Aquatrade Water Treatment Chemicals (Pty) Ltd

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1 Identification

GHS Product Identifier

HYDROGEN PEROXIDE 50%

Other means of identification

CAS:	7722-84-1
EC:	231-765-0
RTECS:	MX0900000
ICSC:	0164
IUPAC:	Peroxol
NSC:	19892
UN:	2014
Chemical Family:	Peroxygen
Type of substance:	mono-constituent; inorganic
Synonyms:	Peroxide 140 Dihydrogen dioxide dihydrogen peroxide Hidrogen Peoxide Hydrogen Peroxide Solution Hydorgen Peroxide Hidrogén-peoxid 30%-os oldat Hydrogen Peroxide Solution
Proper Shipping Name:	HYDROGEN PEROXIDE, AQUEOUS SOLUTION with >20% and <60% hydrogen peroxide (stabilized as necessary)
Molecular Formula:	H_2O_2
Molecular Weight:	34.014 g/mol

Recommended use of the chemical and restriction on use

Industrial Water Treatment. Not for food, drug or household use.

Supplier's details

AQUATRADE WATER TREATMENT CHEMICALS (PTY) LTD

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Emergency phone number

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Spilltech: +27 861 000 366 (Available 24/7)

2 Hazard(s) identification

Classification of the substance or mixture

Classification according to Regulation (EC) No 1272/2008

Oxidizing Liquid (Category 1), H271
Acute Toxicity, Oral (Category 4), H302

Acute Toxicity, Inhalation (Category 4), H332
Skin Corrosion/Irritation (Category 1B), H314
Specific Target Organ Toxicity - Single exposure (Respiratory Sysytem) (Category 3), H335
Aquatic Toxicity Acute & Chronic (Category 3), H412

For the full text of the H-Statements mentioned in this Section, see Section 16.

GHS label elements

Danger

May cause fire or explosion; strong oxidizer

Harmful if swallowed

Causes severe skin burns and eye damage

Harmful if inhaled

May cause respiratory irritation

Harmful to aquatic life with long lasting effects

Do not breathe dust/fume/gas/mist/vapours/spray.

Wash thoroughly after handling.

Do not eat, drink or smoke when using this product.

Use only outdoors or in a well-ventilated area.

Wear protective gloves/protective clothing/eye protection/face protection.

Wear fire/flame resistant/retardant clothing.

IF SWALLOWED: call a POISON CENTER or doctor/physician IF you feel unwell.

IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.

IF ON SKIN (or hair): Remove/Take off Immediately all contaminated clothing. Rinse SKIN with water/shower.

IF INHALED: Remove victim to fresh air and Keep at rest in a position comfortable for breathing.

IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.

IF ON CLOTHING: Rinse Immediately contaminated CLOTHING and SKIN with plenty of water before removing clothes.

Immediately call a POISON CENTER or doctor/physician.

Specific treatment (see P330+P351+P353 on this label).

Wash contaminated clothing before reuse.

In case of fire: Use WATER to extinguish.

In case of major fi re and large quantities: Evacuate area. Fight fire remotely due to the risk of explosion.

Store in a well-ventilated place. Keep container tightly closed.

Store away from other materials.

Dispose of contents and container in accordance with local, regional, national, international regulations.

Keep away from heat/sparks/open flames/hot surfaces. — No smoking. Keep/Store away from clothing/combustible materials.

Other hazards which do not result in classification

PBT status: the substance is not PBT / vPvB

3 Composition/information on ingredients

Description	CAS Number	EINECS Number	%	Note

Hydrogen Peroxide	7722-84-1	0 - 50	Acute toxicity - Oral Cat 4; Acute toxicity - Inhalation (Vapors) Cat 4; Skin corrosion/irritation Cat 1; Serious eye damage/eye irritation Cat 1; Specific target organ toxicity (single exposure) Cat 3; Oxidizing Liquids Cat 2

4 First-aid measures

Description of necessary first-aid measures

Call 112 or 10177 or your local emergency help number immediately, for emergency assistance. Call the Poison Control Center at +27 21 931 6129 – Tygerberg or +27 21 658 5308 – Red Cross, Email: poisonsinformation@uct.ac.za, Website: https://www.afritox.co.za for further instructions. Provide them with information such as the compound taken, quantity and time of ingestion, age, weight and general health status of affected individual. Carefully remove the individual from the exposure area.

First Aid

EYES

1. First check the victim for contact lenses and remove if present.
2. Flush victim's eyes with water or normal saline solution for 20 to 30 minutes while simultaneously calling a hospital or poison control center.
3. **DO NOT** put any ointments, oils, or medication in the victim's eyes without specific instructions from a physician.
4. **IMMEDIATELY** transport the victim after flushing eyes to a hospital even if no symptoms (such as redness or irritation) develop.

SKIN

1. **IMMEDIATELY** flood affected skin with water while removing and isolating all contaminated clothing.
2. Gently wash all affected skin areas thoroughly with soap and water.
3. **IMMEDIATELY** call a hospital or poison control center even if no symptoms (such as redness or irritation) develop.
4. **IMMEDIATELY** transport the victim to a hospital for treatment after washing the affected areas.

INHALATION

1. **IMMEDIATELY** leave the contaminated area; take deep breaths of fresh air.
2. If symptoms (such as wheezing, coughing, shortness of breath, or burning in the mouth, throat, or chest) develop, call a physician and be prepared to transport the victim to a hospital.
3. Provide proper respiratory protection to rescuers entering an unknown atmosphere. Whenever possible, Self-Contained Breathing Apparatus (SCBA) should be used; if not available, use a level of protection greater than or equal to that advised under Protective Clothing.
4. Move victims to fresh air. Emergency personnel should **avoid** self-exposure to hydrogen peroxide.
5. Evaluate vital signs including pulse and respiratory rate, and note any trauma. If no pulse is detected, provide CPR. If not breathing, provide artificial respiration. If breathing is labored, administer oxygen or other respiratory support.
6. Obtain authorization and/or further instructions from the local hospital for administration of an antidote or performance of other invasive procedures.
7. Transport to a health care facility.

INGESTION

1. Evaluate vital signs including pulse and respiratory rate, and note any trauma. If no pulse is detected, provide CPR. If not breathing, provide artificial respiration. If breathing is labored, administer oxygen or other respiratory support.
2. **DO NOT** induce vomiting or attempt to neutralize! Corrosive chemicals will destroy the membranes of the mouth, throat, and esophagus and, in addition, have a high risk of being aspirated into the victim's lungs during vomiting which increases the medical problems.
3. Give the victims water or milk: children up to 1 year old, 125 mL (4 oz or 1/2 cup); children 1 to 12 years old, 200 mL (6 oz or 3/4 cup); adults, 250 mL (8 oz or 1 cup). Water or milk should be given only if victims are conscious and alert.
4. Activated charcoal is of no value.
5. **IMMEDIATELY** call a hospital or poison control center.
6. Obtain authorization and/or further instructions from the local hospital for administration of an antidote or performance of other invasive procedures.

7. **IMMEDIATELY** transport the victim to a hospital.
8. If the victim is convulsing or unconscious, do not give anything by mouth, ensure that the victim's airway is open and lay the victim on his/her side with the head lower than the body.

Excerpt from ERG Guide 140 [Oxidizers] & ERG Guide 143 [Oxidizers (Unstable)]
Ensure that medical personnel are aware of the material(s) involved and take precautions to protect themselves. Move victim to fresh air. Call 112 or 10177 or alternative emergency medical service. Give artificial respiration if victim is not breathing. Administer oxygen if breathing is difficult. Remove and isolate contaminated clothing and shoes. Contaminated clothing may be a fire risk when dry. In case of contact with substance, immediately flush skin or eyes with running water for at least 20 minutes. Keep victim calm and warm.

Most important symptoms/effects, acute and delayed

Signs and symptoms of acute exposure to hydrogen peroxide may be severe and include irritation or burns to the skin, eyes, respiratory tract, mouth, esophagus, stomach, and intestines. Distension or rupture of the stomach and other hollow viscera may occur; vomiting is common. Corneal ulceration may develop.

Indication of immediate medical attention and special treatment needed, if necessary

Hydrogen peroxide at these concentrations is a strong oxidant. Direct contact with the eye is likely to cause corneal damage especially if not washed immediately. Careful opthalmologic evaluation is recommended and the possibility of local corticosteroid therapy should be considered. Because of the likelihood of corrosive effects on the gastrointestinal tract after ingestion, and the unlikelihood of systemic effects, attemps at evacuating the stomach via emesis induction or gastric lavage should be avoided. There is a remote possibility, however, that a nasogastric or orogastric tube may be required for the reduction of severe distension due to gas formation.

Emergency Life-Support Procedures
Acute exposure to hydrogen peroxide may require decontamination and life support for the victims. Emergency personnel should wear protective clothing appropriate to the type and degree of contamination. Air-purifying or supplied-air respiratory equipment should also be worn, as necessary. Rescue vehicles should carry supplies such as plastic sheeting and disposable plastic bags to assist in preventing spread of contamination.

Immediate first aid
Ensure adequate decontamination has been carried out. If patient is not breathing, start artificial respiration, preferably with a demand-valve resuscitator, bag-valve-mask device, or pocket mask, as trained. Perform CPR if necessary. Immediately flush contaminated eyes with gently flowing water. Do not induce vomiting. If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain an open airway and prevent aspiration. Keep patient quiet and maintain normal body temperature. Obtain medical attention.

Basic treatment
Establish a patent airway (oropharyngeal or nasopharyngeal airway, if needed). Suction if necessary. Watch for signs of respiratory insufficiency and assist ventilations if necessary. Administer oxygen by nonrebreather mask at 10 to 15 L/min. Monitor for pulmonary edema and treat if necessary. Monitor for shock and treat if necessary. For eye contamination, flush eyes immediately with water. Irrigate each eye continuously with 0.9% saline (NS) during transport. Do not use emetics. For ingestion, rinse mouth and administer 5 mL/kg up to 200 mL of water for dilution if the patient can swallow, has a strong gag reflex, and does not drool. Do not attempt to neutralize because of exothermic reaction. Cover skin burns with dry, sterile dressings after decontamination.

Advanced treatment
Consider orotracheal or nasotracheal intubation for airway control in the patient who is unconscious, has severe pulmonary edema, or is in severe respiratory distress. Early intubation, at the first sign of upper airway obstruction, may be necessary. Positive-pressure ventilation techniques with a bag-valve-mask device may be beneficial. Consider drug therapy for pulmonary edema. Monitor cardiac rhythm and treat arrhythmias as necessary. Start IV administration of D5W /SRP: "To keep open", minimal flow rate/. Use 0.9% saline (NS) or lactated Ringer's (LR) if signs of hypovolemia are present. For hypotension with signs of hypovolemia, administer fluid cautiously. Watch for signs of fluid overload. Use proparacaine hydrochloride to assist eye irrigation.

5 Fire-fighting measures

Suitable extinguishing media

Excerpt from ERG Guide 140 [Oxidizers]:
SMALL FIRE:
Use water. **DO NOT** use dry chemicals or foams. CO2 or Halon® may provide limited control.
LARGE FIRE:
Flood fire area with water from a distance. **DO NOT** move cargo or vehicle if cargo has been exposed to heat. Move containers from fire area if you can do it without risk.
FIRE INVOLVING TANKS OR CAR/TRAILER LOADS:
Fight fire from maximum distance or use unmanned hose holders or monitor nozzles. Cool containers with flooding quantities of water until well after fire is out. ALWAYS stay away from tanks engulfed in fire. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.

Excerpt from ERG Guide 143 [Oxidizers (Unstable)]
SMALL FIRE:
Use water. **DO NOT** use dry chemicals or foams. CO2 or Halon® may provide limited control.
LARGE FIRE:
Flood fire area with water from a distance. **DO NOT** move cargo or vehicle if cargo has been exposed to heat. Move containers from fire area if you can do it without risk. **DO NOT** get water inside containers: a violent reaction may occur.
FIRE INVOLVING TANKS OR CAR/TRAILER LOADS:
Cool containers with flooding quantities of water until well after fire is out. Dike fire-control water for later disposal. ALWAYS stay away from tanks engulfed in fire. For massive fire, use unmanned hose holders or monitor nozzles; if this is impossible, withdraw from area and let fire burn.

Specific hazards arising from the chemical

In closed unventilated containers, risk of rupture due to the increased pressure from decomposition. Contact with combustible material may cause fire.

Hazardous Combustion Products
On decomposition product releases oxygen which may intensify fire.

Explosion data

Sensitivity to Mechanical Impact.	Not sensitive.
Sensitivity to Static Discharge.	Not sensitive.

Special protective actions for fire-fighters

Keep unnecessary people away; isolate hazard area and deny entry. Stay upwind; keep out of low areas. Wear self-contained (positive pressure if available) breathing apparatus and full protective clothing. Move container from fire area if you can do it without risk. Cool containers that are exposed to flames with water from the side until well after fire is out. For massive fire in cargo area, use unmanned hose holder or monitor nozzles; if this is impossible, withdraw from area and let fire burn. Not flammable. Fires should be fought with water since the use of chemical extinguishants may accelerate decomposition.

Small fires
water only; no dry chemical or carbon dioxide.
Large fires
flood fire area with water.

In case of fire in the surroundings, use appropriate extinguishing media. In case of fire: keep drums, etc., cool by spraying with water.

6 Accidental release measures

Personal precautions, protective equipment and emergency procedures

Caution : Explosion potential is high. Hydrogen peroxide may ignite combustable materials. Keep unnecessary people away; isolate hazard area and deny entry. Stay upwind; keep out of low areas. Keep combustibles (wood, paper, oil, etc.) away from spilled material. **DO NOT** touch spilled material; stop leak if you can do it without risk. Use water spray to reduce vapors; do not get water inside container. Use personal protective equipment. **Avoid** breathing vapors, mist or gas. Ensure adequate ventilation. Evacuate personnel to safe areas.

Precautions for safe handling

Avoid contact with skin and eyes. **Avoid** inhalation of vapor or mist.

Isolation and Evacuation
Excerpt from ERG Guide 140 [Oxidizers]:
As an immediate precautionary measure, isolate spill or leak area in all directions for at least 50 meters (150 feet) for liquids and at least 25 meters (75 feet) for solids.
LARGE SPILL:
Consider initial downwind evacuation for at least 100 meters (330 feet).
FIRE:
If tank, rail car or tank truck is involved in a fire, ISOLATE for 800 meters (1/2 mile) in all directions; also, consider initial evacuation for 800 meters (1/2 mile) in all directions.

Environmental precautions

Environmental precautions
Prevent further leakage or spillage if safe to do so. **DO NOT** let product enter drains. Discharge into the environment must be avoided.

Environmental considerations - land spill
Dig a pit, pond, lagoon, holding area to contain liquid or solid material. Dike surface flow using soil, sand bags, foamed polyurethane, or foamed concrete. Dilute slowly with water. Absorb bulk liquid with fly ash or cement powder.

Small spill
Wear face shield and goggles, laboratory coat, and butyl rubber gloves.

Methods and materials for containment and cleaning up

Excerpt from ERG Guide 140 [Oxidizers]:
Keep combustibles (wood, paper, oil, etc.) away from spilled material. **DO NOT** touch damaged containers or spilled material unless wearing appropriate protective clothing. Stop leak if you can do it without risk. **DO NOT** get water inside containers.

SMALL DRY SPILL
With clean shovel, place material into clean, dry container and cover loosely; move containers from spill area.

SMALL LIQUID SPILL
Cover spill with a 1:1:1 mixture by weight of sodium carbonate or calcium carbonate, clay cat litter (bentonite), and sand. Dampen with water. Using a soft plastic scoop, transfer the mix into a container. Transport to the fume hood. Slowly add to a pail of cold water. Gradually add to an excess of aqueous sodium metabisulfite solution. Decant the liquid to the drain. Treat the solid as normal refuse.

LARGE SPILL
Dike far ahead of liquid spill for later disposal. Following product recovery, flush area with water.

7 Handling and storage

Precautions for safe handling

Use only in well-ventilated areas. Keep/Store away from clothing/ combustible materials. Wear personal protective equipment. Never return unused hydrogen peroxide to original container. Contamination may cause decomposition and generation of oxygen gas which could result in high pressures and possible container rupture. Empty drums should be triple rinsed with water before discarding. Utensils used for handling hydrogen peroxide should only be made of glass, stainless steel, aluminum or plastic. Pipes and equipment should be passivated before first use. Hydrogen peroxide should be stored only in vented containers and transferred only in a prescribed manner.

Conditions for safe storage, including any incompatibilities

Keep container tightly closed in a dry and well-ventilated place. Containers which are opened must be carefully resealed and kept upright to prevent leakage. Recommended storage temperature 2 - 8 deg C.

Store in original closed container. Be sure that the container vent is working properly. **DO NOT** add any other compound to the container. When empty, flush container thoroughly with clean water.

Keep protected from light and in a cool place.

Hydrogen peroxide topical solution should be stored in tight, light-resistant containers at 15 - 30 °C. To ensure greater stability, the inside surfaces of containers should be as free as possible from rough points since these promote decomposition.

Incompatible products
Combustible materials. Copper alloys, galvanized iron. Strong reducing agents. Heavy metals. Iron. Copper alloys. Contact with metals, metallic ions, alkalis, reducing agents and organic matter (such as alcohols or terpenes) may produce self-accelerated thermal decomposition.

Safe Storage
Store in tightly closed original container in a dry, cool and well-ventilated place. Keep container tightly closed. Protect from light, including direct sunrays. Keep away from heat, sparks and open flame.

SANS 10263-0 Warehousing
8.4.3.2 Where flammable or **corrosive** substances are stored, the floor shall slope away from the storage area (primary collection area) to a secondary catch basin or sump of capacity at least 10 % of the total available storage volume of the fire section concerned. The secondary catch basin shall be within the fire section, and shall be such that it can be well ventilated. Care shall be taken in the design of such areas to prevent contamination of the soil or ground water.

9.7.2 Every type of storage area inside a warehouse shall be clearly demarcated, for example separate storage areas for poisons, flammables and **corrosives** shall display the relevant hazard class diamond (see table 1). The dimensions of the hazard class diamonds shall be at least 250 mm x 250 mm.

