Ultimum Long Acting Horse Wormer and Boticide

Virbac (Australia) Pty Limited

Chemwatch Hazard Alert Code: **2**

Chemwatch: **5526-76**
Version No: **3.1**
Safety Data Sheet according to WHS Regulations (Hazardous Chemicals) Amendment 2020 and ADG requirements

Issue Date: **03/07/2022**
Print Date: **03/07/2022**
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SECTION 1 Identification of the substance / mixture and of the company / undertaking

Product Identifier

Product name	Ultimum Long Acting Horse Wormer and Boticide
Chemical Name	Not Applicable
Synonyms	APVMA No.: 90549
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 treatment and control of tapeworm, large strongyles, small strongyles, pinworms, ascarids, hairworms, intestinal threadworms, stomach worms, bots and cutaneous onchocerciasis.

Details of the supplier of the safety data sheet

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

Emergency telephone number

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

SECTION 2 Hazards identification

Classification of the substance or mixture

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

ChemWatch Hazard Ratings

		Min	Max
Flammability	1		
Toxicity	2		
Body Contact	2		
Reactivity	1		
Chronic	2		

0 = Minimum
1 = Low
2 = Moderate
3 = High
4 = Extreme

Poisons Schedule	S5
Classification [1]	Acute Toxicity (Oral) Category 4, Sensitisation (Skin) Category 1, Serious Eye Damage/Eye Irritation Category 2A, Specific Target Organ Toxicity - Single Exposure (Narcotic Effects) Category 3, Germ Cell Mutagenicity Category 2, Specific Target Organ Toxicity - Repeated Exposure 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	**Warning**

Hazard statement(s)

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H302	Harmful if swallowed.
H317	May cause an allergic skin reaction.
H319	Causes serious eye irritation.
H336	May cause drowsiness or dizziness.
H341	Suspected of causing genetic defects.
H373	May cause damage to organs through prolonged or repeated exposure.

Precautionary statement(s) Prevention

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

Precautionary statement(s) Response

P308+P313	IF exposed or concerned: Get medical advice/ attention.
P302+P352	IF ON SKIN: Wash with plenty of water.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P337+P313	If eye irritation persists: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before reuse.
P301+P312	IF SWALLOWED: Call a POISON CENTER/doctor/physician/first aider if you feel unwell.
P304+P340	IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P330	Rinse mouth.

Precautionary statement(s) Storage

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

Precautionary statement(s) Disposal

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

SECTION 3 Composition / information on ingredients

Substances

See section below for composition of Mixtures

Mixtures

CAS No	%[weight]	Name
100-51-6	10-30	benzyl alcohol
55268-74-1	10-30	praziquantel
7631-86-9	1-10	silica amorphous
64-17-5	1-5	ethanol
9005-65-6	1-5	sorbitan monooleate, ethoxylated
113507-06-5	1-5	moxidectin
Not Available	30-60	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: ▸ Immediately hold eyelids apart and flush the eye continuously with running water. ▸ Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids. ▸ Continue flushing until advised to stop by the Poisons Information Centre or a doctor, or for at least 15 minutes. ▸ Transport to hospital or doctor without delay. ▸ Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.
Skin Contact	If skin or hair contact occurs: ▸ Immediately flush body and clothes with large amounts of water, using safety shower if available. ▸ Quickly remove all contaminated clothing, including footwear. ▸ Wash skin and hair with running water. Continue flushing with water until advised to stop by the Poisons Information Centre.

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	▸ Transport to hospital, or doctor. For thermal burns: ▸ Decontaminate area around burn. ▸ Consider the use of cold packs and topical antibiotics. For first-degree burns (affecting top layer of skin) ▸ Hold burned skin under cool (not cold) running water or immerse in cool water until pain subsides. ▸ Use compresses if running water is not available. ▸ Cover with sterile non-adhesive bandage or clean cloth. ▸ Do NOT apply butter or ointments; this may cause infection. ▸ Give over-the counter pain relievers if pain increases or swelling, redness, fever occur. For second-degree burns (affecting top two layers of skin) ▸ Cool the burn by immerse in cold running water for 10-15 minutes. ▸ Use compresses if running water is not available. ▸ Do NOT apply ice as this may lower body temperature and cause further damage. ▸ Do NOT break blisters or apply butter or ointments; this may cause infection. ▸ Protect burn by cover loosely with sterile, nonstick bandage and secure in place with gauze or tape. To prevent shock: (unless the person has a head, neck, or leg injury, or it would cause discomfort): ▸ Lay the person flat. ▸ Elevate feet about 12 inches. ▸ Elevate burn area above heart level, if possible. ▸ Cover the person with coat or blanket. ▸ Seek medical assistance. For third-degree burns Seek immediate medical or emergency assistance. In the mean time: ▸ Protect burn area cover loosely with sterile, nonstick bandage or, for large areas, a sheet or other material that will not leave lint in wound. ▸ Separate burned toes and fingers with dry, sterile dressings. ▸ Do not soak burn in water or apply ointments or butter; this may cause infection. ▸ To prevent shock see above. ▸ For an airway burn, do not place pillow under the person's head when the person is lying down. This can close the airway. ▸ Have a person with a facial burn sit up. ▸ Check pulse and breathing to monitor for shock until emergency help arrives.
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	▸ **IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.** ▸ For advice, contact a Poisons Information Centre or a doctor. ▸ Urgent hospital treatment is likely to be needed. ▸ In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition. ▸ If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the SDS should be provided. Further action will be the responsibility of the medical specialist. ▸ If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the SDS. **Where medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:** ▸ **INDUCE** vomiting with fingers down the back of the throat, **ONLY IF CONSCIOUS**. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration. **NOTE:** Wear a protective glove when inducing vomiting by mechanical means.

Indication of any immediate medical attention and special treatment needed

Treat symptomatically.
As in all cases of suspected poisoning, follow the ABCDEs of emergency medicine (airway, breathing, circulation, disability, exposure), then the ABCDEs of toxicology (antidotes, basics, change absorption, change distribution, change elimination).
For poisons (where specific treatment regime is absent):

BASIC TREATMENT

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

ADVANCED TREATMENT

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

BRONSTEIN, A.C. and CURRANCE, P.L.
EMERGENCY CARE FOR HAZARDOUS MATERIALS EXPOSURE: 2nd Ed. 1994

Continued...

SECTION 5 Firefighting measures

Extinguishing media

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

Special hazards arising from the substrate or mixture

Fire Incompatibility	‣ Avoid contamination with oxidising agents i.e. nitrates, oxidising acids, chlorine bleaches, pool chlorine etc. as ignition may result

Advice for firefighters

Fire Fighting	‣ When silica dust is dispersed in air, firefighters should wear inhalation protection as hazardous substances from the fire may be adsorbed on the silica particles. ‣ When heated to extreme temperatures, (>1700 deg.C) amorphous silica can fuse. ‣ 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 courses. ‣ Use water delivered as a fine spray to control fire and cool adjacent area. ‣ **DO NOT** approach containers suspected to be hot. ‣ Cool fire exposed containers with water spray from a protected location. ‣ If safe to do so, remove containers from path of fire. ‣ Equipment should be thoroughly decontaminated after use.
Fire/Explosion Hazard	‣ Combustible. ‣ Slight fire hazard when exposed to heat or flame. ‣ Heating may cause expansion or decomposition leading to violent rupture of containers. ‣ On combustion, may emit toxic fumes of carbon monoxide (CO). ‣ May emit acrid smoke. ‣ Mists containing combustible materials may be explosive. Combustion products include: carbon monoxide (CO) carbon dioxide (CO2) aldehydes nitrogen oxides (NOx) silicon dioxide (SiO2) other pyrolysis products typical of burning organic material. May emit poisonous fumes. May emit corrosive fumes. **WARNING**: Long standing in contact with air and light may result in the formation of potentially explosive peroxides.
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	Slippery when spilt. ‣ Clean up all spills immediately. ‣ Avoid contact with skin and eyes. ‣ Wear impervious gloves and safety goggles. ‣ Trowel up/scrape up. ‣ Place spilled material in clean, dry, sealed container. ‣ Flush spill area with water.
Major Spills	‣ Clear area of personnel and move upwind. ‣ Alert Fire Brigade and tell them location and nature of hazard. ‣ Wear full body protective clothing with breathing apparatus. ‣ Prevent, by all means available, spillage from entering drains or water courses. ‣ Consider evacuation (or protect in place). ‣ No smoking, naked lights or ignition sources. ‣ Increase ventilation. ‣ Stop leak if safe to do so. ‣ Water spray or fog may be used to disperse / absorb vapour. ‣ Contain or absorb spill with sand, earth or vermiculite. ‣ Collect recoverable product into labelled containers for recycling. ‣ Collect solid residues and seal in labelled drums for disposal. ‣ Wash area and prevent runoff into drains. ‣ After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using. ‣ If contamination of drains or waterways occurs, advise emergency services. Slippery when spilt.

