinary oils are unheated, it is virtually impossible to rule out the presence of traces of LOPs within them (analysis of apparently pure PUFAs or their corresponding triglycerides obtained from reputable commercial sources has revealed that these materials contain traces of CHPDs and/or aldehydes

As expected, the levels of total aldehydes generated increase proportionately with oil PUFA content, and over half are the more highly cytotoxic alpha,beta-unsaturated classes, which include acrolein and 4-hydroxy-trans-2-nonenal (HNE), as well as 4-hydroperoxy-, 4-hydroxy-, and 4,5-epoxy-trans-2-alkenals. Total alpha,beta-unsaturated aldehyde concentrations in culinary oils (heated at 180 deg C for 30-90 minutes or longer) are often higher than 20 mmol/kg and can sometimes approach 50 mmol/kg. Furthermore, relatively low concentrations of detectable aldehydes and their CHPD precursors are even found in newly purchased unheated culinary oils.

Acrylamide (which can exert toxic effects on the nervous system and fertility, and may also be carcinogenic) can also arise from an acrolein source when asparagine-rich foods are deep-fried in PUFA-rich oils. The levels of acrylamide generated in foods during high-temperature cooking/frying processes are substantially lower than those recorded for aldehydes formed in PUFA-rich culinary oils during frying episodes (to date, the very highest reported levels are only ca. 4 ppm, equivalent to 56 umol/kg).

Acrolein is just one of the alpha,beta-unsaturated aldehydes generated in thermally stressed PUFA-rich oils: Many others generated in this manner have comparable toxicological properties. The foregoing considerations exclude possible toxicological properties of their isomeric CHPD precursors (also present in the high millimolar range in thermally stressed oils) in a typical fried food meal. Indeed, in one early investigation, a single intravenous dose of methyl linoleate hydroperoxide (20 mg/kg) administered to rats gave rise to a high mortality within 24 hours (animals dying from lung damage), although a higher dose given orally was without effect. This observation may reflect the limited in vivo absorption of these particular aldehyde precursors, in contrast to the known absorption of aldehydes.

Furthermore, with regard to the risk of inhalation of aldehydes volatilised during frying practices by humans, the maximum US Occupational Safety and Health (OSHA) permissible exposure limit (PEL) for acrolein, which is an (atmospheric) level of 0.1 ppm (equivalent to only 1.8 umol/kg in the fried food model) for a time-weighted long-term (8 hour) exposure, and 0.3 ppm (5.4 umol/kg) for a short-term (15 minute) one. This 15-minute exposure time can be considered to be less than the time taken to consume a typical fried meal.

The concentrations of aldehydes generated in culinary oils during episodes of heating at 180 deg C represent only what remains in the oil: Owing to their low boiling points, many of the aldehydes generated are volatilized at standard frying temperatures. These represent inhalation health hazards, in view of their inhalation by humans, especially workers in inadequately ventilated fast-food retail outlets.

The composition and content of hazardous LOPs available in fried foods depend on the identity of the frying/cooking oil and its PUFA content, the frying conditions employed, the length of the frying process, exposure of the frying medium to atmospheric oxygen, the reactivities of these agents with a range of other biomolecules (e.g., amino acids and proteins), and, to a limited extent, the antioxidant content of the frying matrix. Experiments have shown that shallow frying gives rise to much higher levels of LOPs than deep frying under the same conditions (reflecting the influence of the surface area of the frying medium, its exposure to atmospheric oxygen, and the subsequent dilution of LOPs generated into the bulk medium).

In vivo absorption of dietary LOPs

Except for direct damage to the gastrointestinal epithelium, the toxicological actions exerted by LOPs depend on their rate and extent of absorption from the gut into the systemic circulation where they may cause damage to essential organs, tissues, and cells. Experiments in rats have demonstrated that trans-2-alkenals, which are generated in PUFA-containing culinary oils during thermal stressing episodes, are absorbed. Following absorption, these cytotoxic agents are metabolized by a process involving the primary addition (Michael addition reaction) of glutathione across their electrophilic carbon-carbon double bonds and finally excreted in the urine as C-3 mercapturate derivatives.