12.8.5 Storage of flammable liquids of class 3, toxic substances of division 6.1 and **corrosives** of class 8

Nitro-methane class 3, UN No. 1261, shall be separated from substances of class 6.1, and cyanides of division 6.1 shall be separated from acids of class 8. Concentrated acids and bases shall be segregated by at least 1 m. Packaged flammable liquids of class 3, toxic substances of division 6.1 and **corrosives** of class 8 that are of category 3 can be stored in the same area, provided that

a) they are kept above floor level, and
b) liquid dangerous goods of one class are not stored above dangerous goods of another class.

12.8.8.1 Flammable materials (see division 2.1, and classes 3 and 4 in SANS 10228)) will greatly increase the risk of a toxicant fire if stored in the same area as toxicants, therefore:

a) Flammable non-toxic materials shall be separated from flammable toxicants and from aerosols.
b) Flammable toxicants shall be separated from non-flammable toxicants.
c) Flammable materials shall be segregated from **oxidizing** substances and **corrosives**.

12.8.8.2 **Oxidizing** substances and organic peroxides (see class 5 in SANS 10228) can react violently with other products, and in particular with reducing substances and certain organic substances.

Oxidizing substances and organic peroxides shall be segregated from reducing substances, toxic substances and infectious substances, and from aerosol dispensers, flammables and **corrosives**.

12.8.8.3 Toxic and infectious substances (see class 6 in SANS 10228) can contaminate firefighting water in the event of a fire, therefore:

a) Toxic and infectious substances shall be separated from other flammable products and aerosols.
b) Toxic and infectious substances shall be segregated from **oxidizing** substances, organic peroxides and corrosives.
c) Flammable toxic and infectious substances shall be segregated from non-flammable toxic and infectious substances.

12.8.8.4 **Corrosives** (see class 8 in SANS 10228) that leak or spill from their packaging can cause serious damage to other packages, with potentially hazardous consequences.

Corrosives shall be segregated from toxic substances, infectious substances, aerosols, flammables, **oxidizing** substances and organic peroxides.

12.8.9.3 Aerosol dispensers shall be segregated from **oxidizing** substances, organic peroxides and **corrosives** (see also 12.8.8.2).

SANS 10263-5 The storage and handling of oxidizing substances

5.2.2 **Oxidizing** substances shall be stored to avoid contact with incompatible materials (see 3.6) such as combustible materials, combustible or flammable liquids, greases, or other incompatible or **oxidizing** substances (see note 4 below).

NOTE 1 See SANS 10228 and SANS 10229-1 for the approved packaging for **oxidizing** substances.
NOTE 2 Caution is required in the storage of any unknown materials in the vicinity of **oxidizing** substances.
NOTE 3 Some **oxidizing** substances of Division 5.1 are incompatible with other Division 5.1 substances, for example sodium nitrite and ammonium nitrate, calcium hypochlorite and isocyanurates.
NOTE 4 Hydrogen peroxide categories 1 to 3 stored in, for example drums, should not be stored on wooden pallets, as the wood will combust when the oxidizer spills.

5.2.3 Special care shall be taken to prevent any contamination of **oxidizing** substances in storage.

5.2.4 **Oxidizing** substances shall be segregated from flammable liquids by 5 m but the distance can be reduced to 3 m in certain circumstances (see 5.4.2.3). The separation shall be maintained by dikes, drains, or floor slopes to prevent flammable liquid leakage from encroaching on the separation.

5.2.5 Solid **oxidizing** substances shall not be stored directly beneath liquids.

5.2.6 Electrical installations shall be in accordance with SANS 10142-1 and SANS 10400. Special attention shall be given to the generation of heat by these installations, as this can trigger the **oxidizing** substances to react.

5.2.7 When the storage configuration is being decided on, the potential evolution of large quantities of smoke and toxic fumes shall be taken into consideration, especially as storage affects manual firefighting operations, building egress, and evacuation of adjacent occupancies or communities. EN 121012 and EN 12101-6 can be consulted in this regard.

6.3.2.1 The storage area of category 3 **oxidizing** substances shall be segregated, separated, or detached.

6.3.2.2 The walls separating **oxidizing** substances from other goods shall have a fire-resistance rating of at least 1 h.

6.3.2.3 The storage configuration, the distances of segregation and separation, and the distances of a detached warehouse from other buildings are given in tables 7 and 8.

6.3.2.4 A detached building where sprinklers are not installed and that is used for storage of category 3 **oxidizing** substances, shall be located no less than 15 m from other buildings or a line of property that can be built upon.

6.3.2.5 It is permitted that four times the quantity of category 3 **oxidizing** substances shown in tables 7 and 8 can be stored in a building, provided that all of the following conditions are met:

a) the storage area is separated or detached;
b) the storage area is located in a non-retail occupancy; and
c) non-combustible containers are used or the building is non-combustible.

6.3.2.6 Storage in basements shall be prohibited.

6.3.2.7 The maximum storage requirements for buildings where sprinklers are not installed shall be in accordance with table 7.

Table 7

Storage configuration and quantity limits	Segregated storage	Separated storage	Detached storage
Quality limit per building, t	50	180	300

Stack limit, t	10	18	30
Stack height, m	2	3	3
Stack width, m	3	4	5
Maximum distance from any container to a working aisle, m	1.5	2	3
Distance to next stack, m	See NOTE 1	See NOTE 1	See NOTE 1
Distance to wall, m	1.5	1.5	1.5
Distance to incompatible material, m	4	See NOTE 2	See NOTE 2
NOTE 1 Aisle width equal to stack height. NOTE 2 Not permitted.			

6.3.2.8 The maximum storage requirements for buildings where sprinklers are installed shall be in accordance with table 8.

Table 8

Storage configuration and quantity limits	**Segregated storage**	**Separated storage**	**Detached storage**
Quality limit per building, t	100	1000	2000
Stack limit, t	20	100	200
Stack height, m	See NOTE 1	See NOTE 1	See NOTE 1
Stack width, m	5	8	8
Maximum distance from any container to a working aisle, m	3	4	4
Distance to next stack, m	See NOTE 2	See NOTE 2	See NOTE 2
Distance to wall, m	1	1	1
Distance to incompatible material, m	4	See NOTE 3	See NOTE 3
NOTE 1 See 6.3.3 and table 9.			
NOTE 2 Aisle width equal to stack height.			
NOTE 3 Not permitted.			

The provisions of above apply to the storage of the following quantities of dangerous goods.

Oxidizing substances and organic peroxides Class 5	
Class 5.1 oxidizing substances	
> 200 kg	
Class 5.2 organic peroxides	
All quantities	
Corrosives (acids and bases) Class 8	
Category 1	> 50 kg
Category 2	> 200 kg
Category 3	> 1 000 kg

8 Exposure controls/personal protection

Control parameters

Chemical name	**ACGIH TLV**	**OSHA PEL**	**NIOSH**	**Mexico**
Hydrogen peroxide 7722-84-1	TWA: 1 ppm	TWA: 1 ppm TWA: 1.4 mg/m3	IDLH: 75 ppm TWA: 1 ppm TWA: 1.4 mg/m3	TWA 1 ppm TWA 1.5 mg/m3 STEL 2 ppm STEL 3 mg/m3
	British Columbia	**Quebec**	**Ontario TWAEV**	**Alberta**
		TWA: 1 ppm		TWA: 1 ppm

	TWA: 1 ppm	TWA: 1 ppm TWA: 1.4 mg/m3	TWA: 1 ppm	TWA: 1 ppm TWA: 1.4 mg/m3

Appropriate engineering controls

Ensure that eyewash stations and safety showers are close to the workstation location. Ensure adequate ventilation.

Individual protection measures

The selection of PPE is dependent on a detailed risk assessment. The risk assessment should consider the work situation, the physical form of the chemical, the handling methods, and environmental factors.

Eye/face protection
Face shield and safety glasses with side-shields conforming to EN166 or when handling larger quantities: basket-shaped glasses made of polycarbonate, acetate, polycarbonate/acetate, PETG or thermoplastic. Use equipment for eye protection tested and approved under appropriate government standards such as NIOSH (US) or EN166 (EU).

Hand protection
Handle with gloves made of nitrile, PVC, or neoprene . Gloves must be inspected prior to use. Use proper glove removal technique (without touching glove's outer surface) to avoid skin contact with this product. Dispose of contaminated gloves after use in accordance with applicable laws and good laboratory practices. Wash and dry hands. The selected protective gloves have to satisfy the specifications of EU Directive 89/686/EEC and the standard EN 374 derived from it.

Glove material butyl-rubber, for example, Butoject (898), Kächele-Cama Latex GmbH (KCL), Germany
Material thickness: 0,7 mm
Break through time: > 480 min
Method: DIN EN 374

Glove material: Natural rubber (NR), for example: Combi-Latex 395, Kächele-Cama Latex GmbH (KCL), Germany
Material thickness: 1 mm
Break through time: > 480 min
Method: DIN EN 374

Glove material: Nitrile, for example, Camatril (731), Kächele-Cama Latex GmbH (KCL), Germany
Material thickness: 0,33 mm
Break through time: > 480 min
Method: DIN EN 374

If used in solution, or mixed with other substances, and under conditions which differ from EN 374, contact the supplier of the CE approved gloves. This recommendation is advisory only and must be evaluated by an industrial hygienist and safety officer familiar with the specific situation of anticipated use by our customers. It should not be construed as offering an approval for any specific use scenario.

Body Protection
Wear protective clothing, acid-proof.

Suitable materials are: PVC, neoprene, nitrile rubber (NBR), rubber. Rubber or plastic boots.

The type of protective equipment must be selected according to the concentration and amount of the dangerous substance at the specific workplace.

Respiratory protection
If workplace exposure in excess of 10 ppm are expected apply respiratory protective equipment. If open handling is unavoidable: Wear respiratory protection. If necessary: Provide with fresh air. If necessary: Local ventilation. When handling for a short time: Suitable filter: Type NO-P3, code colour blue-white, in the event of prolonged exposure during handling: Self-contained breathing apparatus (EN 133). Note time limit for wearing respiratory protective equipment.

DO NOT use any form of air-purifying respirator (APR) or filtering facepiece (dust mask), especially those containing oxidizable sorbants such as activated carbon.

Hygiene measures

1. **DO NOT** inhale vapour, aerosols, mist.
2. **Avoid** contact with skin, eyes and clothing.
3. Ensure there is good room ventilation.
4. The work-place related airborne concentrations have to be kept below of the indicated exposure limits. If the limits at the workplace are exeeded and/or larger amounts are released (leakage, spilling, etc.) the indicated respiratory protection should be used.
5. **No** eating, drinking, smoking, or snuffing tobacco at work.
6. Wash face and/or hands before break and end of work.
7. Preventive skin protection
8. **Avoid** contaminating clothes with product.
9. **Immediately** change moistened and saturated work clothes.
10. **Immediately** rinse contaminated or saturated clothing with water.
11. Any contaminated protective equipment is to be cleaned after use.

Protective measures

1. Handle in accordance with good industrial hygiene and safety practice.
2. Wear suitable protective clothing, gloves and eye/face protection.
3. **Avoid** protective gloves, clothes and shoes made from the following materials: Leather
4. The personal protective equipment used must meet the requirements of directive 89/686/EEC and amendments (CE certification).
5. It should be defined in the work place in the form of a risk analysis according to directive 89/686/EEC and amendments.

9 Physical and chemical properties

Physical and chemical properties

Appearance/physical state/colour:	colourless, clear liquid without odour
Melting point/freezing point:	@ 101 325 Pa: 272.57 K
Boiling point:	@ 101 325 Pa: 423.2 K
Density:	@ 20C: 1.442
Particle size distribution (Granulometry):	D50 percentile
Vapour pressure:	299 Pa @ 298 K
Partition coefficient:	-1.57 @ 20 °C
Water solubility:	miscible in water in all proportions.
Solubility inorganic solvents/fat solubility:	study technically not feasible
Surface tension:	80.4 @ 20 °C
Flashpoint:	study technically not feasible
Auto-flammability:	study scientifically not necessary
Flammability:	study scientifically not necessary
Explosiveness:	Non explosive
Oxidising properties:	Yes
Oxidation reduction potential:	Hydrogen peroxide is a strong oxidizer with high oxidation potential.
Stability inorganic solvents and identity of relevant degradation products:	study technically not feasible
	The decomposition of hydrogen peroxide caused by catalytic impurities and the associated release of heat have been described in Chapters 2 and 3. Great care must be taken in production, storage, and transportation to prevent these impurities from entering the hydrogen peroxide solution and to ensure that hydrogen peroxide is put only into perfectly clean containers. Because commercial hydrogen peroxide

Storage stability and reactivity toward scontainer material:	always contains small quantities of catalytic impurities, the stabilization of peroxide solutions is extremely important. The stabilizing effects of inorganic and organic compounds are described in detail in [3]. Sodium pyrophosphate [7722 -88 -5] and sodium stannate [12058 -66 -1] are the preferred stabilizers and are added separately or together [112], [113]. Organic compounds are not stable enough for use with concentrated hydrogen peroxide; they are preferred for dilute solutions [114], [115]. Aluminium (99.5 %), aluminium-magnesium alloys, or stainless steels are good construction materials. Because of their corrosion resistance, polyethylene containers and storage tanks are preferred for hydrogen peroxide concentrations up to 50 wt %. Before metallic tanks and containers can be used, their surfaces must be passivated. Iron particles may become attached to the surface during the rolling of aluminium, and they must be removed. Aluminium is, therefore, treated with dilute sodium hydroxide, safety precautions must be taken to avoid detonating gas atmosphere. It is extremely important to ensure that no hydrogen peroxide is trapped, e.g. between closed valves. If decomposition occurs, extremely high pressures result which lead to very serious explosions
Stability: thermal, sunlight, metals:	Refer above
pH:	2.02 at 21 °C (50 wt %)
Dissociation constant:	2.24 and 2.4E-12 at 25 °C
Viscosity:	1.249 mPa · s (dynamic) @ 20 °C
Additional physico-chemical information:	thermodynamically instable

NOTE: The physical data presented above are typical values and should not be construed as a specification.

10 Stability and reactivity

Reactivity

Air and Water Reactions
An aqueous solution that is readily diluted.

Reactive Group
Oxidizing Agents, Strong. Water and Aqueous Solutions

Reactivity Alerts
Explosive. Strong Oxidizing Agent

CSL Reaction Information

CSL No:	CSL00009
Reactants/Reagents:	Hydrogen peroxide
GHS Category:	Explosive
Warning Message:	Formation of acetone peroxides possible. Try to avoid combination or check for peroxides
Source Reference:	ACS Safety Letters
CSL Status:	Approved
Modified Date:	6/29/2018

CSL No:	CSL00021
Reactants/Reagents:	Hydrogen peroxide
Reaction Class:	oxidation
GHS Category:	Explosive

Warning Message: explosion hazard: anhydride could have combined with peracetic acid to form diacetyl peroxide. This organic peroxide is known to be a shock-sensitive explosive
Source Reference: C&EN
CSL Status: Approved
Modified Date: 8/7/2018

CSL No: CSL00022
Reactants/Reagents: Hydrogen peroxide
GHS Category: Gas Under Pressure
Warning Message: Overpressurization Hazard if heated above 150 degrees C
Source Reference: C&EN
CSL Status: Approved
Modified Date: 8/7/2018

CSL No: CSL00041
Reactants/Reagents: Hydrogen peroxide
Function Group: peroxide
GHS Category: Explosive
Warning Message: Steel drum burst when used for storing peroxide waste
Source Reference: User-Reported
CSL Status: Approved
Modified Date: 5/31/2018

CSL No: CSL00050
Reactants/Reagents: Hydrogen peroxide
Reaction Class: oxidation
GHS Category: Explosive,Oxidizer
Warning Message: When using hydrogen peroxide make sure to completely quench all of the unreacted hydrogen peroxide before concentrating the reaction solution (or workup) to avoid an explosion.
Source Reference: User-Reported
CSL Status: Approved
Modified Date: 5/24/2018

Reactivity Profile

HYDROGEN PEROXIDE, AQUEOUS SOLUTION, STABILIZED, WITH MORE THAN 60% HYDROGEN PEROXIDE is a powerful oxidizing agent. Will react or decompose violently and exothermically with readily oxidizable materials or alkaline substances. May decompose violently in contact with iron, copper, chromium, and most other metals or their salts, which act as catalysts for this reaction, and with ordinary dust (which frequently contain rust, also a catalyst for this reaction). Stabilization operates against such reactions, but does not eliminate their possibility. Contact with combustible materials may result in their spontaneous ignition. Solutions containing over 30% hydrogen peroxide can detonate when mixed with organic solvents (such as acetone, ethanol, glycerol); the violence of the explosion increases with increasing concentration of the hydrogen peroxide. Concentration of solutions of hydrogen peroxide under vacuum led to violent explosions when the concentration was sufficiently high (>90%) [Bretherick 2nd ed., 1979]. Mixtures of aqueous hydrogen peroxide with 1-phenyl-2-methyl propyl alcohol tend to explode if acidified with 70% sulfuric acid [Chem. Eng. News 45(43):73(1967); J, Org. Chem. 28:1893(1963)]. Hydrogen selenide and hydrogen peroxide undergo a very rapid reaction [Mellor 1:941(1946-1947)].

The hazards associated with the use of HYDROGEN PEROXIDE (especially highly concentrated solutions) are well documented. There is a release of enough energy during the catalytic decomposition of 65% peroxide to evaporate all water and ignite nearby combustible materials. Most cellulose materials contain enough catalyst to cause spontaneous ignition with 90% peroxide. Contamination of concentrated peroxide causes the possibility of explosion. Readily oxidizable materials, or alkaline substances containing heavy metals may react violently. Solvents(acetone, ethanol, glycerol) will detonate on mixture with peroxide of over 30% concentration, the violence increasing with concentration. Concentrated peroxide may decompose violently in contact with iron, copper, chromium, and most other metals or their salts, and dust(which frequently contain rust). During concentration under vacuum of aqueous or of aqueous-alcoholic solutions of hydrogen peroxide, violent explosions occurred when the concentration was sufficiently high(>90%), [Bretherick 2nd ed., 1979]. Mixtures of alcohols with concentrated sulfuric acid and strong hydrogen peroxide can cause explosions. Example: An explosion will occur if dimethylbenzylcarbinol is added to 90% hydrogen peroxide then acidified with concentrated sulfuric acid. Mixtures of ethyl alcohol with concentrated hydrogen peroxide form powerful explosives. Mixtures of

hydrogen peroxide and 1-phenyl-2-methyl propyl alcohol tend to explode if acidified with 70% sulfuric acid, [Chem. Eng. News 45(43):73(1967); J, Org. Chem. 28:1893(1963)]. Hydrogen selenide and hydrogen peroxide undergo a very rapid decomposition, [Mellor 1:941(1946-1947)].