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

SECTION 7 Handling and storage

Continued...

Precautions for safe handling

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. ‣ Use good occupational work practice. ‣ Observe manufacturer's storage and handling recommendations contained within this SDS. ‣ Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.
Other information	‣ 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	‣ 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.

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	silica amorphous	Silica - Amorphous: Silica gel	10 mg/m3	Not Available	Not Available	(a) This value is for inhalable dust containing no asbestos and < 1% crystalline silica.
Australia Exposure Standards	silica amorphous	Silica - Amorphous: Diatomaceous earth (uncalcined)	10 mg/m3	Not Available	Not Available	(a) This value is for inhalable dust containing no asbestos and < 1% crystalline silica.
Australia Exposure Standards	silica amorphous	Silica, fused	0.05 mg/m3	Not Available	Not Available	Not Available
Australia Exposure Standards	silica amorphous	Silica - Amorphous: Fumed silica (respirable dust)	2 mg/m3	Not Available	Not Available	Not Available
Australia Exposure Standards	silica amorphous	Silica - Amorphous: Precipitated silica	10 mg/m3	Not Available	Not Available	(a) This value is for inhalable dust containing no asbestos and < 1% crystalline silica.
Australia Exposure Standards	silica amorphous	Silica - Amorphous: Fume (thermally generated)(respirable dust)	2 mg/m3	Not Available	Not Available	(e) Containing no asbestos and < 1% crystalline silica.
Australia Exposure Standards	ethanol	Ethyl alcohol	1000 ppm / 1880 mg/m3	Not Available	Not Available	Not Available

Emergency Limits

Ingredient	TEEL-1	TEEL-2	TEEL-3
benzyl alcohol	30 ppm	52 ppm	740 ppm
silica amorphous	18 mg/m3	200 mg/m3	1,200 mg/m3
silica amorphous	18 mg/m3	100 mg/m3	630 mg/m3
silica amorphous	120 mg/m3	1,300 mg/m3	7,900 mg/m3
silica amorphous	45 mg/m3	500 mg/m3	3,000 mg/m3
silica amorphous	18 mg/m3	740 mg/m3	4,500 mg/m3
ethanol	Not Available	Not Available	15000* ppm

Ingredient	Original IDLH	Revised IDLH
benzyl alcohol	Not Available	Not Available
praziquantel	Not Available	Not Available
silica amorphous	3,000 mg/m3	Not Available
ethanol	3,300 ppm	Not Available

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Ingredient	Original IDLH	Revised IDLH
sorbitan monooleate, ethoxylated	Not Available	Not Available
moxidectin	Not Available	Not Available

Occupational Exposure Banding

Ingredient	Occupational Exposure Band Rating	Occupational Exposure Band Limit
benzyl alcohol	E	≤ 0.1 ppm
sorbitan monooleate, ethoxylated	E	≤ 0.1 ppm
moxidectin	E	≤ 0.01 mg/m³
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.

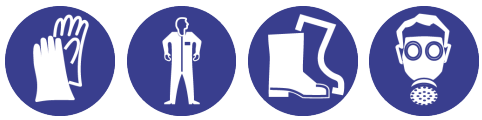
Type of Contaminant:	Air Speed:
solvent, vapours, degreasing etc., evaporating from tank (in still air).	0.25-0.5 m/s (50-100 f/min)
aerosols, fumes from pouring operations, intermittent container filling, low speed conveyer transfers, welding, spray drift, plating acid fumes, pickling (released at low 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

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:
- Chemical goggles.
- Face shield. Full face shield may be required for supplementary but never for primary protection of eyes.
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lenses or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59], [AS/NZS 1336 or national equivalent]

Skin protection

See Hand protection below

Hands/feet protection

NOTE:
- The material may produce skin sensitisation in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact.
- Contaminated leather items, such as shoes, belts and watch-bands should be removed and destroyed.
- Rubber gloves (nitrile or low-protein, powder-free latex, latex/ nitrile). Employees allergic to latex gloves should use nitrile gloves in preference.

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	▸ Double gloving should be considered. ▸ PVC gloves. ▸ 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
Other protection	▸ 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. ▸ 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:
Ultimum Long Acting Horse Wormer and Boticide

Material	CPI
BUTYL	A
NATURAL RUBBER	C
NATURAL+NEOPRENE	C
NEOPRENE	C
NITRILE	C
NITRILE+PVC	C
PE/EVAL/PE	C
PVC	C
VITON	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-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 10 x ES	A-AUS P2	-	A-PAPR-AUS / Class 1 P2
up to 50 x ES	-	A-AUS / Class 1 P2	-
up to 100 x ES	-	A-2 P2	A-PAPR-2 P2 ^

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

SECTION 9 Physical and chemical properties

Information on basic physical and chemical properties

Appearance	Pale yellow to light pink gel.

Physical state	Gel	**Relative density (Water = 1)**	1-1.06
Odour	Not Available	**Partition coefficient n-octanol / water**	Not Available
Odour threshold	Not Available	**Auto-ignition temperature (°C)**	Not Available
pH (as supplied)	6.5-7.5	**Decomposition temperature**	Not Available
Melting point / freezing point (°C)	Not Available	**Viscosity (cSt)**	Not Available
Initial boiling point and boiling range (°C)	Not Available	**Molecular weight (g/mol)**	Not Applicable
Flash point (°C)	Not Available	**Taste**	Not Available
Evaporation rate	Not Available	**Explosive properties**	Not Available
Flammability	Not Available	**Oxidising properties**	Not Available
Upper Explosive Limit (%)	Not Available	**Surface Tension (dyn/cm or mN/m)**	Not Available
Lower Explosive Limit (%)	Not Available	**Volatile Component (%vol)**	Not Available
Vapour pressure (kPa)	Not Available	**Gas group**	Not Available
Solubility in water	Not Available	**pH as a solution (Not Available%)**	Not Available
Vapour density (Air = 1)	Not Available	**VOC g/L**	691.22

SECTION 10 Stability and reactivity

Continued...

