Cipla Amoxicillin and Clavulanate Potassium for Oral Suspension

Cipla Ltd

Chemwatch Hazard Alert Code: **2**

Chemwatch: **5546-16**
Version No: **2.1**
Safety Data Sheet

Issue Date: **17/06/2022**
Print Date: **20/06/2022**
L.GHS.IND.EN

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

Product Identifier

Product name	Cipla Amoxicillin and Clavulanate Potassium for Oral Suspension
Chemical Name	Not Applicable
Synonyms	Not Available
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	Penicillin Antibiotic / Avoid breathing dust and avoid contact with eyes, skin and clothing with drug powder.

Details of the supplier of the safety data sheet

Registered company name	**Cipla Ltd**
Address	Peninsula Business Park, Ganpatrao Kadam Marg, Lower Parel, Mumbai 400013 India
Telephone	022 2576 1928
Fax	Not Available
Website	Not Available
Email	Not Available

Emergency telephone number

Association / Organisation	**CHEMWATCH EMERGENCY RESPONSE**
Emergency telephone numbers	+918000403230
Other emergency telephone numbers	+61 3 9573 3188

Once connected and if the message is not in your prefered language then please dial 01

SECTION 2 Hazards identification

Classification of the substance or mixture

NFPA 704 diamond



Note: The hazard category numbers found in GHS classification in section 2 of this SDSs are NOT to be used to fill in the NFPA 704 diamond. Blue = Health Red = Fire Yellow = Reactivity White = Special (Oxidizer or water reactive substances)

Classification	Skin Corrosion/Irritation Category 2, Sensitisation (Skin) Category 1, Serious Eye Damage/Eye Irritation Category 2, Sensitisation (Respiratory) Category 1, Specific Target Organ Toxicity - Single Exposure (Respiratory Tract Irritation) Category 3, Germ Cell Mutagenicity Category 2, Specific Target Organ Toxicity - Repeated Exposure Category 2

Label elements

Hazard pictogram(s)	
Signal word	**Danger**

Hazard statement(s)

H315	Causes skin irritation.

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H317	May cause an allergic skin reaction.
H319	Causes serious eye irritation.
H334	May cause allergy or asthma symptoms or breathing difficulties if inhaled.
H335	May cause respiratory irritation.
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 dust/fume.
P271	Use only outdoors or in a well-ventilated area.
P280	Wear protective gloves, protective clothing, eye protection and face protection.
P284	[In case of inadequate ventilation] wear respiratory protection.
P264	Wash all exposed external body areas thoroughly after handling.
P272	Contaminated work clothing should not be allowed out of the workplace.

Precautionary statement(s) Response

P304+P340	IF INHALED: Remove person to fresh air and keep comfortable for breathing.
P308+P313	IF exposed or concerned: Get medical advice/ attention.
P342+P311	If experiencing respiratory symptoms: Call a POISON CENTER/doctor/physician/first aider.
P302+P352	IF ON SKIN: Wash with plenty of water.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P312	Call a POISON CENTER/doctor/physician/first aider/if you feel unwell.
P333+P313	If skin irritation or rash occurs: Get medical advice/attention.
P337+P313	If eye irritation persists: Get medical advice/attention.
P362+P364	Take off contaminated clothing and wash it before reuse.

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.

Not Applicable

SECTION 3 Composition / information on ingredients

Substances

See section below for composition of Mixtures

Mixtures

CAS No	%[weight]	Name
69-65-8	40-50	mannitol
188112-75-6	20-25	amoxycillin
61177-45-5	10-15	clavulanic acid, potassium salt
14808-60-7	7-12	silica crystalline - quartz
9004-65-3	2-3	hydroxypropyl methylcellulose
11138-66-2	1-2	gum xanthan
6155-57-3	1-1.5	sodium saccharin
Not Available	3-4	Ingredients determined not to be hazardous

SECTION 4 First aid measures

Description of first aid measures

Eye Contact	If this product comes in contact with the eyes: ▸ Wash out immediately with fresh running water. ▸ Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids. ▸ Seek medical attention without delay; if pain persists or recurs seek medical attention. ▸ Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.
Skin Contact	If skin contact occurs: ▸ Immediately remove all contaminated clothing, including footwear. ▸ Flush skin and hair with running water (and soap if available). ▸ Seek medical attention in event of irritation.

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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 do **NOT** induce vomiting. ▸ If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration. ▸ Observe the patient carefully. ▸ Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious. ▸ Give water to rinse out mouth, then provide liquid slowly and as much as casualty can comfortably drink. ▸ Seek medical advice.

Indication of any immediate medical attention and special treatment needed

Penicillins are widely distributed in body fluids and tissues. They appear in pleural, pericardial, peritoneal and synovial fluids and diffuse across the placenta into foetal circulation. Only small amounts pass into normal cerebrospinal fluid. Plasma half-life is about 30 minutes with about 55-80% bound to plasma proteins. 20-35% appears in the urine within an hour. Only small concentrations appear in the bile.
When cutaneous reactions occur, they may subside spontaneously within a few hours or days following withdrawal of the antibiotic. Administration of antihistamines, or in the absence of a response, corticosteroids, may control reactions. At the first sign of an immediate reaction to penicillin treatment, 0.3 to 1 ml of adrenalin injection should be given intramuscularly (or in severe cases, 0.2 ml well diluted intravenously) followed by a further dose should no improvement occur. This may be followed by an antihistamine such as diphenhydramine or chlorpheniramine, given parenterally and a corticosteroid given intravenously. Should bronchospasm be severe, aminophylline (250 mg in 10 ml) may be given intravenously. Assisted respiration is necessary if there is upper airways obstruction and plasma or suitable electrolyte solutions should be given intravenously if circulatory failure occurs. Severe urticaria and/or joint pains may be treated with oral corticosteroids.
MARTINDALE; The Extra Pharmacopoeia, 29th Edition.
Treatment of penicillin overdose may include the following:
· Perform gastric decontamination in cases of severe ingestion.
· Administer activated charcoal as a slurry.
· Manage anaphylaxis with establishment of patent airway, epinephrine, and diphenhydramine.
· For seizures, administer intravenous diazepam or lorazepam. If seizures recur, consider phenobarbital.
For hypotension, dysrhythmias, respiratory depression, and need for endotracheal intubation.
· Evaluate for hypoglycemia, electrolyte disturbances, and hypoxia.
· Treat dysrhythmias with standard antiarrhythmic drugs, if necessary.
· Monitor fluid and electrolyte status and patients with severe vomiting and/or diarrhea.
· Monitor for renal and hematologic abnormalities.
· For coagulopathies,administer vitamin K.
· For moderate to severe pseudomembranous colitis, manage with fluids and electrolytes, protein supplementation, and treatment with an antibacterial drug clinically effective against Clostridium difficile colitis.
· Hemodialysis may aid in the removal of penicillins from the blood.
[Meditext 2007 and PDR 2007]
Treat symptomatically.

SECTION 5 Firefighting measures

Extinguishing media

- There is no restriction on the type of extinguisher which may be used.
- Use extinguishing media suitable for surrounding area.

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	▸ Alert Fire Brigade and tell them location and nature of hazard. ▸ Wear breathing apparatus plus protective gloves in the event of a fire. ▸ Prevent, by any means available, spillage from entering drains or water courses. ▸ Use fire fighting procedures suitable for surrounding area. ▸ **DO NOT** approach containers suspected to be hot. ▸ Cool fire exposed containers with water spray from a protected location. ▸ If safe to do so, remove containers from path of fire. ▸ Equipment should be thoroughly decontaminated after use.
Fire/Explosion Hazard	Combustion products include: carbon monoxide (CO) carbon dioxide (CO2) nitrogen oxides (NOx) sulfur oxides (SOx) silicon dioxide (SiO2) other pyrolysis products typical of burning organic material. May emit poisonous fumes. May emit corrosive fumes. ▸ Solid which exhibits difficult combustion or is difficult to ignite. ▸ Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. ▸ Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust (420 micron or less) may burn rapidly and fiercely if ignited; once initiated larger particles up to 1400 microns diameter will contribute to the propagation of an explosion. ▸ A dust explosion may release large quantities of gaseous products; this in turn creates a subsequent pressure rise of explosive force capable of damaging plant and buildings and injuring people. ▸ Usually the initial or primary explosion takes place in a confined space such as plant or machinery, and can be of sufficient force to damage or rupture the plant. If the shock wave from the primary explosion enters the surrounding area, it will disturb any settled dust layers, forming a second dust cloud, and often initiate a much larger secondary explosion. All large scale explosions have resulted from chain reactions of this type. ▸ Dry dust can also be charged electrostatically by turbulence, pneumatic transport, pouring, in exhaust ducts and during transport. ▸ Build-up of electrostatic charge may be prevented by bonding and grounding. ▸ Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting.

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	▸ All movable parts coming in contact with this material should have a speed of less than 1-metre/sec.

