



XtraCare Ice Cold Pain Relieving Gel

JTC Import Export Pty Ltd

Chemwatch: 5391-93

Version No: 2.1.1.1

Safety Data Sheet according to WHS and ADG requirements

Chemwatch Hazard Alert Code: 2

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

Product Identifier

Product name	XtraCare Ice Cold Pain Relieving Gel
Synonyms	Product code: 67570
Other means of identification	Not Available

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

Relevant identified uses	For temporary relief of minor discomfort of muscles and joint.
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Details of the supplier of the safety data sheet

Registered company name	JTC Import Export Pty Ltd
Address	98 South Park Drive Dandenong South VIC 3175 Australia
Telephone	+61 3 9532 5100
Fax	+61 3 9532 6102
Website	http://www.jtcimportexport.com.au
Email	sales@jtcimportexport.com.au

Emergency telephone number


Association / Organisation	JTC Import Export Pty Ltd
Emergency telephone numbers	+61 3 9532 5100 (Mon-Thurs 8.30am to 5.30pm; Friday 8.30am to 3pm)
Other emergency telephone numbers	Not Available

SECTION 2 HAZARDS IDENTIFICATION

Classification of the substance or mixture

Poisons Schedule	Not Applicable
Classification ^[1]	Eye Irritation Category 2A, Skin Sensitizer Category 1
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)	
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SIGNAL WORD	WARNING
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Hazard statement(s)

H319	Causes serious eye irritation.
H317	May cause an allergic skin reaction.

Precautionary statement(s) Prevention

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

Precautionary statement(s) Response

P321	Specific treatment (see advice on this label).
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P363	Wash contaminated clothing before reuse.
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.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P337+P313	If eye irritation persists: Get medical advice/attention.

Precautionary statement(s) Storage

Not Applicable

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
67-63-0	1-5	<u>isopropanol</u>
1490-04-6	1-5	<u>menthol</u>
464-49-3	<1	<u>camphor</u>
9003-01-4	<1	<u>Carbomer</u>

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, aerosols or combustion products are inhaled remove from contaminated area. ▶ Other measures are usually unnecessary.
Ingestion	<ul style="list-style-type: none"> ▶ If swallowed do NOT induce vomiting. ▶ If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration. ▶ Observe the patient carefully. ▶ Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious. ▶ Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink. ▶ Seek medical advice.

Indication of any immediate medical attention and special treatment needed

Treat symptomatically.

SECTION 5 FIREFIGHTING MEASURES**Extinguishing media**

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

Special hazards arising from the substrate or mixture

Fire Incompatibility	▶ Avoid contamination with oxidising agents i.e. nitrates, oxidising acids, chlorine bleaches, pool chlorine etc. as ignition may result
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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.
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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) 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	<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>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. ▶ 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"> ▶ 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

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Control parameters

OCCUPATIONAL EXPOSURE LIMITS (OEL)

INGREDIENT DATA

Source	Ingredient	Material name	TWA	STEL	Peak	Notes
Australia Exposure Standards	isopropanol	Isopropyl alcohol	400 ppm / 983 mg/m ³	1230 mg/m ³ / 500 ppm	Not Available	Not Available
Australia Exposure Standards	camphor	Camphor, synthetic	2 ppm / 12 mg/m ³	19 mg/m ³ / 3 ppm	Not Available	Not Available

EMERGENCY LIMITS

Ingredient	Material name	TEEL-1	TEEL-2	TEEL-3
isopropanol	Isopropyl alcohol	400 ppm	2000 ppm	12000 ppm

Ingredient	Original IDLH	Revised IDLH
isopropanol	2,000 ppm	Not Available
menthol	Not Available	Not Available
camphor	200 mg/m ³	Not Available
Carbomer	Not Available	Not Available


OCCUPATIONAL EXPOSURE BANDING

Ingredient	Occupational Exposure Band Rating	Occupational Exposure Band Limit
menthol	E	≤ 0.01 mg/m ³
Carbomer	E	≤ 0.01 mg/m ³

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	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 specific circumstances. If risk of overexposure exists, wear approved respirator. Correct fit is essential to obtain adequate protection. Provide adequate ventilation in warehouse or closed storage areas. Air contaminants generated in the workplace possess varying "escape" velocities which, in turn, determine the "capture velocities" of fresh circulating air required to effectively remove the contaminant.	
	Type of Contaminant:	Air Speed:
	solvent, 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.)
grinding, abrasive blasting, tumbling, high speed wheel generated dusts (released at high initial velocity into zone of very high rapid air motion).	2.5-10 m/s (500-2000 f/min.)	
Within each range the appropriate value depends on:		
Lower end of the range		Upper end of the range
1: Room air currents minimal or 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 m/s (200-400 f/min) for extraction of solvents generated in a tank 2 meters distant from the extraction point. Other mechanical considerations, producing performance deficits within the extraction apparatus, make it essential that theoretical air velocities are multiplied by factors of 10 or more when extraction systems are installed or used.		
Personal protection		
Eye and face protection	<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	

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	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
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
NEOPRENE	A
NITRILE	A
NITRILE+PVC	A
PE/EVAL/PE	A
PVC	B
NAT+NEOPR+NITRILE	C
NATURAL RUBBER	C
NATURAL+NEOPRENE	C