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. Limited evidence or practical experience suggests that the material may produce irritation of the respiratory system, in a significant number of individuals, following inhalation. In contrast to most organs, the lung is able to respond to a chemical insult by first removing or neutralising the irritant and then repairing the damage. The repair process, which initially evolved to protect mammalian lungs from foreign matter and antigens, may however, produce further lung damage resulting in the impairment of gas exchange, the primary function of the lungs. Respiratory tract irritation often results in an inflammatory response involving the recruitment and activation of many cell types, mainly derived from the vascular system. The most common signs of inhalation overexposure to ethanol, in animals, include ataxia, incoordination and drowsiness for those surviving narcosis. The narcotic dose for rats, after 2 hours of exposure, is 19260 ppm.
Ingestion	Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.
Skin Contact	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. Skin contact with the material may damage the health of the individual; systemic effects may result following absorption. The material may produce moderate skin irritation; limited evidence or practical experience suggests, that the material either: ▸ produces moderate inflammation of the skin in a substantial number of individuals following direct contact and/or ▸ produces significant, but moderate, inflammation when applied to the healthy intact skin of animals (for up to four hours), such inflammation being present twenty-four hours or more after the end of the exposure period. Skin irritation may also be present after prolonged or repeated exposure; this may result in a form of contact dermatitis (nonallergic). The dermatitis is often characterised by skin redness (erythema) and swelling (oedema) which may progress to blistering (vesiculation), scaling and thickening of the epidermis. At the microscopic level there may be intercellular oedema of the spongy layer of the skin (spongiosis) and intracellular oedema of the epidermis.
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	Strong evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure. 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. 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 should be appropriate consultation with an occupational health professional over the degree of risk and level of surveillance. Serious damage (clear functional disturbance or morphological change which may have toxicological significance) is likely to be caused by repeated or prolonged exposure. As a rule the material produces, or contains a substance which produces severe lesions. Such damage may become apparent following direct application in subchronic (90 day) toxicity studies or following sub-acute (28 day) or chronic (two-year) toxicity tests. Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems. The synthetic, amorphous silicas are believed to represent a very greatly reduced silicosis hazard compared to crystalline silicas and are considered to be nuisance dusts. When heated to high temperature and a long time, amorphous silica can produce crystalline silica on cooling. Inhalation of dusts containing crystalline silicas may lead to silicosis, a disabling pulmonary fibrosis that may take years to develop. Discrepancies between various studies showing that fibrosis associated with chronic exposure to amorphous silica and those that do not may be explained by assuming that diatomaceous earth (a non-synthetic silica commonly used in industry) is either weakly fibrogenic or nonfibrogenic and that fibrosis is due to contamination by crystalline silica content Long-term exposure to ethanol may result in progressive liver damage with fibrosis or may exacerbate liver injury caused by other agents. Repeated ingestion of ethanol by pregnant women may adversely affect the central nervous system of the developing foetus, producing effects collectively described as foetal alcohol syndrome. These include mental and physical retardation, learning disturbances, motor and language deficiency, behavioural disorders and reduced head size. Consumption of ethanol (in alcoholic beverages) may be linked to the development of Type I hypersensitivities in a small number of individuals. Symptoms, which may appear immediately after consumption, include conjunctivitis, angioedema, dyspnoea, and urticarial rashes. The causative agent may be acetic acid, a metabolite (1). (1) Boehncke W.H., & H.Gall, Clinical & Experimental Allergy, 26, 1089-1091, 1996 Allergic reactions to benzoic acid have been reported. Of 100 patients with asthma undergoing provocation tests with benzoic acid, 47 showed positive reactions. In another study, of 75 patients with recurrent urticaria (skin eruptions) and angio-oedema (a deep dermal condition characterised by large wheals) of more than 4 months duration, 44 were found to be sensitive to sodium benzoate or p-hydroxybenzoic acid (paraben), alone or in conjunction with aspirin or azo- dyes, or both. In a further work there was no significant objective or subjective skin

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response to two 500-mg daily doses of benzoic acid or lactic acid in a double blind study of 150 dermatological patients
Repeated exposure to synthetic amorphous silicas may produce skin dryness and cracking.
Available data confirm the absence of significant toxicity by oral and dermal routes of exposure.
Numerous repeated-dose, subchronic and chronic inhalation toxicity studies have been conducted in a number of species, at airborne concentrations ranging from 0.5 mg/m3 to 150 mg/m3. Lowest-observed adverse effect levels (LOAELs) were typically in the range of 1 to 50 mg/m3. When available, the no-observed adverse effect levels (NOAELs) were between 0.5 and 10 mg/m3. Differences in values may be due to particle size, and therefore the number of particles administered per unit dose. Generally, as particle size diminishes so does the NOAEL/ LOAEL. Exposure produced transient increases in lung inflammation, markers of cell injury and lung collagen content. There was no evidence of interstitial pulmonary fibrosis.
Prolonged or repeated exposure to benzyl alcohol may cause allergic contact dermatitis.
Prolonged or repeated ingestion may affect behavior/central nervous system with symptoms similar to acute ingestion. It may also affect the liver, kidneys, cardiovascular system, and metabolism (weight loss).
Animal studies have shown this compound to cause lung, liver, kidney and CNS disorders. Studies in animals have shown evidence of teratogenicity in the chick embryo. The significance of the information for humans is unknown.
Benzyl alcohol showed no evidence of carcinogenic activity in long-term toxicology and carcinogenesis study.

Harmful: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed.

Ultimum Long Acting Horse Wormer and Boticide	**TOXICITY**	**IRRITATION**
	Not Available	Not Available

benzyl alcohol	**TOXICITY**	**IRRITATION**
	Dermal (rabbit) LD50: 2000 mg/kg[2]	Eye (rabbit): 0.75 mg open SEVERE
	Inhalation(Rat) LC50; >4.178 mg/L4h[1]	Eye: adverse effect observed (irritating)[1]
	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]

praziquantel	**TOXICITY**	**IRRITATION**
	Oral (Dog) LD50; >200 mg/kg[2]	Not Available

silica amorphous	**TOXICITY**	**IRRITATION**
	dermal (rat) LD50: >2000 mg/kg[1]	Eye (rabbit): non-irritating *
	Inhalation(Rat) LC50; >0.139 mg/L4h[1]	Eye: no adverse effect observed (not irritating)[1]
	Oral (Rat) LD50; >1000 mg/kg[1]	Skin (rabbit): non-irritating *
		Skin: no adverse effect observed (not irritating)[1]

ethanol	**TOXICITY**	**IRRITATION**
	Dermal (rabbit) LD50: 17100 mg/kg[1]	Eye (rabbit): 500 mg SEVERE
	Inhalation(Rat) LC50; 64000 ppm4h[2]	Eye (rabbit):100mg/24hr-moderate
	Oral (Rat) LD50; 7060 mg/kg[2]	Eye: adverse effect observed (irritating)[1]
		Skin (rabbit):20 mg/24hr-moderate
		Skin (rabbit):400 mg (open)-mild
		Skin: no adverse effect observed (not irritating)[1]

sorbitan monooleate, ethoxylated	**TOXICITY**	**IRRITATION**
	Oral (Mouse) LD50; 25000 mg/kg[2]	Eye (rabbit): 150 mg - mild
		Skin (rabbit): - slight

moxidectin	**TOXICITY**	**IRRITATION**
	Dermal (rabbit) LD50: >2000 mg/kg[2]	Eye (rabbit): slight irritant *
	Oral (Mouse) LD50; 42 mg/kg[2]	Skin (rabbit): non-irritant *

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*

BENZYL ALCOHOL

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.
For benzoates:
Acute toxicity: Benzyl alcohol, benzoic acid and its sodium and potassium salt can be considered as a single category regarding human health, as they are all rapidly metabolised and excreted via a common pathway within 24 hrs. Systemic toxic effects of similar nature (e.g. liver, kidney)

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were observed. However with benzoic acid and its salts toxic effects are seen at higher doses than with benzyl alcohol.
The compounds exhibit low acute toxicity as for the oral and dermal route. The LD50 values are > 2000 mg/kg bw except for benzyl alcohol which needs to be considered as harmful by the oral route in view of an oral LD50 of 1610 mg/kg bw. The 4 hrs inhalation exposure of benzyl alcohol or benzoic acid at 4 and 12 mg/l as aerosol/dust respectively gave no mortality, showing low acute toxicity by inhalation for these compounds.
Benzoic acid and benzyl alcohol are slightly irritating to the skin, while sodium benzoate was not skin irritating. No data are available for potassium benzoate but it is also expected not to be skin irritating. Benzoic acid and benzyl alcohol are irritating to the eye and sodium benzoate was only slightly irritating to the eye. No data are available for potassium benzoate but it is expected also to be only slightly irritating to the eye.
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 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