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Chemical stability

Stable under normal conditions. Decomposes on heating. Stable under recommended storage conditions.

Possibility of hazardous reactions

Contact with organic substances may cause fire or explosion. Contact with metals, metallic ions, alkalis, reducing agents and organic matter (such as alcohols or terpenes) may produce self-accelerated thermal decomposition.

Hazardous polymerization
Hazardous polymerization does not occur.

Conditions to avoid

Excessive heat; Contamination; Exposure to UV-rays; pH variations.

Incompatible materials

Combustible materials. Copper alloys, galvanized iron. Strong reducing agents. Heavy metals. Iron. Copper alloys. Contact with metals, metallic ions, alkalis, reducing agents and organic matter (such as alcohols or terpenes) may produce self-accelerated thermal decomposition.

Hazardous decomposition products

Oxygen which supports combustion. Liable to produce overpressure in container.

11 Toxicological information

Toxicological (health) effects

Human studies
The dissociation of hydrogen peroxide is a violent and exothermic reaction. Ingestion results in gastrointestinal irritation, the severity of which depends on the concentration of the solution. There is also a risk for a gas embolism. A number of deaths have been reported in the literature. In most cases the exposures were to concentrated solutions of 30% to 40%.

Other reactions include vomiting (the vomitus may be frothy due to the liberation of oxygen), hematemesis, burning of the throat, and gastric distension due to the release of oxygen. Lethargy, coma, convulsions, shock and respiratory arrest have also been reported.

Gastrointestinal bleeding and burns to the stomach and duodenum may occur. In severe cases ischemic ECG changes and EMD (electromechanical dissociation) may be observed because of embolization of the heart restricting blood flow.

Hydrogen peroxide is an irritant to the skin with paraesthesia, blistering and whitening; solutions >10% may cause burns.

Hydrogen peroxide is irritating to the eyes with a burning sensation, conjunctival hyperemia, lacrimation, and severe pain which resolves within a few hours. There are rare cases of temporary corneal injury resulting from the application of 3%

solution to the eye on contact lenses including punctuate staining of the cornea, decreased vision, corneal opacity and edema. Cerebral infarction resulting from gas embolization of the cerebral vasculature has been reported in an 84-year-old man.

Multiple brain embolisms occurred in a 63-year-old who ingested hydrogen peroxide. DNA strand breaks and chromosomal aberrations were studied in human cells treated with hydrogen peroxide. DNA strand breaks could be produced at dose levels of hydrogen peroxide much lower than those which induced chromosomal aberrations.

Animal studies
After ip injection of 0.5 mL of 5% hydrogen peroxide into adult mice, a radiation-like effect was observed; pyknotic nuclei were induced in the intestine and thymus within 2 hr and persisted for up to 24 hr. In rabbits and cats that died after iv administration of hydrogen peroxide, the lungs were found to be pale and emphysematous, with considerable amounts of gas in the great veins and in the right side of the heart.

Application of a drop of 10 to 30% to rabbit's eye caused superficial corneal haze, and, if there were defects in the epithelium, could cause localized swelling and opacities in the corneal stroma. Also, 5% solution caused superficial corneal haze and much conjunctival reaction, but these effects were gone in 24 hr.

Hydrogen peroxide was mutagenic to Salmonella typhimurium TA92 and TA102 and was positive in a forward mutation test in Salmonella typhimurium SV50. Single strand scissions were produced in T7 DNA upon incubation with hydrogen peroxide in aqueous solution at neutral pH.

Ecotoxicity studies
Hydrogen peroxide was not teratogenic in Xenopus developing embryos.

Information on the likely routes of exposure

According to the 2016 TSCA Inventory Update Reporting data, 20 reporting facilities estimate the number of persons reasonably likely to be exposed during the manufacturing, processing, or use of hydrogen peroxide in the United States may be as low as 10 workers to less than 10,000 but unknown or unreasonably ascertainable as to how many workers per plant; the data may be greatly underestimated due to confidential business information (CBI) or unknown values.

NIOSH (NOES Survey 1981-1983) has statistically estimated that 1,006,752 workers (727,702 of these are female) are potentially exposed to 90% solution hydrogen peroxide in the US. Occupational exposure to hydrogen peroxide may occur through inhalation and dermal contact with this compound at workplaces where hydrogen peroxide is produced or used(SRC). The general population is expected to be exposed to hydroperoxide through the use of consumer products containing this compound(SRC).

Symptoms related to the physical, chemical and toxicological characteristics

Potential symptoms of overexposure are irritation of eyes, nose and throat; corneal ulceration; erythema, vesicles on skin; bleaching of hair.

Pure hydrogen peroxide, its solutions, vapors, and mists are very irritating to body tissue. This irritation can vary from mild to severe depending upon the concentration of hydrogen peroxide. For instance, solutions of hydrogen peroxide of 35 wt% and over can easily cause blistering of the skin. The eyes are particularly sensitive to this material.

Large doses presumably produce gastritis and esophagitis. Cases of rupture of the colon, proctitis and ulcerative colitis have been reported following hydrogen peroxide enemas.

Workers exposed to vapors from 90% hydrogen peroxide have noted primarily respiratory irritation, but splash of such high concentration is generally feared as a potential cause of severe corneal damage.

Dropping 1 to 3% hydrogen peroxide solution on the human eye causes severe pain, but this soon subsides.

Although ingestion is unlikely to occur, if it does the hydrogen peroxide will cause irritation of the upper gastrointestinal tract. Decomposition results in rapid liberation of O2, leading to distension of the esophagus or stomach, and possibly severe damage and internal bleeding.

Human exposure by inhalation may result in extreme irritation and inflammation of nose, throat and respiratory tract; pulmonary edema, headache, dizziness, nausea, vomiting, diarrhea, irritability, insomnia, hyper-reflexia; and tremors and

numbness of extremities, convulsions, unconsciousness and shock. The latter symptoms are a result of severe systemic poisoning.

Exposure to mist or spray may cause stinging and tearing of the eyes. If hydrogen peroxide is splashed into the eye, severe damage such as ulceration of the cornea may result; sometimes, though rarely, this may appear as long as a week after exposure.

Skin contact with hydrogen peroxide liquid will result in temporary whitening of the skin; if the contamination is not removed, erythema and vesicle formation may occur.

If swallowed, the sudden evolution of oxygen may cause injury by acute distension of the stomach and also nausea, vomiting, and internal bleeding.

Delayed and immediate effects and also chronic effects from short and long term exposure

Case reports

Human

Cerebral arterial gas embolism (CAGE) is a feared complication of ambient depressurization and can also be a complication of hydrogen peroxide ingestion. We present an unusual case of CAGE in a 57-year-old woman exposed to both of these risk factors. We describe her subsequent successful treatment with hyperbaric oxygen, despite a 72-hour delay in initial presentation and diagnosis, and discuss the safety of aero-medical transfer following hydrogen peroxide ingestions.

54-year-old woman with brain gas emboli after an accidental ingestion of concentrated hydrogen peroxide was described. Hydrogen peroxide (H2O2) is a water-soluble, caustic liquid. Exposure to concentrated (> 30-35%) hydrogen peroxide may cause cardiorespiratory insufficiency, shock, convulsions, coma, and chemical burns of skin and mucous membranes. Arterial gas embolization in central nervous system is a relatively rare complication. There are three possible mechanisms of gas embolization: persisting patent foramen ovale, pulmonary gas emboli caused by aspiration of hydrogen peroxide to the lower respiratory tract, formation of gas emboli after reaching the brain. Absence of gas emboli and cerebral infarction in CT does not exclude intoxication. Hyperbaric therapy is most effective for brain air embolism complicating hydrogen peroxide poisoning in acute phase. Some authors suggested that this therapy is also effective if administered during the subacute phase. Neurologic symptoms after ingestion of hydrogen peroxide may suggest gas embolism of the cerebral vasculature. The absence of atrial septal defect does not exclude the possibility of cerebral air embolism. The absence of gas and cerebral infarction in CT scans does not exclude brain gas embolism. The use of hyperbaric therapy should be considered in treating severe cases of hydrogen peroxide poisoning.

We report several cases of hydrogen peroxide-related colitis that occurred in an epidemic pattern in our gastrointestinal endoscopy center during a 2-month period in early 2007. During colonoscopy using sterilized endoscopes that had been flushed with hydrogen peroxide after the peracetic acid cycle, instantaneous effervescence and blanching (the "snow white sign") were observed on the intestinal mucosa when the water button was depressed. Biopsy specimens revealed features resembling a clinical condition which used to be known as "pseudolipomatosis." At follow-up, no patient was found to have suffered morbidity associated with this peroxidecolitis. Endoscopists should consider hydrogen peroxide colitis when they see a snow white sign during colonoscopy which cannot be attributed to active inflammation or organic disease of the digestive tract.

It is well known that hydrogen peroxide ingestion can cause gas embolism. This study reports a case illustrating that the definitive, most effective treatment for gas embolism is hyperbaric oxygen therapy. We present a case of a woman who presented to the Emergency Department with acute abdominal pain after an accidental ingestion of concentrated hydrogen peroxide. Complete recovery from her symptoms occurred quickly with hyperbaric oxygen therapy. This is a case report of the successful use of hyperbaric oxygen therapy to treat portal venous gas embolism caused by hydrogen peroxide ingestion. Hyperbaric oxygen therapy can be considered for the treatment of symptomatic hydrogen peroxide ingestion.

Complications of hydrogen peroxide have been described in the literature and typically involve the effects of O(2) emboli. We report a 15-year-old male patient undergoing right frontal craniotomy and excision of craniopharyngioma. A sudden bradycardia occurred after instillation of hydrogen peroxide solution at the surgical site. Stimulation of the anterior hypothalamus after removal of the tumor and hydrogen peroxide irrigation may have triggered intense parasympathetic activity leading to bradycardia.

Ingestion of acid-containing household products, either accidentally or as a suicide attempt, is a common form of intoxication. A clear and odorless liquid, hydrogen peroxide is an oxidizing agent found in most households and many

industrial environments. Cardiovascular manifestations of hydrogen peroxide ingestion are extremely rare. Here we report a 60 year-old woman with acute inferolateral myocardial infarction (MI) after hydrogen peroxide ingestion, who had no history of coronary artery disease. Physicians dealing with hydrogen peroxide ingestion in the emergency department should be aware of the probability of MI and obtain an electrocardiogram, even if the patient has no cardiac complaint.

We report a case of acute transitional ischemia of the hand with acute compartment syndrome of the forearm, following hydrogen peroxide irrigation of a wound. We discuss the physiopathology and management of this complication. Along with numerous related cases of gas embolism, this complication emphasizes the risks of using hydrogen peroxide under pressure, notably in hand surgery.

Hydrogen peroxide is commonly used for the decontamination of wounds. We report a case of a probable venous oxygen embolism resulting in cardiovascular collapse following irrigation of a necrotic breast wound with hydrogen peroxide. We discuss the differential diagnosis, mechanism of oxygen embolism and question the relative advantages versus disadvantages of using hydrogen peroxide for wound decontamination.

A 33 yr old woman unintentionally ingested a 1 pint bottle of 35% hydrogen peroxide. She vomited, collapsed, and experienced a brief tonic-clonic seizure within minutes. On examination, the patient was intermittently seizing and markedly cyanotic and had copious white foam emanating from her mouth. Vital signs were blood pressure 156/118 mm Hg; pulse, 126; respirations, 32; and temp, 38.2 deg C. Pupils were 6 mm and weakly reactive to light. The heart was rapid and regular, and no SC emphysema was noted. Deep tendon reflexes were 2/4, and plantar responses were flexor. The patient was given 5 mg diazepam, 4 mg naloxone hydrochloride, 100 mg thiamine, and 50 mL of 50% dextrose iv. Within 30 sec after nasotracheal intubation, the patient became apneic and dependent on mechanical ventilation. Gastric lavage was performed. Preoperative esophagogastroduodenoscopy showed mild erythema of the distal esophagus and diffuse hemorrhages and edema of the gastric mucosa. Recurrent postoperative seizures were well controlled with phenytoin therapy. Bilateral cerebral hemisphere swelling was determined; intracranial pressure of 30 cm H2O responded to hyperventilation. Later neurologic examination demonstrated patchy areas of weakness in the upper and lower extremities and truncal ataxia with inability to maintain a sitting position. After 9 days, the patient was transferred to a rehabilitation facility.

Non-Human

There is so far no generally accepted animal model of chronic cystitis by which potential therapies can be evaluated. In this study, we aimed to establish a new mouse model of cystitis based on the proinflammatory effects of reactive oxygen species. A single intravesical injection of 1.5% hydrogen peroxide (H2O2) significantly increased the numbers of voids by 1 day after injection in female mice, which lasted up to 7 days. The H2O2 injection rapidly increased the bladder weight by 3 hr in parallel with the histological damage and hyperpermeability of urothelial barrier. Although the urothelial dysfunction was recovered to normal by 7 days, increase in bladder weight, edematous thickening of the submucosa, and vascular hyperpermeability were apparent even 7 days after injection. During the time course, massive infiltration of neutrophils and increased expression of inflammatory cytokines were observed in the bladder. An intraperitoneal administration of oxybutynin, amitriptyline, indomethacin, or morphine attenuated the H2O2-induced frequent urination. These findings suggest that an intravesical injection of H2O2 induces relatively long-lasting inflammatory and overactive bladder, compared with existing cystitis models. The intravesical H2O2 injection model may be a simple and useful tool in the pathological study and drug discovery for chronic cystitis.

Some clinicians use hydrogen peroxide (H2O2) to clear the lumen of ventilation tubes that become blocked postoperatively. The ototoxicity associated with H2O2 has been controversial. We designed an experiment to test if H2O2 damages the cochlear hair cells using a Chinchilla laniger animal model. Nine chinchillas (18 ears) were included in this study. Each animal was used as its own control. Following the insertion of ventilation tubes in both ears and baseline recordings of the auditory brain stem responses (ABR), we instilled 2 mL of 3 percent H2O2 into their right external auditory canals (experimental ears). H2O2 was left in the external auditory canal for a total of 5 minutes and then was drained. We instilled a normal saline control solution in their left ears (control ears) in a similar fashion. ABR recordings were performed 1 day after the last instillation of H2O2 and 5 days later. There was no statistically significant difference in the ABR thresholds of the experimental and control ears. H2O2 did not appear to cause ototoxicity in chinchilla ears with tympanostomy tubes exposed to H2O2 instillation using a standard clinical protocol.

We previously established a long-lasting cystitis model by an intravesical injection of hydrogen peroxide (H2O2) into mice. In this study, we assessed the pain-related behaviors in the cystitis model. An intravesical injection of 1.5% H2O2 transiently decreased spontaneous locomotor activity at 3 hr after injection, indicative of acute spontaneous pain. In contrast, licking response to a bladder distention was slowly observed as licks to the lower abdomen at 7 and 14 days after injection, which was attenuated by amitriptyline and morphine, but not by oxybutynin. These results suggest that H2O2-

induced chronic cystitis model shows delayed and long-lasting painful pathological condition.

After ip injection of 0.5 mL of 5% hydrogen peroxide into adult mice, a radiation like effect was observed; pyknotic nuclei were induced in the intestine and thymus within 2 hr and persisted for up to 24 hr.

Experiments on rabbit eyes showed corneal injury from dropped application to depend not only on the concentration of hydrogen peroxide, but also on the integrity of the corneal epithelium, which had a protective influence. Application of a drop of 10 to 30% caused superficial corneal haze, and, if there were defects in the epithelium, could cause localized swelling and opacities in the corneal stroma. Also, 5% solution caused superficial corneal haze and much conjunctival reaction, but these effects were gone in 24 hr. The effect of 10% solution usually took longer to disappear, and occasionally could result in lasting localized opacities.

Dogs /were exposed by inhalation/ 6 hours/day, 5 days/week for 6 months at an average vapor concentration of 7 ppm of 90% hydrogen peroxide. The dogs developed skin irritation, sneezing, lacrimation, and bleaching of the hair. Autopsy disclosed pulmonary irritation and greatly thickened skin, but not hair follicle destruction. No significant changed in blood or urinary parameters were observed.

Rabbits exposed daily /to 90% hydrogen peroxide by inhalation/ for 3 months at 22 ppm showed no eye injury, although the hair was bleached and irritation was noted around nose.

Genotoxicity

Human

We studied DNA-damaging effects of dental bleaching systems containing hydrogen peroxide and/or carbamide peroxide by the "comet assay" (alkaline version). Dental bleaching systems in a hydrogen peroxide concentration range from 0.03 to 30 mM produced a genotoxic effect on isolated HeLa cells in vitro comparable with the effects of pharmacopoeial hydrogen peroxide or urea peroxide. Catalase protected the cells against products containing hydrogen peroxide and had no effect on the genotoxicity of samples containing carbamide peroxide.

DNA damage induced by oxidants includes formation of DNA strand breaks as well as oxidative damage to DNA bases. Both forms of DNA damage were measured concurrently in two model human breast epithelial cell lines treated with hydrogen peroxide to compare the dose-dependent induction of each form of DNA damage with growth inhibition. MCF-7 breast cancer cells had relatively higher levels of non-protein thiols, oxidized glutathione (GSSG) reductase, catalase, and superoxide dismutase than did the MCF-10A line of immortalized, but not transformed human breast epithelial cells. The levels of antioxidant defenses were not predictive of endogenous oxidative DNA damage levels nor of toxicity and DNA damage induced by hydrogen peroxide. The endogenous levels of 5-hydroxymethyl-2'-deoxyuridine were higher in MCF-7 than MCF-10A cells. The cells were treated with 10-200 uM hydrogen peroxide for 15 min at 37 C in complete media. Low concentration of hydrogen peroxide were growth stimulatory to both cell lines. At higher concentration, growth inhibition by hydrogen peroxide was greater in MC-7 than in MCF-10A cells. Accordingly, induction of both single-strand DNA breaks and 5-hydroxymethyl-2'-deoxyuridine in DNA was greater in MCF-7 than MCF-10A cells. In both cell lines, the dose-dependent induction of single-strand breaks paralleled growth inhibition more closely than did formation of 5-hydroxymethyl-2'-deoxyuridine.

