Phenolphthalein

sc-206050

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

PRODUCT NAME
Phenolphthalein

STATEMENT OF HAZARDOUS NATURE

NFPA

SUPPLIER
Company: Santa Cruz Biotechnology, Inc.
Address: 2145 Delaware Ave
Santa Cruz, CA 95060
Telephone: 800.457.3801 or 831.457.3800
Emergency Tel: CHEMWATCH: From within the US and Canada: 877-715-9305
Emergency Tel: From outside the US and Canada: +800 2436 2255
(1-800-CHEMCALL) or call +613 9573 3112

PRODUCT USE
Acid-base indicator useful in the pH range 8.2 (colourless) to 10 (violet red); laxative (cathartic) present in many over-the-counter products; laboratory reagent.

SYNONYMS
C20-H14-O4, "pH indicator", "3, 3-bis(hydroxyphenyl)-1-(3H)-isobenzofuranone", "3, 3-bis(p-hydroxyphenyl)phthalide", "3, 3-bis(4-hydroxyphenyl)phthalide", Chocolax, Darmol, Laxin, Laxettes, "APS UL00002656", "Merck 20088, 20089", "Hach 2545"

Section 2 - HAZARDS IDENTIFICATION

CHEMWATCH HAZARD RATINGS

<table>
<thead>
<tr>
<th>Hazard</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flammability</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Toxicity</td>
<td>2</td>
<td></td>
</tr>
<tr>
<td>Body Contact</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Reactivity</td>
<td>1</td>
<td></td>
</tr>
<tr>
<td>Chronic</td>
<td>3</td>
<td></td>
</tr>
</tbody>
</table>

CANADIAN WHMIS SYMBOLS
Phenolphthalein is used as a laxative. Large doses phenolphthalein and related substances cause nausea, vomiting and diarrhoea. No systemic toxicity has been reported after oral doses except for occasional allergic reactions. Several acute reactions to oral doses have been reported with various types of skin rash described, in some cases followed by persistent pigmentation. Signs of systemic lupus erythematosus have been also been ascribed to phenolphthalein. In one fatal case a child developed cerebral and pulmonary oedema and became comatose following the ingestion of 600 mg of the laxative in chocolate. In another case a 35 year old man developed hypothermia, hypotension, severe acidosis, oedema and oliguria after ingesting a dose of 2 gm in chocolate. If urine or faeces is alkaline it may acquire a red colour; this is not blood.

Phenolphthalein has been widely used as a laxative for many years. The usual dose for an adult is 30-195 mg, although doses of several grams may be swallowed without serious symptoms. In most people ingested phenolphthalein can cause diarrhoea but no other problems. A rare but potentially serious allergic reaction may occur with some people using laxatives but these effects are generally not relevant to occupational exposure to phenolphthalein. (CCINFO)

Abuse of phenolphthalein-containing laxatives (for weight loss), has been associated with gastrointestinal bleeding and iron deficient anaemia, acute pancreatitis, and multiple organ damage in cases of massive overdosage, including fulminant hepatic failure and disseminated intravascular coagulation.

In one study over fifteen per cent of the patients (177) in a gastroenterologic clinic employed phenolphthalein as a habitual laxative. In a large percentage (152) a diagnosis of catarrhal colitis was made. A small percentage (22) had established a tolerance for the drug and exhibited no signs of toxicity. Chronic stomatitis was present in three patients addicted to the drug. In industrial situations, long-term, repeated exposure to high levels of dust will lead to chronic non-specific lung disease (ILO Encyclopaedia).

Indiscriminate use of phenolphthalein results in chronic constipation and laxative dependence, loss of normal bowel function, and bowel irritation. Habitual use over several years may cause a "cathartic colon", i.e., a poorly functioning, atonic dilation of the colon, especially of the right side, resulting in extensive bowel retention. This condition resembles chronic ulcerative colitis both radiologically and pathologically, involves thinning of the intestinal wall and loss of the normal mucosal pattern of the terminal ileum. Long term use or overdose have been associated,
anecdotally, with abdominal pain, diarrhoea, electrolyte imbalance (hypokalaemia, hypocalcaemia, and/or metabolic acidosis or alkalosis), dehydration, malabsorption, protein-losing gastroenteropathy, steatorrhea, anorexia, weight loss, polydipsia, polyuria, cardiac arrhythmias, muscle weakness, prostration and histopathologic lesions. Kidney, muscle, and central nervous system disturbances may be due to electrolyte imbalance. Hypokalaemia contributes to kidney dysfunction associated with rhabdomyolysis (muscle wasting).

Phenolphthalein allergy is often manifested by inflammatory reactions of the skin. In extreme cases recurrences involve progressively more severe lesions characterised by bullous erythema multiforme, with focal haemorrhage and necrosis. Cross-sensitivity reactions in individuals previously sensitised by phthalic anhydride and its congeners, might be the subject of speculation.

Phenolphthalein has weak oestrogenic activity, in fashion similar to that said to be exerted by other phthalates. Phenolphthalein competes with oestrogen for binding sites on cultured MCF-7 human breast cancer cells.