* 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 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 10 x ES	A-AUS	-	A-PAPR-AUS / Class 1
up to 50 x ES	-	A-AUS / Class 1	-
up to 100 x ES	-	A-2	A-PAPR-2 ^

^ - Full-face

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

- 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	Blue flavoured gel; mixes with water.		
Physical state	Liquid	Relative density (Water = 1)	1-1.1
Odour	Not Available	Partition coefficient n-octanol / water	Not Available
Odour threshold	Not Available	Auto-ignition temperature (°C)	Not Available
pH (as supplied)	6-7	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	Miscible	pH as a solution (1%)	Not Available
Vapour density (Air = 1)	Not Available	VOC g/L	Not Available

SECTION 10 STABILITY AND REACTIVITY

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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
Hazardous decomposition products	See section 5

SECTION 11 TOXICOLOGICAL INFORMATION

Information on toxicological effects

Inhaled	The material is not thought to produce adverse health effects or irritation of the respiratory tract (as classified by EC Directives using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable control measures be used in an occupational setting.
Ingestion	The material has NOT been classified by EC Directives or other classification systems as "harmful by ingestion". This is because of the lack of corroborating animal or human evidence. The material may still be damaging to the health of the individual, following ingestion, especially where pre-existing organ (e.g liver, kidney) damage is evident. Present definitions of harmful or toxic substances are generally based on doses producing mortality rather than those producing morbidity (disease, ill-health). Gastrointestinal tract discomfort may produce nausea and vomiting. In an occupational setting however, ingestion of insignificant quantities is not thought to be cause for concern.
Skin Contact	<p>The material is not thought to produce adverse health effects or skin irritation following contact (as classified by EC Directives using animal models). Nevertheless, good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.</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	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.
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>Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.</p>

XtraCare Ice Cold Pain Relieving Gel	TOXICITY	IRRITATION
	Not Available	Not Available
isopropanol	TOXICITY	IRRITATION
	dermal (rat) LD50: =12800 mg/kg ^[2]	Eye (rabbit): 10 mg - moderate
	Inhalation (rat) LC50: 72.6 mg/l/4h ^[2]	Eye (rabbit): 100 mg - SEVERE
	Oral (rat) LD50: =4396 mg/kg ^[2]	Eye (rabbit): 100mg/24hr-moderate
menthol		Skin (rabbit): 500 mg - mild
	TOXICITY	IRRITATION
	Oral (rat) LD50: >2000 mg/kg ^[1]	Eye (rabbit): 0.75 mg - SEVERE
		Eye: adverse effect observed (irritating) ^[1]
		Eye: slight *
camphor		Skin: adverse effect observed (irritating) ^[1]
		Skin: irritant *
Carbomer	TOXICITY	IRRITATION
	Dermal (rabbit) LD50: >2000 mg/kg ^[1]	Eye: adverse effect observed (irreversible damage) ^[1]
	Dermal (rabbit) LD50: >3000 mg/kg ^[2]	Skin: no adverse effect observed (not irritating) ^[1]
	Oral (rat) LD50: >1000 mg/kg ^[2]	
	Oral (rat) LD50: >2500 mg/kg ^[2]	
	Oral (rat) LD50: 146-468 mg/kg ^[1]	
	Oral (rat) LD50: 4100 mg/kg ^[2]	
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	

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ISOPROPANOL

For isopropanol (IPA):

Acute toxicity: Isopropanol has a low order of acute toxicity. It is irritating to the eyes, but not to the skin. Very high vapor concentrations are irritating to the eyes, nose, and throat, and prolonged exposure may produce central nervous system depression and narcosis. Human volunteers reported that exposure to 400 ppm isopropanol vapors for 3 to 5 min. caused mild irritation of the eyes, nose and throat.

Although isopropanol produced little irritation when tested on the skin of human volunteers, there have been reports of isolated cases of dermal irritation and/or sensitization. The use of isopropanol as a sponge treatment for the control of fever has resulted in cases of intoxication, probably the result of both dermal absorption and inhalation. There have been a number of cases of poisoning reported due to the intentional ingestion of isopropanol, particularly among alcoholics or suicide victims. These ingestions typically result in a comatose condition. Pulmonary difficulty, nausea, vomiting, and headache accompanied by various degrees of central nervous system depression are typical. In the absence of shock, recovery usually occurred.

Repeat dose studies: The systemic (non-cancer) toxicity of repeated exposure to isopropanol has been evaluated in rats and mice by the inhalation and oral routes. The only adverse effects-in addition to clinical signs identified from these studies were to the kidney.

Reproductive toxicity: A recent two-generation reproductive study characterised the reproductive hazard for isopropanol associated with oral gavage exposure. This study found that the only reproductive parameter apparently affected by isopropanol exposure was a statistically significant decrease in male mating index of the F1 males. It is possible that the change in this reproductive parameter was treatment related and significant, although the mechanism of this effect could not be discerned from the results of the study. However, the lack of a significant effect of the female mating index in either generation, the absence of any adverse effect on litter size, and the lack of histopathological findings of the testes of the high-dose males suggest that the observed reduction in male mating index may not be biologically meaningful.

Developmental toxicity: The developmental toxicity of isopropanol has been characterized in rat and rabbit developmental toxicity studies. These studies indicate that isopropanol is not a selective developmental hazard. Isopropanol produced developmental toxicity in rats, but not in rabbits. In the rat, the developmental toxicity occurred only at maternally toxic doses and consisted of decreased foetal body weights, but no teratogenicity.