DNA strand breaks and chromosomal aberrations were studied in human cells treated with hydrogen peroxide or with ionizing radiation. DNA strand breaks could be produced at dose levels of hydrogen peroxide much lower than those which induced chromosomal aberrations. Doses as low as 0.5 mM of hydrogen peroxide produced about as many DNA strand breaks as 2 Gy of (60)Co gamma-radiation. On the other hand, as much as 20 mM hydrogen peroxide produced only half as many chromosomal aberrations as 1 Gy of (60)Co gamma-radiation.

Human A549 lung epithelial cells were challenged with (18)O-labeled hydrogen peroxide ([(18)O]-H2O2), the total RNA and DNA extracted in parallel, and analyzed for (18)O-labeled 8-oxo-7,8-dihydroguanosine ([(18)O]-8-oxoGuo) and 8-oxo-7,8-dihydro-2'-deoxyguanosine ([(18)O]-8-oxodGuo) respectively, using high-performance liquid chromatography electrospray ionization tandem mass spectrometry (HPLC-MS/MS). [(18)O]-H2O2 exposure resulted in dose-response formation of both [(18)O]-8-oxoGuo and [(18)O]-8-oxodGuo and (18)O-labeling of guanine in RNA was 14-25 times more common than in DNA. Kinetics of formation and subsequent removal of oxidized nucleic acids adducts were also monitored up to 24 hr. The A549 showed slow turnover rates of adducts in RNA and DNA giving half-lives of approximately 12.5 hr for [(18)O]-8-oxoGuo in RNA and 20.7 hr for [(18)O]-8-oxodGuo in DNA, respectively.

Non-Human

An iron chelate, ferric nitrilotriacetate (Fe-NTA), is a potent nephrotoxic agent, and induces acute and subacute renal

proximal tubular necrosis, a consequence of the Fenton-like reaction that eventually leads to a high incidence of renal adenocarcinoma in rodents. In order to examine the possible mechanism for carcinogenic activity, we investigated the DNA damage with Fe-NTA in the presence of various peroxides/organic hydroperoxides. S1 nuclease hydrolysis and deoxyribose degradation assays were performed. Incubation of calf thymus DNA with ferric nitrilotriacetate (0.1 mM) in the presence of peroxides/organic hydroperoxides at a final concentration of 40 mM of each in phosphate buffer (0.1 M, pH 7.4) augmented DNA damage severalfold as compared to the damage caused by individual treatments. Fe-NTA in the presence of hydrogen peroxide caused DNA single-strand breaks and damage to its deoxyribose sugar moiety as measured, respectively, by S1 nuclease hydrolysis and deoxyribose degradation using calf thymus DNA. However, only deoxyribose degradation could be recorded in the presence of other peroxide/organic hydroperoxides. No DNA single-strand break was observed by this treatment. The observed differences in DNA damage by hydrogen peroxide and organic hydroperoxides/peroxide have been ascribed to the differential reactivity of DNA with hydroxyl and alkoxy/aryloxy free radicals produced, respectively, from these inorganic and organic peroxides. These studies suggest that Fe-NTA not only mediated the production of reactive oxygen species, but also catalyzed the decomposition of these peroxides and organic hydroperoxides, which may cause a clastogenic change in DNA. This reactivity enhances the clastogenic activity in DNA. These changes in the DNA structure may ultimately be responsible, at least in part, for the induction of carcinogenesis in Fe-NTA-exposed animals.

Prophages are induced by treatment of lysogenized bacteria with hydrogen peroxide. In Escherichia coli, hydrogen peroxide induced single strand breaks in DNA and was positive in DNA repair assays.

Hydrogen peroxide was mutagenic to Salmonella typhimurium TA92 and TA102 and was positive in a forward mutation test in Salmonella typhimurium SV50.

Single strand scissions were produced in T7 DNA upon incubation with /hydrogen peroxide/ in aqueous solution at neutral pH. Inhibition of scissions by hydroxyl radical scavengers indicates intermediacy of hydroxyl radicals.

Alternative and In Vitro tests

Human

Hydrogen peroxide (H_2O_2) may have a biphasic effect on melanin synthesis and melanosome transfer. High H_2O_2 concentrations are involved in impaired melanosome transfer in vitiligo. However, low H_2O_2 concentration promotes the beneficial proliferation and migration of melanocytes. The aim of this study was to explore low H_2O_2 and its mechanism in melanosome transfer, protease-activated receptor-2 (PAR-2) expression and calcium balance. Melanosomes were fluorescein-labeled for clear visualization of their transfer. The expression of protease-activated receptor-2 (PAR-2) in keratinocytes was determined by western blot analysis. Flow cytometry was employed to evaluate the effects of H_2O_2 on calcium levels in keratinocytes. Fluorescence microscopy showed the upregulation of melanosome transfer into keratinocytes following 0.3 mM H_2O_2 treatment in the co-cultures rather than in the untreated control groups, which was associated with higher expression of PAR-2 protein and increased calcium concentration. The addition of a PAR-2 antagonist inhibited the positive activity of H_2O_2 and calcium flow in keratinocytes. When calcium flow was blocked by a calcium chelator, the addition of H_2O_2 did not increase the PAR-2 expression level in keratinocytes, therefore, inhibiting dendrite formation and melanosome transfer. Low H_2O_2 concentration promotes melanosome transfer with increased PAR-2 expression level and calcium concentration in keratinocytes. In addition, the interaction between melanocytes and keratinocytes is more beneficial to enhance calcium levels in keratinocytes which mediate melanin transfer. Moreover, low H_2O_2 concentration promotes dendrite formation, in which extracellular calcium and Par-2 were involved.

Intestinal epithelial cells can secrete interleukin-8 (IL-8), among other substances in response to different stimuli, which plays an important role in mucosal immune response. Above a certain concentration range, hydrogen peroxide causes cell death by necrosis or apoptosis. We investigated the time- and dose-dependent induction of IL-8 by hydrogen peroxide in the human colon adenocarcinoma cell line Caco-2. In addition, the changes of transepithelial electrical resistance and cell death induction in response to hydrogen peroxide were studied. Nonfilter-grown and filter-grown Caco-2 cells were employed in our experiments. Interleukin-8 synthesis was measured by ELISA. Necrosis was determined by DAPI staining of cells, apoptosis by measuring caspase-3 enzyme activity or annexin V staining. In nonfilter-grown Caco-2 cells, 1 mM of hydrogen peroxide induced the highest level of IL-8 production 24 hr after treatment. In filter-grown Caco-2 cells, IL-8 was produced only on the apical side in response to 1 mM of hydrogen peroxide. This level was 10-fold lower than that measured in nonfilter-grown Caco-2 cells 24 hr after the treatment. In filter-grown Caco-2 cells 10 mM hydrogen peroxide induced the highest IL-8 level on the apical as well as basolateral side. Transepithelial electrical resistance decreased markedly upon application of 40 mM hydrogen peroxide. Late effect of hydrogen peroxide was observed in nonfilter-grown Caco-2 cells, as 1 mM hydrogen peroxide caused necrosis after 24 hr while early-necrosis induction occurred in filter-grown cells exposed to 40 mM of hydrogen peroxide after 1 hr. Filter-grown Caco-2 cells were less sensitive to hydrogen peroxide than the nonfilter-grown ones.

The effect of low concentrations of hydrogen peroxide (10-100 uM) on sperm motility and on the activity of the sperm enzyme glyceraldehyde-3-phosphate dehydrogenase (GAPDS) was investigated. Incubation of semen samples with 10 and 100 uM hydrogen peroxide increased the content of spermatozoa with progressive motility by 20 and 18%, respectively, and enhanced the activity of GAPDS in the sperm cells by 27 and 20% compared to a semen sample incubated without additions. It was also found that incubation with 10 uM hydrogen peroxide increased the content of reduced glutathione (GSH) in sperm cells by 50% on average compared to that in the control samples. It is supposed that low concentrations of hydrogen peroxide activate the pentose phosphate pathway, resulting in NADPH synthesis and the reduction of the oxidized glutathione by glutathione reductase yielding GSH. The formed GSH reduces the oxidized cysteine residues of the GAPDS active site, increasing the activity of the enzyme, which in turn enhances the content of sperm cells with progressive motility. Thus, the increase in motile spermatozoa in the presence of low concentrations of hydrogen peroxide can serve as an indicator of normal functioning of the antioxidant defense system in sperm cells.

Chinese hamster V79 cells were conditioned by repeated treatment with low doses of hydrogen peroxide. After this treatment, the conditioned cells were compared to parental V79 cells with regard to different endpoints. It was found that, compared to parental cells, the conditioned cells tolerated low serum concentrations better, they suffered from higher levels of aneuploidy, and they showed enhanced antioxidant defense. When exposed to gamma-rays, they suffered from lipid peroxidation to a lesser extent, were more resistant to cell killing, exhibited higher mutation frequency at the HGPRT locus, and showed lower frequency of apoptosis. These cells also induced antioxidant enzymes in response to gamma-ray exposure that differently was from than the parental cells. Overall, the data suggest a stable adaptive response in the conditioned cells.

It has been reported that overproduction of reactive oxygen species occurs after brain injury and mediates neuronal cells degeneration. In the present study, we examined the role of Ras signaling on hydrogen peroxide-induced neuronal cells degeneration in dopaminergic neuroblastoma SH-SY5Y cells. Hydrogen peroxide significantly reduced cell viability in SH-SY5Y cultured cells. An inhibitor of the enzyme that catalyzes the farnesylation of Ras proteins, FTI-277, and a competitive inhibitor of GTP-binding proteins, GDP-beta-S significantly decreased hydrogen peroxide-induced reduction in cell viability in SH-SY5Y cultured cells. The results of this study might indicate that a Ras-dependent signaling pathway plays a role in hydrogen peroxide-induced toxicity in neuronal cells.

Hydrogen peroxide (H2O2), a substance involved in cellular oxidative stress, has been observed to induce an adaptive response, which is characterized by a protection against the toxic effect of H2O2 at higher concentrations. However, the molecular mechanism for the adaptive response remains unclear. In particular, the existing reports on H2O2 -induced adaptive response are limited to animal cells and human tumor cells, and relatively normal human cells have never been observed for an adaptive response to H2O2. In this study, a human embryo lung fibroblast (MRC-5) cell line was used to model an adaptive response to H2O2, and the relevant differential gene expressions by using fluoro mRNA differential display RT-PCR. The results showed significant suppression of cytotoxicity of H2O2 (1100 uM, 1 hr) after pretreatment of the cells with H2O2 at lower concentrations (0.088-8.8 uM, 24 hr), as indicated by cell survival, lactate dehydrogenase release, and the rate of apoptotic cells. Totally 60 mRNA components were differentially expressed compared to untreated cells, and five of them (sizing 400-600 bp) which demonstrated the greatest increase in expression were cloned and sequenced. They showed identity with known genes, such as BCL-2, eIF3S5, NDUFS4, and RPS10. Real time RT-PCR analysis of the five genes displayed a pattern of differential expression consistent with that by the last method. These five genes may be involved in the induction of adaptive response by H2O2 in human cells, at least in this particular cell type.

Hydrogen peroxide (H2O2) produced by members of the mitis group of oral streptococci plays important roles in microbial communities such as oral biofilms. Although the cytotoxicity of H2O2 has been widely recognized, the effects of H2O2 produced by oral streptococci on host defense systems remain unknown. In the present study, we investigated the effect of H2O2 produced by Streptococcus oralis on human macrophage cell death. Infection by S. oralis was found to stimulate cell death of a THP-1 human macrophage cell line at multiplicities of infection greater than 100. Catalase, an enzyme that catalyzes the decomposition of H2O2, inhibited the cytotoxic effect of S. oralis. S. oralis deletion mutants lacking the spxB gene, which encodes pyruvate oxidase, and are therefore deficient in H2O2 production, showed reduced cytotoxicity toward THP-1 macrophages. Furthermore, H2O2 alone was capable of inducing cell death. The cytotoxic effect seemed to be independent of inflammatory responses, because H2O2 was not a potent stimulator of tumor necrosis factor-alpha production in macrophages. These results indicate that streptococcal H2O2 plays a role as a cytotoxin, and is implicated in the cell death of infected human macrophages.

Non-Human

To clarify discrepancies in the literature on the adverse effects of hydrogen peroxide on neurons, this study investigated the application of this peroxide to cultured cerebellar granule neurons /from rats/ with six assays frequently used to test

for viability. Cultured neurons efficiently cleared exogenous H2O2. Although viability was not affected by exposure to 10 uM hydrogen peroxide, an exposure to the peroxide in higher concentrations rapidly lowered, within 15 min, the cellular 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) reduction capacity to 53% +/- 1% (100 uM) and 31% +/- 1% (1,000 uM) and the 3-amino-7-dimethylamino-2-methyl-phenazine hydrochloride (neutral red; NR) uptake to 84% +/- 6% (100 uM) and 33% +/- 1% (1,000 uM) of control cells. The release of glycolytically generated lactate was stopped within 30 min in neurons treated with 1,000 uM peroxide. In contrast, even hours after peroxide application, the cell morphology, the number of propidium iodide-positive cells, and the extracellular activity of the cytosolic enzyme lactate dehydrogenase (LDH) were not significantly altered. The rapid loss in MTT reduction and NR uptake after exposure of neurons to H2O2 for 5 or 15 min correlated well with a strongly compromised MTT reduction and a very high extracellular LDH activity observed after further incubation in peroxide-free medium for a total incubation period of 24 hr. These data demonstrate that cultured neurons do not recover from damage that is inflicted by a short exposure to H2O2 and that the rapid losses in the capacities of neurons for MTT reduction and NR uptake are good predictors of delayed cell damage.

The study objective was to study the effect of hydrogen peroxide (H2O2) on persistent sodium current (I(Na.P)) in guinea pig ventricular myocytes. The whole-cell, cell-attached, and inside-out patch-clamp techniques were applied on isolated ventricular myocytes from guinea pig. H2O2 (0.1 mmol/L, 0.5 mmol/L and 1.0 mmol/L) increased the amplitude of whole-cell I(Na.P) in a concentration-dependent manner, and glutathione (GSH 1 mmol/L) reversed the increased I(Na.P). H2O2 (1 mmol/L) increased persistent sodium channel activity in cell-attached and inside-out patches. The mean open probability was increased from control values of 0.015+/-0.004 and 0.012+/-0.003 to 0.106+/-0.011 and 0.136+/-0.010, respectively (P< 0.01 vs control). They were then decreased to 0.039+/-0.024 and 0.027+/-0.006, respectively, after the addition of 1 mmol/L GSH (P<0.01 vs H2O2). The time when open probability began to increase and reached a maximum was shorter in inside-out patches than that in cell-attached patches (4.8+/-1.0 min vs 11.5+/-3.9 min, P<0.01; 9.6+/-1.6 min vs 18.7+/-4.7 min, P<0.01). H2O2 increased the I(Na.P) of guinea pig ventricular myocytes in a concentration-dependent manner, possibly by directly oxidating the cell membrane.

Reactive oxygen species modify DNA, generating various DNA lesions including modified bases such as 8-oxoguanine (8-oxoG). These base-modified DNA lesions have been shown to trap DNA topoisomerase I (TOP1) into covalent cleavage complexes. In this study, we have investigated the role of TOP1 in hydrogen peroxide toxicity. We showed that ectopic expression of TOP1 in Saccharomyces cerevisiae conferred sensitivity to hydrogen peroxide, and this sensitivity was dependent on RAD9 checkpoint function. Moreover, in the mammalian cell culture system, hydrogen peroxide-induced growth inhibition and apoptosis were shown to be partly TOP1-dependent as evidenced by a specific increase in resistance to hydrogen peroxide in TOP1-deficient P388/CPT45 murine leukemia cells as compared with their TOP1-proficient parental cell line P388. In addition, hydrogen peroxide was shown to induce TOP1-DNA cross-links. These results support a model in which hydrogen peroxide promotes the trapping of TOP1 on oxidative DNA lesions to form TOP1-DNA cleavage complexes that contribute to hydrogen peroxide toxicity.

This study was designed to investigate the effect of hydrogen peroxide on the expression of endoplasmic reticulum stress marker glucose-regulated protein 78 (GRP78) in endothelial cells and reveals the possible role of cyclooxygenase in this effect. The porcine endothelial cell line was cultured in 1640 medium. Western blot and immunocytochemistry were used to detect the expression of GRP78. The caspase-12 activity was analyzed with the immune fluorescence method. The results showed that after the endothelial cells were incubated with 250 uM of hydrogen peroxide for 12 hr, apoptosis increased, which was antagonized by the cyclooxygenase-2 inhibitor nimesulide or the nonselective cyclooxygenase inhibitor aspirin, but not by the cyclooxygenase-1 inhibitor piroxicam. The expression of GRP78 was induced in endothelial cells after exposure to hydrogen peroxide for 12 hr. The overexpression of GRP78 was inhibited by nimesulide and aspirin, but not by piroxicam. There are no significant differences in caspase-12 activity among all groups. The present study provides evidence that hydrogen peroxide induced GRP78 overexpression in endothelial cells by a mechanism involving cyclooxygenase-2-dependent pathway.

This in vitro experiment studied the effects of sodium bicarbonate and hydrogen peroxide on the cariogenic bacteria Streptococcus mutans through analysis with a spectrophotometer. The growth of S. mutans was analyzed using seven different environments. Twelve wells in each of the seven rows of a multi-well plate were used to incubate the test materials. In combinations of 10 uL distilled water, 100 uL broth, 10 uL 10% sucrose, 10 uL S. mutans, 10 uL 10% sodium bicarbonate, and 10 uL 3% hydrogen peroxide, seven different environments were created for testing. Environments had either sodium bicarbonate or hydrogen peroxide with S. mutans, or a combination of sodium bicarbonate and hydrogen peroxide with S. mutans. The plate was incubated at 37 degrees C and measured at 0, 18, 20, 22, 24, 26, 28, 30, and 42 hours by optical density with a spectrophotometer. Results showed bacterial growth was prevented by sodium bicarbonate, hydrogen peroxide, and the combination of sodium bicarbonate and hydrogen peroxide. Although hydrogen peroxide is bacteriocidal and sodium bicarbonate is bacteriostatic, there were no significant differences among the three treatment groups in spectrophotometer readings at any of the nine readings over 42 hours. There was no significant

difference among the effects of hydrogen peroxide, sodium bicarbonate, or the sodium bicarbonate and hydrogen peroxide combination, as measured by optical density. The hydrogen peroxide, sodium bicarbonate, and the sodium bicarbonate and hydrogen peroxide combination prevented bacterial growth of S. mutans. The results show that products containing these agents have the ability to stop the growth of S. mutans. Products containing sodium bicarbonate and/or hydrogen peroxide may be useful to caries-prone patients. More studies are needed to confirm these results on patients.