In a study conducted in Melbourne, Australia, with 1408 subjects, there was no statistically significant increased risk of colorectal cancer in phenolphthalein laxative users (Kune, 1993).

Under the conditions of a 2-year feed study using male rats, there was clear evidence of carcinogenic activity based on a marked increased in the incidence of benign pheochromocytomas of the adrenal medulla, and of renal tubule adenomas, and adenomas or carcinomas (combined). There was some evidence of carcinogenic activity of phenolphthalein in female rats. There was clear evidence in male mice of carcinogenic activity based on increased incidences of histiocytic sarcomas and of malignant lymphomas of thymic origin. In female mice there was also clear evidence of carcinogenic activity based on increased incidences of histiocytic sarcomas, malignant tumours of all types, lymphomas of thymic origin, and benign sex-cord stromal tumours of the ovary.

National Toxicological Program, Technical Reports Series, No. 465, 1996

Phenolphthalein causes enhanced oxygen radical production in in vitro systems. In vivo, reduction of phenoxy radicals could allow reformation of phenolphthalein, establishing a futile cycle of oxidation and reduction, thereby generating more free radical species. Thus, phenolphthalein may be a significant source of oxidative stress in physiological systems.

Abnormal sperm were induced in male mice, but not male rats, treated with phenolphthalein via dosed feed for 13 weeks.

In a mouse carcinogenicity bioassay phenolphthalein produced evidence of carcinogenic effects with significant increases in histiocytic sarcoma and malignant lymphoma. Benign ovary tumours were significantly increased in all treatment groups.

Phenolphthalein induces a significant increase in the frequency of chromosome aberrations in human cells. The lowest dose level at which the clastogenic effect is evident is 23 ug/ml. Similar positive results were obtained in a Chinese hamster liver cell line, which is metabolically competent to activate different classes of promutagens and procarcinogens into biologically active metabolites. Instead, parallel experiments in Chinese hamster ovary cells did not show any clastogenic effect due to phenolphthalein. These latter data suggested that phenolphthalein acts as a promutagen and must be metabolically activated to exert its clastogenic effect. Teratogenesis Carcinog. Mutagen. 20:209-217, 2000.

Extended use of purgatives and laxatives can cause a profuse, watery diarrhea with severe dehydration, mineral losses, weakness and weight loss. Absorption from the bowel may become impaired and damage to the heart and kidneys can also occur.

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Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

<table>
<thead>
<tr>
<th>NAME</th>
<th>CAS RN</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>phenolphthalein</td>
<td>77-09-8</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

Section 4 - FIRST AID MEASURES

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

EYE
- If this product comes in contact with the eyes:
  - Wash out immediately with fresh running water.
  - Ensure complete irrigation of the eye by keeping eyelids apart and away from eye and moving the eyelids by occasionally lifting the upper and lower lids.
  - If pain persists or recurs seek medical attention.
  - Removal of contact lenses after an eye injury should only be undertaken by skilled personnel.

SKIN
- If skin contact occurs:
  - Immediately remove all contaminated clothing, including footwear.
  - Flush skin and hair with running water (and soap if available).
  - Seek medical attention in event of irritation.

INHALED
- If dust is inhaled, remove from contaminated area.
- Encourage patient to blow nose to ensure clear passage of breathing.
- If irritation or discomfort persists seek medical attention.
Section 5 - FIRE FIGHTING MEASURES

<table>
<thead>
<tr>
<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vapour Pressure (mmHG)</td>
<td>Negligible</td>
</tr>
<tr>
<td>Upper Explosive Limit (%)</td>
<td>Not applicable</td>
</tr>
<tr>
<td>Specific Gravity (water=1)</td>
<td>1.28 - 1.30</td>
</tr>
<tr>
<td>Lower Explosive Limit (%)</td>
<td>Not applicable</td>
</tr>
</tbody>
</table>

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

FIRE FIGHTING
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves for fire only.
- Prevent, by any means available, spillage from entering drains or water course.
- Use fire fighting procedures suitable for surrounding area.
- Do not approach containers suspected to be hot.
- Cool fire exposed containers with water spray from a protected location.
- If safe to do so, remove containers from path of fire.
- Equipment should be thoroughly decontaminated after use.

GENERAL FIRE HAZARDS/HAZARDOUS COMBUSTIBLE PRODUCTS
- Combustible solid which burns but propagates flame with difficulty.
- Avoid generating dust, particularly clouds of dust in a confined or unventilated space as dusts may form an explosive mixture with air, and any source of ignition, i.e. flame or spark, will cause fire or explosion. Dust clouds generated by the fine grinding of the solid are a particular hazard; accumulations of fine dust may burn rapidly and fiercely if ignited.
- Dry dust can be charged electrostatically by turbulence, pneumatic transport, pouring, in exhaust ducts and during transport.
- Build-up of electrostatic charge may be prevented by bonding and grounding.
- Powder handling equipment such as dust collectors, dryers and mills may require additional protection measures such as explosion venting.
- Combustion products include: carbon monoxide (CO), carbon dioxide (CO2), other pyrolysis products typical of burning organic material. May emit clouds of acrid smoke.
- May emit poisonous fumes.
- May emit corrosive fumes.

