



Butec OTM Pain Relief for Cattle and Sheep Troy Laboratories Pty Ltd

Chemwatch: 5581-87 Version No: 2.1

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

Chemwatch Hazard Alert Code: 2

Issue Date: 23/01/2023 Print Date: 24/01/2023 L.GHS.AUS.EN.E

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

Product Identifier

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Product name	Butec OTM Pain Relief for Cattle and Sheep
Chemical Name	Not Applicable
Synonyms	ilium Buccalgesic OTM; APVMA number 69874; APVMA number 93151
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	For the alleviation of pain associated with routine husbandry procedures in cattle and sheep. To be used as directed on product label

Details of the manufacturer or supplier of the safety data sheet

Registered company name	Troy Laboratories Pty Ltd	
Address	37 Glendenning Road Glendenning NSW 2761 Australia	
Telephone	8808 3600	
Fax	02 9677 9300	
Website	www.Troylab.com.au	
Email	admin@troylab.com.au	

Emergency telephone number

Association / Organisation	Troy Laboratories Pty Ltd
Emergency telephone numbers	1800 033 111
Other emergency telephone numbers	Not Available

SECTION 2 Hazards identification

Classification of the substance or mixture

Poisons Schedule	S4	
Classification [1]	Skin Corrosion/Irritation Category 2, Sensitisation (Skin) Category 1, Serious Eye Damage/Eye Irritation Category 2A, Carcinogenicity Category 2	
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 W

Warning

Hazard statement(s)

H315	Causes skin irritation.	
H317	May cause an allergic skin reaction.	
H319	Causes serious eye irritation.	
H351	Suspected of causing cancer.	

Precautionary statement(s) Prevention

P201 Obtain special instructions before use.

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P280	Wear protective gloves, protective clothing, eye protection and face protection.	
P261	Avoid breathing mist/vapours/spray.	
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	F exposed or concerned: Get medical advice/ attention.	
P302+P352	ON SKIN: Wash with plenty of water.	
P305+P351+P338	EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.	
P333+P313	skin irritation or rash occurs: Get medical advice/attention.	
P337+P313	eye irritation persists: Get medical advice/attention.	
P362+P364	Take off contaminated clothing and wash it before reuse.	

Precautionary statement(s) Storage

P405 Store locked up.

Precautionary statement(s) Disposal

P501 Dispose of contents/container to authorised hazardous or special waste collection point in accordance with any local regulation.

SECTION 3 Composition / information on ingredients

Substances

See section below for composition of Mixtures

Mixtures

CAS No	%[weight]	Name
57-55-6	30-60	propylene glycol
71125-38-7	1-10	meloxicam
100-51-6	1-10	benzyl alcohol
Not Available	>60	Ingredients determined not to be hazardous
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	If this product comes in contact with the eyes: 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	If skin contact occurs: Immediately remove all contaminated clothing, including footwear. Flush skin and hair with running water (and soap if available). Seek medical attention in event of irritation.		
Inhalation	 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	 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.

SECTION 5 Firefighting measures

Extinguishing media

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

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

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In such an event consider:

- foam.
- dry chemical powder.
- carbon dioxide.

Special hazards arising from the substrate or mixture

Special hazards arising from the substrate or mixture			
Fire Incompatibility	None known.		
Advice for firefighters			
Fire Fighting	 Alert Fire Brigade and tell them location and nature of hazard. Wear full body protective clothing with breathing apparatus. Prevent, by any means available, spillage from entering drains or water course. Use water delivered as a fine spray to control fire and cool adjacent area. Avoid spraying water onto liquid pools. DO NOT approach containers suspected to be hot. Cool fire exposed containers with water spray from a protected location. If safe to do so, remove containers from path of fire. 		
Fire/Explosion Hazard	 The material is not readily combustible under normal conditions. However, it will break down under fire conditions and the organic component may burn. Not considered to be a significant fire risk. Heat may cause expansion or decomposition with violent rupture of containers. Decomposes on heating and may produce toxic fumes of carbon monoxide (CO). May emit acrid smoke. Decomposes on heating and produces toxic fumes of: carbon dioxide (CO2) nitrogen oxides (NOx) other pyrolysis products typical of burning organic material. May emit poisonous fumes. 		

SECTION 6 Accidental release measures

HAZCHEM

Personal precautions, protective equipment and emergency procedures

Not Applicable

May emit corrosive fumes.