Genotoxicity: All genotoxicity assays reported for isopropanol have been negative.

Carcinogenicity: rodent inhalation studies were conducted to evaluate isopropanol for cancer potential. The only tumor rate increase seen was for interstitial (Leydig) cell tumors in the male rats. Interstitial cell tumors of the testis is typically the most frequently observed spontaneous tumor in aged male Fischer 344 rats. These studies demonstrate that isopropanol does not exhibit carcinogenic potential relevant to humans.

Furthermore, there was no evidence from this study to indicate the development of carcinomas of the testes in the male rat, nor has isopropanol been found to be genotoxic. Thus, the testicular tumors seen in the isopropanol exposed male rats are considered of no significance in terms of human cancer risk assessment.

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

The substance is classified by IARC as Group 3:

NOT classifiable as to its carcinogenicity to humans.

Evidence of carcinogenicity may be inadequate or limited in animal testing.

MENTHOL

With few exceptions * (see below) there are no safety concerns regarding certain cyclic and non-cyclic terpene alcohols **, as fragrance ingredients, under the present declared levels of use and exposure for the following reasons

- The non-cyclic and cyclic terpene alcohols have a low order of acute toxicity
- No significant toxicity was observed in repeated dose toxicity tests; it is concluded that these materials have dermal and oral NOAELs of 50 mg/kg body weight/day or greater.
- These materials were inactive in mutagenicity and genotoxicity tests.
- Based on data on metabolism it is concluded that members of this category exhibit similar chemical and biochemical fate.
- Although there is some indication for the production of reactive metabolites by some materials, these metabolites appear to be efficiently detoxicated and not expected to result in overt toxicity. There is no indication for the production of persistent metabolites.
- The results from materials studied to date are indicative of the group and there are no grounds for environmental concern with respect to cyclic and non-cyclic terpene alcohol compounds as currently used in fragrance compounds.
- Human dermatological studies show that, at current use levels, these materials are practically non-irritating.
- The sensitization potential is generally low.
- The margin of safety is generally greater than 100 times the maximum daily exposure.

Sufficient data are available from farnesol, linalool, menthol and α-terpineol, i.e., compounds that contain all key structural elements and potential sites of metabolism of all other members in the group, to demonstrate that the non-cyclic and cyclic terpenes share common metabolic pathways. In most cases, metabolism yields innocuous metabolites. Some materials, however, may generate α,β-unsaturated compounds or be oxidized to hydroperoxides. Such compounds have the capacity to participate in a range of nucleophilic and electrophilic addition reactions with biological material.

* Safety concerns exist for the following substances for the following reasons.

- 6,7-Dihydrogeraniol, hydroabietyl alcohol and 6-isopropyl-2-decahydro-naphthalenol are potent skin sensitizers. These materials are prohibited for use in fragrance materials by IFRA Standards.
- Farnesol is a weak sensitizer. Its use in fragrance materials is therefore restricted by IFRA Standards.
- Sclareol and linalool may contain impurities and/or oxidation products that are strong sensitizers. For use in fragrance materials, these compounds must comply with the purity criteria stated in their IFRA Standards.
- No sensitization test results were available for 2(10)-pinen-3-ol, 2,6-dimethyloct-3,5-dien-2-ol, and 3,7-dimethyl-4,6-octadien-3-ol. These materials should be regarded as potential sensitizers until tested.

** The common characteristic structural element of acyclic -noncyclic- and cyclic terpene alcohols is the typically branched isoprene unit 2-methyl-1,3-butadiene

The Research Institute for Fragrance Materials (RIFM) Expert Panel for kappa-opioid agonists:

kappa-Opioid receptors are widely distributed in the brain (hypothalamus, periaqueductal gray, and claustrum), spinal cord (substantia gelatinosa), and in pain neurons

kappa-Opioid receptor agonists are dysphoric (produce uncomfortable/unpleasant moods such as sadness) but dysphoria from kappa-opioid receptor agonists has been shown to differ between sexes. The kappa-opioid receptor has been strongly implicated as an integral neurochemical component of addiction and the remission thereof. The kappa-opioid receptor also mediates the action of the hallucinogenic side effects of opioids such as pentazocine

It is now widely accepted that kappa-opioid receptor (partial) agonists have dissociative effects (reduce/block signals to the conscious mind from other parts of the brain) and deliriant effects (producing stupor, confusion), as exemplified by salvinorin A. These effects are generally undesirable in medicinal drugs and could have had frightening or disturbing effects in the tested humans. It is thought that the hallucinogenic effects of drugs such as butorphanol, nalbuphine, and pentazocine serve to limit their opiate abuse potential. In the case of salvinorin A, a structurally novel neoclerodane diterpene kappa-opioid receptor agonist, these hallucinogenic, more specifically deliriant and dissociative, effects are sought after, even though the substance is inherently dysphoric. While salvinorin A is considered a hallucinogen, it is not a psychedelic, and its effects are qualitatively different than those produced by the classical psychedelic hallucinogens such as LSD or mescaline.