FIRE INCOMPATIBILITY
- Avoid contamination with oxidizing agents i.e. nitrates, oxidizing acids, chlorine bleaches, pool chlorine etc. as ignition may result.

PERSONAL PROTECTION
- Glasses:
  Chemical goggles.
- Gloves:
  1. NATURAL RUBBER 2. NEOPRENE
- Respirator:
  Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS
- Clean up waste regularly and abnormal spills immediately.
- Avoid breathing dust and contact with skin and eyes.
- Wear protective clothing, gloves, safety glasses and dust respirator.
- Use dry clean up procedures and avoid generating dust.
- Vacuum up or sweep up. NOTE: Vacuum cleaner must be fitted with an exhaust micro filter (HEPA type) (consider explosion-proof machines designed to be grounded during storage and use).
- Dampen with water to prevent dusting before sweeping.
- Place in suitable containers for disposal.

MAJOR SPILLS
- Clear area of personnel and move upwind.
- Alert Emergency Responders and tell them location and nature of hazard.
- Wear full body protective clothing with breathing apparatus.
- Prevent, by all means available, spillage from entering drains or water courses.
Consider evacuation (or protect in place).
No smoking, naked lights or ignition sources.
Increase ventilation.
Stop leak if safe to do so.
Water spray or fog may be used to disperse / absorb vapour.
Contain or absorb spill with sand, earth or vermiculite.
Collect recoverable product into labelled containers for recycling.
Collect solid residues and seal in labelled drums for disposal.
Wash area and prevent runoff into drains.
After clean up operations, decontaminate and launder all protective clothing and equipment before storing and re-using.
If contamination of drains or waterways occurs, advise emergency services.

PROTECTIVE ACTIONS FOR SPILL

From US Emergency Response Guide 2000
Guide No guide found.

From IERG (Canada/Australia)

Isolation Distance

Downwind Protection Distance

FOOTNOTES
1 PROTECTIVE ACTION ZONE is defined as the area in which people are at risk of harmful exposure. This zone assumes that random changes in wind direction confines the vapour plume to an area within 30 degrees on either side of the predominant wind direction, resulting in a crosswind protective action distance equal to the downwind protective action distance.
2 PROTECTIVE ACTIONS should be initiated to the extent possible, beginning with those closest to the spill and working away from the site in the downwind direction. Within the protective action zone a level of vapour concentration may exist resulting in nearly all unprotected persons becoming incapacitated and unable to take protective action and/or incurring serious or irreversible health effects.
3 INITIAL ISOLATION ZONE is determined as an area, including upwind of the incident, within which a high probability of localised wind reversal may expose nearly all persons without appropriate protection to life-threatening concentrations of the material.
4 SMALL SPILLS involve a leaking package of 200 litres (55 US gallons) or less, such as a drum (jerican or box with inner containers). Larger packages leaking less than 200 litres and compressed gas leaking from a small cylinder are also considered "small spills". LARGE SPILLS involve many small leaking packages or a leaking package of greater than 200 litres, such as a cargo tank, portable tank or a "one-tonne" compressed gas cylinder.
5 Guide No guide found. is taken from the US DOT emergency response guide book.
6 IERG information is derived from CANUTEC - Transport Canada.

ACUTE EXPOSURE GUIDELINE LEVELS (AEGL) (in ppm)
AEGL 1: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience notable discomfort, irritation, or certain asymptomatic nonsensory effects. However, the effects are not disabling and are transient and reversible upon cessation of exposure.
AEGL 2: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience irreversible or other serious, long-lasting adverse health effects or an impaired ability to escape.
AEGL 3: The airborne concentration of a substance above which it is predicted that the general population, including susceptible individuals, could experience life-threatening health effects or death.

Section 7 - HANDLING AND STORAGE

PROCEDURE FOR HANDLING

Avoid all personal contact, including inhalation.
Wear protective clothing when risk of exposure occurs.
Use in a well-ventilated area.
Prevent concentration in hollows and sumps.
DO NOT enter confined spaces until atmosphere has been checked.
DO NOT allow material to contact humans, exposed food or food utensils.
Avoid contact with incompatible materials.
When handling, DO NOT eat, drink or smoke.
Keep containers securely sealed when not in use.
Avoid physical damage to containers.
Always wash hands with soap and water after handling.
Work clothes should be laundered separately.
Launder contaminated clothing before re-use.
Use good occupational work practice.
Observe manufacturer's storing and handling recommendations.
Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.
In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

- Polyethylene or polypropylene container.
- Check all containers are clearly labelled and free from leaks.