See section 8

Environmental precautions

See section 12

Methods and material for containment and cleaning up

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

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

SECTION 7 Handling and storage

Safe handling

Precautions for safe handling

▶ Avoid all personal contact, including inhalation.

- Wear protective clothing when risk of exposure occurs.
- Use in a well-ventilated area.
- ▶ Prevent concentration in hollows and sumps.
- ► DO NOT enter confined spaces until atmosphere has been checked.
- ▶ DO NOT allow material to contact humans, exposed food or food utensils. Avoid contact with incompatible materials.
- ▶ When handling, **DO NOT** eat, drink or smoke
- Keep containers securely sealed when not in use.
- Avoid physical damage to containers.
- Always wash hands with soap and water after handling. ▶ Work clothes should be laundered separately. Launder contaminated clothing before re-use.

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- Use good occupational work practice.
 - Dbserve manufacturer's storage and handling recommendations contained within this SDS.
 - Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.
 - ▶ Store in original containers.
- ► Keep containers securely sealed.

Other information

- 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

- ▶ Packaging as recommended by manufacturer.
- Check that containers are clearly labelled.
- Tamper-proof containers.
- Suitable container
- Polyethylene or polypropylene containers.
- Metal drum with sealed plastic liner.
- Glass container is suitable for laboratory quantities
- Metal can or drum
- Packaging as recommended by manufacturer.
- ▶ Check all containers are clearly labelled and free from leaks.
- Storage incompatibility
- Avoid strong acids, bases.
- Avoid reaction with oxidising agents

SECTION 8 Exposure controls / personal protection

Control parameters

Occupational Exposure Limits (OEL)

INGREDIENT DATA

Source	Ingredient	Material name	TWA	STEL	Peak	Notes
Australia Exposure Standards	propylene glycol	Propane-1,2-diol: particulates only	10 mg/m3	Not Available	Not Available	Not Available
Australia Exposure Standards	propylene glycol	Propane-1,2-diol total: (vapour & particulates)	150 ppm / 474 mg/m3	Not Available	Not Available	Not Available

Emergency Limits

Ingredient	TEEL-1	TEEL-2	TEEL-3
propylene glycol	30 mg/m3	1,300 mg/m3	7,900 mg/m3
benzyl alcohol	30 ppm	52 ppm	740 ppm

Ingredient	Original IDLH	Revised IDLH
propylene glycol	Not Available	Not Available
meloxicam	Not Available	Not Available
benzyl alcohol	Not Available	Not Available

Occupational Exposure Banding

Ingredient	Occupational Exposure Band Rating	Occupational Exposure Band Limit
meloxicam	E	≤ 0.01 mg/m³
benzyl alcohol	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

Enclosed local exhaust ventilation is required at points of dust, fume or vapour generation.

HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapours.

Barrier protection or laminar flow cabinets should be considered for laboratory scale handling.

A fume hood or vented balance enclosure is recommended for weighing/ transferring quantities exceeding 500 mg.

When handling quantities up to 500 gram in either a standard laboratory with general dilution ventilation (e.g. 6-12 air changes per hour) is preferred. Quantities up to 1 kilogram may require a designated laboratory using fume hood, biological safety cabinet, or approved vented enclosures. Quantities exceeding 1 kilogram should be handled in a designated laboratory or containment laboratory using appropriate barrier/ containment technology.

Manufacturing and pilot plant operations require barrier/ containment and direct coupling technologies

Appropriate engineering controls

Barrier/ containment technology and direct coupling (totally enclosed processes that create a barrier between the equipment and the room) typically use double or split butterfly valves and hybrid unidirectional airflow/ local exhaust ventilation solutions (e.g. powder containment booths). Glove bags, isolator glove box systems are optional. HEPA filtration of exhaust from dry product handling areas is required. Fume-hoods and other open-face containment devices are acceptable when face velocities of at least 1 m/s (200 feet/minute) are achieved.

Partitions, barriers, and other partial containment technologies are required to prevent migration of the material to uncontrolled areas. For non-routine emergencies maximum local and general exhaust are necessary. 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, etc. evaporating from tank (in still air)	0.25-0.5 m/s (50-100 f/min.)