Cell cycle arrest is associated with differentiation, senescence and apoptosis. We investigated alterations in the cell cycle during the development of hypertrophy induced by hydrogen peroxide (H(2)O(2)) in the H9c2 clonal myoblastic cell line. H(2)O(2) induced hypertrophy in H9c2 cells that was indicated by an increase in atrial natriuretic peptide (ANP) gene expression, a marker of cardiomyocyte hypertrophy, and a larger cell size. On induction of hypertrophy by H(2)O(2) in H9c2 cells, cell proliferation was arrested, indicated by the number of cells remaining constant during a 72-hr incubation period. The cell cycle was arrested at the G1 and G2/M phases with an increase in p21 expression, a negative cell cycle regulator. Cell cycle arrest and increase in p21 expression were significantly inhibited by 1,2-bis(o-aminophenoxy)ethane-N,N,N',N'-tetraacetic acid tetra (acetoxymethyl) ester (BAPTA-AM), an intracellular calcium chelator. Although ANP gene expression was induced significantly, H(2)O(2) failed to induce hypertrophy in the presence of BAPTA-AM, and the cell cycle progressed. We concluded that H(2)O(2) induced cell cycle arrest in H9c2 cells, which was related to cellular hypertrophy.

The effect of hydrogen peroxide on perfusion flow, airway conductance and dynamic compliance of isolated perfused and ventilated guinea pig lungs was investigated. Hydrogen peroxide (50 uM in the perfusion buffer) induced a decrease in airway conductance and dynamic compliance and perfusion flow during 5 min. of exposure. Hydrogen peroxide also caused an increase in the levels of thromboxane in the perfusate of the lung. The constrictor effects as well as the formation of thromboxane were inhibited by the cyclooxygenase inhibitor ibuprofen (50 uM). The thromboxane/prostaglandin endoperoxide receptor antagonist L-670,596 (1 uM) abolished the effects of hydrogen peroxide on perfusion flow, airway conductance and dynamic compliance, but did not affect the formation of thromboxane. The thromboxane synthetase inhibitor carboxyheptylimidazole (100 uM) reduced both the hydrogen peroxide induced formation of thromboxane and vaso and bronchoconstriction, suggesting a predominant role for thromboxane A2 versus prostaglandin H2 in these effects. A role for platelet activating factor in mediating the effect of hydrogen peroxide could not be supported, as the platelet activating factor receptor antagonist WEB 2086 (10 uM) did not affect hydrogen peroxide induced vaso and bronchoconstriction. Hydrogen peroxide induces thromboxane A2 mediated vaso and bronchoconstriction in the isolated perfused an ventilated guinea pig lung. Platelet activating factor does not appear to play a significant role in the hydrogen peroxide induced vaso and bronchoconstriction. The perfused guinea pig lung is more sensitive to hydrogen peroxide than the perfused rat lung.

Hydrogen peroxide resistant sublines of Chinese hamster ovary cells were isolated by in vitro exposure to the oxidant (treatment for 1 hr followed by 3 days of growth in peroxide free medium). Stepwise increase in low level hydrogen peroxide concentration produced variants which were progressively more resistant to the growth inhibitory effect elicited by the oxidant. Removal from hydrogen peroxide decreased resistance and the curve describing this process was biphasic in nature. The protein content constantly increased during the adaptation process and decreases upon removal from hydrogen peroxide. Catalase activity did not show large variations in resistant sublines with respect to the parental cell line, and these changes were at least partially related to differences in cell size/amount of total cell proteins of the sublines. In addition, the minor changes observed for catalase activity did not correlate with the degree of resistance to growth inhibition elicited by the oxidant.

To understand the role of protein-thiol mixed disulfide formation in relation to the sequence of events during cataract induction, we conducted a long term hydrogen peroxide exposure study for up to 96 hr to monitor the dynamic changes in glutathione and protein-glutathione mixed disulfide levels, the formation of protein-protein disulfide aggregate, protein solubility, and the progression in lens opacity. Rat lenses were cultured in 0.5 mM hydrogen peroxide and harvested at intervals of 24, 48, 72 and 96 hr for the examination of morphological and biochemical changes. Contralateral lenses cultured in hydrogen peroxide free media were used as controls. It was found that the lenses had only patchy opacity at the equator after 24 hr, but became hydrated suddenly at 48 hr (31% heavier than the control), with an opacity which involved the entire outer cortical region. By 72 hr incubation, the nucleus was opacified. Lens glutathione progressively decreased with time of hydrogen peroxide exposure, 40% was lost by 24 hr and over 95% by 48 hr. There was a concomitant elevation of protein-glutathione mixed disulfide, 16 fold over the controls by 24 hr and 45 fold by 48 hr followed by a decline to 34 fold after 72 hr. In addition, the level of protein-cysteine mixed disulfide was elevated after 48 hr incubation in hydrogen peroxide. At this time, protein-protein disulfide aggregates began to appear both in water soluble and urea soluble fractions along with a drastic reduction in protein solubility. Western blot analysis of the protein fractions identified beta and gamma, but not alpha-crystallin in the disulfide containing aggregates. The lens clarity and biochemical changes partially recovered if the oxidant was removed within 24 hr, indicating a potential therapeutic role for antioxidants.

An oxidant burden established by hydrogen peroxide overload may elicit postischemic myocardial damage. Exposure of neonatal rat cardiomyocytes to 50 uM-1.0 mM hydrogen peroxide bolus rapidly shifted their pyridine-nucleotide redox balance toward oxidation. At least 30% of the observed NADPH oxidation was independent of glutathione cycle activity and appeared chemical in nature with hydrogen peroxide itself, and not a radical metabolite, acting as oxidant. Cell exposure to hydrogen peroxide also depleted cardiomyocyte pyridine nucleotides as a consequence of enhanced utilization. The oxidative stress activated one major route of pyridine nucleotide catabolism (i.e., protein ADP-ribosylation) without acute inhibitory effect upon the other (cleavage by NAD glycohydrolase). The limited NAD sparing by metal chelators and inhibitors of ADP-ribosylation reflected pyridine nucleotide utilization for repair of single-strand DNA breaks caused by hydroxyl-like radicals formed intracellularly through iron-dependent hydrogen peroxide reduction. Cardiomyocyte NAD depletion during hydrogen peroxide induced oxidative stress was independent of cell integrity and lipid peroxidation. The NAD lost after a discrete hydrogen peroxide pulse was only partly replenished over a 24 hr postinjury period. Cardiomyocyte pyridine nucleotide metabolism is a nonperoxidative injury target that is chronically affected by hydrogen peroxide overload.

The effect of the oxidant hydrogen peroxide on the vulnerability of the myocardium to reperfusion induced arrhythmias following global ischemia was investigated. After a 15 min equilibration period with or without experimental intervention, isolated perfused rat hearts were made globally ischemic for 5 min by cross-clamping the aortic line. No dysrhythmias were evoked upon reperfusion at the 5 min global ischemia time period. Hydrogen peroxide was added to the perfusate 5 min into the equilibration period with a total exposure of 10 min. Global ischemia was then induced for 5 min followed by 10 min of reperfusion. All hearts exposed to 200 uM hydrogen peroxide developed ventricular dysrhythmias during the reperfusion period. Coronary flow increased after 5 min of exposure to 200 uM hydrogen peroxide and remained elevated during reperfusion. Toxic oxygen derived products are capable of increasing the susceptibility of the myocardium to reperfusion induced arrhythmias.

The superoxide dismutase mimic, 4-hydroxy TEMPO (TEMPOL), was used to investigate the mechanism by which hydrogen peroxide damages cultured rabbit lens epithelial cells and to identify some of the targets of hydrogen peroxide insult. Most studies aimed at determining the mechanism by which hydrogen peroxide exerts its cytotoxic effect have used iron chelators to prevent the generation of the damaging hydroxyl radical. TEMPOL does not chelate transition metals. Cells at low or high density were cultured in MEM containing 5 mM TEMPOL and exposed to a single sub-lethal dose of 0.05 or 0.5 mM hydrogen peroxide, respectively. Analysis of EPR spectra indicated that TEMPOL was stable in MEM, did not destroy hydrogen peroxide and penetrated the intracellular fluid. TEMPOL prevented or curtailed the hydrogen peroxide induced inhibition of cell growth, blebbing of the cell membrane, the decrease in NAD+, the activation of poly ADP-ribose polymerase, an enzyme involved in DNA repair, and limited the induction of single strand breaks in DNA normally brought about by hydrogen peroxide. TEMPOL did not prevent the hydrogen peroxide induced decrease in reduced glutathione, lactate production, and the activity of glyceraldehyde 3-phosphate dehydrogenase, or the hydrogen peroxide induced increases in oxidized glutathione and hexose monophosphate shunt activity. Addition of TEMPOL 1-15 min after exposure of cells to hydrogen peroxide offered partial protection from the inhibition of cell division. TEMPOL at 5 mM did not inhibit cell growth. Some of the hydrogen peroxide induced damage in cultured rabbit LECs is mediated by intracellular redox-active metals involved in the Haber-Weiss cycle. Cellular changes not protected by TEMPOL, including attack of hydrogen peroxide on the thiol groups of glutathione (mediated through glutathione peroxidase) and G3PDH, are likely brought about by hydrogen peroxide itself and not by reactions of oxygen free-radicals generated from hydrogen peroxide.

The effect of extracellular acidosis on different types of cell injury and death was examined using suspensions of rabbit renal proximal tubules. Cell death produced by the mitochondrial inhibitors rotenone, antimycin A, carbonyl cyanide p-trifluoromethoxyphenylhydrazone and oligomycin and by the ion exchangers valinomycin, nigericin and monensin was ameliorated by reducing extracellular pH from 7.4 to 6.4. The protection lasted for more than 5 hr and was not due to the release of mitochondrial inhibition or to the maintenance of tubular ATP levels. In contrast, extracellular acidosis potentiated the cell injury and death produced by the oxidants t-butyl hydroperoxide, hydrogen peroxide and ochratoxin A. Because a decrease in extracellular pH resulted in an increase in lipid peroxidation and in glutathione disulfide formation, and caused a decrease in glutathione peroxidase and glutathione reductase activities, the mechanism of this potentiation is most likely the result of an increase in free-radical production or a decrease in free-radical detoxification. The findings with the oxidants are in marked contrast to those in hepatocytes.

Hydrogen peroxide induced contractions of isolated rabbit intrapulmonary arteries mounted in standard tissue baths were studied. All vessels were pretreated with a thromboxane A2/prostaglandin H2 receptor antagonist, SQ 29,548, to block immediate transient contractions to hydrogen peroxide and to isolate slowly developing sustained contractions. When exposed to hydrogen peroxide (0.1, 0.2, 0.3, 0.6, and 1.0 mM) for 30 min, vessels contracted in a concn-dependent fashion between 0.1 and 0.3 mM hydrogen peroxide; contractions at 0.6 and 1.0 mM hydrogen peroxide were not significantly

different from those at 0.3 mM hydrogen peroxide. During recovery (90 min) from hydrogen peroxide exposures, baseline tension was significantly greater, but active tension (10 uM phenylephrine) was significantly less for vessels previously exposed to 0.6 and 1.0 mM hydrogen peroxide.

Our previous work indicated that energy transduction, as measured by myocyte respiration, was inhibited by hydrogen peroxide, but the mitochondrial membrane potential was relatively unaffected. Therefore, we determined in the present study the critical steps in mitochondrial energy transduction by measuring the sensitivity to hydrogen peroxide of NADH-CoQ reductase, ATP synthase, and adenine nucleotide translocase in situ in myocytes. Adult rat heart cells were isolated using collagenase and incubated in the presence of 0.1-10 mM hydrogen peroxide for 30 min. Activities of NADH-CoQ reductase and oligomycin-sensitive ATP synthase were assayed enzymatically with sonicated myocytes, and adenine nucleotide translocase activities were determined by atractyloside-inhibitable [(14)C]ADP uptake of myocytes, permeabilized by saponin. The NADH-CoQ reductase and ATP synthase activities were inhibited to 77% and 67% of control, respectively, following an exposure to 10 mM hydrogen peroxide for 30 min. The adenine nucleotide translocase activities were inhibited in a concentration- and time-dependent manner and by 10 mM hydrogen peroxide to 44% of control. The dose-response relationship indicated that the translocase was the most susceptible to hydrogen peroxide among the three enzymes studied. Combined treatment of myocytes with 3-amino-1,2,4-triazole, 1,3-bis(2-chloroethyl)-1-nitrosourea and diethyl maleate (to inactivate catalase, to inhibit glutathione reductase activity, and to deplete glutathione, respectively) enhanced the sensitivity of translocase to hydrogen peroxide, supporting the view that the cellular defense mechanism is a significant factor in determining the toxicity of hydrogen peroxide. The results indicate that hydrogen peroxide can cause dysfunction in mitochondrial energy transduction, principally as the result of inhibition of adenine nucleotide translocase.

Other toxicity information

Human

The safety of tooth bleaching, which is based upon hydrogen peroxide (HP) as the active agent, has been questioned. Our aim was to investigate the effects of 30% HP on human tooth enamel. The specimens were divided randomly into three groups and treated with distilled water, HCl, and HP, respectively. Raman scattering and laser-induced fluorescence of enamel were determined before and after treatment. Microhardness testing and scanning electron microscopy were also used. The results of Raman scattering showed that the Raman relative intensity of enamel changed significantly after HP and HCl treatment. These findings were consistent with the results of microhardness testing and morphological observations. In addition, a small band at 876 cm(-1) due to O-O stretching of HP became pronounced during HP treatment, which provided direct evidence that HP has the ability to penetrate enamel. Meanwhile, the results of laser-induced fluorescence revealed that HP caused the greatest fluorescence reduction. This suggested that the organic matter in enamel might be greatly affected by HP, which was also supported by the results of microhardness. It can be concluded, therefore, that the 30% HP may have adverse effects on the mineral and the organic matter of human tooth enamel.

It was observed that externally applied bleaching gels may penetrate into the pulp chamber. This study was conducted to evaluate the peroxide diffusion from two whitening strips into the pulp chamber. Twenty-four, human, extracted, maxillary central teeth were separated into three groups (n = 8). All teeth were sectioned 3-mm apical to cementoenamel junction, the intracoronal pulp tissue was removed, and the pulp chamber was filled with acetate buffer. Vestibuler crown surfaces of teeth in the experimental groups were subjected to whitening strips; the teeth in the control group were exposed only to distilled water. The acetate buffer solution in each tooth was transferred to the tube. Leuco-crystal violet and enzyme horseradish peroxidase also were added to the tube. The pulpal peroxide was determined spectrophotometrically. The results indicated that the whitening strip containing 14% hydrogen peroxide presented a higher pulpal peroxide penetration than 6.5 % hydrogen peroxide ($p < 0.001$).

Limited data are available to assess the safety of high levels of hydrogen peroxide in overnight tooth-whitening formulas. The purpose of this study was to assess the effects of hydrogen peroxide on enamel microhardness, pulp penetration, and enamel morphology. Colgate Platinum Professional Overnight Whitening System (10% carbamide peroxide, equivalent to 3.5% hydrogen peroxide) was compared with two prototype formulations containing either 7.0% or 12.0% hydrogen peroxide. In the pulp chamber studies, human extracted teeth were exposed to 3.5%, 7.0%, or 12.0% hydrogen peroxide for 30 minutes, 4 hours, or 7 hours. Microhardness, electron spectroscopy for chemical analysis, and atomic force microscopy evaluations were made from enamel blocks cut from human extracted molars. The enamel blocks were evaluated following 14 7-hour treatments (98 hr total). At 7 hours' post-treatment, hydrogen peroxide penetrated the pulp chamber at 23.12 +/- 10.09, 24.58 +/- 6.90, and 26.39 +/- 5.43 ug for 3.5%, 7.0%, and 12.0% hydrogen peroxide, respectively. With regard to enamel morphology, pulp penetration, microhardness, and elemental composition, no statistically significant differences were observed between treatment groups following 98 hours of treatment. Hydrogen peroxide does not adversely affect enamel morphology or microhardness. The levels recovered in pulp indicate that hydrogen peroxide is not expected to inhibit pulpal enzymes. Overnight tray products containing levels of hydrogen peroxide of 3.5%, 7.0%, and 12.0% are not expected to adversely affect the enamel or pulpal enzymes. Additional safety

studies are needed to assess the potential for tooth sensitivity and gingival irritation.

Non-Human
The objective was to assess the effect of hydrogen peroxide applied to the middle ear on cochlear and vestibular function. Sand rats underwent a right-side total labyrinthectomy, and a polyethylene tube was inserted into the left-side middle ear. Following baseline recordings of vestibular evoked potentials in response to linear acceleration stimuli and auditory brainstem response, each experimental animal received five daily applications of hydrogen peroxide into the left-side middle ear. Two control groups received saline and gentamicin, respectively. Subsequently, recordings were repeated and compared with baseline measurements. Saline administration affected neither vestibular evoked potentials nor auditory brainstem response. In contrast, both responses could not be recorded following gentamicin application. After hydrogen peroxide administration, auditory brainstem response could not be recorded in 25% (3 of 12) of the animals, whereas in the remaining nine animals the average auditory brainstem response threshold was significantly elevated by 55 dB (P =.000002). Linear vestibular evoked potentials could not be recorded in 42% (5 of 12) of the animals. It appears that topical hydrogen peroxide adversely affects both cochlear and vestibular function of the sand rat. The study demonstrated the effect of a reactive oxygen species on inner ear function and may be useful in the study of mechanisms responsible for this damage and its protection. Clinically, although an animal model was used in the present study, caution should be exercised when large amounts of hydrogen peroxide are applied to a dry, perforated ear.