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	▸ Clean up waste regularly and abnormal spills immediately. ▸ Avoid breathing dust and contact with skin and eyes. ▸ Wear protective clothing, gloves, safety glasses and dust respirator. ▸ Use dry clean up procedures and avoid generating dust. ▸ Vacuum up or sweep up. **NOTE:** Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use). ▸ Dampen with water to prevent dusting before sweeping. ▸ Place in suitable containers for disposal.
Major Spills	▸ Absorb or contain isothiazolinone liquid spills with sand, earth, inert material or vermiculite. ▸ The absorbent (and surface soil to a depth sufficient to remove all of the biocide) should be shovelled into a drum and treated with an 11% solution of sodium metabisulfite ($Na_2S_2O_5$) or sodium bisulfite ($NaHSO_3$), or 12% sodium sulfite (Na_2SO_3) and 8% hydrochloric acid (HCl). ▸ Glutathione has also been used to inactivate the isothiazolinones. ▸ Use 20 volumes of decontaminating solution for each volume of biocide, and let containers stand for at least 30 minutes to deactivate microbicide before disposal. ▸ If contamination of drains or waterways occurs, advise emergency services. ▸ After clean up operations, decontaminate and launder all protective clothing ▸ and equipment before storing and re-using.

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

SECTION 7 Handling and storage

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. ▸ Organic powders when finely divided over a range of concentrations regardless of particulate size or shape and suspended in air or some other oxidizing medium may form explosive dust-air mixtures and result in a fire or dust explosion (including secondary explosions) ▸ Minimise airborne dust and eliminate all ignition sources. Keep away from heat, hot surfaces, sparks, and flame. ▸ Establish good housekeeping practices. ▸ Remove dust accumulations on a regular basis by vacuuming or gentle sweeping to avoid creating dust clouds. ▸ Use continuous suction at points of dust generation to capture and minimise the accumulation of dusts. Particular attention should be given to overhead and hidden horizontal surfaces to minimise the probability of a "secondary" explosion. According to NFPA Standard 654, dust layers 1/32 in.(0.8 mm) thick can be sufficient to warrant immediate cleaning of the area. ▸ Do not use air hoses for cleaning. ▸ Minimise dry sweeping to avoid generation of dust clouds. Vacuum dust-accumulating surfaces and remove to a chemical disposal area. Vacuums with explosion-proof motors should be used. ▸ Control sources of static electricity. Dusts or their packages may accumulate static charges, and static discharge can be a source of ignition. ▸ Solids handling systems must be designed in accordance with applicable standards (e.g. NFPA including 654 and 77) and other national guidance. ▸ Do not empty directly into flammable solvents or in the presence of flammable vapors. ▸ The operator, the packaging container and all equipment must be grounded with electrical bonding and grounding systems. Plastic bags and plastics cannot be grounded, and antistatic bags do not completely protect against development of static charges. Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source. ▸ Do NOT cut, drill, grind or weld such containers. ▸ In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.
Other information	▸ Store in original containers. ▸ Keep containers securely sealed. ▸ Store in a cool, dry area protected from environmental extremes. ▸ 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. For major quantities: ▸ Consider storage in bunded areas - ensure storage areas are isolated from sources of community water (including stormwater, ground water, lakes and streams}.

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	▸ Ensure that accidental discharge to air or water is the subject of a contingency disaster management plan; this may require consultation with local authorities.

Conditions for safe storage, including any incompatibilities

Suitable container	▸ Glass container is suitable for laboratory quantities ▸ Polyethylene or polypropylene container. ▸ Check all containers are clearly labelled and free from leaks.
Storage incompatibility	▸ Avoid reaction with oxidising agents

SECTION 8 Exposure controls / personal protection

Control parameters

Occupational Exposure Limits (OEL)

INGREDIENT DATA

Not Available

Emergency Limits

Ingredient	TEEL-1	TEEL-2	TEEL-3
silica crystalline - quartz	0.075 mg/m3	33 mg/m3	200 mg/m3

Ingredient	Original IDLH	Revised IDLH
mannitol	Not Available	Not Available
amoxycillin	Not Available	Not Available
clavulanic acid, potassium salt	Not Available	Not Available
silica crystalline - quartz	25 mg/m3 / 50 mg/m3	Not Available
hydroxypropyl methylcellulose	Not Available	Not Available
gum xanthan	Not Available	Not Available
sodium saccharin	Not Available	Not Available

Occupational Exposure Banding

Ingredient	Occupational Exposure Band Rating	Occupational Exposure Band Limit
amoxycillin	E	≤ 0.01 mg/m³
clavulanic acid, potassium salt	E	≤ 0.01 mg/m³
silica crystalline - quartz	E	≤ 0.01 mg/m³
sodium saccharin	D	> 0.01 to ≤ 0.1 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. ▸ Employees exposed to confirmed human carcinogens should be authorized to do so by the employer, and work in a regulated area. ▸ Work should be undertaken in an isolated system such as a "glove-box" . Employees should wash their hands and arms upon completion of the assigned task and before engaging in other activities not associated with the isolated system. ▸ Within regulated areas, the carcinogen should be stored in sealed containers, or enclosed in a closed system, including piping systems, with any sample ports or openings closed while the carcinogens are contained within. ▸ Open-vessel systems are prohibited. ▸ Each operation should be provided with continuous local exhaust ventilation so that air movement is always from ordinary work areas to the operation. ▸ Exhaust air should not be discharged to regulated areas, non-regulated areas or the external environment unless decontaminated. Clean make-up air should be introduced in sufficient volume to maintain correct operation of the local exhaust system. ▸ For maintenance and decontamination activities, authorized employees entering the area should be provided with and required to wear clean, impervious garments, including gloves, boots and continuous-air supplied hood. Prior to removing protective garments the employee should undergo decontamination and be required to shower upon removal of the garments and hood. ▸ Except for outdoor systems, regulated areas should be maintained under negative pressure (with respect to non-regulated areas). ▸ Local exhaust ventilation requires make-up air be supplied in equal volumes to replaced air. ▸ Laboratory hoods must be designed and maintained so as to draw air inward at an average linear face velocity of 0.76 m/sec with a minimum of 0.64 m/sec. Design and construction of the fume hood requires that insertion of any portion of the employees body, other than hands and arms, be disallowed.
Personal protection	

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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. The selection of suitable gloves does not only depend on the material, but also on further marks of quality which vary from manufacturer to manufacturer. Where the chemical is a preparation of several substances, the resistance of the glove material can not be calculated in advance and has therefore to be checked prior to the application. The exact break through time for substances has to be obtained from the manufacturer of the protective gloves and has to be observed when making a final choice. Personal hygiene is a key element of effective hand care. Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended. Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: · frequency and duration of contact, · chemical resistance of glove material, · glove thickness and · dexterity Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739, AS/NZS 2161.1 or national equivalent). · When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended. · When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374, AS/NZS 2161.10.1 or national equivalent) is recommended. · Some glove polymer types are less affected by movement and this should be taken into account when considering gloves for long-term use. · Contaminated gloves should be replaced. As defined in ASTM F-739-96 in any application, gloves are rated as: · Excellent when breakthrough time > 480 min · Good when breakthrough time > 20 min · Fair when breakthrough time < 20 min · Poor when glove material degrades For general applications, gloves with a thickness typically greater than 0.35 mm, are recommended. It should be emphasised that glove thickness is not necessarily a good predictor of glove resistance to a specific chemical, as the permeation efficiency of the glove will be dependent on the exact composition of the glove material. Therefore, glove selection should also be based on consideration of the task requirements and knowledge of breakthrough times. Glove thickness may also vary depending on the glove manufacturer, the glove type and the glove model. Therefore, the manufacturers technical data should always be taken into account to ensure selection of the most appropriate glove for the task. Note: Depending on the activity being conducted, gloves of varying thickness may be required for specific tasks. For example: · Thinner gloves (down to 0.1 mm or less) may be required where a high degree of manual dexterity is needed. However, these gloves are only likely to give short duration protection and would normally be just for single use applications, then disposed of. · Thicker gloves (up to 3 mm or more) may be required where there is a mechanical (as well as a chemical) risk i.e. where there is abrasion or puncture potential Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended. ▸ Rubber gloves (nitrile or low-protein, powder-free latex, latex/ nitrile). Employees allergic to latex gloves should use nitrile gloves in preference. ▸ 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. ▸ Butyl rubber gloves · Nitrile rubber gloves (Note: Nitric acid penetrates nitrile gloves in a few minutes.) Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present. ▸ polychloroprene. ▸ nitrile rubber. ▸ butyl rubber. ▸ fluorocaoutchouc. ▸ polyvinyl chloride. Gloves should be examined for wear and/ or degradation constantly.
Body protection	See Other protection below
Other protection	▸ Employees working with confirmed human carcinogens should be provided with, and be required to wear, clean, full body protective clothing (smocks, coveralls, or long-sleeved shirt and pants), shoe covers and gloves prior to entering the regulated area. [AS/NZS ISO 6529:2006 or national equivalent] ▸ Employees engaged in handling operations involving carcinogens should be provided with, and required to wear and use half-face filter-type respirators with filters for dusts, mists and fumes, or air purifying canisters or cartridges. A respirator affording higher levels of protection may be substituted. [AS/NZS 1715 or national equivalent] ▸ Emergency deluge showers and eyewash fountains, supplied with potable water, should be located near, within sight of, and on the same level with locations where direct exposure is likely. ▸ Prior to each exit from an area containing confirmed human carcinogens, employees should be required to remove and leave protective clothing and equipment at the point of exit and at the last exit of the day, to place used clothing and equipment in impervious containers at the point of exit for purposes of decontamination or disposal. The contents of such impervious containers must be identified with suitable labels. For maintenance and decontamination activities, authorized employees entering the area should be provided with and required to wear clean, impervious garments, including gloves, boots and continuous-air supplied hood. ▸ Prior to removing protective garments the employee should undergo decontamination and be required to shower upon removal of the