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aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers (released at 0.5-1 m/s (100-200 f/min.) low velocity into zone of active generation) direct spray, drum filling, conveyer loading, crusher dusts, gas discharge (active generation into zone of rapid air 1-2.5 m/s (200-500 f/min.) motion)

Within each range the appropriate value depends on:

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

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 1-2.5 m/s (200-500 f/min.) for extraction of gases discharged 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.

The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated: Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied respirators should be evaluated.

The following protective devices are recommended where exposures exceed the recommended exposure control guidelines by factors of: 10; high efficiency particulate (HEPA) filters or cartridges

10-25; loose-fitting (Tyvek or helmet type) HEPA powered-air purifying respirator.

25-50; a full face-piece negative pressure respirator with HEPA filters

50-100; tight-fitting, full face-piece HEPA PAPR

100-1000; a hood-shroud HEPA PAPR or full face-piece supplied air respirator operated in pressure demand or other positive pressure mode.

Personal protection











When handling very small quantities of the material eye protection may not be required.

For laboratory, larger scale or bulk handling or where regular exposure in an occupational setting occurs:

- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes.

Eye and face protection

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

preference

- Rubber gloves (nitrile or low-protein, powder-free latex, latex/ nitrile). Employees allergic to latex gloves should use nitrile gloves in
- Double gloving should be considered.
- PVC gloves. Hands/feet protection
 - ▶ Change gloves frequently and when contaminated, punctured or torn.
 - Wash hands immediately after removing gloves.
 - ▶ Protective shoe covers. [AS/NZS 2210]
 - Head covering.

Body protection

See Other protection below

- ▶ For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs

Other protection

- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers. For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
- ▶ Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies: Vinyl suit

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	С
BUTYL/NEOPRENE	С
HYPALON	С
NATURAL RUBBER	С
NATURAL+NEOPRENE	С
NEOPRENE	С
NEOPRENE/NATURAL	С

Respiratory protection

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

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

Required Minimum Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
up to 5 x ES	AK-AUS / Class 1 P2	-	AK-PAPR-AUS / Class 1 P2
up to 25 x ES	Air-line*	AK-2 P2	AK-PAPR-2 P2
up to 50 x ES	-	AK-3 P2	-
50+ x ES	-	Air-line**	-

- * Continuous-flow; ** Continuous-flow or positive pressure demand
- ^ Full-face

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NITRILE	С
NITRILE+PVC	С
PE/EVAL/PE	С
PVA	С
PVC	С
VITON	С

* 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.

2.37 @20C

Not Available

Miscible

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 $\label{eq:conditional} \mbox{dioxide}(SO2), \ G = \mbox{Agricultural chemicals}, \ K = \mbox{Ammonia}(\mbox{NH3}), \ \mbox{Hg} = \mbox{Mercury}, \ \mbox{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	Clear blue viscous liquid with no odour; mixes with water.		
Physical state	Liquid	Relative density (Water = 1)	1.035
Odour	Not Available	Partition coefficient n-octanol / water	Not Available
Odour threshold	Not Available	Auto-ignition temperature (°C)	Not Applicable
pH (as supplied)	Not Available	Decomposition temperature (°C)	Not Available
Melting point / freezing point (°C)	~0	Viscosity (cSt)	Not Available
Initial boiling point and boiling range (°C)	~100	Molecular weight (g/mol)	Not Applicable
Flash point (°C)	Not Applicable	Taste	Not Available
Evaporation rate	Not Available	Explosive properties	Not Available
Flammability	Not Applicable	Oxidising properties	Not Available
Upper Explosive Limit (%)	Not Applicable	Surface Tension (dyn/cm or mN/m)	Not Available
Lower Explosive Limit (%)	Not Applicable	Volatile Component (%vol)	Not Available

SECTION 10 Stability and reactivity

Vapour pressure (kPa)

Vapour density (Air = 1)

Solubility in water

Reactivity	See section 7
Chemical stability	 Unstable in the presence of incompatible materials. Product is considered stable. Hazardous polymerisation will not occur.
Possibility of hazardous reactions	See section 7
Conditions to avoid	See section 7
Incompatible materials	See section 7
Hazardous decomposition products	See section 5

SECTION 11 Toxicological information

Information on toxicological effects

Inhaled	Inhalation of vapours may cause drowsiness and dizziness. This may be accompanied by narcosis, reduced alertness, loss of reflexes, lack of coordination and vertigo. Inhalation of vapours or aerosols (mists, fumes), generated by the material during the course of normal handling, may be damaging to the health of the individual. Inhalation hazard is increased at higher temperatures.
Ingestion	Accidental ingestion of the material may be damaging to the health of the individual.
Skin Contact	The material produces moderate skin irritation; evidence exists, or practical experience predicts, that the material either produces moderate inflammation of the skin in a substantial number of individuals following direct contact, and/or produces significant, but moderate, inflammation when applied to the healthy intact skin of animals (for up to four hours), such inflammation

being present twenty-four hours or more after the end of the exposure period.