STORAGE REQUIREMENTS

- Store in original containers.
- Keep containers securely sealed.
- Store in a cool, dry, well-ventilated area.
- Store away from incompatible materials and foodstuff containers.
- Protect containers against physical damage and check regularly for leaks.
- Observe manufacturer's storing and handling recommendations.

SAFE STORAGE WITH OTHER CLASSIFIED CHEMICALS

| X | X | + | X | X | + |

X: Must not be stored together
O: May be stored together with specific precautions
+: May be stored together

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

ENDOELTABLE

<table>
<thead>
<tr>
<th>Source</th>
<th>Material</th>
<th>TWA mg/m³</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>US - Oregon Permissible Exposure Limits (Z-3)</td>
<td>phenolphthalein (Inert or Nuisance Dust: Total dust)</td>
<td>10</td>
<td>(d)</td>
</tr>
<tr>
<td>US OSHA Permissible Exposure Levels (PELs) - Table Z3</td>
<td>phenolphthalein (Inert or Nuisance Dust: (d) Respirable fraction)</td>
<td>5</td>
<td></td>
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<tr>
<td>US OSHA Permissible Exposure Levels (PELs) - Table Z3</td>
<td>phenolphthalein (Inert or Nuisance Dust: (d) Total dust)</td>
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<tr>
<td>US - Hawaii Air Contaminant Limits</td>
<td>phenolphthalein (Particulates not other wise regulated - Total dust)</td>
<td>10</td>
<td></td>
</tr>
<tr>
<td>US - Hawaii Air Contaminant Limits</td>
<td>phenolphthalein (Particulates not other wise regulated - Respirable fraction)</td>
<td>5</td>
<td></td>
</tr>
<tr>
<td>US - Oregon Permissible Exposure Limits (Z-3)</td>
<td>phenolphthalein (Inert or Nuisance Dust: Respirable fraction)</td>
<td>5</td>
<td>(d)</td>
</tr>
<tr>
<td>US ACGIH Threshold Limit Values (TLV)</td>
<td>phenolphthalein (Particles (Insoluble or Poorly Soluble) [NOS] Inhalable particles)</td>
<td>10</td>
<td>See Appendix B current TLV/BEI Book</td>
</tr>
</tbody>
</table>
MATERIAL DATA

PHENOLPHTHALEIN:
■ It is the goal of the ACGIH (and other Agencies) to recommend TLVs (or their equivalent) for all substances for which there is evidence of health effects at airborne concentrations encountered in the workplace. At this time no TLV has been established, even though this material may produce adverse health effects (as evidenced in animal experiments or clinical experience). Airborne concentrations must be maintained as low as is practically possible and occupational exposure must be kept to a minimum.

NOTE: The ACGIH occupational exposure standard for Particles Not Otherwise Specified (P.N.O.S) does NOT apply.

PERSONAL PROTECTION

Consult your EHS staff for recommendations

EYE
■ Safety glasses with side shields.
■ Chemical goggles.
■ Contact lenses pose a special hazard; soft lenses may absorb irritants and all lenses concentrate them. DO NOT wear contact lenses.

HANDS/FEET
■ NOTE: The material may produce skin sensitization in predisposed individuals. Care must be taken, when removing gloves and other protective equipment, to avoid all possible skin contact. Suitability and durability of glove type is dependent on usage. Important factors in the selection of gloves include: such as:
   ■ frequency and duration of contact,
   ■ chemical resistance of glove material,
   ■ glove thickness and
   ■ dexterity
Select gloves tested to a relevant standard (e.g. Europe EN 374, US F739).
■ When prolonged or frequently repeated contact may occur, a glove with a protection class of 5 or higher (breakthrough time greater than 240 minutes according to EN 374) is recommended.
■ When only brief contact is expected, a glove with a protection class of 3 or higher (breakthrough time greater than 60 minutes according to EN 374) is recommended.
■ Contaminated gloves should be replaced.
Gloves must only be worn on clean hands. After using gloves, hands should be washed and dried thoroughly. Application of a non-perfumed moisturiser is recommended.
Experience indicates that the following polymers are suitable as glove materials for protection against undissolved, dry solids, where abrasive particles are not present.
■ polychloroprene
■ nitrile rubber
■ butyl rubber
■ fluorocaoutchouc
■ polyvinyl chloride
Gloves should be examined for wear and/ or degradation constantly.

OTHER
■ Employees working with confirmed human carcinogens should be provided with, and be required to wear, clean, full body protective clothing (smocks, coveralls, or long-sleeved shirt and pants), shoe covers and gloves prior to entering the regulated area.
■ Employees engaged in handling operations involving carcinogens should be provided with, and required to wear and use half-face filter-type respirators with filters for dusts, mists and fumes, or air purifying canisters or cartridges. A respirator affording higher levels of protection may be substituted.
■ Emergency deluge showers and eyewash fountains, supplied with potable water, should be located near, within sight of, and on the same level with locations where direct exposure is likely.
■ Prior to each exit from an area containing confirmed human carcinogens, employees should be required to remove and leave protective clothing and equipment at the point of exit and at the last exit of the day, to place used clothing and equipment in impervious containers at the point of exit for purposes of decontamination or disposal. The contents of such impervious containers must be identified with suitable
labels. For maintenance and decontamination activities, authorized employees entering the area should wear clean, impervious garments, including gloves, boots and continuous-air supplied hood.