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garments and hood.
- 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

Respiratory protection

Particulate. (AS/NZS 1716 & 1715, EN 143:2000 & 149:001, ANSI Z88 or national equivalent)

Required Minimum Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
up to 10 x ES	P1 Air-line*	- -	PAPR-P1 -
up to 50 x ES	Air-line**	P2	PAPR-P2
up to 100 x ES	-	P3	-
		Air-line*	-
100+ x ES	-	Air-line**	PAPR-P3

* - Negative pressure demand ** - Continuous flow
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)

If inhalation risk above the TLV exists, wear approved dust respirator.
Use respirators with protection factors appropriate for the exposure level.
- Up to 5 X TLV, use valveless mask type; up to 10 X TLV, use 1/2 mask dust respirator
- Up to 50 X TLV, use full face dust respirator or demand type C air supplied respirator
- Up to 500 X TLV, use powered air-purifying dust respirator or a Type C pressure demand supplied-air respirator
- Over 500 X TLV wear full-face self-contained breathing apparatus with positive pressure mode or a combination respirator with a Type C positive pressure supplied-air full-face respirator and an auxiliary self-contained breathing apparatus operated in pressure demand or other positive pressure mode

· Respirators may be necessary when engineering and administrative controls do not adequately prevent exposures.
· The decision to use respiratory protection should be based on professional judgment that takes into account toxicity information, exposure measurement data, and frequency and likelihood of the worker's exposure - ensure users are not subject to high thermal loads which may result in heat stress or distress due to personal protective equipment (powered, positive flow, full face apparatus may be an option).
· Published occupational exposure limits, where they exist, will assist in determining the adequacy of the selected respiratory protection. These may be government mandated or vendor recommended.
· Certified respirators will be useful for protecting workers from inhalation of particulates when properly selected and fit tested as part of a complete respiratory protection program.
· Where protection from nuisance levels of dusts are desired, use type N95 (US) or type P1 (EN143) dust masks. Use respirators and components tested and approved under appropriate government standards such as NIOSH (US) or CEN (EU)
· Use approved positive flow mask if significant quantities of dust becomes airborne.
· Try to avoid creating dust conditions.
Where significant concentrations of the material are likely to enter the breathing zone, a Class P3 respirator may be required.
Class P3 particulate filters are used for protection against highly toxic or highly irritant particulates.
Filtration rate: Filters at least 99.95% of airborne particles
Suitable for:
· Relatively small particles generated by mechanical processes eg. grinding, cutting, sanding, drilling, sawing.
· Sub-micron thermally generated particles e.g. welding fumes, fertilizer and bushfire smoke.
· Biologically active airborne particles under specified infection control applications e.g. viruses, bacteria, COVID-19, SARS
· Highly toxic particles e.g. Organophosphate Insecticides, Radionuclides, Asbestos
Note: P3 Rating can only be achieved when used with a Full Face Respirator or Powered Air-Purifying Respirator (PAPR). If used with any other respirator, it will only provide filtration protection up to a P2 rating.

SECTION 9 Physical and chemical properties

Information on basic physical and chemical properties

Appearance	White to off-white blend powder; partly soluble in water.

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

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Solubility in water	Partly miscible	**pH as a solution (Not Available%)**	Not Available
Vapour density (Air = 1)	Not Available	**VOC g/L**	Not Available

SECTION 10 Stability and reactivity

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

SECTION 11 Toxicological information

Information on toxicological effects

Inhaled	Evidence shows, or practical experience predicts, that the material produces irritation of the respiratory system, in a substantial number of individuals, following inhalation. In contrast to most organs, the lung is able to respond to a chemical insult by first removing or neutralising the irritant and then repairing the damage. The repair process, which initially evolved to protect mammalian lungs from foreign matter and antigens, may however, produce further lung damage resulting in the impairment of gas exchange, the primary function of the lungs. Respiratory tract irritation often results in an inflammatory response involving the recruitment and activation of many cell types, mainly derived from the vascular system. Cellulose, after a single intratracheal dose (15 mg per animal) brought about fibrosing granulomatous bronchioloalveolitis and an increase of IgA production in the bronchioalveolar lavage. Fibrosing alveolitis showed moderate progression as a function of time. Injury of Type I pneumocytes and incomplete repair of Type II pneumocytes were detected. The damage of alveolar epithelium initiated and activated a series of processes that led to definite pulmonary alterations and pulmonary fibrosis leading to disintegration of the alveolo-capillary morphological functional unit. Tatrai, E. et al: Journal of Applied Toxicology; 16(2) 129-135 (1996) Some health effects associated with wood, cotton, flax, jute and hemp particles or fibres are not attributable to cellulose content but to other substances and/or impurities. Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled. If prior damage to the circulatory or nervous systems has occurred or if kidney damage has been sustained, proper screenings should be conducted on individuals who may be exposed to further risk if handling and use of the material result in excessive exposures. Effects on lungs are significantly enhanced in the presence of respirable particles. Overexposure to respirable dust may produce wheezing, coughing and breathing difficulties leading to or symptomatic of impaired respiratory function.
Ingestion	beta-Lactam antibiotics often produce allergic reactions including skin rash, urticaria, eosinophilia,superinfection (including candidiasis) and on occasion, anaphylaxis. Gastro-intestinal effects include diarrhoea, nausea and vomiting. Infrequent adverse effects include fever, vomiting, erythema, dermatitis, angioedema, pseudomembranous colitis. Pain and inflammation at the injection site is also common for parenterally administered ß-lactam antibiotics. This group of antibiotics is related to the cephalosporins and cephamycins. The most serious side-effect of the cephalosporins is acute and potentially fatal renal failure due to proximal tubular necrosis. Neurological disturbances may occasionally occur. Rarely, there may be mild neutropenia, elevated serum aspartate aminotransferase (SGOT) values and increased prothrombin times. Cephalothin (a congener) is reported to produce eosinophilia, thrombocytopenia and an autoimmune type of haemolytic anaemia. Immunological cross-sensitivities may occur with penicillin derivatives, cephalosporins and cephamycins. Research shows that all beta lactams have the intrinsic hazard of very serious hazardous reactions in susceptible patients. Only the frequency of these reactions vary, based on the. A major feature in determining frequency of immunological reactions is the similarity of the side chains (e.g., first generation cephalosporins are similar to penicillins), and this is the reason the beta-lactams are associated with different frequencies of serious reactions (e.g., anaphylaxis) Immunologically mediated adverse reactions to any beta-lactam antibiotic may occur in up to 10% of patients receiving that agent (a small fraction of which are truly IgE-mediated allergic reactions, see amoxicillin rash). Anaphylaxis will occur in approximately 0.01% of patients.There is perhaps a 5-10% cross-sensitivity between penicillin-derivatives, cephalosporins, and carbapenems; but this figure has been challenged by various investigators. Nevertheless, the risk of cross-reactivity is sufficient to warrant the contraindication of all beta-lactam antibiotics in patients with a history of severe allergic reactions (urticaria, anaphylaxis, interstitial nephritis) to any beta-lactam antibiotic. Rarely, allergic reactions have been triggered by exposure from kissing and sexual contact with a partner who is taking these antibiotics A Jarisch-Herxheimer reaction may occur after initial treatment of a spirochetal infection such as syphilis with a beta-lactam antibiotic. A Jarisch-Herxheimer reaction is a reaction to endotoxin-like products released by the death of harmful microorganisms within the body during antibiotic treatment. Efficacious antimicrobial therapy results in lysis (destruction) of bacterial cell membranes, and in the consequent release into the bloodstream of bacterial toxins, resulting in a systemic inflammatory response. Jarisch-Herxheimer reactions can be life-threatening as they can cause a significant drop in blood pressure and cause acute end-organ injury, eventually leading to multi-organ failure . The use of clavulanic acid with penicillins has been associated with an increased incidence of cholestatic jaundice and acute hepatitis during therapy or shortly after, in particular, in men and those over the age of 65. The associated jaundice is usually self-limiting and very rarely fatal. The UK Committee on Safety of Medicines (CSM) recommends that treatments such as amoxicillin/clavulanic acid preparations be reserved for bacterial infections likely to be caused by amoxicillin-resistant beta-lactamase-producing strains, and that treatment should not normally exceed 14 day. Allergy has been reported Administration of penicillins by mouth may produce transient diarrhoea, nausea, heartburn, pruritus ani. In non-allergic individuals even large doses are generally non-toxic although convulsions and other signs of toxicity to the central nervous system may occur at very high doses. In hypersensitive patients anaphylactic shock, with collapse and sometimes death, may occur within minutes. Acute interstitial nephritis has also been described in hypersensitive patients. A generalised sensitivity reaction may occur within 1 to 3 weeks. This may produce urticaria, angioneurotic oedema with marked swelling of the lips, face and periorbital tissues, erythema multiforme, exfoliative dermatitis, purpuric skin lesions, localised oedema, extreme weakness, abdominal pains and cramps, fever and joint pain, bronchoconstriction with severe asthma, chest pains, severe hypotension, cyanosis, circulatory collapse and pulmonary oedema. Maculopapular dermatitis may also occur. Symptom of serum sickness type reactions include chills with or without fever, leukopenia, purpura, arthralgia or arthritis, myalgia, generalised oedema, malaise, mental changes, lymphadenopathy, and splenomegaly. Signs of hypersensitivity include wheezing, flushing of the skin, pruritus, vasculitis of the skin and other organs, haematuria, haemolytic anaemia, neutropenia, thrombocytopenia, eosinophilia, granulocytopenia and anaemia. Relatively uncommon are jaundice, liver necrosis and neuropathies. Immunological cross-sensitivity may occur with other penicillic acid derivatives,