Gas group

VOC g/L

pH as a solution (1%)

Not Available

Not Available

Not Available

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 Chemwatch: 5581-87 Page 7 of 13 Issue Date: 23/01/2023 Version No: 2.1

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thickening of the epidermis. At the microscopic level there may be intercellular oedema of the spongy layer of the skin (spongiosis) and intracellular gedema of the epidermis

Open cuts, abraded or irritated skin should not be exposed to this material

Entry into the blood-stream through, for example, cuts, abrasions, puncture wounds or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

Limited evidence suggests that repeated exposure may cause skin cracking, flaking or drying following normal handling and use.

Eve

Evidence exists, or practical experience predicts, that the material may cause eye irritation in a substantial number of individuals and/or may produce significant ocular lesions which are present twenty-four hours or more after instillation into the eye(s) of experimental animals. 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

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.

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.

Chronic

Substances than can cuase 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 Wherever it is reasonably practicable, exposure to substances that can cuase 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. 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

Exposure to the material may cause concerns for humans owing to possible developmental toxic effects, generally on the basis that results in appropriate animal studies provide strong suspicion of developmental toxicity in the absence of signs of marked maternal toxicity, or at around the same dose levels as other toxic effects but which are not a secondary non-specific consequence of other toxic effects.

should be appropriate consultation with an occupational health professional over the degree of risk and level of surveillance.

Butec OTM Pain Relief for	TOXICITY	IRRITATION
Cattle and Sheep	Not Available	Not Available
	TOXICITY	IRRITATION
	Dermal (rabbit) LD50: 11890 mg/kg ^[2]	Eye (rabbit): 100 mg - mild
	Inhalation(Rat) LC50: >44.9 mg/l4h ^[1]	Eye (rabbit): 500 mg/24h - mild
propylene glycol	Oral (Rat) LD50: 20000 mg/kg ^[2]	Eye: no adverse effect observed (not irritating) ^[1]
		Skin(human):104 mg/3d Intermit Mod
		Skin(human):500 mg/7days mild
		Skin: no adverse effect observed (not irritating) ^[1]
	TOXICITY	IRRITATION
meloxicam	Oral (Rabbit) LD50; 320 mg/kg ^[2]	Eye (rabbit): Not irritating *
		Skin (rabbit) : Not irritating *
	TOXICITY	IRRITATION
	Dermal (rabbit) LD50: 2000 mg/kg ^[2]	Eye (rabbit): 0.75 mg open SEVERE
	Inhalation(Rat) LC50: >4.178 mg/L4h ^[2]	Eye: adverse effect observed (irritating) ^[1]
benzyl alcohol	Oral (Rat) LD50: 1230 mg/kg ^[2]	Skin (man): 16 mg/48h-mild
		Skin (rabbit):10 mg/24h open-mild
		Skin: no adverse effect observed (not irritating) ^[1]
Legend:	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	

PROPYLENE GLYCOL

The acute oral toxicity of propylene glycol is very low, and large quantities are required to cause perceptible health damage in humans. Serious toxicity generally occurs only at plasma concentrations over 1 g/L, which requires extremely high intake over a relatively short period of time. It would be nearly impossible to reach toxic levels by consuming foods or supplements, which contain at most 1 g/kg of PG. Cases of propylene glycol poisoning are usually related to either inappropriate intravenous administration or accidental ingestion of large quantities by children. The potential for long-term oral toxicity is also low. Because of its low chronic oral toxicity, propylene glycol was classified by the U. S. Food and Drug Administration as "generally recognized as safe" (GRAS) for use as a direct food additive.