- Prior to removing protective garments the employee should undergo decontamination and be required to shower upon removal of the garments and hood.
- Overalls.
- P.V.C. apron.
- Barrier cream.
- Skin cleansing cream.
- Eye wash unit.

**RESPIRATOR**

- Respirators may be necessary when engineering and administrative controls do not adequately prevent exposures.
- The decision to use respiratory protection should be based on professional judgment that takes into account toxicity information, exposure measurement data, and frequency and likelihood of the worker's exposure - ensure users are not subject to high thermal loads which may result in heat stress or distress due to personal protective equipment (powered, positive flow, full face apparatus may be an option).
- Published occupational exposure limits, where they exist, will assist in determining the adequacy of the selected respiratory. These may be government mandated or vendor recommended.
- Certified respirators will be useful for protecting workers from inhalation of particulates when properly selected and fit tested as part of a complete respiratory protection program.
- Use approved positive flow mask if significant quantities of dust becomes airborne.
- Try to avoid creating dust conditions.

**GLOVE SELECTION INDEX**

- Glove selection is based on a modified presentation of the: "Forsberg Clothing Performance Index".
- The effect(s) of the following substance(s) are taken into account in the computer-generated selection: phenolphthalein
- Protective Material CPI *

<table>
<thead>
<tr>
<th>Material</th>
<th>CPI</th>
</tr>
</thead>
<tbody>
<tr>
<td>NATURAL RUBBER</td>
<td>A</td>
</tr>
<tr>
<td>NEOPRENE</td>
<td>A</td>
</tr>
<tr>
<td>NITRILE</td>
<td>A</td>
</tr>
<tr>
<td>PVC</td>
<td>A</td>
</tr>
</tbody>
</table>

* CPI - Chemwatch Performance Index

A: Best Selection
B: Satisfactory; may degrade after 4 hours continuous immersion
C: Poor to Dangerous Choice for other than short term immersion

**NOTE:** As a series of factors will influence the actual performance of the glove, a final selection must be based on detailed observation.

* Where the glove is to be used on a short term, casual or infrequent basis, factors such as "feel" or convenience (e.g. disposability), may dictate a choice of gloves which might otherwise be unsuitable following long-term or frequent use. A qualified practitioner should be consulted.

**RESPIRATOR**

<table>
<thead>
<tr>
<th>Protection Factor</th>
<th>Half-Face Respirator</th>
<th>Full-Face Respirator</th>
<th>Powered Air Respirator</th>
</tr>
</thead>
<tbody>
<tr>
<td>10 x PEL</td>
<td>P1</td>
<td>-</td>
<td>PAPR-P1</td>
</tr>
<tr>
<td>50 x PEL</td>
<td>Air-line*</td>
<td>P2</td>
<td>PAPR-P2</td>
</tr>
<tr>
<td>100 x PEL</td>
<td>Air-line**</td>
<td>P3</td>
<td>-</td>
</tr>
<tr>
<td>100+ x PEL</td>
<td>Air-line*</td>
<td>Air-line**</td>
<td>PAPR-P3</td>
</tr>
</tbody>
</table>

* - Negative pressure demand ** - Continuous flow

Explanation of Respirator Codes:
Class 1 low to medium absorption capacity filters.
Class 2 medium absorption capacity filters.
Class 3 high absorption capacity filters.
PAPR Powered Air Purifying Respirator (positive pressure) cartridge.
Type A for use against certain organic gases and vapors.
Type AX for use against low boiling point organic compounds (less than 65ºC).
Type B for use against certain inorganic gases and other acid gases and vapors.
Type E for use against sulfur dioxide and other acid gases and vapors.
Type K for use against ammonia and organic ammonia derivatives
Class P1 intended for use against mechanically generated particulates of sizes most commonly encountered in industry, e.g. asbestos, silica.
Class P2 intended for use against both mechanically and thermally generated particulates, e.g. metal fume.
Class P3 intended for use against all particulates containing highly toxic materials, e.g. beryllium.
The local concentration of material, quantity and conditions of use determine the type of personal protective equipment required.

Use appropriate NIOSH-certified respirator based on informed professional judgement. In conditions where no reasonable estimate of exposure can be made, assume the exposure is in a concentration IDLH and use NIOSH-certified full face pressure demand SCBA with a
minimum service life of 30 minutes, or a combination full facepiece pressure demand SAR with auxiliary self-contained air supply. Respirators provided only for escape from IDLH atmospheres shall be NIOSH-certified for escape from the atmosphere in which they will be used.