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	cephalosporins and cephamycins. Large doses of cellulose may be administered orally as non-nutritive bulk. Doses of up to 30 g/day can be tolerated as bulk laxative. Extremely large oral doses may produce gastrointestinal disturbances. Large daily doses of saccharin (5-25 gm) produce digestive disorders, anorexia, nausea, vomiting, gastric hyperacidity and diarrhoea Small quantities are normally tolerated by the body and are eliminated almost quantitatively via the kidneys. Large doses (or small doses in hypersensitive individuals) may produce headache, diuresis, loss of appetite, gastric cramps with pain, acute myalgia with muscular fibrillation and twitching, delirium and hallucinations especially those of an auditory type. Allergic reactions include wheezing, urticaria, pruritus, and oedematous papules may occur. Frothing at the mouth, muscle spasm, and convulsions may also be symptomatic. Isothiazolinones are moderately to highly toxic by oral administration. The major signs of toxicity were severe gastric irritation, lethargy, and ataxia Polysaccharides are not substantially absorbed from the gastrointestinal tract but may produce a laxative effect. Larger doses may produce intestinal obstruction or stomach concretions. Large quantities of the substituted polysaccharide, methylcellulose (as with other bulk laxatives), may temporarily increase flatulence. Oesophageal obstruction, by swelling, may occur if the material is swallowed dry. Doses of 3-9 gm hydroxypropylcellulose, fed to human subjects, at least one week apart, were eliminated within 96 hours. Animals fed on diets containing 3% or less, experienced no adverse effects. Higher levels produced malnutrition due to excessive bulk but caused no organic damage. In one dog, an oral dose of hydroxypropylcellulose produced diarrhoea and blood cell depression. Ingestion of hetastarch (hydroxyethyl amylopectin) has reportedly produced fever, chills, urticaria and salivary gland enlargement. Several of these effects may be due to contamination by other naturally occurring macromolecules extracted from the source material. Large volumes of ingested hetastarch may interfere with coagulation mechanisms and increase the risk of haemorrhage. Anaphylaxis has occurred. Infusions of dextrans may occasionally produce allergic reactions such as urticaria, hypotension and bronchospasm. Severe anaphylactic reactions may occasionally occur and death may result from cardiac and respiratory arrest. Nausea, vomiting, fever, joint pains, and flushing may also occur. Similarly, allergic reactions, sometimes severe (but rare) have been reported following ingestion or inhalation of tragacanth gums.
Skin Contact	Evidence exists, or practical experience predicts, that the material either produces inflammation of the skin in a substantial number of individuals following direct contact, and/or produces significant 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. The material may accentuate any pre-existing dermatitis condition Aqueous solutions of isothiazolinones may be irritating or even corrosive depending on concentration. Solutions containing more than 0.5% (5000 ppm active substance) may produce severe irritation of human skin whilst solutions containing more than 100 ppm may irritate the skin. Open cuts, abraded or irritated skin should not be exposed to this material Entry into the blood-stream through, for example, cuts, abrasions, puncture wounds or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.
Eye	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. Solutions containing isothiazolinones may produce corrosion of the mucous membranes and cornea. Instillation of 0.1 ml of an aqueous solution containing 560 ppm isothiazolinone into rabbit eye did not produce irritation whereas concentrations, typically around 3% and 5.5 %, were severely irritating or corrosive to the eye.. Symptoms included clouding of the cornea, chemosis and swelling of the eyelids.
Chronic	Long-term exposure to respiratory irritants may result in disease of the airways involving difficult breathing and related systemic problems. Strong evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure. Practical evidence shows that inhalation of the material is capable of inducing a sensitisation reaction in a substantial number of individuals at a greater frequency than would be expected from the response of a normal population. Pulmonary sensitisation, resulting in hyperactive airway dysfunction and pulmonary allergy may be accompanied by fatigue, malaise and aching. Significant symptoms of exposure may persist for extended periods, even after exposure ceases. Symptoms can be activated by a variety of nonspecific environmental stimuli such as automobile exhaust, perfumes and passive smoking. 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. Toxic: danger of serious damage to health by prolonged exposure through inhalation, in contact with skin and if swallowed. 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. The celluose derivatives pass essentially unchanged through the gastrointestinal tract following oral administration to rats, dogs and man. Acute, subchronic, chronic toxicity, reproductive and developmental toxicity, genotoxicity and carcinogenicity studies of cellulose derivatives indicated that they are practically non-toxic when administered by oral, intraperitoneal, subcutaneous or dermal routes. While no clinical inhalation studies have been conducted, long term exposure to the dusts of cellulose ethers in manufacturing operations has not lead to any significant adverse effects. Ocular and dermal irritation studies indicate that the cellulose derivatives are, at most, minimally irritating and are not dermal sensitisers. Clinical studies confirm these results. Amended Safety Assessment of Cellulose and Related Polymers as used in Cosmetics: Final Report of the Cosmetic Ingredient Review (CIR) Expert Panel: March 2009 Inhalation studies indicate that cellulose fibres may be fibrogenic; this finding continues to be the subject of extensive research. Cellulose is not considered an inert substance because : · in rats, it causes granulomatous fibrosing alveolitis at the end of the third month after exposure, · in rats there was an increase in the secretion of plasminogen activator and interleukin 1 as well as the release of lactate dehydrogenase from macrophages, in a manner similar to asbestos, · there were increases in the incidence of obstructive lung diseases and bronchial asthma in humans at work and in the residential environment where exposure to cellulose was common, · the substance may induce free radical production in human leucocytes. Byssinosis is an occupational disease of the lungs caused by inhalation of cotton dust or dusts from other vegetable fibres such as flax, hemp, or sisal. Byssinosis is a chronic, asthma-like narrowing of the airways. Also called brown lung disease, byssinosis occurs almost exclusively in