The involvement of the kappa-opioid receptor in stress response has been elucidated. kappa-Opioid agonists have very marked effects on all types of addiction including alcohol and opiate abuse. There are numerous studies which reflect a reduction in self-administration of alcohol; heroin dependence has also been shown to be effectively treated with kappa-opioid agonism by reducing the immediate rewarding effects and by causing the curative effect of up-regulation of mu opioid receptors which have been down-regulated during opiate abuse

Activation of the kappa-opioid receptor appears to antagonise many of the effects of the mu-opioid receptor.

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	<p>kappa-Opioid receptor ligands are also known for their characteristic diuretic effects, due to their negative regulation of antidiuretic hormone (ADH).</p> <p>kappa-Opioid agonism is neuroprotective against hypoxia/ ischaemia; as such, kappa-opioid receptors may represent a novel therapeutic target</p> <p>Bacterial mutagenicity (Ames) test: negative * No evidence of carcinogenic, mutagenic or teratogenic effects After inhalation ; mucosal irritation</p> <p>After swallowing: gastric spasms, nausea, vomiting Systemic effects: dizziness, ataxia (impaired locomotor coordination), tiredness, depressed respiration. Risk of methaemoglobin formation. *Merck MSDS</p>
CAMPHOR	<p>Camphor appears to have moderate acute oral toxicity, with an LD50 of 1310 mg/kg in mice. It demonstrated moderate to high toxicity in acute inhalation studies(450 mg/m3 (72 ppm) in mice and 500 mg/m3 (80 ppm) in rats). In subchronic studies,inhaled camphor resulted in emphysema in mice at 210 mg/m3 (33 ppm) and rabbits at 33 mg/m3 (5 ppm). In 13-week subchronic dermal studies, camphor had NOAELs of 1000 mg/kg bw/day in mice and 250 mg/kg bw/day in rats. IPCS reported negative results in carcinogenicity tests for camphor. In addition, camphor was negative for genotoxicity in a microsome mutagenesis test, and a peripheral blood micronucleus assay. Reproductive toxicity studies were not available for camphor, however, in developmental toxicity studies, camphor demonstrated no foetal toxicity (with NOAELs 800 mg/kg bw/day in rats) at dose levels that resulted in maternal toxicity</p> <p>For bicyclic terpenes:</p> <p>Acute toxicity: The literature abounds with clinical reports of accidental and intentional acute poisoning with pinene-based turpentine. Rat oral LD50 values are available for <i>alpha</i>-pinene, <i>beta</i>-pinene, camphene and turpentine oil and indicate these materials to be very low in oral acute toxicity with LD50 values in the range from 3388 mg/kg to greater than 5000 mg/kg. Rabbit dermal LD50 values similarly indicate very low toxicities with values greater than the limit doses of 2000 or 5000 mg/kg.</p> <p>Acute inhalation toxicity has been measure in different animal species. The acute LC50 was reported to be 13,500 mg/m3 in rats, 13,500 mg/m3 in guinea pigs, and 9000 mg/m3 in mice . The acute inhalation LC50 of commercial grade turpentine in Wistar rats is reported to be in the range of 12,000-20,000 mg/m3 for 1 to 6 hour exposures and the LC50 for a 2-hour exposure in Swiss-Webster mice is 29,000 mg/m3 . Based on these results the acute oral, dermal, and inhalation toxicities of bicyclic terpene hydrocarbons is concluded to be low.</p> <p>Repeat dose toxicity: A 28-day repeat dose study has been performed with camphene according to an OECD Guideline 407 in both sexes of Wistar rats. Animals of both sexes at the 1000 mg/kg bw/day dose exhibited vacuolization of hepatocytes and increase liver weights. Male rats also exhibited <i>alpha</i>-2-microglobulin-type nephrotoxicity at all dose levels.</p> <p>Subsequent investigations have shown that the <i>alpha</i>-2-microglobulin nephropathy found in the F344/N male rat does not develop in mammals that do not express the hepatic form of <i>alpha</i>-2-microglobulin (e.g. other strains of rats, mice, dogs, humans). Therefore, the nephrotoxicity observed in the camphene study in male F344 rats is not relevant to the human health risk assessment. Based on liver toxicity, the NOAEL for this study is concluded to be 250 mg/kg bw/day</p> <p>Reproductive toxicity: In the a-animal species study, no reproductive effects were observed when dose levels of up to 260 to 600 mg/kg bw of an essential oil predominantly composed of bicyclic terpene hydrocarbons (<i>alpha</i>-pinene, <i>beta</i>-pinene, and sabinene) was administered daily to mice, rats, or hamsters during gestation. When this data is combined with the fact that no adverse effects were observed to the reproductive organs in a 28-day study with camphene at dose levels up to 250 mg/kg bw/day, it is concluded that bicyclic terpene hydrocarbons including <i>alpha</i>-pinene and <i>beta</i>-pinene are not reproductive toxicants</p> <p>Two ninety day inhalation studies have been performed for alpha-pinene in which a full complement of male and female sex organs and tissues were subjected to histopathological examination. Both studies reported no microscopic changes that could be associated with exposure to the test substance. Taking into account the lack of any effects to females in a earlier teratology study, the absence of any maternal or developmental effects in a reproductive/developmental study of a pinene-based oil and for a structurally related monoterpene hydrocarbon, myrcene, it can be concluded that the members of this category show no significant reproductive or developmental toxicity</p> <p>Developmental toxicity: Based on the NOAELs for maternal and developmental toxicity in studies with camphene (250 and 1000 mg/kg bw/day) and a terpene hydrocarbon mixture containing <i>alpha</i>- and <i>beta</i>-pinene and camphene (688 mg/kg bw/day) , and the lack of any signs of maternal or developmental toxicity in a mice, rats, or hamsters given 260 to 600 mg/kg bw/day of a mixture composed primarily (>80%) of <i>alpha</i>- and <i>beta</i>-pinene and sabinene, it is concluded that bicyclic terpene hydrocarbons are not maternal or developmental toxicants.