ENGINEERING CONTROLS

- Employees exposed to confirmed human carcinogens should be authorized to do so by the employer, and work in a regulated area.
- Work should be undertaken in an isolated system such as a “glove-box”. Employees should wash their hands and arms upon completion of the assigned task and before engaging in other activities not associated with the isolated system.
- Within regulated areas, the carcinogen should be stored in sealed containers, or enclosed in a closed system, including piping systems, with any sample ports or openings closed while the carcinogens are contained within.
- Open-vessel systems are prohibited.
- Each operation should be provided with continuous local exhaust ventilation so that air movement is always from ordinary work areas to the operation.
- Exhaust air should not be discharged to regulated areas, non-regulated areas or the external environment unless decontaminated. Clean make-up air should be introduced in sufficient volume to maintain correct operation of the local exhaust system.
- For maintenance and decontamination activities, authorized employees entering the area should be provided with and required to wear clean, impervious garments, including gloves, boots and continuous-air supplied hood. Prior to removing protective garments the employee should undergo decontamination and be required to shower upon removal of the garments and hood.
- Except for outdoor systems, regulated areas should be maintained under negative pressure (with respect to non-regulated areas).
- Local exhaust ventilation requires make-up air be supplied in equal volumes to replaced air.
- Laboratory hoods must be designed and maintained so as to draw air inward at an average linear face velocity of 150 feet/min. with a minimum of 125 feet/min. Design and construction of the fume hood requires that insertion of any portion of the employees body, other than hands and arms, be disallowed.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES
Solid.
Does not mix with water.
Solvents in water:

<table>
<thead>
<tr>
<th>State</th>
<th>Divided solid</th>
<th>Molecular Weight</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melting Range (°F)</td>
<td>496.4-505.4</td>
<td>Viscosity</td>
</tr>
<tr>
<td>Boiling Range (°F)</td>
<td>(decomp)</td>
<td>Solubility in water (g/L)</td>
</tr>
<tr>
<td>Flash Point (°F)</td>
<td>Not applicable</td>
<td>pH (1% solution)</td>
</tr>
<tr>
<td>Decomposition Temp (°F)</td>
<td>Not available.</td>
<td>pH (as supplied)</td>
</tr>
<tr>
<td>Autoignition Temp (°F)</td>
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<td>Vapour Pressure (mmHG)</td>
</tr>
<tr>
<td>Upper Explosive Limit (%)</td>
<td>Not applicable</td>
<td>Specific Gravity (water=1)</td>
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<tr>
<td>Lower Explosive Limit (%)</td>
<td>Not applicable</td>
<td>Relative Vapor Density (air=1)</td>
</tr>
<tr>
<td>Volatile Component (%vol)</td>
<td>Not available</td>
<td>Evaporation Rate</td>
</tr>
</tbody>
</table>

APPEARANCE
White to off-white minute odourless crystals; practically insoluble in water. Soluble in acetone, toluene and moderately soluble in alcohol. Slightly soluble in chloroform. Insoluble in petroleum ether.

Section 10 - CHEMICAL STABILITY

CONDITIONS CONTRIBUTING TO INSTABILITY
- Presence of incompatible materials.
- Product is considered stable.
- Hazardous polymerization will not occur.

STORAGE INCOMPATIBILITY
Avoid reaction with oxidizing agents.

For incompatible materials - refer to Section 7 - Handling and Storage.

Section 11 - TOXICOLOGICAL INFORMATION

PHENOLPHTHALEIN

TOXICITY AND IRRITATION
- unless otherwise specified data extracted from RTECS - Register of Toxic Effects of Chemical Substances.

TOXICITY

<p>| |</p>
<table>
<thead>
<tr>
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<tbody>
<tr>
<td>IRITATION</td>
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</tbody>
</table>

9 of 12
Phenolphthalein is absorbed in the small bowel and is conjugated in the liver to form phenolphthalein glucuronide, which is eliminated in the bile. As it passes through the small intestine, it is partially deconjugated and reabsorbed. Phenolphthalein and its glucuronide enhance oxygen radical production and cause oxidative damage in vitro. Phenolphthalein has also been shown to have low oestrogenic activity in some model systems. Phenolphthalein induced micronucleated erythrocytes in mice given multiple but not single treatments by gavage or in feed. Abnormal spermatozoa were induced in male mice but not male rats treated with phenolphthalein in the feed for 13 weeks. The malignant thymic lymphomas induced by phenolphthalein in female heterozygous p53-deficient mice showed loss of the normal p53 allele.

Phenolphthalein induced chromosomal aberrations, Hprt gene mutations and morphological transformation but not aneuploidy or ouabain-resistant mutations or sister chromatid exchange in cultured mammalian cells. It did not induce gene mutations in bacteria.