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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. A prohapten is a chemical that itself is non- or low-sensitising but that is transformed into a hapten in the skin (bioactivation) usually via enzyme catalysis. It is not always possible to know whether a particular allergen that is not directly reactive acts as a prehapten or as a prohapten, or both, because air oxidation and bioactivation can often give the same product (geraniol is an example). Some chemicals might act by all three pathways. **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
PRAZIQUANTEL	**NOTE:** Substance has been shown to be mutagenic in at least one assay, or belongs to a family of chemicals producing damage or change to cellular DNA. * Bayer ADI: 0.02 mg/kg/day NOEL: 20 mg/kg/day
SILICA AMORPHOUS	Reports indicate high/prolonged exposures to amorphous silicas induced lung fibrosis in experimental animals; in some experiments these effects were reversible. [PATTYS] For silica amorphous: Derived No Adverse Effects Level (NOAEL) in the range of 1000 mg/kg/d. In humans, synthetic amorphous silica (SAS) is essentially non-toxic by mouth, skin or eyes, and by inhalation. Epidemiology studies show little evidence of adverse health effects due to SAS. Repeated exposure (without personal protection) may cause mechanical irritation of the eye and

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	drying/cracking of the skin. When experimental animals inhale synthetic amorphous silica (SAS) dust, it dissolves in the lung fluid and is rapidly eliminated. If swallowed, the vast majority of SAS is excreted in the faeces and there is little accumulation in the body. Following absorption across the gut, SAS is eliminated via urine without modification in animals and humans. SAS is not expected to be broken down (metabolised) in mammals. After ingestion, there is limited accumulation of SAS in body tissues and rapid elimination occurs. Intestinal absorption has not been calculated, but appears to be insignificant in animals and humans. SASs injected subcutaneously are subjected to rapid dissolution and removal. There is no indication of metabolism of SAS in animals or humans based on chemical structure and available data. In contrast to crystalline silica, SAS is soluble in physiological media and the soluble chemical species that are formed are eliminated via the urinary tract without modification. Both the mammalian and environmental toxicology of SASs are significantly influenced by the physical and chemical properties, particularly those of solubility and particle size. SAS has no acute intrinsic toxicity by inhalation. Adverse effects, including suffocation, that have been reported were caused by the presence of high numbers of respirable particles generated to meet the required test atmosphere. These results are not representative of exposure to commercial SASs and should not be used for human risk assessment. Though repeated exposure of the skin may cause dryness and cracking, SAS is not a skin or eye irritant, and it is not a sensitiser. Repeated-dose and chronic toxicity studies confirm the absence of toxicity when SAS is swallowed or upon skin contact. Long-term inhalation of SAS caused some adverse effects in animals (increases in lung inflammation, cell injury and lung collagen content), all of which subsided after exposure. Numerous repeated-dose, subchronic and chronic inhalation toxicity studies have been conducted with SAS in a number of species, at airborne concentrations ranging from 0.5 mg/m3 to 150 mg/m3. Lowest-observed adverse effect levels (LOAELs) were typically in the range of 1 to 50 mg/m3. When available, the no-observed adverse effect levels (NOAELs) were between 0.5 and 10 mg/m3. The difference in values may be explained by different particle size, and therefore the number of particles administered per unit dose. In general, as particle size decreases so does the NOAEL/LOAEL. Neither inhalation nor oral administration caused neoplasms (tumours). SAS is not mutagenic in vitro. No genotoxicity was detected in in vivo assays. SAS does not impair development of the foetus. Fertility was not specifically studied, but the reproductive organs in long-term studies were not affected. For Synthetic Amorphous Silica (SAS) Repeated dose toxicity Oral (rat), 2 weeks to 6 months, no significant treatment-related adverse effects at doses of up to 8% silica in the diet. Inhalation (rat), 13 weeks, Lowest Observed Effect Level (LOEL) =1.3 mg/m3 based on mild reversible effects in the lungs. Inhalation (rat), 90 days, LOEL = 1 mg/m3 based on reversible effects in the lungs and effects in the nasal cavity. For silane treated synthetic amorphous silica: Repeated dose toxicity: oral (rat), 28-d, diet, no significant treatment-related adverse effects at the doses tested. There is no evidence of cancer or other long-term respiratory health effects (for example, silicosis) in workers employed in the manufacture of SAS. Respiratory symptoms in SAS workers have been shown to correlate with smoking but not with SAS exposure, while serial pulmonary function values and chest radiographs are not adversely affected by long-term exposure to SAS. 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.
SORBITAN MONOOLEATE, ETHOXYLATED	Polyoxyethylene sorbitan monooleate (TW80) is widely used as an emulsifier or solubilizer in a variety of foods, cosmetics and other commercial Products. In addition, TW80 in water has been used as a vehicle for the delivery of other chemical agents to pregnant laboratory animals by the oral route of administration (eg. by gavage or in the drinking water). Based upon the large population of pregnant women potentially exposed to TW80, and because of its use as a vehicle in laboratory animal studies, TW80 was evaluated for potential developmental toxicity. Timed-mated Sprague-Dawley-derived (CD®) rats (25 per group) were exposed to 0, 500 or 5000 mg/kg/day of TW80. Aqueous solutions were delivered by gavage in a volume of 5 ml/kg of body weight on gestational days (gd) 6 through 15. At termination (gd 20), the uterus was removed and examined to determine pregnancy status, and to evaluate the number of resorptions, and dead or live foetuses. Dead or live foetuses were weighed, and live foetuses were examined for external, visceral and skeletal defects. All treated females survived to scheduled necropsy and 19-23 pregnancies per group were confirmed. No dose-related signs of toxicity were observed for individual animals during the in-life phase of the study or at scheduled necropsy. Average maternal body weight (gd 0, 3, 6, 9, 12, 15, 18, or 20) did not differ among treatment groups, nor was there a treatment related change in maternal weight gain during treatment or gestation (absolute or corrected). There were no treatment-related effects upon the following maternal organ weights: gravid weight (absolute), kidney weight (absolute or relative), and heart weight (absolute or relative). Relative maternal liver weight (% body weight on gd 20 or % corrected body weight) was elevated in both TW80 groups and absolute liver weight was elevated at 500 mg/kg/day. Maternal food intake was comparable across groups during the pre- and post-treatment periods, but was decreased by 14% during the first 3 days of treatment at 5000 mg/kg/day relative to the vehicle control group. Maternal relative water intake was comparable among treatment groups throughout gestation. No differences among groups were noted for the number of corpora lutea per dam, the number of implantation sites per dam or the percent preimplantation loss per litter. No adverse effects were noted on the growth, viability or morphological development of the conceptuses. In conclusion, the maternal LOAEL was 500 mg/kg/day (based upon an increase in maternal relative liver weight). No definitive adverse effects of TW80 upon prenatal development were noted in this study. Thus, the developmental NOAEL was greater than 5000 mg/kg/day . Exposure to the material may result in a possible risk of irreversible effects. The material may produce mutagenic effects in man. This concern is raised, generally, on the basis of appropriate studies using mammalian somatic cells in vivo. Such findings are often supported by positive results from in vitro mutagenicity studies. Asthma-like symptoms may continue for months or even years after exposure to the material ceases. This may be due to a non-allergenic condition known as reactive airways dysfunction syndrome (RADS) which can occur following exposure to high levels of highly irritating compound. Key criteria for the diagnosis of RADS include the absence of preceding respiratory disease, in a non-atopic individual, with abrupt onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. A reversible airflow pattern, on spirometry, with the presence of moderate to severe bronchial hyperreactivity on methacholine challenge testing and the lack of minimal lymphocytic inflammation, without eosinophilia, have also been included in the criteria for diagnosis of RADS. RADS (or asthma) following an irritating inhalation is an infrequent disorder with rates related to the concentration of and duration of exposure to the irritating substance. Industrial bronchitis, on the other hand, is a disorder that occurs as result of exposure due to high concentrations of irritating substance (often particulate in nature) and is completely reversible after exposure ceases. The disorder is characterised by dyspnea, cough and mucus production. The Cosmetic Ingredient Review (CIR) Expert Panel concluded that listed polysorbates are safe in cosmetics when formulated to be non-irritating. This conclusion supersedes the conclusion reached in the 1984, 2000, and 2001 CIR safety assessments. This safety assessment combines polysorbates reviewed in 3 previous safety assessments with other polysorbates that have not been reviewed by the CIR Panel into a group of 80 polyethoxylated sorbitan or sorbitol esters of fatty acid. Following oral administration of polysorbate 20 to rats, ester bonds of polysorbates are hydrolyzed within the digestive tract by pancreatic lipase.24 Free fatty acids were absorbed from the digestive tract and oxidized and excreted, mainly as carbon dioxide in exhaled breath. No migration of the polyoxyethylene sorbitan into the thymus lymph nodes has been demonstrated. No sex difference has been detected in the disposition of polysorbates in rats. Following oral ingestion of polysorbate 20 in humans, 90% or more of the administered substance was excreted in the feces as metabolites, with the polyoxyethylene sorbitan structure maintained, and 2%-3% of these metabolites were excreted in the urine The Panel considered the data available to characterize the potential for polysorbates to cause systemic toxicity, irritation, sensitization, reproductive and developmental toxicity, and genotoxicity. They noted the lack of systemic toxicity at low and moderate doses in several acute and repeated-dose oral exposure studies, and low toxicity at high doses; little or no irritation or sensitization in multiple tests of dermal and ocular exposure; the absence of genotoxicity in multiple Ames tests and chromosome aberration tests, and minimal irritation and lack of sensitization in tests of dermal exposure at concentration of use. The Panel recognizes that there are data gaps regarding use and concentration of these ingredients. However, the overall