Prolonged contact with propylene glycol is essentially non-irritating to the skin. Undiluted propylene glycol is minimally irritating to the eye, and can produce slight transient conjunctivitis (the eye recovers after the exposure is removed). Exposure to mists may cause eye irritation, as well as upper respiratory tract irritation. Inhalation of the propylene glycol vapours appears to present no significant hazard in ordinary applications. However, limited human experience indicates that inhalation of propylene glycol mists could be irritating to some individuals It is therefore recommended that propylene glycol not be used in applications where inhalation exposure or human eye contact with the spray mists of these materials is likely, such as fogs for theatrical productions or antifreeze solutions for emergency eye wash stations.

Propylene glycol is metabolised in the human body into pyruvic acid (a normal part of the glucose-metabolism process, readily converted to energy), acetic acid (handled by ethanol-metabolism), lactic acid (a normal acid generally abundant during digestion), and propionaldehyde (a potentially hazardous substance).

Propylene glycol shows no evidence of being a carcinogen or of being genotoxic.

Research has suggested that individuals who cannot tolerate propylene glycol probably experience a special form of irritation, but that they only rarely develop allergic contact dermatitis. Other investigators believe that the incidence of allergic contact dermatitis to propylene glycol may be greater than 2% in patients with eczema.

One study strongly suggests a connection between airborne concentrations of propylene glycol in houses and development of asthma and allergic reactions, such as rhinitis or hives in children

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Another study suggested that the concentrations of PGEs (counted as the sum of propylene glycol and glycol ethers) in indoor air, particularly bedroom air, is linked to increased risk of developing numerous respiratory and immune disorders in children, including asthma, hav fever, eczema, and allergies, with increased risk ranging from 50% to 180%. This concentration has been linked to use of water-based paints and water-based system cleansers.

Patients with vulvodynia and interstitial cystitis may be especially sensitive to propylene glycol. Women suffering with yeast infections may also notice that some over the counter creams can cause intense burning. Post menopausal women who require the use of an eostrogen cream may notice that brand name creams made with propylene glycol often create extreme, uncomfortable burning along the vulva and perianal area. Additionally, some electronic cigarette users who inhale propylene glycol vapor may experience dryness of the throat or shortness of breath . As an alternative, some suppliers will put Vegetable Glycerin in the "e-liquid" for those who are allergic (or have bad reactions) to propylene glycol. Adverse responses to intravenous administration of drugs which use PG as an excipient have been seen in a number of people, particularly with large dosages thereof. Responses may include "hypotension, bradycardia... QRS and T abnormalities on the ECG, arrhythmia, cardiac arrest, serum hyperosmolality, lactic acidosis, and haemolysis". A high percentage (12% to 42%) of directly-injected propylene glycol is eliminated/secreted in urine unaltered depending on dosage, with the remainder appearing in its glucuronide-form. The speed of renal filtration decreases as dosage increases, which may be due to propylene glycol's mild anesthetic / CNS-depressant -properties as an alcohol. In one case, intravenous administration of propylene glycol-suspended nitroglycerin to an elderly man may have induced coma and acidosis. Propylene glycol is an approved food additive for dog food under the category of animal feed and is generally recognized as safe for dogs with an LD50 of 9 mL/kg. The LD50 is higher for most laboratory animals (20 mL/kg)

Similarly, propylene glycol is an approved food additive for human food as well. The exception is that it is prohibited for use in food for cats due to links to Heinz body anemia

Carcinogenicity: No carcinogenic effect of meloxicam was observed in rats given oral doses up to 0.8 mg/kg/day (approximately 0.4-fold the human dose at 15 mg/day for a 50 kg adult based on body surface area conversion) for 104 weeks or in mice given oral doses up to 8.0 mg/kg/day (approximately 2.2-fold the human dose, as noted above) for 99 weeks. Reproductive Toxicity: Meloxicam did not impair male and female fertility in rats at oral doses up to 9 and 5 mg/kg/day, respectively (4.9-fold and 2.5-fold the human dose, as noted above). However, an increased incidence of embryolethality at oral doses >/= 1 mg/kg/day (0.5-fold the human dose, as noted above) was observed in rats when dams were given meloxicam 2 weeks prior to mating and during early embryonic development. Teratogenicity: Pregnancy Category C: Meloxicam caused an increased incidence of septal defect of the heart, a rare event, at an oral dose of 60 mg/kg/day (64.5-fold the human dose at 15 mg/day for a 50 kg adult based on body surface area conversion) and embryolethality at oral doses >/= 5 mg/kg/day (5.4-fold the human dose, as noted above) when rabbits were treated throughout organogenesis. Meloxicam was not teratogenic in rats up to an oral dose of 4 mg/kg/day (approximately 2.2-fold the human dose, as noted above) throughout organogenesis. An increased incidence of stillbirths was observed when rats were given oral doses >/= 1 mg/kg/day throughout organogenesis. Meloxicam crosses the placental barrier. There are no adequate and well-controlled studies in pregnant women. Mutagenicity: Meloxicam was not mutagenic in an Ames assay, or clastogenic in a chromosome aberration assay with human lymphocytes and an in vivo micronucleus test in mouse bone marrow. * Apotex SDS Accumulated studies have proved that non-steroidal anti-inflammatory drugs (NSAIDs) which block inflammation by their actions on arachidonic acid (AA) metabolism have a potential role in cancer chemotherapy and chemoprevention.