</p> <p>Genotoxicity:</p> <p>In vitro: <i>In vitro</i> genotoxicity assays available for <i>alpha</i>-pinene, <i>beta</i>-pinene and camphene demonstrate that these substances have a little, if any, genotoxic potential. In standard Ames assays of <i>alpha</i>-pinene, <i>beta</i>-pinene and camphene, <i>Salmonella typhimurium</i> strains TA97, TA98, TA100, TA1535, TA1537, and TA1538 provided no evidence of mutagenicity at any dose tested.</p> <p>In vivo: Based on the lack of any evidence of genotoxicity in numerous <i>in vitro</i> assays with and without metabolic activation, it is unlikely that any of these bicyclic terpenes would exhibit a significant genotoxic potential <i>in vivo</i>.</p> <p>for (+/-) -camphor: [CAS No. 21368-68-3] Nil reported</p>
CARBOMER	<p>Polycarboxylates are of low toxicity by all exposure routes examined.</p> <p>Homopolymers(P-AA) are of low acute toxicity to the rat (LD50 > 5 g/kg bw/d) and are not irritating to the rabbit's skin and, at the most, slightly irritating to the eye. Further P-AA has no sensitising potential.</p> <p>The adverse effect after repeated inhalation dosing (91-d/rat) was a mild, reversible pulmonary irritation. This effect is considered as not substance related owing to the physical property of the respirable dust, which caused local and not systemic lung effects.</p> <p>There was neither evidence for a genotoxic potential of PAA using a variety of genetic endpoints in-vitro and in-vivo,nor for developmental toxicity or reprotoxicity in the rat. Based upon the available data, it is considered that exposure to polycarboxylates does not imply any particular hazard to humans</p> <p>No significant acute toxicological data identified in literature search.</p> <p>The Cosmetic Ingredient Review (CIR) Expert Panel noted that these crosslinked alkyl acrylates are macromolecules that are not expected to pass through the stratum corneum of the skin, so significant dermal absorption is not expected. Therefore, topically applied cosmetics are not expected to result in systemic or reproductive and developmental toxicity or to have genotoxic or carcinogenic effects upon use.</p> <p>The Panel noted that cosmetic products containing these ingredients are reportedly used around the eyes, on the lips, and on other mucous membranes. Thus, crosslinked alkyl acrylates could be absorbed systemically through the relatively moist,n stratum cornea of the conjunctiva, lips,and other mucous membranes, and through ingestion when applied to the lips. However, the Panel noted that any absorption through healthy intact mucous membranes is likely to be not significant,primarily because of the relatively large molecular sizes. Furthermore, the chemically inert nature of the polymers precludes degradation to smaller absorbable species.</p> <p>Absorption of the polymers and their residual monomers in cosmetic products also would be limited after application to the lips or eye area based on the relatively small fractions of the applied products that might be inadvertently ingested or make direct contact with the conjunctiva.</p> <p>The Carbomers (Carbopols) are synthetic, high molecular weight, nonlinear polymers of acrylic acid, cross-linked with a polyalkenyl polyether.</p> <p>The Carbomer polymers are used in cosmetics and emulsifying agents at concentrations up to 50%. Acute oral animal studies showed that Carbomers-910, -934, -934P, -940, and -941 have low toxicities when ingested. Rabbits showed minimal skin irritation and zero to moderate eye irritation when tested with Carbomers-910 and -934. Subchronic feeding of rats and dogs with Carbomer-934 in the diet resulted in lower than normal body weights, but no pathological changes were observed. Dogs chronically fed Carbomer-934P manifested gastrointestinal irritation and marked pigment deposition within Kupffer cells of the liver. Clinical studies with Carbomers showed that these polymers have low potential for skin irritation and sensitization at concentrations up to 100%. Carbomer-934 demonstrated low potential for phototoxicity and photo-contact allergenicity. On the basis of the available information presented and as qualified in the report, it is concluded that the Carbomers are safe as cosmetic ingredients.</p> <p>Little toxicity data is available for acrylic crosspolymers; the acute dermal and oral toxicity data that were found indicated that these ingredients are not very toxic. The little genotoxicity data that were available reported negative results in Ames tests. Carcinogenicity data were not found in the published literature for the polymers, but data were available for the monomers.</p> <p>In an alternative method study, acrylates/vinyl neodecanoate crosspolymer was predicted to be a non-irritant. The non-human studies reported no to slight irritation with undiluted and weak sensitization with 2% aq., acrylates/C10-30 alkyl acrylate crosspolymer, no irritation with acrylates crosspolymer at 30% in olive oil, and no irritation or sensitization with sodium acrylates crosspolymer-2 (concentration not specified). Mostly, human testing with undiluted acrylates/C10-30 alkyl acrylate crosspolymer, acrylates crosspolymer, and acrylates/ethylhexyl acrylate crosspolymer, up to 2.5% aq. acrylates/vinyl isodecanoate crosspolymer, 1% aq. dilutions of formulations containing 2% acrylates/vinyl</p>