This aim of the present study was to evaluate the pulp chamber penetration of 35% hydrogen peroxide activated by LED (light-emitting diode) or Nd:YAG laser in bovine teeth, after an in-office bleaching technique. Forty-eight bovine lateral incisors were divided into four groups, acetate buffer was placed into the pulp chamber and bleaching agent was applied as follows: for group A (n = 12), activation was performed by LED; for group B (n = 12), activation was performed by Nd:YAG laser (60 mJ, 20 Hz); group C (n = 12) received no light or laser activation; and the control group (n = 12) received no bleaching gel application or light or laser activation. The acetate buffer solution was transferred to a glass tube and Leuco Crystal Violet and horseradish peroxidase were added, producing a blue solution. The optical density of this solution was determined spectrophotometrically and converted into microgram equivalents of hydrogen peroxide. The results were analyzed using ANOVA and Tukey's test (5%). It was verified that the effect of activation was significant, as groups activated by LED or laser presented greater hydrogen peroxide penetration into the pulp chamber (0.499 +/- 0.622 ug) compared with groups that were not (0.198 +/- 0.218 ug). There was no statistically significant difference in the penetration of hydrogen peroxide into the pulp chamber between the two types of activation (LED or laser). The results suggest that activation by laser or LED caused an increase in hydrogen peroxide penetration into the pulp chamber.

Carbamide peroxide and hydrogen peroxide are used as the main agents in vital tooth bleaching. In this study, the influence of peroxide treatment on cross-sectional morphology and mechanical property was investigated. A 3 x 5-mm window of enamel on the labial surface of a bovine tooth was exposed to immersion in 10% or 30% carbamide peroxide or hydrogen peroxide for 30 or 180 min. After immersion, the cross-sectional structure of each specimen was examined by nanoindentation and SEM. Nanohardness in the enamel showed a decrease at 2 um below the surface, but none at 50 um. High concentrations of peroxide caused erosion to a depth of 5 um below the surface. In conclusion, decrease in nanohardness and change in morphology were limited to an area less than 50 um below the surface, regardless of either concentration of peroxide or period of immersion.

In rabbits and cats that died after iv administration of hydrogen peroxide, the lungs were found to be pale and emphysematous, with considerable amounts of gas in the great veins and in the right side of the heart.

Carcinogenicity
This product contains hydrogen peroxide. The International Agency for Research on Cancer (IARC) has concluded that there is inadequate evidence for carcinogenicity of hydrogen peroxide in humans, but limited evidence in experimental animals, (Group 3 - not classifiable as to its carcinogenicity to humans). The American Conference of Governmental Industrial Hygienists (ACGIH) has concluded that hydrogen peroxide is a Confirmed Animal Carcinogen with Unknown Relevance to Humans' (A3).

Mutagenicity
This product is not recognized as mutagenic by Research Agencies In vivo tests did not show mutagenic effects

Reproductive toxicity
Pregnant rats /were fed/ a diet containing up to 10% hydrogen peroxide. Maternal and fetal weights were reduced but no significant malformations were reported.

STOT - single exposure

May cause respiratory irritation.

STOT - repeated exposure
Not classified. Target organ effects Eyes, Respiratory System, Skin.

Aspiration hazard
Aspiration risk: may cause lung damage if swallowed.

Numerical measures of toxicity (such as acute toxicity estimates)

Acute toxicity		Category
LD_{50} Oral Rat	> 2 000 mg/kg	4
LD_{50} Dermal Rat Pig	4 060 mg/kg > 2 000 mg/kg	Not classifiable
LC_{50} Inhalation Rat (4hrs)	2 000 mg/m^3	4

Interactive effects

To explore the cardiac effects of iron with or without hydrogen peroxide, the isolated perfused rat heart and enzymatically isolated ventricular cardiomyocyte were used. It was shown that treatment with cell-permeable iron (Fe-HQ) for 10 min reduced the contractile amplitude and velocity and end diastolic cell length in the cardiomyocyte and increased the contents of lactate dehydrogenase (LDH) and creatine kinase (CK) in the coronary effluent and malondialdehyde (MDA) in the myocardium. The left ventricular developed pressure (LVDP), +/-dP/dtmax, and heart rate and coronary flow showed a biphasic phase, an increase at first followed by a decline. Treatment with hydrogen peroxide for 10 min following Fe-HQ augmented the effect of iron with an increase in coronary LDH and CK release and myocardial MDA content, and decrease in LVDP, +/-dP/dtmax and heart rate. Perfusion of reduced glutathione with hydrogen peroxide counteracted these effects of Fe-HQ and hydrogen peroxide while dimethyl sulfoxide had no effect on the injury induced by Fe-HQ and hydrogen peroxide in the isolated rat heart. This suggests that augmentation of myocardial injury as a result of an increase in intracellular iron by hydrogen peroxide might involve the dysfunction of sulfydryl group containing proteins but not the hydroxyl radicals.

It has been shown that the mucolytic agent erdosteine (N-carboxymethylthio-acetyl-homocysteine thiolactone) has anti-inflammatory and anti-oxidant properties, and an active metabolite I (MET I) containing pharmacologically active sulphydryl group has been found to have a free radical scavenging activity. The aim of this study was to assess the ability of erdosteine metabolite I to protect A549 human lung adenocarcinoma cell against hydrogen peroxide (H2O2)-mediated oxidative stress and oxidative DNA damage. When A549 cells were pre-treated with the active metabolite I (2.5-5-10 ug/mL) for 10-30 min and then exposed to H2O2 (1-4 mM) for two additional hours at 37 degrees C, 5% at CO2, the intracellular peroxide production, reflected by dichlorofluorescein (DCF) fluorescence, decreased in a concentration-dependent manner. Furthermore, using a comet assay as an indicator for oxidative DNA damage, it was found that the metabolite I prevented damage to cells exposed to short-term H2O2 treatment. The data suggest that this compound is effective in preventing H2O2-induced oxidative stress and DNA damage in A549 cells. The underlying mechanisms involve the scavenging of intracellular reactive oxygen species (ROS).

Oxidative stress reduces cell viability and contributes to disease processes. Flavonoids including anthocyanins and proanthocyanidins reportedly induce intracellular antioxidant defense systems. Thus, in this study, we examined the antioxidant effects of a commercial extract from black soybean seed coats (BE), which are rich in anthocyanin and proanthocyanidin, and investigated the associated intracellular mechanisms in HepG2 cells. HepG2 cells treated with hydrogen peroxide (HPO) showed 60% viability, whereas pretreatment with BE-containing media for 2 hr ameliorated HPO-mediated cell death by up to 90%. Pretreatment with BE for 2 hr partially blocked HPO-mediated activation of extracellular-signal-regulated kinase (ERK) in HepG2 cells, and that for 1 hr led to a 20% increase in intracellular total protein phosphatase (PP) activity, which is known to deactivate protein kinases. These results indicate that BE prevents HPO-mediated cell damage by inhibiting ERK signaling, potentially via PPs.

Hydrogen peroxide (HP) or cyanide (CN) are bacteriostatic at low-millimolar concentrations for growing Escherichia coli, whereas CN+HP mixture is strongly bactericidal. We show that this synergistic toxicity is associated with chromosomal fragmentation. Since CN alone does not kill at any concentration, while HP alone kills at 20 mM, CN must potentiate HP poisoning. The CN+HP killing is blocked by iron chelators, suggesting Fenton's reaction. Indeed, we show that CN enhances

plasmid DNA relaxation due to Fenton's reaction in vitro. However, mutants with elevated iron or HP pools are not acutely sensitive to HP-alone treatment, suggesting that, in addition, in vivo CN recruits iron from intracellular depots. We found that part of the CN-recruited iron pool is managed by ferritin and Dps: ferritin releases iron on cue from CN, while Dps sequesters it, quelling Fenton's reaction. We propose that disrupting intracellular iron trafficking is a common strategy employed by the immune system to kill microbes.

The effect of Co(II) ion on the reaction of hydrogen peroxide with DNA was investigated by a DNA sequencing technique using (32)P-5'-end-labeled DNA fragments obtained from human c-Ha-ras-1 protooncogene. 20 uM Co(II) (as cobalt chloride, CoCl2) induced strong DNA cleavage in the presence of 0.4 mM hydrogen peroxide even without alkali treatment. Guanine residues were the most alkali-labile site, and the extent of cleavages at the positions of thymine and cytosine was dependent on the sequence. Adenine residues were relatively resistant. Neither Co(II) nor hydrogen peroxide alone caused DNA cleavage. Diethylenetriaminepentaacetic acid, present in excess over Co(II), inhibited DNA cleavage. Singlet oxygen scavengers (dimethylfuran, 0.05 M sodium azide, 0.05 M 1,4-diazabicyclo(2.2.2)octane, 0.025 M dGMP), sulfur compounds (methional, methionine), and superoxide dismutase inhibited DNA cleavage completely. Hydroxyl radical scavengers, such as dimethyl sulfoxide and sodium formate, were not so effective as singlet oxygen scavengers. Electron spin resonance studies performed in the presence of ADP using 2,2,6,6-tetramethyl-4-piperidone as a single oxygen trap suggest that Co(II) reacts with hydrogen peroxide to produce singlet oxygen or its equivalent. Electron spin resonance studies using 5,5-dimethylpyrroline N-oxide showed that the hydroxyl radical adduct of 5,5-dimethylpyrroline N-oxide was also formed.

Free radical generation from hydrogen peroxide and lipid hydroperoxides in the presence of chromium(III) was investigated by electron spin resonance spin trapping methodology. Incubation of chromium(III) with hydrogen peroxide at physiological pH generated hydroxyl radical, the yield of which reached saturation level in about 6 min. Deferoxamine reduced the hydroxyl radical yield by only about 20%, diethylenetriamine pentaacetic acid reduced it by about 70%, while cysteine, glutathione, and NADH exhibited no significant effect. The yield of hydroxyl radical formation also depended on the pH being 15 times higher at pH 10 than that at pH 7.2. At pH 3.0, hydroxyl radical generation became nondetectable, and addition of hydrogen peroxide to chromium(III) solution did not affect the intensity of the chromium(III) electron spin resonance signal while at pH 10, addition of hydrogen peroxide reduced the chromium(II) intensity by about 40%, showing that reaction of chromium(III) with hydrogen peroxide occurred only at higher pH. Chromium(III) is capable of producing free radicals from hydrogen peroxide and lipid hydroperoxides.

Electron spin resonance spin trapping was utilized to investigate the generation of free radicals from cumene hydroperoxide, tert-butyl hydroperoxide, and hydrogen peroxide at pH 7.2 by cobalt(II) in the presence of cysteinyl and histidyl chelating agents. Incubation of cobalt(II) with cumene hydroperoxide or tert-butyl hydroperoxide did not generate any detectable amounts of free radicals. However, in the presence of glutathione, cysteine, penicillamine, or N-acetylcysteine, cobalt(II) generated cumene hydroperoxide-derived carbon-centered radicals, cumene alkoxyl radicals, and hydroxyl radicals. Oxidized glutathione and cysteine used instead of reduced glutathione or cysteine did not generate any free radical, indicating an important role of the -SH group in radical generation. While the addition of diethylenetriamine pentaacetic acid prevented radical generation, deferoxamine had only a slightly inhibitory effect. Incubation of cobalt(II) with hydrogen peroxide produced only a small amount of hydroxyl radicals. Addition of glutathione to the mixture of cobalt(II) and hydrogen peroxide resulted in generation of both glutathionyl and hydroxyl radicals, which could be inhibited by diethylenetriamine pentaacetic acid and deferoxamine. Under the same experimental conditions, cysteine, penicillamine, and N-acetylcysteine inhibited free radical generation from the reaction of cobalt(II) with hydrogen peroxide. Histidine and histidyl oligopeptides, homocarnosine, and carnosine did not have a significant effect. However, anserine enhanced the hydroxyl radical generation from this reaction. Cobalt(II) is capable of generating free radicals from lipid hydroperoxides and hydrogen peroxide in the presence of certain chelating agents.

This in vitro experiment studied the effects of sodium bicarbonate and hydrogen peroxide on the cariogenic bacteria Streptococcus mutans through analysis with a spectrophotometer. The growth of S. mutans was analyzed using seven different environments. Twelve wells in each of the seven rows of a multi-well plate were used to incubate the test materials. In combinations of 10 uL distilled water, 100 uL broth, 10 uL 10% sucrose, 10 uL S. mutans, 10 uL 10% sodium bicarbonate, and 10 uL 3% hydrogen peroxide, seven different environments were created for testing. Environments had either sodium bicarbonate or hydrogen peroxide with S. mutans, or a combination of sodium bicarbonate and hydrogen peroxide with S. mutans. The plate was incubated at 37 degrees C and measured at 0, 18, 20, 22, 24, 26, 28, 30, and 42 hours by optical density with a spectrophotometer. Results showed bacterial growth was prevented by sodium bicarbonate, hydrogen peroxide, and the combination of sodium bicarbonate and hydrogen peroxide. Although hydrogen peroxide is bacteriocidal and sodium bicarbonate is bacteriostatic, there were no significant differences among the three treatment groups in spectrophotometer readings at any of the nine readings over 42 hours. There was no significant difference among the effects of hydrogen peroxide, sodium bicarbonate, or the sodium bicarbonate and hydrogen peroxide combination, as measured by optical density. The hydrogen peroxide, sodium bicarbonate, and the sodium

bicarbonate and hydrogen peroxide combination prevented bacterial growth of S. mutans. The results show that products containing these agents have the ability to stop the growth of S. mutans. Products containing sodium bicarbonate and/or hydrogen peroxide may be useful to caries-prone patients. More studies are needed to confirm these results on patients.

We determined whether the cytotoxicity of doxorubicin hydrochloride would be enhanced by adding hydrogen peroxide as a source of oxygen free radicals. Mouse bladder tumor cells (MBT-2) were grown in RPMI 1640 medium and treated with various concentrations of doxorubicin hydrochloride for 2 hours. Protein content was assayed as a measure of cell growth. A similar set of experiments was done with cells exposed to hydrogen peroxide only and combined doxorubicin and hydrogen peroxide. Protein content was again assayed as a measure of cell growth. Cells were also assayed for glutathione peroxidase and malonyl dialdehyde, a product of lipid peroxidation, to determine the mechanism of cell damage. Furthermore, MBT-2 cells were incubated with 100 M. alpha-tocopherol, a free radical scavenger, before exposure to hydrogen peroxide to determine whether the effects of hydrogen peroxide could be reversed. We observed a dose dependent inhibition of MBT-2 cell growth after exposure to doxorubicin hydrochloride. Exposure to doxorubicin and hydrogen peroxide resulted in greater cell growth inhibition than exposure to either agent alone. The effects of hydrogen peroxide on cell proliferation were reversed by pre-incubation with alpha-tocopherol. As a source of oxygen free radicals, hydrogen peroxide enhances the antiproliferative effect of doxorubicin hydrochloride on a mouse bladder tumor cell line. Thus, hydrogen peroxide may be a relatively inexpensive, nontoxic method of augmenting the cytotoxicity of doxorubicin hydrochloride. Further studies are warranted to determine whether these observations may have clinical application.

Where specific chemical data are not available

No additional data available.

Mixtures

No additional data available.

Mixture versus ingredient information

No additional data available.

Other information

Populations at Special Risk
Individuals with eye, skin, and chronic respiratory diseases may be at an increased risk.

12 Ecological information

Toxicity

Hazard for aquatic organisms

Freshwater

Hazard assessment conclusion:	PNEC aqua (freshwater)
PNEC value:	0.013 mg/L
Assessment factor:	50
PNEC freshwater (intermittent releases):	0.014 mg/L

Marine water

Hazard assessment conclusion:	PNEC aqua (marine water)
PNEC value:	0.013 mg/L
Assessment factor:	50

STP

Hazard assessment conclusion:	PNEC STP
PNEC value:	4.66 mg/L
Assessment factor:	100

Sediment (freshwater)

Hazard assessment conclusion:	PNEC sediment (freshwater)
PNEC value:	0.047 mg/kg sediment dw
Extrapolation method:	equilibrium partitioning method

Sediment (marine water)

Hazard assessment conclusion:	PNEC sediment (marine water)
PNEC value:	0.047 mg/kg sediment dw
Extrapolation method:	equilibrium partitioning method

Soil

Hazard assessment conclusion:	PNEC soil

PNEC value:	0.002 mg/kg soil dw
Extrapolation method:	equilibrium partitioning method

The available ecotoxicological information does not imply the classification of hydrogen peroxide for environmental hazards.

Aquatic Toxicity
The acute aquatic toxicity of hydrogen peroxide to fish, invertebrates and aquatic algae has been investigated in a number of valid assays and the following (lowest) EC50 values have been derived from acute studies: 16.4 mg/L in fish, 2.4 mg/L in daphnia and 1.38 mg/L in algae (marine diatoms). It appears that algae represent the most sensitive species with regard to acute toxicity of hydrogen peroxide. Valid prolonged toxicity studies were performed in Daphnia magna (NOEC of 0.63 mg/L) and in the marine diatom Skeletonema costatum (NOEC of 0.63 mg/L) indicating that there is no significant difference in the sensitivity of these species to the aquatic toxicity of hydrogen peroxide. The PNEC aqua for freshwater and marine organisms can be derived from the available data by applying an assessment factor of 50. The resulting PNEC aqua is 0.0126 mg/L. A valid respiration inhibition test with hydrogen peroxide using activated sludge from a primarily domestic wastewater treatment plant resulted in an EC50 value of 466 mg/L determined for an incubation duration of 30 minutes. The respiration inhibition was reversible in the test. An assessment factor of 100 is applied to calculate the PNEC STP of 4.66 mg/L.

Short-term toxicity to fish
According to the EU Risk Assessment Report for hydrogen peroxide (European Commission 2003), three tests on the acute toxicity of hydrogen peroxide to three fish species are available. Acute LC50 values for fish range from 16.4 to 37.4 mg/L. The test with the lowest LC50 for Pimephales promelas (Shurtleff 1989) was done according to US EPA guidelines, the test solution was renewed and the concentration of the test substance was measured every 24 hours. The other two LC50 values for fish are somewhat higher but the results are based on nominal concentrations. Taking into account the instability of the test substance these two results cannot be considered as reliable. The LC50 value of 16.4 mg/L for Pimephales promelas will be taken into consideration with the test results of other taxonomic groups for the derivation of PNEC for the aquatic environment.