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information available on the types of products in which these ingredients are used, concentrations of use and the similar pattern of use raise no safety concerns. The Panel note that polysorbate 20, polysorbate 65, and polysorbate 80 were shown to enhance dermal drug absorption. The Panel cautions that care should be taken in formulating cosmetic products that may contain these ingredients in combination with any ingredients whose safety was based on their lack of dermal absorption, or when dermal absorption was a concern. Especially, care should be taken when creating formulations intended for use on infants.
To address the possible presence of 1,4-dioxane and ethylene oxide impurities in these ingredients, the Panel
stressed that the cosmetics industry should continue to use the necessary procedures to limit these impurities from the PEG ingredients before blending them into cosmetic formulations. The Panel expressed concern about pesticide residues and heavy metals that may be present in botanical (ie, coconut-derived) ingredients. They stressed that the cosmetics industry should continue to use current good manufacturing practices (cGMPs) to limit impurities. Data from the 1984 safety assessment suggested that polysorbates caused a slight enhancement of tumor development caused by 7,12-dimethyl-benz[a]anthracene (DMBA) and N-methyl-N -nitro-N-nitrosoguanidine (MNNG); however, the data were not consistent. For other compounds, the tumorigenic properties of 3-methyl-cholanthrene (MCA) and 3,4-benz[a]pyrene (BP) were not enhanced by polysorbates. Since the tumor enhancement effects were inconsistent and depended on the simultaneous exposure to strong chemical carcinogens, which are not present in cosmetics, the Panel felt that the weak tumor enhancement effects were not relevant to cosmetic formulations. Because some studies showed minimal irritation at concentrations that are used in cosmetics, the Panel cautioned that products containing these ingredients should be formulated to be non-irritating. It was noted that at the time of the 2001 safety assessment on sorbeth beeswaxes, the Panel had recommended that
cosmetic formulations containing PEGs not be used on damaged skin because of the possibility of renal toxicity when PEGs were applied to severely damaged skin, such as in burn patients. Since then, PEGs have been re-reviewed and the additional data demonstrated minimal dermal penetration of low-molecular weight PEGs. The amount of PEGs that would penetrate the stratum corneum barrier, even if damaged, from the use of cosmetics was well below the level of renal toxicity. Therefore, the Panel has removed the caveat that PEGs should not be used on damaged skin. The Panel strongly asserted that it is inappropriate to apply cosmetic products containing high concentrations of PEGs to individuals exhibiting barrier skin disruption through both the stratum corneum and the epidermis.
The Panel discussed the issue of incidental inhalation exposure from spray products, including aerosol and pump hair sprays, spray deodorants, spray body and hand products, and spray moisturizing products. The limited acute exposure
data available from 1 new inhalation study and 1 historical tracheal study suggest little potential for respiratory effects at
relevant doses. These ingredients are reportedly used at concentrations up to 4% in cosmetic products that may be
aerosolized. The Panel noted that 95%-99% of droplets/particles would not be respirable to any appreciable amount.
Coupled with the small actual exposure in the breathing zone and the concentrations at which the ingredients are used, the
available information indicates that incidental inhalation would not be a significant route of exposure that might lead to local
respiratory or systemic effects.
Safety Assessment of Polysorbates as Used in CosmeticJuly 2015
http://www.cir-safety.org/sites/default/files/PSorba_062015_FR_0.pdf
No significant acute toxicological data identified in literature search.
For sorbitan esters, ethoxylated (syn: polyoxyethylene sorbitan esters):
Some of the early short-term studies with these polyoxyethylene sorbitan esters in rats and hamsters showed deleterious effects. Subsequent work suggests that these were largely due to diarrhoea resulting from a large amount of unabsorbed polyglycol, possibly aggravated in some experiments by the use of an unsuitable basal diet. Since that time there has been considerable improvement in testing procedures,and more extensive long-term studies have been carried out. It seems reasonable therefore to base the evaluation of these substances on the levels causing no adverse effects indicated by the results of the more recent investigations.
The significance of the local tumours which were produced by injection has been discussed at the meeting of the Scientific Group (1966). No increase in tumour incidence has followed the oral intake of polyoxyethylene sorbitan esters. Furthermore, large doses of the oleate and stearate have been well tolerated by human subjects.
Polyoxyethylene (20) sorbitan monoester of lauric, oleic, palmitic and stearic acid and triester of stearic acid
Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives, Wld Hlth Org. Techn. Rep. Ser., 1974, No. 539; FAO Nutrition Meetings Report Series, 1974, No. 53.
Polyethers, for example, ethoxylated surfactants and polyethylene glycols, are highly susceptible towards air oxidation as the ether oxygens will stabilize intermediary radicals involved. Investigations of a chemically well-defined alcohol (pentaethylene glycol mono-n-dodecyl ether) ethoxylate, showed that polyethers form complex mixtures of oxidation products when exposed to air.
Sensitization studies in guinea pigs revealed that the pure nonoxidized surfactant itself is nonsensitizing but that many of the investigated oxidation products are sensitizers. Two hydroperoxides were identified in the oxidation mixture, but only one (16-hydroperoxy-3,6,9,12,15-pentaoxaheptacosan-1-ol) was stable enough to be isolated. It was found to be a strong sensitizer in LLNA (local lymph node assay for detection of sensitization capacity). The formation of other hydroperoxides was indicated by the detection of their corresponding aldehydes in the oxidation mixture .
On the basis of the lower irritancy, nonionic surfactants are often preferred to ionic surfactants in topical products. However,
their susceptibility towards autoxidation also increases the irritation. Because of their irritating effect, it is difficult
to diagnose ACD to these compounds by patch testing.
Allergic Contact Dermatitis—Formation, Structural Requirements,and Reactivity of Skin Sensitizers.
Ann-Therese Karlberg et al; Chem. Res. Toxicol.2008,21,53-69
Polyethylene glycols (PEGs) have a wide variety of PEG-derived mixtures due to their readily linkable terminal primary hydroxyl groups in combination with many possible compounds and complexes such as ethers, fatty acids, castor oils, amines, propylene glycols, among other derivatives. PEGs and their derivatives are broadly utilized in cosmetic products as surfactants, emulsifiers, cleansing agents, humectants, and skin conditioners.
PEGs and PEG derivatives were generally regulated as safe for use in cosmetics, with the conditions that impurities and by-products, such as ethylene oxides and 1,4-dioxane, which are known carcinogenic materials, should be removed before they are mixed in cosmetic formulations. Most PEGs are commonly available commercially as mixtures of different oligomer sizes in broadly- or narrowly-defined molecular weight (MW) ranges. For instance, PEG-10,000 typically designates a mixture of PEG molecules (n = 195 to 265) having an average MW of 10,000. PEG is also known as polyethylene oxide (PEO) or polyoxyethylene (POE), with the three names being chemical synonyms. However, PEGs mainly refer to oligomers and polymers with molecular masses below 20,000 g/mol, while PEOs are polymers with molecular masses above 20,000 g/mol, and POEs are polymers of any molecular mass. Relatively small molecular weight PEGs are produced by the chemical reaction between ethylene oxide and water or ethylene glycol (or other ethylene glycol oligomers), as catalyzed by acidic or basic catalysts. To produce PEO or high-molecular weight PEGs, synthesis is performed by suspension polymerization. It is necessary to hold the growing polymer chain in solution during the course of the poly-condensation process. The reaction is catalyzed by magnesium-, aluminum-, or calcium-organoelement compounds. To prevent coagulation of polymer chains in the solution, chelating additives such as dimethylglyoxime are used
Safety Evaluation of Polyethyene Glycol (PEG) Compounds for Cosmetic Use: Toxicol Res 2015; 31:105-136 The Korean Society of Toxicology
http://doi.org/10.5487/TR.2015.31.2.105
For Group D aliphatic esters:(sorbitan fatty esters)
Sorbitan fatty acid esters are mono-, di-, and triesters of fatty acids and sorbitol-derived hexitol anhydrides.
Sorbitan fatty acid esters were relatively nontoxic via ingestion in acute and long-term studies. They were generally minimal to mild skin irritants in animal studies, except that sorbitan isostearate applied to the skin was a moderate irritant in one rabbit study and when injected intradermally caused mild to severe irritation in guinea pigs. Sorbitan fatty acid esters did not sensitise guinea pigs. The fatty acid component, tested alone, typically caused only slight irritation and sensitisation, and was not photosensitising. Sorbitan fatty acid esters were not ocular irritants. Fatty acids are normal components of diet for which no data were available concerning reproductive or developmental toxicity, but Sorbitol had no adverse effects on the reproduction of CD rats during a multigeneration feeding study and was not a reproductive toxin at doses of 3000 to 7000 mg/kg/day for 2 years. Overall these esters and their corresponding fatty acids were not mutagenic, but sorbitan oleate was reported to reduce DNA repair following ultraviolet radiation exposure in human lymphocytes in culture. Sorbitan laurate and sorbitan trioleate were cocarcinogens in one mouse study, but sorbitan trioleate and sorbitan oleate were not tumour promoters in another study. In clinical tests, Sorbitan fatty acid esters were generally minimal to mild skin irritants and were nonsensitizing, but sorbitan sesquioleate did produce an allergic reaction in fewer than 1%