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	<p>neodecanoate crosspolymer, and formulations containing up to 2.6% lauryl methacrylate/glycol dimethacrylate crosspolymers do not indicate any dermal irritation or sensitization. The only exception was a weak irritant response noted during an intensified Shelanski human repeated insult patch test (HRIPT) with undiluted acrylates/C10-30 alkyl acrylate crosspolymer.</p> <p>Alternative test methods for ocular irritation indicated that acrylates/vinyl isodecanoate crosspolymer and a formulation containing 1% lauryl methacrylate/glycol dimethacrylate crosspolymer are not likely ocular irritants. In studies using rabbits, undiluted acrylates/C10-30 alkyl acrylate crosspolymer produced minimal to moderate irritation, and it was considered a borderline irritant in untrained rabbit eyes. Acrylates crosspolymer, at 50% in olive oil, and sodium acrylates crosspolymer-2 did not appear to be ocular irritants in rabbit eyes. Two different risk assessments evaluating the carcinogenic endpoint for benzene that may be present in acrylates/ C10-30 alkyl acrylates crosspolymer resulted in different lifetime risk. One found that the risk was within the range associated with a 10exp 6 cancer risk, while the other reported a 20-fold greater risk. Final Safety Assessment: Crosslinked Alkyl Acrylates as Used in Cosmetics. Nov 2011</p> <p>Cosmetic Ingredient Review (CIR) Expert Panel http://ntp.niehs.nih.gov/ntp/roc/nominations/2013/publiccomm/attachmentcir_508.pdf</p> <p>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.</p>
ISOPROPANOL & MENTHOL & CAMPHOR & CARBOMER	<p>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 hyperactivity 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.</p>
MENTHOL & CAMPHOR	<p>The following information refers to contact allergens as a group and may not be specific to this product.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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.</p> <p>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</p>

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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.

In the case of prehapten, it is possible to prevent activation outside the body to a certain extent by different measures, e.g. prevention of air exposure during handling and storage of the ingredients and the final product, and by the addition of suitable antioxidants. When antioxidants are used, care should be taken that they will not be activated themselves and thereby form new sensitisers.

Prehapten

Most terpenes with oxidisable allylic positions can be expected to autoxidise on air exposure due to their inherent properties. Depending on the stability of the oxidation products that are formed, a difference in the sensitisation potency of the oxidised terpenes can be seen. Autoxidation is a free radical chain reaction in which hydrogen atom abstraction in combination with addition of oxygen forms peroxy radicals. The reaction shows selectivity for positions where stable radicals can be formed. So far, all fragrance substances that have been investigated with regard to the influence of autoxidation on the allergenic potential, including identification of formed oxidation products, have oxidisable allylic positions that are able to form hydroperoxides and/or hydrogen peroxide as primary oxidation products upon air exposure. Once the hydroperoxides have been formed outside the skin they form specific antigens and act as skin sensitisers. Secondary oxidation products such as aldehydes and epoxides can also be allergenic, thus further increasing the sensitisation potency of the autoxidation mixture. The process of photoactivation may also play a role, but further research is required to establish whether this activation route is currently underestimated in importance due to insufficient knowledge of the true haptens in this context.

It should be noted that activation of substances via air oxidation results in various haptens that might be the same or cross-reacting with other haptens (allergens). The main allergens after air oxidation of linalool and linalyl acetate are the hydroperoxides. If linalyl acetate is chemically hydrolysed outside the skin it can thereafter be oxidised to the same haptens as seen for linalool. A corresponding example is citronellol and citronellyl acetate. In clinical studies, concomitant reactions to oxidised linalool and oxidised linalyl acetate have been observed. Whether these reactions depend on cross-reactivity or are due to exposure to both fragrance substances cannot be elucidated as both have an allergenic effect themselves. Linalool and linalyl acetate are the main components of lavender oil. They autoxidise on air exposure also when present in the essential oil, and form the same oxidation products found in previous studies of the pure synthetic terpenes. Experimental sensitisation studies showed that air exposure of lavender oil increased the sensitisation potency. Patch test results in dermatitis patients showed a connection between positive reactions to oxidised linalool, linalyl acetate and lavender oil.

Prohapten

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

In the case of prohapten, the possibility to become activated is inherent to the molecule and activation cannot be avoided by extrinsic measures. Activation processes increase the risk for cross-reactivity between fragrance substances. Crossreactivity has been shown for certain alcohols and their corresponding aldehydes, i.e. between geraniol and geranial (citral) and between cinnamyl alcohol and cinnamal.

The human skin expresses enzyme systems that are able to metabolise xenobiotics, modifying their chemical structure to increase hydrophilicity and allow elimination from the body. Xenobiotic metabolism can be divided into two phases: phase I and phase II. Phase I transformations are known as activation or functionalisation reactions, which normally introduce or unmask hydrophilic functional groups. If the metabolites are sufficiently polar at this point they will be eliminated. However, many phase I products have to undergo subsequent phase II transformations, i.e. conjugation to make them sufficiently water soluble to be eliminated. Although the purpose of xenobiotic metabolism is detoxification, it can also convert relatively harmless compounds into reactive species. Cutaneous enzymes that catalyse phase I transformations include the cytochrome P450 mixed-function oxidase system, alcohol and aldehyde dehydrogenases, monoamine oxidases, flavin-containing 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 prohapten 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 prohapten) 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 prohapten. 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 alicyclic substance generally regarded as safe (GRAS).