Long-term toxicity to fish
Hydrogen peroxide has a short half-life in natural waters due to the activity of micro-organisms, and therefore long-term exposure of aquatic biota, i.a. invertebrates to hydrogen peroxide originating from anthropogenic sources is considered rather improbable. Furthermore, hydrogen peroxide is continuously formed in the environment and is ubiquitous in fresh- and seawater at natural background concentrations from some micrograms to some tens of microgram per litre. Accordingly, fish can be considered evolutionary adapted to hydrogen peroxide in this range of concentrations. In consideration of these points, a prolonged toxicity test in fish is deemed not necessary.

A long-term test is available from public literature addressing potential carcinogenic effects of hydrogen peroxide on fish (Kelly et al. 1992). During the 8-month test period, rainbow trout were exposed to hydrogen peroxide via the diet at nominal levels of 600 or 3000 ppm. However, dosing via the diet is not considered appropriate because hydrogen peroxide does not persist in food but would be rapidly degraded before the food is eaten by the fish. Therefore, the study is not considered valid. Furthermore, dietary uptake is not a relevant exposure route.

Short-term toxicity to invertebrates
Data on the acute toxicity of hydrogen peroxide to aquatic invertebrates is available for four different species from two phyla. Hydrogen peroxide was more toxic to crustacea than to molluscs with the waterflea Daphnia pulex representing the most sensitive test species (EC50: 2.4 mg/L) followed by the amphipod Gammarus (EC50: 4.4 mg/L) and the snail Physa (EC50 : 17.7 mg/L). The acute toxicity of hydrogen peroxide to invertebrates was tested in a semi-static, 48 - hours assay with Daphnia pulex (Shurtleff 1989b) according to USEPA Toxic Substances Control Act Test Guidelines (1985, 1987). Tested hydrogen peroxide concentrations ranged from 0.5 to 500 mg/L. The validity criteria of the test were fulfilled in the sense that no mortality was observed in the controls. Significant dissipation of the test material ranging from 10% to 60% occurred within 24 hours with the four lowest test concentrations (0.5 to 50 mg/L, nominal). The LC50 value was determined to be 2.4 mg/L in the test. No reliable confidence intervals could be calculated.

Long-term toxicity to invertebrates
Data are available from the public domain on a reproduction test in Daphnia magna (Meinertz et al. 2008) conducted according to ASTM guidance (E 1193-97). Daphnids were exposed under flow-through conditions for 21 days to a range of concentrations, i.e., 0.32, 0.63, 1.25, 2.5 and 5.0 mg/L. Survival and reproduction of parent generation was not affected at concentrations up to and including 1.25 mg/L. Body length of adult water flea was statistically significantly reduced after

21 days at 0.32 mg/L compared to the control, however, the difference was so small that it is considered not biologically meaningful. Therefore, a NOEC of 0.63 mg/L is considered under the test conditions.

A further supporting long-term test with invertebrates is available from public literature addressing potential adverse effects of Fenton's reagent (hydrogen peroxide in combination with ferrous ion) on zebra mussel Dreissena polymorpha (Klerks and Fraleigh, 1991). In the 56-day flow-through test (11 °C; pH 8.25; average concentrations hydrogen peroxide/total iron: 0.79/0.33, 1.62/0.61 and 4.47/1.53 mg/L), the NOECmortality for zebra mussel was 1.62 mg/L.

Toxicity to cyanobacteria
Effects of hydrogen peroxide to primary producers were investigated in numerous freshwater algal species and, in addition, in two marine diatoms. Most of the data is from the public domain, summarising the findings from experiments conducted with a scientific background rather than gearing to registration requirements. Therefore, the test methods are often not in compliance with standard methods and the set-ups are not optimised for EC50 or NOEC value calculation. Despite these technical limitations, the findings are considered quite consistent with no indication of significant differences in the sensitivity of freshwater and marine species. It is considered a reasonable approach to use the endpoint for the risk assessment that was derived from the test most closely approaching the standard test guidelines, i.e., the NOEC of 0.63 mg/L in the marine diatom Skeletonema costatum was considered in the calculation of the PNEC aquatic.

Toxicity to micro-organisms
A valid respiration inhibition test using activated sludge from a primarily domestic wastewater treatment plant was carried out with hydrogen peroxide according to OECD Guideline No. 209 and to GLP. Concentrations of hydrogen peroxide were tested over the range of 1 to 1000 mg/L. Two controls with no exposure to hydrogen peroxide were included. Test solutions were incubated for 30 minutes or 3 hours, before the oxygen demand was measured once per minute during a period of 11 minutes. Hydrogen peroxide inhibited the respiration of activated sludge in a concentration dependent manner. However, the effect was reversible with time due to the rapid degradation of hydrogen peroxide mediated by the biological matrix. The EC50 value determined for the test solution incubated for 30 minutes was 466 mg/L, whereas the EC50 value determined for the test solution incubated for 3 hours was greater than 1000 mg/L.

Toxicity to other aquatic organisms
An EC50 value of 4.8 mg/L H2O2 with a 95% confidence range of 4.2-5.6 mg/L was determined for the rotifer. The NOEC was 3.5 mg/ H2O2. Based on the results of the first test, a more confined concentration series was applied. The second test revealed an EC50 value of 5.9 mg/L with a 95% confidence interval of 5.7-6.2 mg/L. The NOEC was measured at 3.5 mg/L.

Sediment toxicity
Moreover, microbial activity, which is considered the key parameter of the rate of degradation of hydrogen peroxide in aquatic systems, is known to be particularly high at the boundary layer between the water and the sediment phase. Therefore, concentrations of hydrogen peroxide in the sediment and also risk to sediment organisms are considered to be negligible. In consideration of these points, testing on sediment dwelling organisms is deemed not necessary. This statement is also supported by the calculated bioconcentration factors for fish and earthworm of 1.4 and 3.3, respectively.

Terrestrial toxicity
A trend towards fast decomposition of hydrogen peroxide occurs in soil and groundwater. Decomposition in soil or groundwater typically takes minutes to several hours, depending on the concentrations of microorganisms present. This is true whether hydrogen peroxide is initially present at relatively low naturally occurring concentrations (Cooper and Zepp 1990, Cooper et al. 1994), or at much higher concentrations (several thousand fold) characteristic of in situ soil and groundwater remediation treatments (Spain et al. 1989, Pardieck et al. 1992). Difficulty has been encountered in maintaining hydrogen peroxide at the desired in situ treatment concentrations (above 100 mg/L) because of its rapid environmental decomposition (Morgan and Watkinson 1992).

A number of laboratory and field studies have reported effects of catalysed hydrogen peroxide on microbial activity in soil and groundwater. Negligible long-term observable adverse effects of oxidant addition on microbial biomass or the effectiveness of bioremediation ability were found (Sahl and Munakata-Marr 2006). This may be explained by the fact that many microbes in times of stress caused by the presence of hydrogen peroxide and other oxidative compounds are able to produce antioxidative enzymes, such as catalase and superoxide dismutase. These enzymes protect the cells against reactive oxygen species. The majority of aerobic and anaerobic microbes present in soil and groundwater are catalase-positive (Pardieck et al. 1992) and thus potentially protected from exposure to hydrogen peroxide and other oxidative compounds formed by its decomposition. The microbial cell numbers declined at hydrogen peroxide concentrations greater than 77 mg/L (Büyuksönmez et al. 1999). An initial decrease in microbial populations following the introduction of

hydrogen peroxide was observed after application of hydrogen peroxide in a laboratory study, which was followed by a rebound with cell numbers exceeding the initial microbial biomass after two weeks (Allen and Reardon 2000). A reestablishment of microbial populations was also observed in a field study using hydrogen peroxide to support the aerobic biodegradation of organic contaminants (Kastner et al. 2000). A rebound of microbial activity following exposure to a chemical oxidant may be attributed to different factors including lower concentrations of contaminants after the oxidation (Chapelle et al. 2005), repopulation of oxidized areas by underlying groundwater or new growth of indigenous microbes after reestablishment of pre-oxidation conditions (Klens et al. 2001). The use of a chemical oxidant in soil and groundwater remediation can lead to a decrease in microbial diversity (Macbeth et al. 2005, Miller et al. 1996), which may be due to microbial specialisation. Evidence exists that methanogenic micro-organisms may be most sensitive to chemical oxidation agents (Klens et al. 2001) as the introduction of oxygen into the ground significantly changes the redox-potential and thus may influence the metabolism of anaerobic micro-organisms.

No direct studies are known on the effect of rapid hydrogen peroxide breakdown in soil to the microbial organisms themselves. The literature seems to suggest that when microbial density and biomass are high compared with the concentration and total amount of available hydrogen peroxide, or if oxygen demand is high, there are no adverse effects to microbial populations (Larish and Duff 1997). In the opposite situation, short-term toxicity to microorganisms is evident, but acclimation and rebound of the populations always takes place (Balvay 1981, Spain et al. 1989, Xenopoulos and Bird 1997). No long-term or irreversible damage to a given microbial biomass as the result of such exposure has been recorded.

Other soil organisms
A prominent representative of soil macro-fauna is the earthworm Eisenia foetida which plays an important role in the decomposition of organic material in the soil. These earthworms seem to be well-equipped with effective antioxidant defences (glutathione, glutathione-related enzymes, catalase, glycoliprotein) that may protect them against potentially harmful effects of hydrogen peroxide exposure (Saint-Denis et al. 1998). Similar defence mechanisms are also found in other earthworms, such as Lampito mauritii (Maity et al. 2008).

Toxicity to soil macroorganisms except arthropods
study scientifically not necessary / other information available

Toxicity to terrestrial arthropods
study scientifically not necessary / other information available

Toxicity to terrestrial plants
The terrestrial compartment is not the primary environmental compartment affected by environmental emissions of the substance. Hydrogen peroxide occurs naturally in the environment, for example in rain water. In addition, hydrogen peroxide is continuously generated in physiological processes of the plants, for example in the mitochondria (e.g. Rasmusson et al. 1998). A complex system of enzymes, such as superoxide dismutase, ascorbate oxidase, catalase and glutathione peroxidase, exists in plants that scavenges reactive oxygen species like hydrogen peroxide (e.g. Mittler et al. 2004). There is evidence that hydrogen peroxide activates defence responses of plants to various environmental stresses (e.g. Bhattachrjee 2005, Neill et al. 2002). It has also been suggested that hydrogen peroxide at lower doses acts as a signal molecule during plant growth and development. From this it is concluded that terrestrial plants can cope with the levels of exposure to hydrogen peroxide that are to be expected from the identified uses of the substance. No additional testing is deemed necessary.

Toxicity to soil microorganisms
study scientifically not necessary / other information available

Toxicity to birds
study scientifically not necessary / other information available

Additional ecotoxological information
Memo: H202 is produced by metabolism on all living cells with the exeption of anaerobic bacteria. To prevent oxidative cell damage cells have developed ability to to decompose H2O2.

Persistence and degradability

Hydrogen peroxide is ubiquitous in air and all types of natural waters. Highest concentrations are typically found in water of clouds or in raindrops.

Air

A complex equilibrium exists in air among molecular oxygen, hydroxyl radicals, nitrogen oxides and other photooxidants. This equilibrium system is influenced by solar radiation and natural as well as anthropogenic emissions. Hydrogen peroxide is part of this equilibrium system, being formed from hydrogen superoxide (HO_2) radicals (e.g. Sakugawa et al. 1990). The formation of hydrogen peroxide is favoured by factors leading to high radical concentrations (e.g., solar radiation or emissions of volatile organic carbon (VOC) or carbon monoxide), while the presence of radical scavengers such as NOx counteracts the formation of hydrogen peroxide. Major sinks for atmospheric hydrogen peroxide are the oxidation of sulphur dioxide, reaction with hydroxyl radicals as well as wet deposition (see table on high concentrations found in rain water). The photochemical dissociation of hydrogen peroxide is considered to be a minor sink (Sakugawa et al. 1990).

Surface water

Formation of hydrogen peroxide in surface waters was found to be due to UV radiation in the presence of DOC and oxygen (Sturzenegger 1998, Scully et al. 1996). Other processes are deemed not to contribute significantly to the overall formation rate (Herrmann and Herrmann 1994). Hydrogen peroxide is decomposed in water to form water and oxygen, both compounds of no concern: H_2O_2 --> H_2O + 0.5 O_2 This reaction has been investigated and discussed by many authors (e.g. Degussa AG 1997, Goor et al. 1989, Schumb et al. 1955). The main conclusions are that a catalyst is needed for the decomposition reaction to proceed at a significant rate under environmental conditions.

Suitable catalysts are ions of transition metals such as iron, manganese or copper, as well as the enzyme catalase (e.g. Spain et al. 1989). Biotic and abiotic catalysis of the decomposition reaction proceeds in parallel under environmental conditions, and are in equilibrium with formation reactions.

Soil

Hydrogen peroxide is present in the soil water, due to its high polarity and full miscibility with water. Therefore, the same decomposition mechanisms apply for soil as discussed for surface water (Aggarwal et al. 1991, Spain et al. 1989, Pardieck et al. 1992).

In summary, hydrogen peroxide concentrations in environmental media depend on the equilibrium of formation and decomposition reactions. Environmental media are therefore expected to possess substantial capacities to buffer anthropogenic emissions of hydrogen peroxide.

Furthermore, the decomposition of hydrogen peroxide in air, water or soil generally cannot be investigated by standard guideline tests designed for biotic or abiotic degradation of organic compounds.

Degradation in air

The following text was copied from the EU Risk Assessment Report (2003), pg. 30:
"In polluted urban air half-lives of few hours have been reported (Sakugawa et al., 1990). No clear figures of overall photolysis rates have been presented in the literature. A study done by Olzyna in Whitetop Mountain indicates that in unpolluted air at night time (during 8-10 hours) indirect photolytic degradation decreases H_2O_2 levels by about 25% and consequently 50% decrease would take 16-20 hours (it is assumed that the night time production rate of H_2O_2 is low or negligible). In polluted air diurnal variations in concentrations seem to be more or less larger than in unpolluted air.

According to the existing test data from different atmospheric conditions (Olszyna, 1988; Sakugawa et al., 1990; Kleinman 1986) a half-life of 24 hours (rate constant of 0.029 h^{-1}) will be chosen to represent the average degradation half-life in the atmosphere."

Decomposition in natural waters

Hydrogen peroxide is not hydrolysed, due to its molecular structure. Furthermore, no direct photolysis of hydrogen peroxide is expected based on the following text copied from the EU Risk Assessment Report (2003), pg. 30:
"Direct photolysis is not expected to be an important degradation process in the aquatic environment. Hydrogen peroxide has absorption bands in the infrared, but is not decomposed by the light of these frequencies. The UV absorption spectrum is a continuous spectrum but the measured molar extinction coefficient values are low. Highest value is $\varepsilon = 4.2$ l/mole.cm (at 280 nm) decreasing continuously to 0.22 l/mole.cm (at 320 nm) and 0.00066 l/mole.cm (at 400 nm) (Schumb et al., 1955)."

Degradation in soil

The following text was copied from the EU Risk Assessment Report (2003), pp. 34/35:
In soil H_2O_2 is normally a short-lived substance. Rapid degradation will occur due to high concentration of catalytic material like transition metals, enzymes, easily oxidised/reduced organic substances and living microbes (Spain et al., 1989).

Hydrogen peroxide is used as a source of oxygen (for aerobic microbes) in polluted groundwater sites (enhanced bioremediation). Therefore specific information on degradability in soil is available. The problem in these applications where hydrogen peroxide is introduced directly into the ground is linked to a too rapid degradation. Observed half-lives of H2O2 in soil vary from 15 hours (soil without microbiological activity and few minerals) to several minutes (soils with 108-109 cells/g total solids, and in the presence of iron and manganese (Aggarwal et al., 1991; ECETOC 1993; Hinchee and Downey 1988 ; Pardieck et al., 1992).

In the assessment it is estimated that the degradation half-life in soil is 12 hours.

Phototransformation in air
The following text was copied from the EU Risk Assessment Report (2003), pg. 30: "In polluted urban air half-lives of few hours have been reported (Sakugawa et al. 1990). No clear figures of overall photolysis rates have been presented in the literature. A study done by Olzyna (1988) in Whitetop Mountain indicates that in unpolluted air at night time (during 8-10 hours) indirect photolytic degradation decreases H2O2 levels by about 25% and consequently 50% decrease would take 16-20 hours (it is assumed that the night time production rate of H2O2 is low or negligible). In polluted air diurnal variations in concentrations seem to be more or less larger than in unpolluted air. According to the existing test data from different atmospheric conditions (Olszyna 1988, Sakugawa et al. 1990, Kleinman 1986) a half-life of 24 hours (rate constant of 0.029 h-1) will be chosen to represent the average degradation half-life in the atmosphere."

Phototransformation in water
study scientifically not necessary / other information available

Phototransformation in soil
The following text was copied from the EU Risk Assessment Report (2003), pp. 34/35: “In soil H2O2 is normally a short-lived substance. Rapid degradation will occur due to high concentration of catalytic material like transition metals, enzymes, easily oxidised/reduced organic substances and living microbes (Spain et al. 1989). Hydrogen peroxide is used as a source of oxygen (for aerobic microbes) in polluted groundwater sites (enhanced bioremediation). Therefore specific information on degradability in soil is available. The problem in these applications where hydrogen peroxide is introduced directly into the ground is linked to a too rapid degradation. Observed half-lives of H2O2 in soil vary from 15 hours (soil without microbiological activity and few minerals) to several minutes (soils with 108-109 cells/g total solids, and in the presence of iron and manganese (Aggarwal et al. 1991, ECETOC 1993, Hinchee and Downey 1988, Pardieck et al. 1992). In the assessment it is estimated that the degradation half-life in soil is 12 hours.”

Hydrolysis
study scientifically not necessary / other information available.

Biodegradation
The EU risk assessment report for hydrogen peroxide (European Commission 2003) comes to the following conclusion with regard to biodegradation of the substance (pp. 33/34): “On the basis of the available biodegradation tests it is possible to conclude that the substance is biodegraded under environmental conditions. The observed biodegradation rates of hydrogen peroxide are high and half-lives are short enough to fulfil the criterion “readily biodegradable” (10-day window criterion fulfilled) concerning the degradation rate. Hydrogen peroxide can therefore be considered as readily biodegradable in the aquatic compartment including sewage treatment plant. The simulation test results show that in most cases biodegradation seems to be the dominant and rate determining degradation pathway of hydrogen peroxide in the aquatic environment. The rate of biodegradation is proportional to the microbial population density and the concentration of hydrogen peroxide. Typical natural concentrations of hydrogen peroxide in freshwater and sea are from a few micrograms to some tens of micrograms per litre. Degradation half-lives observed are typically of the order of some hours. The microorganism/hydrogen peroxide ratio is high and degradation is favoured because there is a substantially large amount of catalase active microbes present compared to the concentration of hydrogen peroxide. If the concentration of hydrogen peroxide is remarkably higher than natural concentrations, other factors remaining constant, the inhibitive effect of hydrogen peroxide on naturally occurring microbes is beginning to have more influence thus giving longer half-lives. In extreme cases the toxicity of hydrogen peroxide will slower the degradation process remarkably (test by L'Air Liquide 1991).