There is a general acceptance that NSAIDs induce colon cancer in humans. One suggested reason is that the balance between COX and lipoxygenase (LOX) activity determines tumorigenesis critically. Under low COX activity, arachidonic acid released from cell membranes in response to external stimuli is preferentially metabolized by LOX enzymes. The oxygenated lipids (metabolites) produced by LOXs initiate subsequent biological reactions, activate cellular signaling mechanisms through specific cell surface receptors, or are further metabolized into potent lipid mediators

There is evidence that a 15-LOX metabolite 13S-HPODE (13S-hydroperoxyoctadecaenoic acid) generated from linoleic acid induces apoptosis in colon cancer.

Ingestion of aspirin or other NSAIDs may elicit respiratory, nasal, and gastrointestinal symptoms, as well as dermal changes in a subset of patients with asthma. The sensitivity to cyclooxygenase (COX) inhibitors has led to the hypothesis that NSAIDs may be causing upregulation of the 5-lipoxygenase pathway and its attendant products, the leukotrienes, in these patients. It has been shown increase in urinary leukotriene E 4 (LTE4) after aspirin ingestion or inhalation of lysine-aspirin in aspirin-sensitive patients with asthma. It has also been demonstrated that pharmacologic blockade at the level of the cysteinyl leukotriene receptor(s) can blunt the bronchospastic response to aspirin. Cysteinyl leukotrienes are potent bronchoconstrictors, induce mucus secretion, and increase vascular permeability. Importantly, inhibition of 5-lipoxygenase blocks not only the respiratory but also the gastrointestinal and dermal reactions to aspirin in aspirin-sensitive patients with asthma. Although these results establish the importance of 5-lipooxygenase products in mediating reactions to aspirin, the cellular source and mechanism of release of these mediators remain unclear.

Mast cells, which are a known source of leukotrienes, are activated in the nasal response to aspirin as demonstrated by the detection of nasal tryptase after aspirin challenge. Tryptase is an enzyme specific to mast cells and is an indicator of mast cell activation. Cysteinyl leukotrienes and histamine, which can be produced by mast cells, were detected as well. The occurrence of nasal symptoms, as well as activation of mast cells, in response to aspirin was blocked by zileuton, an inhibitor of 5-lipoxygenase. This confirms that 5-lipoxygenase products are critical to the development of aspirin-induced asthma (ASA- induced) reactions in the nose. It also suggests that 5-lipoxygenase products may have a role in the activation of mast cells during this reaction.

The following information refers to contact allergens as a group and may not be specific to this product.

Contact allergies quickly manifest themselves as contact eczema, more rarely as urticaria or Quincke's oedema. The pathogenesis of contact eczema involves a cell-mediated (T lymphocytes) immune reaction of the delayed type. Other allergic skin reactions, e.g. contact urticaria, involve antibody-mediated immune reactions. The significance of the contact allergen is not simply determined by its sensitisation potential: the distribution of the substance and the opportunities for contact with it are equally important. A weakly sensitising substance which is widely distributed can be a more important allergen than one with stronger sensitising potential with which few individuals come into contact. From a clinical point of view, substances are noteworthy if they produce an allergic test reaction in more than 1% of the persons tested. For benzyl alkyl alcohols:

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

Acute toxicity: Benzyl alcohol, benzoic acid and its sodium and potassium salt can be considered as a single category regarding human health, as they are all rapidly metabolised and excreted via a common pathway within 24 hrs. Systemic toxic effects of similar nature (e.g. liver, kidney) were observed. However with benzoic acid and its salts toxic effects are seen at higher doses than with benzyl alcohol.