The majority of alicyclic substances used as flavour ingredients are mono- and bicyclic terpenes which occur naturally in a wide variety of foods. Alicyclic compounds have one or more all-carbon rings which may be either saturated or unsaturated, but do not have aromatic character; alicyclic compounds may have one or more aliphatic side chains attached.

With the exception of pulegone, alicyclic substances exhibit very low oral acute toxicity (i.e. LD50 > 1000 mg/kg). Rodent LD50 values in the range from 1000 to more than 5000 mg/kg have been reported for 83 of the 1199 alicyclic substances in this group. The majority of these LD50 values are greater than 2000 mg/kg.

In most of the reported subchronic studies, no adverse effects were observed at any dose level. In studies that showed adverse effects (e.g. studies for alpha- and beta ionone and iso-bornyl acetate), NOAELs were in the range from 15 mg/kg/day to 500 mg/kg/day. The dose levels that resulted in no adverse effects for a parent or representative substance was at least 1000 times the total daily per capita intake, as flavour ingredients, for all members of this group.

The metabolic options available to alicyclic substances increase with an increase in the number and types of functional groups and ring substituents in the molecule. If a primary alcohol, aldehyde or carboxylic acid function is present on an alkyl side-chain, the substance may undergo beta-oxidation and cleavage. If the number of carbons in the side-chain is even, beta oxidation may lead to cleavage of the alicyclic ring. If the number of carbons in the side-chain is odd, beta-oxidation may lead to cleavage of the alicyclic ring. Alicyclic terpenoid primary alcohols which contain alkyl ring substituents generally oxidize to the corresponding carboxylic acid, conjugate with glucuronic acid, and are excreted. Terpenoid aldehydes also undergo oxidation to the corresponding carboxylic acid or, to a lesser extent, reduction to the corresponding alcohol with subsequent conjugation and excretion. If the substance has an endocyclic alkene function and is excreted into the bile, intestinal microflora may promote hydrogenation of the double bond. Excretion metabolites, therefore, may include conjugates of the reduced form of the alcohol or acid.

As with acyclic substances, simple, unsubstituted, alicyclic secondary alcohols and ketones are readily interconverted by oxidation-reduction reactions. For low molecular weight, polar alicyclic substances the ketone is stereoselectively reduced by cytosolic carbonyl reductases to yield the secondary alcohol which is conjugated primarily with glucuronic acid. The resulting conjugate may be

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excreted in the faeces or, more importantly, enter enterohepatic circulation and be excreted in the urine. For higher molecular weight, more lipophilic substances or those with sterically hindered functional groups, oxidation of a ring position by non-specific cytochrome P-450 mixed-function oxidases may compete with reduction of the ketone function or oxidation of the alcohol function.

If the alicyclic alcohol or ketone contains an endocyclic double bond, oxidation or hydrogenation of the alkene may lead to additional metabolites. If a secondary alcohol or ketone function is located on a ring containing alkyl substituents, as in simple terpenoid derivatives, oxidation of the alkyl substituents competes with oxidation-reduction reactions of the alcohol or ketone function. If the substance contains allylic or tertiary hydrogens, the rate of oxidation increases often leading to polyoxygenated metabolites.

Substances exhibiting greater lipophilicity may undergo oxidation of the secondary alcohol function to the corresponding ketone in addition to oxidation of alkyl substituents.

If the functional group is on an alkyl side-chain, as in the ionone derivatives, the ketone may be reduced to the corresponding alcohol. In addition, oxidation of activated ring positions may also occur.

Tertiary alcohol functions are relatively stable in vivo and eventually are excreted as the glucuronic acid conjugates. Ring alkyl substituents of tertiary alcohols are generally oxidized to diols and hydroxyacids, similar to that of secondary alcohols and ketones. Tertiary alcohols with ring unsaturation would yield products of hydrogenation or oxidation of the alkene.

Flavor and Extract Manufacturers' Association (FEMA)

MENTHOL & CARBOMER

The material may produce severe irritation to the eye causing pronounced inflammation. Repeated or prolonged exposure to irritants may produce conjunctivitis.

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

XtraCare Ice Cold Pain Relieving Gel	ENDPOINT	TEST DURATION (HR)	SPECIES	VALUE	SOURCE
	Not Available	Not Available	Not Available	Not Available	Not Available
isopropanol	ENDPOINT	TEST DURATION (HR)	SPECIES	VALUE	SOURCE
	LC50	96	Fish	9-640mg/L	2
	EC50	48	Crustacea	12500mg/L	5
	EC50	96	Algae or other aquatic plants	993.232mg/L	3
	EC0	24	Crustacea	5-102mg/L	2
	NOEC	5760	Fish	0.02mg/L	4
menthol	ENDPOINT	TEST DURATION (HR)	SPECIES	VALUE	SOURCE
	LC50	96	Fish	2.609mg/L	3
	EC50	48	Crustacea	26.6mg/L	2
	EC50	72	Algae or other aquatic plants	0.33mg/L	2
	NOEC	72	Algae or other aquatic plants	0.089mg/L	2
camphor	ENDPOINT	TEST DURATION (HR)	SPECIES	VALUE	SOURCE
	LC50	96	Fish	33.25mg/L	2
	EC50	48	Crustacea	4.23mg/L	2
	EC50	72	Algae or other aquatic plants	0.3mg/L	2
	NOEC	72	Algae or other aquatic plants	0.032mg/L	2
Carbomer	ENDPOINT	TEST DURATION (HR)	SPECIES	VALUE	SOURCE
	LC50	96	Fish	27mg/L	2
	EC50	48	Crustacea	47mg/L	2
	EC50	72	Algae or other aquatic plants	0.75mg/L	2
	NOEC	72	Algae or other aquatic plants	0.03mg/L	2
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				

DO NOT discharge into sewer or waterways.