The main target organ for the toxic effects of phenolphthalein is reported to be the intestine. Indiscriminate use of phenolphthalein results in chronic constipation and laxative dependence, loss of normal bowel function and bowel irritation. Habitual use for several years may cause a "cathartic colon", i.e. a poorly functioning colon with atonic dilatation, especially on the right side, resulting in extensive retention of the bowel contents. The clinical condition, which resembles chronic ulcerative colitis both radiologically and pathologically, involves thinning of the intestinal wall and loss of the normal pattern of the submucosal plexus. Anecdotal cases of long-term use or overdose of phenolphthalein have been associated with abdominal pain, diarrhea, vomiting, electrolyte imbalance (hypokalaemia, hypocapniaemia and/or metabolic acidosis or alkalosis), dehydration, malabsorption, protein-losing gastroenteropathy, steatorrhea, anorexia, weight loss, polydipsia, polyuria, cardiac arrhythmia, muscle weakness, prostration and histopathological lesions. Kidney, muscle and central nervous system disturbances are thought to be due to electrolyte imbalance. Loss of intestinal sodium and water stimulates compensatory renal production and secondary aldosteronism, leading to sodium conservation and potassium loss by the kidney. The hypokalaemia contributes to renal insufficiency and is sometimes associated with rhabdomyolysis.

A few epidemiological studies have investigated the association between the use of phenolphthalein containing laxatives and colon cancer or polyp formation. phenolphthalein has been associated with gastrointestinal bleeding, iron-deficient anaemia, acute pancreatitis and multiple organ damage in cases of massive overdose, including fulminant hepatic failure and disseminated intravascular coagulation. Allergy to phenolphthalein is often manifested as cutaneous inflammatory reactions or fixed drug eruptions, i.e. solitary or multiple, well-defined, erythematous macules that may progress to vesicles and/or bullae. These lesions characteristically recur in the same location with each subsequent dose of phenolphthalein and generally leave residual hyperpigmentation that increases in intensity with each exposure; numerous melanin-containing dermal macrophages have been found in pigmented areas. In extreme cases, recurrences have involved progressively more severe lesions characterised as bullous erythema multiforme, with focal haemorrhage and necrosis and perivascular lymphocytic infiltration and, in one case report, toxic epidermal necrolysis.

A review of 204 cases of phenolphthalein ingestion in children aged five years and younger reported to the Pittsburgh Poison Center (USA) over a 30-month period indicated that ingestion of < 1 g was associated with a minimal risk of developing dehydration due to excessive diarrhoea and resulting fluid loss. Despite the profile of low acute toxicity documented in this study, cases of fatal poisoning of children have been reported; symptoms of pulmonary and cerebral oedema, multiple organ effects and encephalitis were attributed to hypersensitivity reactions. Repeated administration of phenolphthalein-containing laxatives to children has led to serious illness and multiple hospitalisations.

Analogy with related biphenolic compounds suggests that phenolphthalein has oestrogenic activity; however, studies with MCF-7 human breast cancer cells in tissue culture and in rat uteri in vivo suggest only a weak oestrogenic response.

Phenolphthalein is a partial oestrogen in immature rat uteri. Doses of 1-10 mg given subcutaneously twice daily for two days to female Wistar rats weighing 35-40 g induced a dose-related increase in uterine weight, but the maximum increase was only about half of that induced by oestradiol. Phenolphthalein was shown to bind to the oestrogen receptor and was a competitive antagonist to oestradiol.

In a study reported in an abstract, exposure of female B6C3F1 mice to 1895 mg/kg bw phenolphthalein orally [method not stated] daily for 30 or 60 days caused no changes in weight gain, oestrous cycles or the numbers of oocyte-containing follicles of any class (primordial, primary, growing or antral), or any detectable pathological change in ovarian cells. In a 1993 study there was no evidence of reproductive toxicity in female B6C3F1 mice or male or female Fischer 344/N rats. Lower epididymal weights and lower sperm density (number of sperm/g of crude epididymal tissue) were observed in male mice at 12 000, 25 000 and 50 000 mg/kg.

Studies have shown that phenolphthalein, at high dose levels, is carcinogenic in mice and has a weak genotoxic (clastogenic) activity in vivo. With respect to the carcinogenicity study, the US FDA has stated that "...the systemic exposures in rodents are approximately 10 to 100 fold the human exposure for rats and mice, respectively. Phenolphthalein is reasonably anticipated to be a human carcinogen based on sufficient evidence of increased incidence of malignant and/or combination of malignant and benign tumors in multiple tissue sites and in multiple species (IARC 2000). In a two-year B6C3F1 mouse carcinogenicity study, NTP (1996) concluded that phenolphthalein, administered in feed, induced significant increases in the incidence of histocytic sarcoma and lymphomas of thymic origin in males and females and malignant lymphoma (all types) and benign ovarian sex cord stromal tumors in females. In the corresponding Fischer 344 rat dietary carcinogenicity study, phenolphthalein induced significant increases in the incidence of benign pheochromocytoma of the adrenal medulla in males and females and renal tubule adenoma in males (NTP 1996). In a 6-month dietary study with female heterozygous p53-deficient transgenic mice, phenolphthalein induced a significant increase in the incidence of malignant lymphoma of thymic origin.

A few epidemiological studies have investigated the association between the use of phenolphthalein-containing laxatives and colon cancer or adenomatous colorectal polyps. No consistent association was found.