The compounds exhibit low acute toxicity as for the oral and dermal route. The LD50 values are > 2000 mg/kg bw except for benzyl alcohol which needs to be considered as harmful by the oral route in view of an oral LD50 of 1610 mg/kg bw. The 4 hrs inhalation exposure of benzyl alcohol or benzoic acid at 4 and 12 mg/l as aerosol/dust respectively gave no mortality, showing low acute toxicity by inhalation for these

Benzoic acid and benzyl alcohol are slightly irritating to the skin, while sodium benzoate was not skin irritating. No data are available for potassium benzoate but it is also expected not to be skin irritating. Benzoic acid and benzyl alcohol are irritating to the eye and sodium benzoate was only slightly irritating to the eye. No data are available for potassium benzoate but it is expected also to be only slightly irritating to the eye. Sensitisation: The available studies for benzoic acid gave no indication for a sensitising effect in animals, however occasionally very low positive reactions were recorded with humans (dermatological patients) in patch tests. The same occurs for sodium benzoate. It has been suggested that the very low positive reactions are non-immunologic contact urticaria. Benzyl alcohol gave positive and negative results in animals, Benzyl alcohol also demonstrated a maximum incidence of sensitization of only 1% in human patch testing. Over several decades no sensitization with these compounds has been seen among workers.

Repeat dose toxicity: For benzoic acid repeated dose oral toxicity studies give a NOAEL of 800 mg/kg/day. For the salts values > 1000 mg/kg/day are obtained. At higher doses increased mortality, reduced weight gain, liver and kidney effects were observed. For benzyl alcohol the long-term studies indicate a NOAEL > 400 mg/kg bw/d for rats and > 200 mg/kg bw/d for mice. At higher doses effects on bodyweights, lesions in the brains, thymus, skeletal muscle and kidney were observed. It should be taken into account that administration in

MELOXICAM

BENZYL ALCOHOL

compounds

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these studies was by gavage route, at which saturation of metabolic pathways is likely to occur.

Mutagenicity: All chemicals showed no mutagenic activity in in vitro Ames tests. Various results were obtained with other in vitro genotoxicity assays. Sodium benzoate and benzyl alcohol showed no genotoxicity in vivo. While some mixed and/or equivocal in vitro

chromosomal/chromatid responses have been observed, no genotoxicity was observed in the *in vivo* cytogenetic, micronucleus, or other assays. The weight of the evidence of the *in vitro* and *in vivo* genotoxicity data indicates that these chemicals are not mutagenic or clastogenic. They also are not carcinogenic in long-term carcinogenicity studies.

In a 4-generation study with benzoic acid no effects on reproduction were seen (NOAEL: 750 mg/kg). No compound related effects on reproductive organs (gross and histopathology examination) could be found in the (sub) chronic studies in rats and mice with benzyl acetate, benzyl alcohol, benzaldehyde, sodium benzoate and supports a non-reprotoxic potential of these compounds. In addition, data from reprotoxicity studies on benzyl acetate (NOAEL >2000 mg/kg bw/d; rats and mice) and benzaldehyde (tested only up to 5 mg/kg bw; rats) support the non-reprotoxicity of benzyl alcohol and benzoic acid and its salts.

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

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

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

Cases of occupational asthma induced by perfume substances such as 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 suffcient 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 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 prehapten is a chemical that itself is non- or low-sensitising, but that is transformed into a hapten outside the skin by simple chemical transformation (air oxidation, photoactivation) and without the requirement of specific enzymatic systems. A prohapten is a chemical that itself is non- or low-sensitising but that is transformed into a hapten in the skin (bioactivation) usually via enzyme catalysis. It is not always possible to know whether a particular allergen that is not directly

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reactive acts as a prehapten or as a prohapten, or both, because air oxidation and bioactivation can often give the same product (geraniol is an example). Some chemicals might act by all three pathways.