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	of patients with suspected contact dermatitis and addition of sorbitan sesquioleate to the components of a fragrance mix used in patch testing increased both irritant and allergic reactions to the fragrance mix. Careful consideration was made of the data on the cocarcinogenesis of sorbitan laurate and sorbitan trioleate, but the high exposure levels, high frequency of exposure, and absence of a dose-response led to the conclusion that there was not a cocarcinogenesis risk with the use of these ingredients in cosmetic formulations. Accordingly, these ingredients were considered safe for use in cosmetic formulations under the present practices of use. Final report on the safety assessment of sorbitan caprylate, sorbitan cocoate, sorbitan diisostearate, sorbitan dioleate, sorbitan distearate, sorbitan isostearate, sorbitan olivate, sorbitan sesquiisostearate, sorbitan sesquistearate, and sorbitan triisostearate Lanigan et al Int J. Toxicol 2002, pp 93-112 According to a classification scheme described by the American Chemistry Council' Aliphatic Esters Panel, Group D substances are esters of monoacids, mainly common fatty acids, and sorbitan (which is derived from sorbitol - a natural carbohydrate sweetener). The fatty acids include lauric, stearic, oleic acids and coca fatty acids (mainly lauric and myristic acids). The hydroxy group in the sorbitan represents the alcohol portion of the ester linkage. The Group D esters are carbohydrate-derived esters since the ester linkage is connected to the hydroxy group(s) of sorbitan. They may have single ester linkages (i.e., sorbitan monoester) or may have multiple ester linkages, as in the case of sorbitan sesquioleate and sorbitan trioleate. Multiple ester linkages with long-chain fatty acids increase lipophilicity and also tend to diminish water solubility. The sorbitan esters are non-ionic surfactant-active agents that typically find use as emulsifiers, stabilizers, and thickeners in foods, cosmetics and medical products. Acute toxicity: Sorbitan esters do not represent a toxicological concern since they are derived from naturally occurring materials and the parent esters are ultimately metabolised back to these same natural constituents: namely, sorbitan and common fatty acids, both of which have low orders of toxicity. The oral LD50 in rats ranged from >2.9 g/kg to > 39.8 g/kg. Numerous sorbitan esters have been studied by acute oral and dermal administration. Results from these studies support the general conclusion that sorbitan fatty acid esters have low orders of acute toxicity. Repeated Dose Toxicity. A large number of subchronic oral and dermal studies and chronic oral feeding studies have been carried out for sorbitan monolaurate, sorbitan monostearate and sorbitan monooleate , For sorbitan monostearate, no adverse effects were reported in rats fed 5% concentrations of the test substance in the diet for 6 weeks. The NOAEL was estimated to be 5% or approximately 2500 mg/kg/day. In 2-year feeding studies at 5, 10 and 20% in the diet rats tolerated sorbitan moonostearate with no adverse effects. However, at 20%, there was a small but significant decrease on growth rate in male rates. Hence, the NOAEL was 10% in the diet or approximately 5000 mg/kg/day in rats, based on these findings. In a 80-week dietary study in mice, no adverse effects were observed for sorbitan monostearate at 2% concentration in the diet and the NOAEL was 2% or approximately 2600 mg/kg/day . Subchronic studies have also been carried out with sorbitan, fatty acids C6-10, tetraester (CAS 228573-47-5).. Oral gavage studies for 28 days at dose levels up to 1000 mg/kg /day resulted in no systemic toxicity. Therefore, the NOAEL was 1000 mg/kg/day for this tetraester. Since the sesquioleate and trioleate of sorbitan are merely multiple ester homologs of sorbitan monooleate, they would be expected to show similar effects, given their structural similarities and potential to be metabolised to the monooleate. Sensitisation: Sorbitan fatty acid esters were generally minimal to mild skin irritants and were nonsensitising, but sorbitan sesquioleate did produce an allergic reaction in fewer than 1% of patients with suspected contact dermatitis and addition of sorbitan sesquioleate to the components of a fragrance mix used in patch testing increased both irritant and allergic reactions to the fragrance mix. Reproductive and developmental toxicity: Limited reproductive toxicity data have been reported for the sorbitan esters. In a 2-year feeding studies in rats with sorbitan monostearate, there were no effects on gestation and fertility at any dose level (0, 5, 10 and 20% in the diet) but survival of the newborn animals and maternal lactation were slightly diminished at the 20% level. Sorbitol was also studied indirectly as part of a mixture of hydrogenated starch hydrolysates (HSH) which contained about 7% sorbitol as part of the polyhydric alcohol mixture. The HSH mixture was investigated as part of a two-year ingestion study, a multigeneration reproduction study and a teratology study. At concentrations of 18% in drinking water (3000-7000 mg/kg/day), HSH did not produce reproductive or developmental effects . These results indicate that sorbitol does not cause reproductive/ developmental toxicity in animals. Given these findings and the low order of toxicity of natural fatty acids, it seems unlikely that sorbitan esters would present reproductive and developmental toxicity concerns. Genotoxicity: Sorbitan monostearate (CAS 1338-41-6) was found to be negative in the Ames assay. In addition, the non-HPV substance, sorbitan fatty acid C6-10 tetraester (CAS 228573-47-5), did not cause any mutagenic effects in the Salmonella in vitro test. These substances bridge the low and high carbon range of most of the sorbitan esters and the chemistry of the sorbitan esters (i.e., sorbitan/ sorbitol, natural fatty acids) does not suggest the likelihood that the sorbitan esters are electrophilic or reactive in nature. Thus, it is not likely that the substances in Group D cause mutagenic effects. Sorbitan monostearate did not transform primary Syrian golden hamster embryo cells. As discussed above for point mutation, the chemistry of the sorbitan esters does not suggest the likelihood that these substances, or their constituent substructures (i.e., sorbitol, fatty acids) are reactive or electrophilic in nature. Carcinogenicity: Overall these esters and their corresponding fatty acids were not mutagenic, but sorbitan oleate was reported to reduce DNA repair following ultraviolet radiation exposure in human lymphocytes in culture. sorbitan laurate and sorbitan trioleate were cocarcinogens in one mouse study, but sorbitan trioleate and sorbitan oleate were not tumour promoters in another study. **WARNING:** This substance has been classified by the IARC as Group 1: **CARCINOGENIC TO HUMANS**. The material may be irritating to the eye, with prolonged contact causing inflammation. Repeated or prolonged exposure to irritants may produce conjunctivitis. 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.
MOXIDECTIN	For avermectins: Technical avermectin exhibits high mammalian acute toxicity. In vertebrates, the effects occur via poisoning of the central nervous system (CNS) through reactions at the receptor for the inhibitory neurotransmitter GABA. The avermectins open the GABAA receptor chloride channel by binding to the GABA recognition site (receptor protein) and act as partial agonists.. Chloride ions then flow into the postsynaptic neuron. This chloride permeability increase can significantly hyperpolarize (make more negative) the membrane potential, which has a dampening effect on nerve impulse firing. There is also a reversible dose-dependent increase in chloride ion permeability in response to very low doses of avermectins. In GABA-insensitive neurons with no inhibitory innervation, the avermectins induce an irreversible increase in chloride ion conductance through interacting with voltage-dependent chloride channels. Avermectin intoxication in mammals begins with hyperexcitability, tremors, and incoordination and later develops into ataxia and coma-like sedation. This is similar to the mode of action of ethanol and barbiturates and benzodiazepine sedatives However, the avermectins are less specific in their action and can affect a variety of other ligand- and voltage-gated chloride channels. The general safety of the avermectins depends on the presence of an intact P-glycoprotein blood-brain barrier Avermectin is not considered to be mutagenic and does not sensitise skin. It is not readily absorbed by mammals and the majority of the residue is excreted in the faeces within 2 days. The 24-month rat chronic feeding/ oncogenicity study and 94-week mouse chronic toxicity oncogenicity study were negative for oncogenic potential. The results of a series of developmental toxicity studies (rat, rabbit, mouse) have been evaluated and showed that avermectin B1 produces developmental toxicity (cleft palate) in the CF1 mouse. Toxicology data were also evaluated for the delta-8,9-isomer of avermectin B1 which is a plant photodegradate that can range between 5 and 20 percent of the residue on/in cottonseed. This isomer possesses avermectin-like toxicological activity. It was concluded that the delta 8,9-isomer also produces developmental toxicity (cleft palate) in mice, but not in rats. In addition to avermectin and its delta 8,9-isomer, toxicology data were also evaluated for the "polar degradates" of avermectin, which constitute a large percentage (up to 70%) of the total residue on cottonseed. Review of the toxicology data indicated that these polar degradates do not possess avermectin-like toxicological activity and for this reason need not be included in the tolerance expression for residues in/on cottonseed. Abamectin (a mixture of avermectin isomers) is a reproductive toxin in laboratory animals at doses which are acutely toxic to the mother. In development toxicity studies with abamectin, cleft palates were seen in mice and rabbits and clubbing of the forepaws was seen in rabbits. The no-observed-adverse-effect-level (NOAEL) for maternal and developmental toxicity in rabbits was 1 mg/kg/day. In CF-1 mice, a strain recognised to be particularly sensitive to avermectins, the NOAEL for maternal toxicity was 0.05 mg/kg/day and the NOAEL for malformations was 0.2 mg/kg/day. Studies show that the sensitivity of a subpopulation of CF-1 mice to avermectins is due to the absence of a transmembrane P-glycoprotein, a significant component of the blood-brain interface that normally acts as a non-selective protective barrier in a wide range of