Phenolphthalein has been identified as a multisite carcinogen in rodents, but the molecular species responsible for the carcinogenicity is not known. A catechol metabolite hydroxyphenolphthalein , was recently identified and may be the molecular species responsible for at least part of the toxicity/carcinogenicity The metabolite is an extremely potent mixed-type inhibitor of the O-methylation of the catechol estrogens. It has been suggested that chronic administration of phenolphthalein may enhance metabolic redox cycling of both the metabolite and the catechol estrogens and this, in turn, may contribute to hydroxyphenolphthalein-induced tumourigenesis.

Toxicol Appl Pharmacol Vol 162(2) pp 124-131 2000

Although negative for mutagenicity and DNA damage in bacteria, phenolphthalein exhibits genetic activity in several in vitro and in vivo mammalian assays. Phenolphthalein was positive for the induction of chromosomal aberrations in cultured Chinese hamster ovary cells in the presence of metabolic activation and induced hprt gene mutations, chromosomal aberrations, and morphological transformation in Syrian mice.
hamster embryo cells. Phenolphthalein was also positive for the induction of micronucleated erythrocytes in mice following multiple, but not single, treatments administered by gavage or dosed feed. Phenolphthalein also induced micronuclei in female heterozygous p53-deficient transgenic mice exposed via dosed feed for 26 weeks. Phenolphthalein was negative for Na/K ATPase gene mutations and aneuploidy in Syrian hamster embryo cells.

Tenth Annual Report on Carcinogens: Substance anticipated to be Carcinogen [National Toxicology Program: U.S. Dep. of Health & Human Services 2002].

WARNING: This substance has been classified by the IARC as Group 2B: Possibly Carcinogenic to Humans.

Oral (rat) TDLo: 324000 mg/kg/13W-C

<table>
<thead>
<tr>
<th>CARCINOGEN</th>
<th>International Agency for Research on Cancer (IARC) - Agents Reviewed by the IARC Monographs</th>
<th>Group</th>
<th>P65</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phenolphthalein</td>
<td>US Environmental Defense Scorecard Recognized Carcinogens</td>
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<td></td>
</tr>
<tr>
<td>PHENOLPHTHALEIN</td>
<td>US Environmental Defense Scorecard Suspected Carcinogens</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

PHENOLPHTHALEIN:

- DO NOT discharge into sewer or waterways.

Ecotoxicity

<table>
<thead>
<tr>
<th>Ingredient</th>
<th>Persistence: Water/Soil</th>
<th>Persistence: Air</th>
<th>Bioaccumulation</th>
<th>Mobility</th>
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<tbody>
<tr>
<td>phenolphthalein</td>
<td>HIGH</td>
<td>LOW</td>
<td>LOW</td>
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</tr>
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</table>

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

All waste must be handled in accordance with local, state and federal regulations.

Puncture containers to prevent re-use and bury at an authorized landfill.

Legislation addressing waste disposal requirements may differ by country, state and/ or territory. Each user must refer to laws operating in their area. In some areas, certain wastes must be tracked.

A Hierarchy of Controls seems to be common - the user should investigate:

- Reduction
- Reuse
- Recycling
- Disposal (if all else fails)

This material may be recycled if unused, or if it has not been contaminated so as to make it unsuitable for its intended use. Shelf life considerations should also be applied in making decisions of this type. Note that properties of a material may change in use, and recycling or reuse may not always be appropriate.

DO NOT allow wash water from cleaning equipment to enter drains. Collect all wash water for treatment before disposal.

- Recycle wherever possible.
- Consult manufacturer for recycling options or consult Waste Management Authority for disposal if no suitable treatment or disposal facility can be identified.
- Dispose of by: Burial in a licensed land-fill or Incineration in a licensed apparatus (after admixture with suitable combustible material)
- Decontaminate empty containers. Observe all label safeguards until containers are cleaned and destroyed.

Section 14 - TRANSPORTATION INFORMATION

NOT REGULATED FOR TRANSPORT OF DANGEROUS GOODS: DOT, IATA, IMDG

Section 15 - REGULATORY INFORMATION

phenolphthalein (CAS: 77-09-8) is found on the following regulatory lists;

- Canada Domestic Substances List (DSL)
- Canada Toxicological Index Service - Workplace Hazardous Materials Information System - WHMIS (English)
- International Agency for Research on Cancer (IARC) - Agents Reviewed by the IARC Monographs
- US - California Proposition 65 - Carcinogens
- US - California Proposition 65 - Priority List for the Development of NSRLs for Carcinogens
- US - Maine
Section 16 - OTHER INFORMATION

LIMITED EVIDENCE
- Ingestion may produce health damage*.
- Cumulative effects may result following exposure*.
- Possible respiratory and skin sensitizer*.
* (limited evidence).

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Classification of the mixture and its individual components has drawn on official and authoritative sources as well as independent review by the Chemwatch Classification committee using available literature references. A list of reference resources used to assist the committee may be found at: www.chemwatch.net/references.

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

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Issue Date: Jun-2-2010
Print Date: Aug-24-2010