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. 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 prohaptens 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 prohaptens) 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 prohaptens. 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 derivate 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

PROPYLENE GLYCOL & BENZYL ALCOHOL

The material may cause skin irritation after prolonged or repeated exposure and may produce a contact dermatitis (nonallergic). This form of dermatitis is often 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	×

Leaend:

— Data either not available or does not fill the criteria for classification

Data available to make classification

SECTION 12 Ecological information

Toxicity

Dutas OTM Dain Dalief for	Endpoint	Test Duration (hr)	Species	Value	Source
Butec OTM Pain Relief for Cattle and Sheep	Not Available	Not Available	Not Available	Not Available	Not Available

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	Endpoint	Test Duration (hr)	Species	Value	Source
	NOEC(ECx)	336h	Algae or other aquatic plants	<5300mg/	1 1
	EC50	72h	Algae or other aquatic plants	19300mg/	2
propylene glycol	EC50	96h	Algae or other aquatic plants	19000mg/	2
	LC50	96h	Fish	710mg/l	4
	EC50	48h	Crustacea	>114.4mg	′L 4
	Endpoint	Test Duration (hr)	Species	Value	Source
meloxicam	NOEC(ECx)	144h	Fish	0.1mg	ı/l 4
	Endpoint	Test Duration (hr)	Species	Value	Source
	LC50	96h	Fish	10mg/l	4
harred also ball	EC50	72h	Algae or other aquatic plants	500mg/l	2
benzyl alcohol	EC50	48h	Crustacea	230mg/l	2
	NOEC(ECx)	336h	Fish	5.1mg/l	2
	EC50	96h	Algae or other aquatic plants	76.828mg	y/l 2
Legend:			HA Registered Substances - Ecotoxicological Information		

DO NOT discharge into sewer or waterways.

Persistence and degradability

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

Bioaccumulative potential

Ingredient	Bioaccumulation
propylene glycol	LOW (BCF = 1)
benzyl alcohol	LOW (LogKOW = 1.1)

Mobility in soil

Ingredient	Mobility
propylene glycol	HIGH (KOC = 1)
benzyl alcohol	LOW (KOC = 15.66)

SECTION 13 Disposal considerations

Waste treatment methods

- ▶ 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.
- Containers may still present a chemical hazard/ danger when empty.
- Return to supplier for reuse/ recycling if possible.

Product / Packaging disposal

- Otherwise:

 If container can not be cleaned sufficiently well to ensure that residuals do not remain or if the container cannot be used to store the same product, then puncture containers, to prevent re-use, and bury at an authorised landfill.
- Where possible retain label warnings and SDS and observe all notices pertaining to the product.
- ▶ DO NOT allow wash water from cleaning or process equipment to enter drains.
- It may be necessary to collect all wash water for treatment before disposal.
- In all cases disposal to sewer may be subject to local laws and regulations and these should be considered first.
- Where in doubt contact the responsible authority.

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

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Not Applicable

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

Product name	Group
propylene glycol	Not Available
meloxicam	Not Available
benzyl alcohol	Not Available

Transport in bulk in accordance with the ICG Code

Product name	Ship Type
propylene glycol	Not Available
meloxicam	Not Available
benzyl alcohol	Not Available

SECTION 15 Regulatory information

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

propylene glycol is found on the following regulatory lists

Australian Inventory of Industrial Chemicals (AIIC)

meloxicam is found on the following regulatory lists

Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) -Schedule 4

FEI Equine Prohibited Substances List - Controlled Medication

FEI Equine Prohibited Substances List (EPSL)

benzyl alcohol is found on the following regulatory lists

Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals

Australian Inventory of Industrial Chemicals (AIIC)

National Inventory Status

National Inventory	Status
Australia - AIIC / Australia Non-Industrial Use	No (meloxicam)
Canada - DSL	No (meloxicam)
Canada - NDSL	No (propylene glycol; meloxicam; benzyl alcohol)
China - IECSC	No (meloxicam)
Europe - EINEC / ELINCS / NLP	No (meloxicam)
Japan - ENCS	No (meloxicam)
Korea - KECI	No (meloxicam)
New Zealand - NZIoC	Yes
Philippines - PICCS	No (meloxicam)
USA - TSCA	No (meloxicam)
Taiwan - TCSI	Yes
Mexico - INSQ	Yes
Vietnam - NCI	Yes
Russia - FBEPH	No (meloxicam)
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	23/01/2023
Initial Date	23/01/2023

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 Chemwatch: 5581-87 Page 13 of 13 Issue Date: 23/01/2023 Version No: 2.1

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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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