* Martin Grootveld, Victor Ruiz Rodado, and Christopher J.L. Silwood

Detection, monitoring, and deleterious health effects of lipid oxidation products generated in culinary oils during thermal stressing episodes American Oil Chemists' Society, 25 (10), pp. 614-624. November/December 2014

Refined grades are edible. Non irritant.

No significant acute toxicological data identified in literature search.

Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergenic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production.

The material may cause 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 the epidermis. Histologically there may be intercellular oedema of the spongy layer (spongiosis) and intracellular oedema of the epidermis.

Acute Toxicity	✗	Carcinogenicity	✗
Skin Irritation/Corrosion	✓	Reproductivity	✓
Serious Eye Damage/Irritation	✓	STOT - Single Exposure	✓
Respiratory or Skin sensitisation	✓	STOT - Repeated Exposure	✗
Mutagenicity	✗	Aspiration Hazard	✗

Legend: ✗ – Data either not available or does not fill the criteria for classification
 ✓ – Data available to make classification

SECTION 12 Ecological information

Toxicity

Continued...

Virbac Virbamec LV Pour-On Endectocide for Cattle

Virbac Virbamec LV Pour-On Endectocide for Cattle	Endpoint	Test Duration (hr)	Species	Value	Source
	Not Available	Not Available	Not Available	Not Available	Not Available
ivermectin	Endpoint	Test Duration (hr)	Species	Value	Source
	NOEC(ECx)	48h	Crustacea	<0.001mg/L	4
	LC50	96h	Fish	0.003-0.004mg/L	4
benzyl alcohol	Endpoint	Test Duration (hr)	Species	Value	Source
	EC50	72h	Algae or other aquatic plants	500mg/l	2
	LC50	96h	Fish	10mg/l	2
	EC50	48h	Crustacea	230mg/l	2
	NOEC(ECx)	336h	Fish	5.1mg/l	2
	EC50	96h	Algae or other aquatic plants	76.828mg/l	2
soybean oil	Endpoint	Test Duration (hr)	Species	Value	Source
	Not Available	Not Available	Not Available	Not Available	Not Available
Legend:	Extracted from 1. IUCLID Toxicity Data 2. Europe ECHA Registered Substances - Ecotoxicological Information - Aquatic Toxicity 3. EPIWIN Suite V3.12 (QSAR) - 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				

On the basis of available evidence concerning either toxicity, persistence, potential to accumulate and/or observed environmental fate and behaviour, the material may present a danger, immediate or long-term and/or delayed, to the structure and/ or functioning of natural ecosystems.

Harmful to aquatic organisms.

DO NOT discharge into sewer or waterways.

Persistence and degradability

Ingredient	Persistence: Water/Soil	Persistence: Air
benzyl alcohol	LOW	LOW

Bioaccumulative potential

Ingredient	Bioaccumulation
benzyl alcohol	LOW (LogKOW = 1.1)

Mobility in soil

Ingredient	Mobility
benzyl alcohol	LOW (KOC = 15.66)

SECTION 13 Disposal considerations

Waste treatment methods

Product / Packaging disposal	
	<ul style="list-style-type: none"> ▶ 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	
	NO
HAZCHEM	
	Not Applicable

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

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

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

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

Not Applicable

Transport in bulk in accordance with MARPOL Annex V and the IMSBC Code

Product name	Group
ivermectin	Not Available
benzyl alcohol	Not Available
soybean oil	Not Available

Transport in bulk in accordance with the ICG Code

Product name	Ship Type
ivermectin	Not Available
benzyl alcohol	Not Available
soybean oil	Not Available

SECTION 15 Regulatory information**Safety, health and environmental regulations / legislation specific for the substance or mixture****ivermectin is found on the following regulatory lists**

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 4

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 5

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 7

benzyl alcohol is found on the following regulatory lists

Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals

Australian Inventory of Industrial Chemicals (AIIC)

soybean oil is found on the following regulatory lists

Australian Inventory of Industrial Chemicals (AIIC)