Persistence and degradability

Ingredient	Persistence: Water/Soil	Persistence: Air
isopropanol	LOW (Half-life = 14 days)	LOW (Half-life = 3 days)
menthol	HIGH	HIGH

Continued...

XtraCare Ice Cold Pain Relieving Gel

camphor	HIGH	HIGH
Carbomer	LOW	LOW

Bioaccumulative potential

Ingredient	Bioaccumulation
isopropanol	LOW (LogKOW = 0.05)
menthol	LOW (BCF = 15)
camphor	LOW (LogKOW = 2.74)
Carbomer	LOW (LogKOW = 0.4415)

Mobility in soil

Ingredient	Mobility
isopropanol	HIGH (KOC = 1.06)
menthol	LOW (KOC = 66.19)
camphor	LOW (KOC = 106)
Carbomer	HIGH (KOC = 1.201)

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.
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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

SECTION 15 REGULATORY INFORMATION

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

ISOPROPANOL IS FOUND ON THE FOLLOWING REGULATORY LISTS

Australia Dangerous Goods Code (ADG Code) - Dangerous Goods List
Australia Dangerous Goods Code (ADG Code) - List of Emergency Action Codes
Australia Exposure Standards
Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals
Australia Inventory of Chemical Substances (AICS)
GESAMP/EHS Composite List - GESAMP Hazard Profiles
IMO IBC Code Chapter 17: Summary of minimum requirements
IMO IBC Code Chapter 18: List of products to which the Code does not apply

IMO MARPOL 73/78 (Annex II) - List of Other Liquid Substances

IMO Provisional Categorization of Liquid Substances - List 2: Pollutant only mixtures containing at least 99% by weight of components already assessed by IMO

IMO Provisional Categorization of Liquid Substances - List 3: (Trade-named) mixtures containing at least 99% by weight of components already assessed by IMO, presenting safety hazards

International Agency for Research on Cancer (IARC) - Agents Classified by the IARC Monographs

International Air Transport Association (IATA) Dangerous Goods Regulations

International Maritime Dangerous Goods Requirements (IMDG Code)

United Nations Recommendations on the Transport of Dangerous Goods Model Regulations

MENTHOL IS FOUND ON THE FOLLOWING REGULATORY LISTS

Australia Inventory of Chemical Substances (AICS)

CAMPBOR IS FOUND ON THE FOLLOWING REGULATORY LISTS

Australia Dangerous Goods Code (ADG Code) - Dangerous Goods List
Australia Dangerous Goods Code (ADG Code) - List of Emergency Action Codes
Australia Exposure Standards
Australia Inventory of Chemical Substances (AICS)
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 6

International Air Transport Association (IATA) Dangerous Goods Regulations

International Maritime Dangerous Goods Requirements (IMDG Code)

United Nations Recommendations on the Transport of Dangerous Goods Model Regulations

CARBOMER IS FOUND ON THE FOLLOWING REGULATORY LISTS

XtraCare Ice Cold Pain Relieving Gel

Australia Dangerous Goods Code (ADG Code) - Dangerous Goods List
 Australia Dangerous Goods Code (ADG Code) - List of Emergency Action Codes
 Australia Inventory of Chemical Substances (AICS)
 GESAMP/EHS Composite List - GESAMP Hazard Profiles
 IMO IBC Code Chapter 17: Summary of minimum requirements

IMO MARPOL (Annex II) - List of Noxious Liquid Substances Carried in Bulk
 International Agency for Research on Cancer (IARC) - Agents Classified by the IARC Monographs
 International Air Transport Association (IATA) Dangerous Goods Regulations
 International Maritime Dangerous Goods Requirements (IMDG Code)
 United Nations Recommendations on the Transport of Dangerous Goods Model Regulations

National Inventory Status

National Inventory	Status
Australia - AICS	Yes
Canada - DSL	Yes
Canada - NDSL	No (menthol; Carbomer; isopropanol)
China - IECSC	Yes
Europe - EINEC / ELINCS / NLP	No (Carbomer)
Japan - ENCS	Yes
Korea - KECI	Yes
New Zealand - NZIoC	Yes
Philippines - PICCS	Yes
USA - TSCA	Yes
Taiwan - TCSI	Yes
Mexico - INSQ	Yes
Vietnam - NCI	Yes
Russia - ARIPS	Yes
Legend:	Yes = All CAS declared ingredients are on the inventory No = One or more of the CAS listed ingredients are not on the inventory and are not exempt from listing(see specific ingredients in brackets)

SECTION 16 OTHER INFORMATION

Revision Date	19/02/2020
Initial Date	19/02/2020

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
 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

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