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	species including humans. CF-1 mice are therefore an unlikely candidate for assessing human risk. No evidence of developmental toxicity was seen in oral studies in rats in the absence of maternal toxicity (NOAEL = 1.6 mg/kg/day). In a rat multigenerational reproduction study, pup toxicity and deaths were seen at 0.4 mg/kg/day (NOAEL = 0.12 mg/kg/day). Neonatal rats are not an appropriate model for assessing human risk in humans because (a) rat milk has a greater fat content than human breast milk and abamectin concentrates in fat; (b) on a weight basis, the neonatal rat consumes significantly greater quantities of milk than the newborn human and(c) the blood brain barrier in rodents is formed post-natally (as evidenced by low P-glycoprotein levels) while in humans this membrane is formed pre-natally. Ivermectin, a close structural analogue, has been used extensively in the treatment of human onchocerciasis at an oral therapeutic dose of 0.2 mg/kg, without serious drug-related effects. Despite its wide usage in animals and humans, ivermectin does dot appear to produce birth defects. Abamectin is non-mutagenic in the Ames test and the micronucleus test. Dietary carcinogenicity studies in mice and rats showed negative results. In a 14-week oral study in monkeys no effects were seen at 0.2, 0.5 or 1.0 mg/kg/day; emesis was seen at 2.0 mg/kg/day; delayed pupillary obstruction at 6 and 8 mg/kg/day and mydriasis at 12 mg/kg/day. In chronic oral toxicity, abamectin produced decreased body weight gain in mice (no-observed-adverse-effect-level (NOAEL) = 1.5 mg/kg/day); tremors in rats (NOAEL = 1.5 mg/kg/day), weight loss, tremors, mydriasis, liver and gall bladder changes and death in dogs (NOAEL = 0.25 mg/kg/day); and emesis, mydriasis and sedation in monkeys (NOAL = 1 mg/kg/day). May produce developmental toxicity in rat offspring at maternally toxic doses. This does not occur in rabbits. * * Cyanamid The ADI for Moxidectin is set at 0.01mg/kg/day. The corresponding NOEL is set at 1mg/kg/day. ADI means Acceptable Daily Intake and NOEL means No-observable-effect-level. In rats given oral doses of moxidectin, decreased activity, prostration, tremors, chromodacryorrhea, decreased respiration, diarrhoea, hypersensitivity to touch and sound, and epistaxis occurred. Congestion of the liver, kidneys and lungs were observed in animals that died, but animals which were sacrificed at the end of the 14-day observation period showed no abnormalities. No overt signs of toxicity were noted in rabbits treated dermally with moxidectin. Studies of moxidectin show the side effects vary by animal and may be affected by the product's formulation, application method and dosage. An overdose of moxidectin enhances the effect of gamma-aminobutyric acid (GABA) in the central nervous system. In horses, overdose may lead to depression, drooping of the lower lip, tremor, lack of coordination when moving (ataxia), decreased rate of breathing (respiratory rate), stupor and coma. If a dog licks moxidectin from the skin which was applied as a "spot-on" (topical) treatment, this has the same effect as an overdose, and may cause vomiting, salivation and neurological signs such as ataxia, tremor, and nystagmus Collie dogs cannot be administered moxidectin
BENZYL ALCOHOL & ETHANOL	The material may cause skin irritation after prolonged or repeated exposure and may produce a contact dermatitis (nonallergic). This form of dermatitis is often characterised by skin redness (erythema) and swelling the epidermis. Histologically there may be intercellular oedema of the spongy layer (spongiosis) and intracellular oedema of the epidermis.