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people who work with unprocessed cotton.
Cotton dust disease, "byssinosis", is well known among cotton mill workers. Cotton dust consists largely of cellulose fibre. Exposure to two components of the total dust, the "respirable" and "medium" fraction correlated significantly with the prevalence of respiratory symptoms. Inhalation exposure to a concentration of 0.3 to 0.4 mg/m3 of "fly-free" dust results in a 20% occurrence of byssinosis. "Fly-free" dust is the sum of respirable and medium-length fibres. At 0.46 mg/m3, Grade II byssinosis occurs. A byssinosis (all grades) prevalence of 20%, at 0.3 mg/m3 occurs when the fibre length is less than 15 um (aerodynamic equivalent diameter). Byssinosis is not caused by mechanical irritation but by reactions caused by pharmacologically active substances producing oedema or contraction of the smooth musculature of the airways. The causative agent is suspected to be an endotoxin, in turn, thought to be a cell wall component of bacteria found in cotton. Symptoms of byssinosis include chest tightness, wheezing and dyspnoea. Symptoms usually appear after an absence from work and may subside after 2-days of exposure. As the disease progresses, symptoms may persist for longer periods until they are constant. The individual may eventually exhibit chronic bronchitis and emphysema. Increased physical exertion may produce shortness of breath.
Allergic contact dermatitis is relatively common amongst those handling the penicillins or following repeated topical application of penicillin containing ointments.
Saccharin is suspected of causing urinary bladder cancer.
When saccharin was administered in the diet or drinking water, increased lymphomas/ leukaemias and transitional cell carcinomas of the urinary bladder were seen in rats. In a multigeneration study using rats dietary saccharin induced transitional cell carcinomas and papillomas of the urinary bladder in the first generation male off-spring. Surgical insertion of pellets containing saccharin resulted in urinary bladder cancer in mice and urinary bladder carcinomas in female mice.
Transplacental exposure of rats to sodium saccharin and saccharin did not produce treatment-related neoplasms. Pretreatment with a single instillation in the urinary bladder of a low dose of N-methyl-N-
nitrosourea or feeding of N-(4-(5-nitro-2-furyl)-2-thiazoyl)formamide followed by oral administration of sodium saccharin increased the incidence of urinary bladder neoplasms in rats. Simultaneous administration of N-nitroso-N-(4-hydroxybutyl)butylamine and sodium saccharin produced significant increases in urinary bladder papillomas.
The results of many case-control studies with humans have proved to be largely inconsistent. One large study showed a significant trend of increasing risk with increasing daily consumption in female non-smokers and male heavy smokers. Subsequent analysis of the data confirmed the original findings overall but cast doubt on the significance of the findings in the two subgroups because of inconsistent dose-response trends.
Repeated ingestion of the penicillins may produce nausea (with or without vomiting), epigastric distress, mild or severe diarrhoea, sore or dry throat, sore or black hairy tongue.
In some tests, the class of beta-lactam antibiotics is clastogenic at high concentrations; no evidence exists, however, that this is a significant finding in humans.
Common (= 1% of people) adverse drug reactions associated with use of the penicillins include diarrhoea, hypersensitivity, nausea, rash, neurotoxicity, urticaria, and superinfection (including candidiasis). Infrequent adverse effects (0.1-1% of people) include fever, vomiting, erythema, dermatitis, angioedema, seizures (especially in people with epilepsy), and pseudomembranous colitis. Penicillin can also induce serum sickness or a serum sickness-like reaction in some individuals. Serum sickness is a type III hypersensitivity reaction that occurs one to three weeks after exposure to drugs including penicillin. It is not a true drug allergy, because allergies are type I hypersensitivity reactions, but repeated exposure to the offending agent can result in an anaphylactic reaction.. Allergy will occur in 1-10% of people, presenting as a skin rash after exposure. IgE-mediated anaphylaxis will occur in approximately 0.01% of patients
Pain and inflammation at the injection site are also common for parenterally administered benzathine benzylpenicillin, benzylpenicillin, and, to a lesser extent, procaine benzylpenicillin. The condition is known as livedoid dermatitis or Nicolau syndrome.
Angioedema and anaphylaxis may occur in penicillin-allergic patients. Convulsions can occur if very high doses are given
The penicillins are metabolized in the body and some of their metabolites are released to the environment. Among the metabolites are penicilloyl, penicilloic acid, and penilloic acid, in addition to the parent compound itself.
Under physiologic conditions, 95% of penicillin spontaneously degrades to penicilloyl – also called the major antigenic determinant. The remaining portion of penicillin degrades mainly to penicilloate and penilloate, which, along with penicillin, are called the minor antigenic determinants. Penilloic acids are most common degradation products in penicillin derivatives. The highly strained beta-lactam ring and its amide bond break open in the presence of acid giving an array of complex products, including penilloic acid, penicillamine and penilloaldehyde through the highly unstable intermediate, viz. penillic acid, penicilloic acid and penicillenic acid. The main cause of degradation of penicillin's is the reactivity of the strained beta-lactam ring, particularly to hydrolysis. The course of hydrolysis and nature of the degradation products are influenced by the pH of the solutions.
The carbonyl group of penicillin undergoes nucleophilic attack by the water or hydroxide ion to form the inactive penicilloic acids, which are identified as major metabolites of penicillin's in humans. The formation of these degradation products of penicillin leads to the total loss of activity. Penicilloic acid derivatives may be converted into corresponding penilloic acid derivatives by using mild reduced pressure (vacuum) in presence of inorganic acid either in water or in a mixture of water and water miscible organic solvent in high yields.
The penicilloyl moiety, which constitutes about 95% of all penicillin metabolites, is referred to as the major determinant because it is the major metabolite in terms of quantity. The other 5% of penicillin metabolites are referred to as the minor determinants. Although they are minor in quantity, these determinants actually cause most of the immediate-type anaphylactic reactions, whereas the major determinant is associated with later and less severe reactions
These metabolites are released in urine that ultimately goes to wastewater treatment plants and then is introduced into the environment. However, these metabolites are nontoxic, unlike other antibiotic residues, whose metabolites are more toxic than their parent compound.
Penicilloyl and penicillanic acid derivatives are the major determinants of penicillin allergy. The penicilloyl determinant, which is produced through opening of the beta-lactam ring, thereby allowing amide linkage to body proteins is the most important antigenic component. Penicillanic acid and its derivatives are produced when reconstituted penicillins break down in solution from acidity or temperature elevation. Minor determinants of allergy are benzyl penicillin (penilloic acid) itself and sodium benzyl penicilloate, which can act either as sensitizing agents or on their own elicit an allergic reaction. Both major and minor determinants may be involved in anaphylactic reactions, as well as in urticarial reactions. These reactions are mediated by immunoglobulin (Ig) E (IgE) antibody. A person who has been sensitized by the hapten-carrier complex can have a reaction to penicillin alone or to penicillin that has formed dimers or polymers in solution. Although a history of penicillin allergy is quite common less than 2% will have an allergic reaction if challenged, but the risk is higher for those with history of an immediate hypersensitivity reaction or a positive skin test.
Serum sickness may occur with penicillins, but it is very uncommon. The illness is characterized by fever, urticaria, joint pains, and angioneurotic edema. Exfoliative dermatitis and Stevens-Johnson syndrome are rare forms of allergic reactions to penicillins. The morbilliform eruptions that develop after penicillin therapy probably are due to IgM antibodies to the benzyl penicilloyl hapten and to the minor determinants. In many patients, these rashes disappear, even if the penicillin is continued, owing to the production of IgG-blocking antibody. There is a risk, however, that the rash could progress to generalized desquamation. If a hypersensitivity reaction does occur, epinephrine given intramuscularly or intravenously usually aborts the reaction. Antihistamines and corticosteroids have not been shown to be of benefit.
Prolonged or repeated use of antibiotics, at therapeutic doses, may produce bacterial resistance for some types of bacteria. Prolonged use may result in the overgrowth of non-susceptible organisms (i.e. super-infection). Rarely, antibiotic-associated pseudomembranous colitis, is associated with penicillin therapy.
Another allergic reaction to penicillins is that of allergic vasculitis with the development of cutaneous and visceral lesions similar to that found with periarteritis nodosa. This reaction is extremely rare.
Hematologic toxicity is rare, although neutropenia has been encountered with the use of all types of penicillins, particularly when large doses are used. The mechanisms of the neutropenia are unknown, and white blood cell counts return to normal rapidly if the offending agent is discontinued. Sometimes a lower dose of drug can be used without production of neutropenia. Coombs-positive haemolytic anemia occurs rarely. All penicillins at high concentrations, particularly ticarcillin, bind to the adenosine diphosphate receptor site in platelets, preventing normal platelet aggregation. Clinically significant bleeding occurs relatively infrequently.
Renal toxicity from penicillins is variable, ranging from allergic angiitis to interstitial nephritis. Interstitial nephritis, most common with methicillin, is seen with all penicillins. The clinical syndrome is one of fever, macular rash, eosinophilia, proteinuria, eosinophiluria, and haematuria. Initially, the reaction is one of nonoliguric renal failure with a decrease in creatinine clearance and a rise in serum urea nitrogen and serum creatinine concentrations. This reaction can progress to anuria and renal failure. Biopsy specimens of the kidney show an interstitial infiltrate of

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mononuclear and eosinophilic cells with tubular damage but no glomerular lesions. Discontinuation of the penicillin results in the return of renal function to normal in most cases.
Administration of massive doses of any penicillin, but most often ticarcillin, may result in hypokalaemia, owing to the large dose of nonreabsorbable anion presented to the distal renal tubules, which alters hydrogen ion excretion and secondarily results in potassium loss.
Central nervous system toxicity in the form of myoclonic seizures can follow the administration of massive doses of penicillin G (40 to 100 million units a day). If there is reduced renal function, the drugs accumulate and this form of toxicity becomes more likely. Direct instillation of small doses of oxacillin or nafcillin into the ventricles at the time of surgery for placement of atrioventricular shunts has not resulted in seizures, but direct application of penicillin to the cortex provokes seizure activity.
Gastrointestinal disturbances may follow the use of any of the oral forms but are most pronounced with ampicillin. Antibiotic-associated colitis due to Clostridium difficile has followed the use of each of the penicillins. All penicillins used at high doses for prolonged periods alter the normal microbiota, with resulting colonization with resistant gram-negative bacilli or with fungi such as Candida.
Chronic symptoms produced by crystalline silicas included decreased vital lung capacity and chest infections. Lengthy exposure may cause silicosis a disabling form of pneumoconiosis which may lead to fibrosis, a scarring of the lining of the air sacs in the lung.
The form and severity in which silicosis manifests itself depends in part on the type and extent of exposure to silica dusts: chronic, accelerated and acute forms are all recognized. In later stages the critical condition may become disabling and potentially fatal. Restrictive and/or obstructive lung function changes may result from chronic exposure. A risk associated with silicosis is development of pulmonary tuberculosis (silico-tuberculosis). Respiratory insufficiencies due to massive fibrosis and reduced pulmonary function, possibly with accompanying heart failure, are other potential causes of death due to silicosis.
Not all individuals with silicosis will exhibit symptoms (signs) of the disease. However, silicosis can be progressive, and symptoms may potentially appear years after exposures have ceased. Symptoms of silicosis may include (but are
not limited to): Shortness of breath; difficulty breathing with or without exertion; coughing; diminished work capacity; diminished chest expansion; reduction of lung volume; heart enlargement and/or failure.
Respirable dust containing newly broken particles has been shown to be more hazardous to animals in laboratory tests than
respirable dust containing older silica particles of similar size. Respirable silica particles which had aged for sixty days or more showed less lung injury in animals than equal exposures of respirable dust containing newly broken pieces of silica. There are reports in the literature indicating that crystalline silica exposure may be associated with adverse health effects involving the kidney, scleroderma (thickening of the skin caused by swelling and thickening of fibrous tissue) and other autoimmune and immunity-related disorders. Several studies of persons with silicosis or silica exposure also indicate or suggest increased risk of developing lung cancer, a risk that may increase with the duration of exposure. Many of these studies of silicosis do not account for lung cancer confounders, especially smoking.
Symptoms may appear 8 to 18 months after initial exposure. Smoking increases this risk. Classic silicosis is a chronic disease characterised by the formation of scattered, rounded or stellate silica-containing nodules of scar tissue in the lungs ranging from microscopic to 1.0 cm or more. The nodules isolate the inhaled silica particles and protect the surrounding normal and functioning tissue from continuing injury. Simple silicosis (in which the nodules are less than 1.0 cm in diameter) is generally asymptomatic but may be slowly progressive even in the absence of continuing exposure. Simple silicosis can develop in complicated silicoses (in which nodules are greater than 1.0 cm in diameter) and can produce disabilities including an associated tuberculous infection (which 50 years ago accounted for 75% of the deaths among silicotic workers).
Crystalline silica deposited in the lungs causes epithelial and macrophage injury and activation. Crystalline silica translocates to the interstitium and the regional lymph nodes and cause the recruitment of inflammatory cells in a dose dependent manner. In humans, a large fraction of crystalline silica persists in the lungs. The question of potential carcinogenicity associated with chronic inhalation of crystalline silica remains equivocal with some studies supporting the proposition and others finding no significant association. The results of recent epidemiological studies suggest that lung cancer risk is elevated only in those patients with overt silicosis. A relatively large number of epidemiological studies have been undertaken and in some, increased risk gradients have been observed in relation to dose surrogates - cumulative exposure, duration of exposure, the presence of radiographically defined silicosis, and peak intensity exposure. Chronic inhalation in rats by single or repeated intratracheal instillation produced a significant increase in the incidences of adenocarcinomas and squamous cell carcinomas of the lung. Lifetime inhalation of crystalline silica (87% alpha-quartz) at 1 mg/m3 (74% respirable) by rats, produced an increase in animals with keratinising cystic squamous cell tumours, adenomas, adenocarcinomas, adenosquamous cell carcinomas, squamous cell carcinoma and nodular bronchiolar alveolar hyperplasia accompanied by extensive subpleural and peribronchiolar fibrosis, increased pulmonary collagen content, focal lipoproteinosis and macrophage infiltration. Thoracic and abdominal malignant lymphomas developed in rats after single intrapleural and intraperitoneal injection of suspensions of several types of quartz.
Some studies show excess numbers of cases of schleroderma, connective tissue disorders, lupus, rheumatoid arthritis chronic kidney diseases, and end-stage kidney disease in workers
NOTE: Some jurisdictions require health surveillance be conducted on workers occupationally exposed to silica, crystalline. Such surveillance should emphasise