National Inventory Status

National Inventory	Status
Australia - AIIC / Australia Non-Industrial Use	No (ivermectin)
Canada - DSL	Yes
Canada - NDSL	No (ivermectin; benzyl alcohol)
China - IECSC	No (ivermectin)
Europe - EINEC / ELINCS / NLP	Yes
Japan - ENCS	No (ivermectin)
Korea - KECI	No (ivermectin)
New Zealand - NZIoC	Yes
Philippines - PICCS	No (ivermectin)
USA - TSCA	No (ivermectin)
Taiwan - TCSI	Yes
Mexico - INSQ	No (ivermectin)
Vietnam - NCI	No (ivermectin)
Russia - FBEPH	No (ivermectin)
Legend:	Yes = All CAS declared ingredients are on the inventory No = One or more of the CAS listed ingredients are not on the inventory. These ingredients may be exempt or will require registration.

SECTION 16 Other information

Revision Date	08/20/2021
Initial Date	05/13/2016

SDS Version Summary

Version	Date of Update	Sections Updated
4.1.1.1	11/01/2019	One-off system update. NOTE: This may or may not change the GHS classification
4.1.2.1	04/26/2021	Regulation Change
4.1.3.1	05/03/2021	Regulation Change
4.1.4.1	05/06/2021	Regulation Change
4.1.5.1	05/10/2021	Regulation Change
4.1.5.2	05/30/2021	Template Change
4.1.5.3	06/04/2021	Template Change
4.1.5.4	06/05/2021	Template Change
4.1.6.4	06/07/2021	Regulation Change
4.1.6.5	06/09/2021	Template Change
4.1.6.6	06/11/2021	Template Change
4.1.6.7	06/15/2021	Template Change
4.1.7.7	06/17/2021	Regulation Change
4.1.8.7	06/21/2021	Regulation Change
4.1.8.8	07/05/2021	Template Change
4.1.9.8	07/14/2021	Regulation Change

Virbac Virbamec LV Pour-On Endectocide for Cattle

Version	Date of Update	Sections Updated
4.1.10.8	07/19/2021	Regulation Change
4.1.10.9	08/01/2021	Template Change
4.1.11.9	08/02/2021	Regulation Change
4.1.12.9	08/05/2021	Regulation Change
4.1.13.9	08/09/2021	Regulation Change
5.1.13.9	08/20/2021	Classification change due to full database hazard calculation/update.
5.1.14.9	08/23/2021	Regulation Change
5.1.15.9	08/26/2021	Regulation Change
5.1.15.10	08/29/2021	Template Change
5.1.16.10	08/30/2021	Regulation Change
5.1.17.10	09/06/2021	Regulation Change

Other information

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.

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
 ES: Exposure Standard
 OSF: Odour Safety Factor
 NOAEL :No Observed Adverse Effect Level
 LOAEL: Lowest Observed Adverse Effect Level
 TLV: Threshold Limit Value
 LOD: Limit Of Detection
 OTV: Odour Threshold Value
 BCF: BioConcentration Factors
 BEI: Biological Exposure Index
 AIIC: Australian Inventory of Industrial Chemicals
 DSL: Domestic Substances List
 NDSL: Non-Domestic Substances List
 IECSC: Inventory of Existing Chemical Substance in China
 EINECS: European INventory of Existing Commercial chemical Substances
 ELINCS: European List of Notified Chemical Substances
 NLP: No-Longer Polymers
 ENCS: Existing and New Chemical Substances Inventory
 KECI: Korea Existing Chemicals Inventory
 NZIoC: New Zealand Inventory of Chemicals
 PICCS: Philippine Inventory of Chemicals and Chemical Substances
 TSCA: Toxic Substances Control Act
 TCSI: Taiwan Chemical Substance Inventory
 INSQ: Inventario Nacional de Sustancias Químicas
 NCI: National Chemical Inventory
 FBEPH: Russian Register of Potentially Hazardous Chemical and Biological Substances

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