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

Legend: ✘ *– Data either not available or does not fill the criteria for classification*
✔ *– Data available to make classification*

SECTION 12 Ecological information

Toxicity

Ultimum Long Acting Horse Wormer and Boticide

Endpoint	Test Duration (hr)	Species	Value	Source
Not Available	Not Available	Not Available	Not Available	Not Available

benzyl alcohol

Endpoint	Test Duration (hr)	Species	Value	Source
NOEC(ECx)	336h	Fish	5.1mg/l	2
LC50	96h	Fish	10mg/l	2
EC50	72h	Algae or other aquatic plants	500mg/l	2
EC50	48h	Crustacea	230mg/l	2
EC50	96h	Algae or other aquatic plants	76.828mg/l	2

praziquantel

Endpoint	Test Duration (hr)	Species	Value	Source
NOEC(ECx)	504h	Fish	24.7mg/L	4
LC50	96h	Fish	22.17-38.51mg/l	4

silica amorphous

Endpoint	Test Duration (hr)	Species	Value	Source
EC0(ECx)	24h	Crustacea	>=10000mg/l	1
LC50	96h	Fish	1033.016mg/l	2
EC50	72h	Algae or other aquatic plants	14.1mg/l	2
EC50	48h	Crustacea	>86mg/l	2
EC50	96h	Algae or other aquatic plants	217.576mg/l	2

ethanol

Endpoint	Test Duration (hr)	Species	Value	Source
EC50(ECx)	96h	Algae or other aquatic plants	<0.001mg/L	4
LC50	96h	Fish	>100mg/l	2
EC50	72h	Algae or other aquatic plants	275mg/l	2
EC50	48h	Crustacea	>79mg/L	4
EC50	96h	Algae or other aquatic plants	<0.001mg/L	4

Continued...

sorbitan monooleate, ethoxylated	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	Not Available	Not Available	Not Available	Not Available	Not Available
moxidectin	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	Not Available	Not Available	Not Available	Not Available	Not Available
Legend:	*Extracted from 1. IUCLID Toxicity Data 2. Europe ECHA Registered Substances - Ecotoxicological Information - Aquatic Toxicity 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.
Harmful to aquatic organisms.

Persistence and degradability

Ingredient	Persistence: Water/Soil	Persistence: Air
benzyl alcohol	LOW	LOW
silica amorphous	LOW	LOW
ethanol	LOW (Half-life = 2.17 days)	LOW (Half-life = 5.08 days)

Bioaccumulative potential

Ingredient	Bioaccumulation
benzyl alcohol	LOW (LogKOW = 1.1)
silica amorphous	LOW (LogKOW = 0.5294)
ethanol	LOW (LogKOW = -0.31)

Mobility in soil

Ingredient	Mobility
benzyl alcohol	LOW (KOC = 15.66)
silica amorphous	LOW (KOC = 23.74)
ethanol	HIGH (KOC = 1)

SECTION 13 Disposal considerations

Waste treatment methods

Product / Packaging disposal	▸ Containers may still present a chemical hazard/ danger when empty. ▸ Return to supplier for reuse/ recycling if possible. 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. ▸ Recycle wherever possible or consult manufacturer for recycling options. ▸ Consult State Land Waste Authority for disposal. ▸ Bury or incinerate residue at an approved site. ▸ Recycle containers if possible, or dispose of in an authorised landfill.

SECTION 14 Transport information

Labels Required

Marine Pollutant	NO
HAZCHEM	Not Applicable

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

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

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

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

Not Applicable

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

Product name	Group
benzyl alcohol	Not Available
praziquantel	Not Available
silica amorphous	Not Available

Continued...

Product name	Group
ethanol	Not Available
sorbitan monooleate, ethoxylated	Not Available
moxidectin	Not Available

Transport in bulk in accordance with the ICG Code

Product name	Ship Type
benzyl alcohol	Not Available
praziquantel	Not Available
silica amorphous	Not Available
ethanol	Not Available
sorbitan monooleate, ethoxylated	Not Available
moxidectin	Not Available

SECTION 15 Regulatory information

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

benzyl alcohol is found on the following regulatory lists

Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals
Australian Inventory of Industrial Chemicals (AIIC)

praziquantel is found on the following regulatory lists

Australia Chemicals with non-industrial uses removed from the Australian Inventory of Chemical Substances (old Inventory)
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 4

silica amorphous is found on the following regulatory lists

Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals
Australia Model Work Health and Safety Regulations - Hazardous chemicals (other than lead) requiring health monitoring
Australian Inventory of Industrial Chemicals (AIIC)
Chemical Footprint Project - Chemicals of High Concern List
International Agency for Research on Cancer (IARC) - Agents Classified by the IARC Monographs
International WHO List of Proposed Occupational Exposure Limit (OEL) Values for Manufactured Nanomaterials (MNMS)

ethanol is found on the following regulatory lists

Australia Hazardous Chemical Information System (HCIS) - Hazardous Chemicals
Australian Inventory of Industrial Chemicals (AIIC)

sorbitan monooleate, ethoxylated is found on the following regulatory lists

Australian Inventory of Industrial Chemicals (AIIC)

moxidectin is found on the following regulatory lists

Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 4
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 5
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 6
Australia Standard for the Uniform Scheduling of Medicines and Poisons (SUSMP) - Schedule 7

National Inventory Status

National Inventory	Status
Australia - AIIC / Australia Non-Industrial Use	No (moxidectin)
Canada - DSL	No (praziquantel; moxidectin)
Canada - NDSL	No (benzyl alcohol; praziquantel; ethanol; sorbitan monooleate, ethoxylated; moxidectin)
China - IECSC	No (moxidectin)
Europe - EINEC / ELINCS / NLP	No (moxidectin)
Japan - ENCS	No (praziquantel; moxidectin)
Korea - KECI	No (praziquantel; moxidectin)
New Zealand - NZIoC	Yes
Philippines - PICCS	No (moxidectin)
USA - TSCA	No (praziquantel; moxidectin)
Taiwan - TCSI	Yes
Mexico - INSQ	No (praziquantel; moxidectin)
Vietnam - NCI	No (moxidectin)
Russia - FBEPH	No (moxidectin)
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	03/07/2022
Initial Date	03/04/2022

Continued...

SDS Version Summary

Version	Date of Update	Sections Updated
3.1	03/07/2022	Classification, Ingredients

Other information

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

The SDS is a Hazard Communication tool and should be used to assist in the Risk Assessment. Many factors determine whether the reported Hazards are Risks in the workplace or other settings. Risks may be determined by reference to Exposures Scenarios. Scale of use, frequency of use and current or available engineering controls must be considered.

Definitions and abbreviations

PC—TWA: Permissible Concentration-Time Weighted Average
PC—STEL: Permissible Concentration-Short Term Exposure Limit
IARC: International Agency for Research on Cancer
ACGIH: American Conference of Governmental Industrial Hygienists
STEL: Short Term Exposure Limit
TEEL: Temporary Emergency Exposure Limit。
IDLH: Immediately Dangerous to Life or Health Concentrations
ES: Exposure Standard
OSF: Odour Safety Factor
NOAEL :No Observed Adverse Effect Level
LOAEL: Lowest Observed Adverse Effect Level
TLV: Threshold Limit Value
LOD: Limit Of Detection
OTV: Odour Threshold Value
BCF: BioConcentration Factors
BEI: Biological Exposure Index
AIIC: Australian Inventory of Industrial Chemicals
DSL: Domestic Substances List
NDSL: Non-Domestic Substances List
IECSC: Inventory of Existing Chemical Substance in China
EINECS: European INventory of Existing Commercial chemical Substances
ELINCS: European List of Notified Chemical Substances
NLP: No-Longer Polymers
ENCS: Existing and New Chemical Substances Inventory
KECI: Korea Existing Chemicals Inventory
NZIoC: New Zealand Inventory of Chemicals
PICCS: Philippine Inventory of Chemicals and Chemical Substances
TSCA: Toxic Substances Control Act
TCSI: Taiwan Chemical Substance Inventory
INSQ: Inventario Nacional de Sustancias Químicas
NCI: National Chemical Inventory
FBEPH: Russian Register of Potentially Hazardous Chemical and Biological Substances