- demography, occupational and medical history and health advice
- standardised respiratory function tests such as FEV1, FVC and FEV1/FVC
- standardised respiratory function tests such as FV1, FVC and FEV1/FVC
- chest X-ray, full size PA view
- records of personal exposure

Studies indicate that diets containing large amounts of non-absorbable polysaccharides, such as cellulose, might decrease absorption of calcium, magnesium, zinc and phosphorus.
Polysaccharides are polymeric carbohydrates that consist of monosaccharide units, which are connected together with glycosidic bonds. Due to the structural variation of different monosaccharides as well as the innumerable ways that these building blocks link with each other, polysaccharides can be considered as structurally complex biomacromolecules. Polysaccharides originating from plants (e.g., starch and guar gum), microbes (e.g., xanthan), algae (e.g., alginates and carrageenans) and animals (e.g., glycogen and chitin) are frequently used in food.
Starch, a high molar mass compound consisting of (1->4)-linked alpha-D-glucopyranosyl units, is an important energy nutrient that is abundant in common foods, such as cereals and root crops. Although many other food polysaccharides are not digested in the upper gastrointestinal tract of humans, they often serve functions other than being components giving nutritional value. For example, plant cell-wall polysaccharides, such as arabinoxylans and beta-glucan, exist in cereal-based foods, and “plant gums” are used as thickeners, emulsifiers, emulsion stabilizers, gelling agents and encapsulating agents. These non-digestible polysaccharides are important for health because they are considered as dietary fibre, which promote colon health, regulate post-prandial blood glucose levels and reduce serum cholesterol levels.
Despite the fact that nature provides various sources of polysaccharides, and that scientific research on their exploitation as food materials is increasingly active, a relatively low number of polysaccharides are authorized for use as food ingredients. For example, in the European Union (EU) and in Switzerland, among the permitted food additives (identified by an E number) only a small percentage are polysaccharide-based (native or structurally modified). The difference between other food ingredients and food additives is mainly the quantity used in any given product. Food ingredients can be consumed alone as food (e.g., starch), whereas food additives (e.g., carboxymethyl cellulose) are used in small quantities (usually less than 2%) relative to the total food composition but they, nonetheless, play an important role in the food products.
Regarding food additive use in Europe, the European Food Safety Authority (EFSA) has an expert Panel on Food Additives and Nutrient Sources Added to Food (ANS), which evaluates the safety of food additives. Similarly, if new ingredients are released into the market, EFSA's Panel on Dietetic Products, Nutrition and Allergies (NDA) has the responsibility of evaluating the safety of Novel Food ingredients
The vast majority of polysaccharides used as food ingredients are plant-based. In addition to the cellulosic polysaccharides, other types of food-grade ingredients or additives, such as, vanillin aroma, glycerol esters of wood rosins (E445), xylitol (E967) and steryls/stanols, are derived from wood. The main components of wood are polysaccharides: cellulose (40–50 wt%) and hemicelluloses (20–35%), while lignin comprises 15–30% of wood mass.
The material contains a substantial proportion of a polymer considered to be of low concern (PLC). The trend towards production of lower molecular weight polymers (thus reducing the required level of solvent use and creating a more "environmentally-friendly" material) has brought with it the need to define PLCs as those
having molecular weights of between 1000 and 10000 and containing less than 10% of the molecules with molecular weight below 500 and less than 25% of the molecules with a molecular weight below 1000. These may contain unlimited low concern functional groups or moderate concern reactive functional groups with a combined functional group equivalent weight (FGEW, a concept developed by the US EPA describing whether

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the reactive functional group is sufficiently diluted by polymeric material) of a 1000 or more (provided no high concern groups are present) or high concern reactive functional groups with a FGEW of 5000 or more (FGEW includes moderate concern groups if present).
having molecular weights exceeding 10000 (without restriction on reactive groups).
inhalation of polymers with molecular weights > 70,000 Da has been linked with irreversible lung damage due to lung overloading and impaired clearance of particles from the lung, particularly following repeated exposure. If the polymer is inhaled at low levels and/or infrequently, it is assumed that it will be cleared from the lungs.
Reactive functional groups are in turn classified as being of low, moderate or high concern Classification of the polymer as a PLC, in accordance with established criteria, does not mean that hazards will not be associated with the polymer (during its import, manufacture, use, storage, handling or disposal). The polymer may, for example, contain a large number of particles in the respirable range, a hazard which may need to assessed in the health and safety risk assessment. Similarly a polymer with low concern reactive may be released into the environment in large quantities and produce an environmental hazard.
Whilst it is generally accepted that polymers with a molecular weight exceeding 1000 are unlikely to pass through biological membranes, oligomers with lower molecular weight and specifically, those with a molecular weight below 500, may. Estimations based on a "highly" dispersed polymer population (polydispersity = 10) suggests that the molecular weight of the polymer carrying a reactive group of high concern must be 5000 to be considered a PLC; similarly a polymer of approximate molecular weight 1000 could contain no more than one reactive group of moderate concern (for two moderate concern groups, the molecular weight would be about 2500).
Prolonged or repeated use of antibiotics, at therapeutic doses, may produce bacterial resistance for some types of bacteria. Prolonged use may result in the overgrowth of non-susceptible organisms (i.e. super- infection).
Clostridium difficile associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agent and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile.*
C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use or exposure.
The isothiazolinones are known contact sensitisers. Data are presented which demonstrate that, in comparison with the chlorinated and dichlorinated compounds which share immunological cross-reactivity, the non-chlorinated isothiazolinones have a lower potential for sensitization and no documented immunological cross-reaction with the chlorinated isothiazolinones. The risk of sensitization depends on how contact with the product occurs. The risk is greater when the skin barrier has been damaged and smaller when the skin is healthy. Dermatological studies have demonstrated that mixed isothiazolinone concentrations below 20 ppm may cause sensitisation and that allergic reactions can be provoked in sensitized persons even with concentrations in the range of 7-15 ppm active isothiazolinones.
The isothiazolinones are a group of heterocyclic sulfur-containing compounds. In general all are electrophilic molecules containing an activated N-S bond that enables them with nucleophilic cell entities, thus exerting biocidal activity. A vinyl activated chlorine atom makes allows to molecule to exert greater antimicrobial efficiency but at the same time produces a greater potential for sensitisation.
Several conclusions relating to the sensitising characteristics of the isothiazolinones may therefore be drawn* :

- The strongest sensitisers are the chlorinated isothiazolinones.
- There are known immunological cross-reactions between at least 2 different chlorinated isothiazolinones.
- There appears to be no immunological cross reaction between non-chlorinated isothiazolinones and chlorinated isothiazolinones.
- Although classified as sensitisers, the nonchlorinated isothiazolinones are considerably less potent sensitisers than are the chlorinated isothiazolinones.
- By avoiding the use of chlorinated isothiazolinones, the potential to induce sensitisation is greatly reduced.
- Despite a significant percentage of the population having been previously sensitised to chlorinated and non-chlorinated species, it is likely that careful and judicious use of non-chlorinated isothiazolinones will result in reduced risk of allergic reactions in those persons.
- Although presently available data promise that several non-chlorinated isothiazolinones will offer effective antimicrobial protection in industrial and personal care products, it is only with the passage of time that proof of their safety in use or otherwise will become available.