Shortest half-lives <<1d can be found in surface waters of eutrophic lakes. These tests are carried out in summer time in warm surface waters and do not represent very well average degradation rates in natural waters of more unfavourable conditions and seasons. Half-lives of 1-3 days may represent quite well annual average degradation rate in mesotrophic/oligotrophic surface waters with low microbial density. Longest half-lives can be found in oligotrophic cold

waters with low microbial density and low transition metal concentrations (Fe/Mn). A half-life of 5 days in surface water has been estimated to represent realistic (worst case) half-life in surface water.

As a conclusion half-lives of 2 minutes and 5 days in STP and in surface water, respectively, will be used in the risk assessment."

The biodegradation of the substance in sediment is of no relevance as hydrogen peroxide will not partition into sediments. The degradation of hydrogen peroxide in soil is expected to be fast in the presence of organic material with half-lives of a few minutes. However, degradation may be slower in soils with low bioactivity and a half-life of 12 hours for biodegradation in soil is considered as a reasonable worst case in the present assessment.

Biodegradation in water: screening tests
Biodegradation in water: readily biodegradable

The decomposition of hydrogen peroxide in municipal sewage sludge was rapid, resulting in a half-life of 2 minutes (Groeneveld and de Groot 1999). This value is conservative, since there was no adaptation of the sludge, and because 2 minutes is the maximum half-life observed in the test. Similar findings on the rapid decomposition of hydrogen peroxide were made in a simulation study by Larish and Duff (1997) in a laboratory-scale simulated STP for pulp and paper mill effluents. A half-life in the range of several minutes can be extracted from the data determined for 25°C and 20 - 200 mg activated sludge/L. However, the amounts of mixed liquor used in the tests were very low (10 mL) and the documentation is insufficient. Therefore, this study can only serve as additional information confirming the rapid biologically catalysed decomposition of hydrogen peroxide. Spain et al. (1989) determined degradation half-lives of maximally 6 minutes for hydrogen peroxide in microbial communities present in an infiltration gallery of a contaminated soil remediation site. Since microbial counts were in the range of those in sewage sludge, these tests provide additional information on ready biodegradability. All references demonstrated that degradation in sludge is mainly biologically mediated, since no degradation was observed in substrates deactivated by autoclaving and/or treatment with HgCl2. While the respiration of activated sludge can be reversibly inhibited by shock doses of hydrogen peroxide, it was also shown that adaptation to a concentration of 500 mg/L hydrogen peroxide led to increased resistance against shock dosing (Larish and Duff 1997). Hydrogen peroxide is therefore considered as readily biodegradable in sewage treatment plants, with a half-life of 2 minutes (rate constant of 21 h-1).

Biodegradation in water and sediment: simulation tests
According to the EU risk assessment report for hydrogen peroxide (European Commission 2003) a number of simulation tests on biodegradation are available. Degradation in lake water (Jacks Lake, Ontario) during summer time was studied (Cooper and Lean 1989). The lake was characterised as oligotrophic with a pH value of 7.2, a Ca2+ concentration of 14 mg/L, a mean phosphorous content of 0.012 mg/L and a DOC of 6 mg/L. The initial concentration of hydrogen peroxide in the lake water was 0.003 mg/L. Dark decay of the substance followed first order kinetics and the following half-lives were observed: 7.8 hours for unfiltered water, 8.6 hours for filtered water (5 micrometre), 31 hours for filtered water (1 micrometre) and >24 hours for filtered water (0.45 micrometre). It appeared from the results that the fraction containing pico plankton contained also the major portion of the biological agent degrading hydrogen peroxide. Hydrogen peroxide degradation was also measured in Lake Ontario (Cooper et al. 1989). The half-lives ranged from 14.7 to 21.6 hours. No degradation of hydrogen peroxide over a period of 7 hours was observed when water was filtered through 0.45 micrometre membranes. The dark decay time of hydrogen peroxide was also measured in sea water at room temperature (Johnson et al. 1989). The initial concentration of hydrogen peroxide was between 3 and 5 microgram/L. The degradation rate was 0.13 microgram/L/hour and hydrogen peroxide disappeared after 23 to 39 hours.

Biodegradation in soil
The following text was copied from the EU Risk Assessment Report (2003), pp. 34/35: "In soil H2O2 is normally a short-lived substance. Rapid degradation will occur due to high concentration of catalytic material like transition metals, enzymes, easily oxidised/reduced organic substances and living microbes (Spain et al. 1989). Hydrogen peroxide is used as a source of oxygen (for aerobic microbes) in polluted groundwater sites (enhanced bioremediation). Therefore specific information on degradability in soil is available. The problem in these applications where hydrogen peroxide is introduced directly into the ground is linked to a too rapid degradation. Observed half-lives of H2O2 in soil vary from 15 hours (soil without microbiological activity and few minerals) to several minutes (soils with 108-109 cells/g total solids, and in the presence of iron and manganese (Aggarwal et al. 1991, ECETOC 1993, Hinchee and Downey 1988, Pardieck et al. 1992). In the assessment it is estimated that the degradation half-life in soil is 12 hours." Though shorter half-lives are expected for the majority of soils, the half-life of 12 hours for degradation of hydrogen peroxide in soil will be considered as a reasonable worst case in the present assessment.

Bioaccumulative potential

Bioaccumulation

The following text is copied from the EU Risk Assessment Report for hydrogen peroxide (European Commission 2003, page 35): "There are no experimental results on bioaccumulation available. Hydrogen peroxide is reactive and short-lived polar substance and no bioaccumulation is expected. Also the estimated log Kow of about -1.5 indicates negligible potential of bioconcentration in aquatic organisms. BCFs calculated according to the TGD for fish and earthworm are low, 1.4 and 3.3, respectively." In addition, the enzyme catalase is almost ubiquitously distributed in biotic systems enabling organisms to convert hydrogen peroxide into water and oxygen. In consideration of these points, a bioconcentration test in fish or other aquatic organisms is deemed not necessary.

Bioaccumulation: aquatic / sediment

study scientifically not necessary / other information available

Bioaccumulation: terrestrial

study scientifically not necessary / other information available

Mobility in soil

Transport and Distribution

No experimental results were located concerning adsorption and desorption behaviour of hydrogen peroxide. Being highly soluble in water (in all proportions) and a highly polar substance, no remarkable adsorption to soil and sediment is expected for hydrogen peroxide and the mobility in soil is expected to be high. Modelling of the environmental distribution of hydrogen peroxide at equilibrium conditions using a Mackay Level 1 model indicate that the substance will partition into the aquatic compartment (99.98 %) at 20 °C and that negligible fractions will be found in the air, soil or sediment compartments. Using QSAR, a value for the Koc may be calculated: log Koc = 0.52*log Kow + 1.02 = 0.2 L/kg (TGD, QSAR for nonhydrophobics), which means a value for the Koc = 1.58 L/kg.

Adsorption / desorption

The modelled Koc = 1.58 L/kg indicates that hydrogen peroxide has no potential for adsorption.
No experimental results were located concerning adsorption and desorption behavior of hydrogen peroxide. Being highly soluble in water (in all proportions) and a highly polar substance, no remarkable adsorption to soil and sediment is expected for hydrogen peroxide and the mobility in soil is expected to be high. Modeling of the environmental distribution of hydrogen peroxide at equilibrium conditions using a Mackay Level 1 model indicate that the substance will partition into the aquatic compartment (99.98%) at 20 °C and that negligible fractions will be found in the air, soil or sediment compartments. Using QSAR, a value for the KOC may be calculated: log KOC = 0.52 * log KOW + 1.02 = 0.2 L/kg (TGD, QSAR for nonhydrophobics), which means a value for the KOC = 1.58 L/kg.

Henry's Law constant

Hydrogen peroxide is fully miscible with water. The low value for the Henry’s Law Constant of hydrogen peroxide of 7.5 x 10-4 Pa x m3 x mol-1 (Hwang and Dasgupta 1985) indicates that the substance has a low ability to volatilise from water. Indeed, hydrogen peroxide tends to evaporate to a much lesser extent from a mixture of water and hydrogen peroxide than the water (European Commission 2003).

Other adverse effects

Decomposes into oxygen and water. No adverse effects.

13 Disposal considerations

Disposal methods

Waste disposal recommendations

Dispose of waste and container in accordance with local and/or national regulations. Hazardous waste shall not be mixed together with other waste. Different types of hazardous waste shall not be mixed together if this may entail a risk of pollution or create problems for the further management of the waste. Hazardous waste shall be managed responsibly. All entities that store, transport or handle hazardous waste shall take the necessary measures to prevent risks of pollution or damage to people or animals. Recycle/reuse. Remove for physico-chemical/biological treatment. **DO NOT** discharge into drains or the environment.

Ecology - waste materials

DO NOT release to the environment.

Empty Container

Avoid reuse container. Triple rinse thoroughly before discarding in trash or return to supplier. Dispose of in accordance with local regulations. Drums - Empty as thoroughly as possible. **Avoid** contamination; impurities accelerate decomposition. **Never** return product to original container.

US EPA Waste Number

D001 D003

14 Transport information

UN Number

TRANSPORTATION CLASSIFICATION	ADR/RID	ADN(R)	IMDG	IATA
Identification Number	2014	2014	2014	FORBIDDEN
Proper Shipping Name	HYDROGEN PEROXIDE, AQUEOUS SOLUTION with >20% and <60% hydrogen peroxide (stabilized as necessary)	HYDROGEN PEROXIDE, AQUEOUS SOLUTION with >20% and <60% hydrogen peroxide (stabilized as necessary)	HYDROGEN PEROXIDE, AQUEOUS SOLUTION with >20% and <60% hydrogen peroxide (stabilized as necessary)	
Transport Hazard Class(es)	5.1(8) 	5.1(8) 	5.1(8) 	
Packing Group	II	II	II	
Classification code	OC1	OC1	N/A	
Special Provisions	Tunnel Restriction Code (ADR): (E)	N/A	N/A	
Environmental Hazards				
Emergency Response	ERG: 140	N/A	EMS: F-S, S-Q	
Additional Information	None	None	None	

UN Proper Shipping Name

HYDROGEN PEROXIDE, AQUEOUS SOLUTION with >20% and <60% hydrogen peroxide (stabilized as necessary)

Transport hazard class(es)

5.1(8)

Packing group, if applicable

II **Exempt quantity** 20Kg **Factor** 50

Environmental hazards

Not expected to have significant environmental effects. Prevent product from entering water sources.

Special precautions for user

DO NOT load with Classes 1, 2, 3, 6.1 and 6.2.
May be loaded with Classes 3, 4.1, 4.2, 4.3 and 8B if kept at least 1 metre apart.
Can be loaded with all other classes.
Goods of different classes **must** be segregated by an air space of at least 100mm or by an approved segregation device or non-dangerous goods.

P, B, L and O provisions as per SANS 10231:2006

L24
Before loading, vehicles and containers shall be thoroughly cleaned and in particular be free of any combustible debris (straw, hay, paper, etc.). The use of flammable materials for stowing packages is prohibited.

ICAO/IATA Hydrogen peroxide (>40%) is forbidden on Passenger and Cargo Aircraft. Air regulation permit shipment of Hydrogen Peroxide (<=40%) in non-vented containers for Air Cargo Only aircraft, as well as for Passenger and Cargo aircraft. HOWEVER, all Hydrogen Peroxide containers are vented and therefore, air shipments of H_2O_2 are not permitted. IATA air regulations state that venting of packages containing oxidizing substances is not permitted for air transport.

OTHER INFORMATION
Protect from physical damage. Keep drums in upright position. Drums should not be stacked in transit. **DO NOT** store drums on wooden pallets.

Transport in bulk according to Annex II of MARPOL 73/78 and the IBC Code

Not applicable.

15 Regulatory information

Safety, health and environmental regulations specific for the product in question

SA NATIONAL LEGISLATION
Hazardous Substances Act 15 of 1973 and Regulations.
Occupational Health and Safety Act 85 of 1993 and Regulations.

SA NATIONAL STANDARDS
SANS 10228 : 2006 : Identification and Classification of Dangerous Goods for Transport by Road and Rail.
SANS 10231 : 2018 : Transport of dangerous goods - Operational requirements for road vehicles.
SANS 10234 : 2008 : Globally Harmonized System of classification and labelling of chemicals (GHS).
SANS 11014 : 2010 : Safety Data Sheets for chemical Products.

REACH Regulation (EC) No 1907/2006
This product contains only components that have been either pre-registered, registered, are exempt from registration, are regarded as registered or are not subject to registration according to Regulation (EC) No. 1907/2006 (REACH)., The aforementioned indications of the REACH registration status are provided in good faith and believed to be accurate as of the effective date shown above. However, no warranty, express or implied, is given. It is the buyer´s/user´s responsibility to ensure that his/her understanding of the regulatory status of this product is correct.

Seveso III: Directive 2012/18/EU
Listed in Regulation: Not applicable

U.S. Federal Regulations
SARA 313
Section 313 of Title III of the Superfund Amendments and Reauthorization Act of 1986 (SARA). This product does not contain any chemicals which are subject to the reporting requirements of the Act and Title 40 of the Code of Federal Regulations, Part 372

SARA 311/312

Hazard Categories	
Acute health hazard	Yes
Chronic health hazard	No
Fire hazard	Yes
Sudden release of pressure hazard	No
Reactive Hazard	No

Clean Water Act
This product does not contain any substances regulated as pollutants pursuant to the Clean Water Act (40 CFR 122.21 and 40 CFR 122.42)

CERCLA
Extremely Hazardous Substances RQs 1000lb

Hydrogen Peroxide RQ is for concentrations of > 52% only.

International Inventories

Component	TSCA - United States	DSL - Canada	EINECS/ELINCS - Europe
Hydrogen peroxide 7722-84-1 (50%)	X	X	X
	ENCS - Japan	IECSC - China	KECL - Korea
	X	X	X
	PICCS - Philippines	AICS - Australia	NZIoC - New Zealand
	X	X	X

Chemical safety report (CSR)
Performed for this substance: Yes

16 Other information

Other information

Full text of H & P - Statements referred to under section 2
Hazard statements

H271	May cause fire or explosion; strong oxidizer.
H302	Harmful if swallowed.
H314	Causes severe skin burns and eye damage.
H332	Harmful if inhaled.
H335	May cause respiratory irritation.
H412	Harmful to aquatic life with long lasting effects.

Precautionary statements

P210+P220	Keep away from heat/sparks/open flames/hot surfaces. — No smoking. Keep/Store away from clothing/combustible materials.
P260	Do not breathe dust/fume/gas/mist/vapours/spray.
P264	Wash thoroughly after handling.
P270	Do not eat, drink or smoke when using this product.
P271	Use only outdoors or in a well-ventilated area.
P280	Wear protective gloves/protective clothing/eye protection/face protection.
P283	Wear fire/flame resistant/retardant clothing.
P301+P330+P331	IF SWALLOWED: Rinse mouth. Do NOT induce vomiting.
P301+P312	IF SWALLOWED: call a POISON CENTER or doctor/physician IF you feel unwell.
P303+P361+P353	IF ON SKIN (or hair): Remove/Take off Immediately all contaminated clothing. Rinse SKIN with water/shower.
P304+P340	IF INHALED: Remove victim to fresh air and Keep at rest in a position comfortable for breathing.
P305+P351+P338	IF IN EYES: Rinse cautiously with water for several minutes. Remove contact lenses, if present and easy to do. Continue rinsing.
P306+P360	IF ON CLOTHING: Rinse Immediately contaminated CLOTHING and SKIN with plenty of water before removing clothes.
P337+P313	IF eye irritation persists: Get medical advice/attention.
P310	Immediately call a POISON CENTER or doctor/physician.
P321	Specific treatment (see P330+P351+P353 on this label).
P330	Rinse mouth.
P363	Wash contaminated clothing before reuse.
P370+P378	In case of fire: Use water to extinguish.
P371+P380+P375	In case of major fire and large quantities: Evacuate area. Fight fire remotely due to the risk of explosion.
P403+P233	Store in a well-ventilated place. Keep container tightly closed.
P405	Store locked up.
P420	Store away from other materials.
P501	Dispose of contents and container in accordance with local, regional, national, international regulations.

Labelling REGULATION (EC) No 1272/2008
Signal Word
Danger
Pictograms Hazard to Human

GHS03	Oxidizing hazard
GHS05	Corrosive hazard
GHS07	Health hazard

Pictogram Hazard during Transport

Class 5.1	Oxidizing substance
Class 8	Corrosive substance

Training advice
Provide adequate information, instruction and training for operators.

Information Sources

1. ECHA https://echa.europa.eu/de/registration-dossier/-/registered-dossier/15701/1
2. National Center for Biotechnology Information. PubChem Database. Hydrogen peroxide, CID=784, https://pubchem.ncbi.nlm.nih.gov/compound/784 (accessed on Apr. 21, 2019)
3. ILO - International Labour Organisation https://www.ilo.org/dyn/icsc/showcard.display?p_card_id=0164
4. CDC The National Institute for Occupational Safety and Health (NIOSH) https://www.cdc.gov/niosh-rtecs/MXDBBA0.html
5. Preventize - Safety Consulting https://www.hazmattool.com/info.php?a=Hydrogen%2C+peroxide%2C+aqueous+solutions+with+more+than+40+percent+but+not+more+than+60+percent+hydrogen+peroxide+%28stabilized+as+necessary%29&b=UN2014&c=5.1

Compiled by Aquatrade Water Treatment Chemicals (Pty) Ltd, R. van Rooyen, SHEQ Co-ordinator and E. Le Sar, Director.

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Revision History

Revision	Date	Change
1.0	2019/04/21	Preparation of the safety data sheet according to SANS 11014:2010