* B.R. Alexander: Contact Dermatitis 2002, 46, pp 191-196
Although there have been conflicting reports in the literature, it has been reported by several investigators that isothiazolinones are mutagenic in *Salmonella typhimurium* strains (Ames test). Negative results were obtained in studies of the DNA-damaging potential of mixed isothiazolinones (Kathon) in mammalian cells *in vitro* and of cytogenetic effects and DNA-binding *in vivo.* The addition of rat liver S-9 (metabolic activation) reduced toxicity but did not eliminate mutagenicity. These compounds bind to the proteins in the S-9. At higher concentrations of Kathon the increase in mutagenicity may be due to an excess of unbound active compounds.
A study of cutaneous application of Kathon CG in 30 months, three times per week at a concentration of 400 ppm (0.04%) a.i. had no local or systemic tumourigenic effect in male mice. No dermal or systemic carcinogenic potential was observed.
Reproduction and teratogenicity studies with rats, given isothiazolinone doses of 1.4-14 mg/kg/day orally from day 6 to day 15 of gestation, showed no treatment related effects in either the dams or in the foetuses
Overexposure to the breathable dust may cause coughing, wheezing, difficulty in breathing and impaired lung function. Chronic symptoms may include decreased vital lung capacity and chest infections. Repeated exposures in the workplace to high levels of fine-divided dusts may produce a condition known as pneumoconiosis, which is the lodgement of any inhaled dusts in the lung, irrespective of the effect. This is particularly true when a significant number of particles less than 0.5 microns (1/50000 inch) are present. Lung shadows are seen in the X-ray. Symptoms of pneumoconiosis may include a progressive dry cough, shortness of breath on exertion, increased chest expansion, weakness and weight loss. As the disease progresses, the cough produces stringy phlegm, vital capacity decreases further, and shortness of breath becomes more severe. Other signs or symptoms include changed breath sounds, reduced oxygen uptake during exercise, emphysema and rarely, pneumothorax (air in the lung cavity).
Removing workers from the possibility of further exposure to dust generally stops the progress of lung abnormalities. When there is high potential for worker exposure, examinations at regular period with emphasis on lung function should be performed.
Inhaling dust over an extended number of years may cause pneumoconiosis, which is the accumulation of dusts in the lungs and the subsequent tissue reaction. This may or may not be reversible.

Cipla Amoxicillin and Clavulanate Potassium for Oral Suspension	**TOXICITY**	**IRRITATION**
	Not Available	Not Available
mannitol	**TOXICITY**	**IRRITATION**
	Oral (Rat) LD50; 13500 mg/kg[2]	Not Available
amoxycillin	**TOXICITY**	**IRRITATION**
	dermal (rat) LD50: >2000 mg/kg[1]	Not Available
	Oral (Rat) LD50; >2000 mg/kg[1]	
clavulanic acid, potassium salt	**TOXICITY**	**IRRITATION**
	Oral (Mouse) LD50; 4526 mg/kg[2]	Not Available
silica crystalline - quartz	**TOXICITY**	**IRRITATION**
	Oral (Rat) LD50; 500 mg/kg[2]	Not Available

Continued...

hydroxypropyl methylcellulose	**TOXICITY**	**IRRITATION**
	Oral (Rat) LD50; >10000 mg/kg[2]	Not Available
gum xanthan	**TOXICITY**	**IRRITATION**
	Not Available	Not Available
sodium saccharin	**TOXICITY**	**IRRITATION**
	dermal (rat) LD50: >2000 mg/kg[1]	Eye: no adverse effect observed (not irritating)[1]
	Oral (Rat) LD50; >8440<9710 mg/kg[1]	Skin: no adverse effect observed (not irritating)[1]
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*	

AMOXYCILLIN	Recordings from specific areas of the central nervous system, diarrhoea recorded. ADI: 0.2 mg/kg/day NOEL: 200 mg/kg/day Asthma-like symptoms may continue for months or even years after exposure to the material ends. This may be due to a non-allergic condition known as reactive airways dysfunction syndrome (RADS) which can occur after exposure to high levels of highly irritating compound. Main criteria for diagnosing RADS include the absence of previous airways disease in a non-atopic individual, with sudden onset of persistent asthma-like symptoms within minutes to hours of a documented exposure to the irritant. Other criteria for diagnosis of RADS include a reversible airflow pattern on lung function tests, moderate to severe bronchial hyperreactivity on methacholine challenge testing, and the lack of minimal lymphocytic inflammation, without eosinophilia. 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. On the other hand, industrial bronchitis is a disorder that occurs as a result of exposure due to high concentrations of irritating substance (often particles) and is completely reversible after exposure ceases. The disorder is characterized by difficulty breathing, cough and mucus production. Allergic reactions which develop in the respiratory passages as bronchial asthma or rhinoconjunctivitis, are mostly the result of reactions of the allergen with specific antibodies of the IgE class and belong in their reaction rates to the manifestation of the immediate type. In addition to the allergen-specific potential for causing respiratory sensitisation, the amount of the allergen, the exposure period and the genetically determined disposition of the exposed person are likely to be decisive. Factors which increase the sensitivity of the mucosa may play a role in predisposing a person to allergy. They may be genetically determined or acquired, for example, during infections or exposure to irritant substances. Immunologically the low molecular weight substances become complete allergens in the organism either by binding to peptides or proteins (haptens) or after metabolism (prohaptens). Particular attention is drawn to so-called atopic diathesis which is characterised by an increased susceptibility to allergic rhinitis, allergic bronchial asthma and atopic eczema (neurodermatitis) which is associated with increased IgE synthesis. Exogenous allergic alveolitis is induced essentially by allergen specific immune-complexes of the IgG type; cell-mediated reactions (T lymphocytes) may be involved. Such allergy is of the delayed type with onset up to four hours following exposure.
CLAVULANIC ACID, POTASSIUM SALT	Somnolence, dyspnea, altered sleep time, dermatitis after systemic exposure, specific developmental abnormalities (musculoskeletal system), effects on newborn, foetotoxicity, maternal effects recorded. Animal studies failed to reveal any evidence of amoxicillin-clavulanate teratogenicity. There are no controlled data in human pregnancies. The results of a study suggest an increased risk of necrotising enterocolitis in neonates if amoxicillin-clavulanate is given prophylactically to women with premature rupture of membranes. Amoxicillin-clavulanate should only be given during pregnancy when need has been clearly established. In the Collaborative Perinatal Project involving 50,282 mother-child pairs, there were 3,546 mother-child pairs exposed to penicillin derivatives in the first trimester. As a group, there was no significant increase in the risk of malformations. In the Michigan Medicaid Birth Defects Study involving 229,101 pregnancies from 1985 to 1992, there were 8,538 first trimester exposures to amoxicillin. Overall, 317 cases of birth defects were observed (363 expected). There was no evidence of an association between first trimester use of amoxicillin and major groups of malformations. In the Michigan Medicaid Birth Defects Study, there were 556 first trimester exposures to clavulanate. Overall, 24 cases of birth defects were observed (24 expected). Two cases of spina bifida occurred compared with only 0.3 cases expected, representing a statistically significant increase in the incidence of this anomaly. In one study, six women were administered a single 1000 mg dose of amoxicillin on the third postpartum day. Amoxicillin milk concentrations ranged from 0.10 to 0.81 mcg/mL, with a peak concentration measured at 5 hours post-dose. The milk to maternal serum concentration ratio ranged from 0.013 to 0.043. Amoxicillin is excreted into human milk in small amounts and is considered compatible with breast-feeding by the American Academy of Pediatrics. Clavulanate has not been detected in human milk. Adverse effects in the nursing infant are unlikely. The manufacturer recommends caution when amoxicillin-clavulanate is administered to a nursing woman.
SILICA CRYSTALLINE - QUARTZ	**WARNING:** For inhalation exposure ONLY: This substance has been classified by the IARC as Group 1: **CARCINOGENIC TO HUMANS** The International Agency for Research on Cancer (IARC) has classified occupational exposures to **respirable** (<5 um) crystalline silica as being carcinogenic to humans . This classification is based on what IARC considered sufficient evidence from epidemiological studies of humans for the carcinogenicity of inhaled silica in the forms of quartz and cristobalite. Crystalline silica is also known to cause silicosis, a non-cancerous lung disease. Intermittent exposure produces; focal fibrosis, (pneumoconiosis), cough, dyspnoea, liver tumours. * Millions of particles per cubic foot (based on impinger samples counted by light field techniques). NOTE : the physical nature of quartz in the product determines whether it is likely to present a chronic health problem. To be a hazard the material must enter the breathing zone as respirable particles.
HYDROXYPROPYL METHYLCELLULOSE	Intraperitoneal (rat) 5200 mg/kg
GUM XANTHAN	Evaluation of workers exposed to xanthan gum dust found evidence of a link to respiratory symptoms.. On May 20, 2011, the FDA issued a press release about SimplyThick, a food-thickening additive containing xanthan gum as the active ingredient, warning parents, caregivers and health care providers not to feed SimplyThick, a thickening product, to premature infants[. The concern is that the product may cause premature infants to suffer necrotizing enterocolitis. According to a 2017 safety review by a scientific panel of the European Food Safety Authority (EFSA), xanthan gum (European food additive number E 415) is extensively digested during intestinal fermentation, and causes no adverse effects, even at high intake amounts. The EFSA panel found no concern about genotoxicity from long-term consumption. EFSA concluded that there is no safety concern for the general population when xanthan gum is consumed as a food additive. Xanthan gum (E 415) can be regarded as non-toxic based on the results of acute oral toxicity studies.From short-term and subchronic toxicity studies, no toxicological relevant changes were reported apart from a decrease in red blood cell count and haemoglobin concentration in dogs receiving 2,000 mg/kg body weight (bw) per day for 12 weeks. This effect was marginal and it was not reproduced in a dog chronic toxicity study at 1,000 mg/kg bw per day, the highest dose tested. The EFSA Panel noted that decreased total serum cholesterol was frequently reported.For genotoxicity, insufficient experimental data were available. However, taking into account the information on structure–activity relationships and considering that xanthan gum has a molecular w eight far

Continued...

	above the threshold for absorption, according to absorption, distribution, metabolism, and excretion (ADME) data, it was not degraded in the intestine and is slightly fermented to non-hazardous short-chain fatty acids by the gut microbiota, the Panel concluded that xanthan gum (E 415) does not give rise to concerns for genotoxicity.In chronic and long-term studies, no adverse effects, including biochemical and haematological parameters, were reported in dogs and rats. The Panel noted that decreased red blood cell counts reported in a subchronic toxicity study in dogs receiving 2,000 mg/kg bw per day at 6 and 12 weeks,effect which was marginal and not reproduced in a dog chronic toxicity study at 1,000 mg/kg bw per day for 107 weeks, the highest dose tested.Dietary feeding of xanthan gum at levels of 0 (control), 250 and 500 mg/kg bw per day to groups of albino rats of both sexes during a three-generation reproduction study had no adverse effect on reproduction as judged by all the endpoints evaluated. No prenatal developmental toxicity studies were available to the Panel.In special studies in neonatal piglets, no test substance-related effects in haematology or clinical chemistry parameters were observed at any dose. In the high-dose group (3,750 mg/kg bw per day) histopathological findings rated from minimal to moderate were observed in the large intestine(caecum, colon, rectum) and small intestine (duodenum). These effects were observed in fewer animals in the lower dose groups (375 and 750 mg/kg bw per day) and the severity was considered minimal. The Panel considered the no-observed-effect-level (NOEL) for xanthan gum in neonatal piglets to be 375 mg/kg bw per day, based on the changes of the faeces (green, soft, watery,increased defaecation) in the mid-dose and high dose group, and the no-observed-adverse-effect-level(NOAEL) was 750 mg/kg bw per day based on histopathological changes in the intestine in the high dose. From a human study with repeated intake ranging from 10.4 to 12.9 g of xanthan gum per day(assuming a body weight of 70 kg corresponding to 149–184 mg/kg bw per day), it was reported that xanthan gum acts as a bulk laxative causing no adverse dietary nor physiological effects. The only effects observed were moderate (10%) reduction in serum cholesterol ($p<0.05$) and a significant increase in faecal bile acid concentrations ($p<0.05$) .A study investigating the effect of repeated intake of 15 g xanthan gum/day (assuming a bodyweight of 70 kg corresponding to 214 mg/kg bw per day) on colonic function showed significant increases in stool output ($p<0.01$), frequency of defecation ($p<0.05$) and flatulence ($p<0.01$) due to the ingestion of the xanthan gum.In clinical studies involving infants, the Panel noted that consumption of xanthan gum in infant formula or formula for special medical purposes in infant was well tolerated, did not influence minerals(Ca, P, Mg), fat and nitrogen balance and did not affect growth characteristics up to concentration of 1,500 mg/L (232 mg/kg bw per day). These results were supported by the outcome of the post-marketing surveillance with formulae containing xanthan gum at a concentration of approximately 750 mg/L of reconstituted formula. No significant acute toxicological data identified in literature search.
SODIUM SACCHARIN	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. Human embryo cell mutagen Reproductive effector in rats. Equivocal tumorigen by RTECS criteria
AMOXYCILLIN & SODIUM SACCHARIN	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.

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

Cipla Amoxicillin and Clavulanate Potassium for Oral Suspension

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

mannitol

Endpoint	Test Duration (hr)	Species	Value	Source
EC10(ECx)	168h	Algae or other aquatic plants	4773.64mg/L	4

amoxycillin

Endpoint	Test Duration (hr)	Species	Value	Source
EC50	72h	Algae or other aquatic plants	56.3mg/l	2
NOEC(ECx)	96h	Algae or other aquatic plants	0.001mg/l	2
EC50	48h	Crustacea	>1000mg/l	2
EC50	96h	Algae or other aquatic plants	0.002mg/l	2
LC50	96h	Fish	>100mg/l	2

clavulanic acid, potassium salt

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

silica crystalline - quartz

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

hydroxypropyl methylcellulose

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

Continued...

gum xanthan	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	Not Available	Not Available	Not Available	Not Available	Not Available

sodium saccharin	**Endpoint**	**Test Duration (hr)**	**Species**	**Value**	**Source**
	EC50	72h	Algae or other aquatic plants	187mg/l	2
	EC50(ECx)	336h	Crustacea	4.4mg/l	2
	EC50	48h	Crustacea	>100mg/l	2
	EC50	96h	Algae or other aquatic plants	15.838mg/l	2
	LC50	96h	Fish	>400mg/l	2

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.

Persistence and degradability

Ingredient	Persistence: Water/Soil	Persistence: Air
mannitol	LOW	LOW
amoxycillin	HIGH	HIGH
sodium saccharin	HIGH	HIGH

Bioaccumulative potential

Ingredient	Bioaccumulation
mannitol	LOW (LogKOW = -3.0108)
amoxycillin	LOW (LogKOW = 0.87)
sodium saccharin	LOW (LogKOW = 0.4488)

Mobility in soil

Ingredient	Mobility
mannitol	LOW (KOC = 10)
amoxycillin	LOW (KOC = 865.5)
sodium saccharin	LOW (KOC = 32.13)

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.

SECTION 14 Transport information

Labels Required

Marine Pollutant	NO

Land transport (UN): 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
mannitol	Not Available
amoxycillin	Not Available
clavulanic acid, potassium salt	Not Available
silica crystalline - quartz	Not Available

Continued...

Product name	Group
hydroxypropyl methylcellulose	Not Available
gum xanthan	Not Available
sodium saccharin	Not Available

Transport in bulk in accordance with the ICG Code

Product name	Ship Type
mannitol	Not Available
amoxycillin	Not Available
clavulanic acid, potassium salt	Not Available
silica crystalline - quartz	Not Available
hydroxypropyl methylcellulose	Not Available
gum xanthan	Not Available
sodium saccharin	Not Available

SECTION 15 Regulatory information

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

mannitol is found on the following regulatory lists

Not Applicable

amoxycillin is found on the following regulatory lists

Not Applicable

clavulanic acid, potassium salt is found on the following regulatory lists

Not Applicable

silica crystalline - quartz is found on the following regulatory lists

Chemical Footprint Project - Chemicals of High Concern List
International Agency for Research on Cancer (IARC) - Agents Classified by the IARC Monographs
International Agency for Research on Cancer (IARC) - Agents Classified by the IARC Monographs - Group 1: Carcinogenic to humans

hydroxypropyl methylcellulose is found on the following regulatory lists

Not Applicable

gum xanthan is found on the following regulatory lists

Not Applicable

sodium saccharin is found on the following regulatory lists

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

National Inventory Status

National Inventory	Status
Australia - AIIC / Australia Non-Industrial Use	No (clavulanic acid, potassium salt)
Canada - DSL	No (clavulanic acid, potassium salt)
Canada - NDSL	No (mannitol; amoxycillin; clavulanic acid, potassium salt; silica crystalline - quartz; hydroxypropyl methylcellulose; gum xanthan; sodium saccharin)
China - IECSC	No (amoxycillin; clavulanic acid, potassium salt)
Europe - EINEC / ELINCS / NLP	No (hydroxypropyl methylcellulose)
Japan - ENCS	No (amoxycillin; clavulanic acid, potassium salt)
Korea - KECI	No (clavulanic acid, potassium salt)
New Zealand - NZIoC	Yes
Philippines - PICCS	No (clavulanic acid, potassium salt)
USA - TSCA	No (amoxycillin; clavulanic acid, potassium salt)
Taiwan - TCSI	Yes
Mexico - INSQ	No (clavulanic acid, potassium salt)
Vietnam - NCI	Yes
Russia - FBEPH	No (amoxycillin; clavulanic acid, potassium salt)
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	17/06/2022
Initial Date	17/06/2022

Continued...

Other information

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

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

Definitions and abbreviations

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

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