

Irinotecan, Hydrochloride, Trihydrate

sc-207762

Material Safety Data Sheet



The Power is Question

Hazard Alert Code
Key:

EXTREME

HIGH

MODERATE

LOW

Section 1 - CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

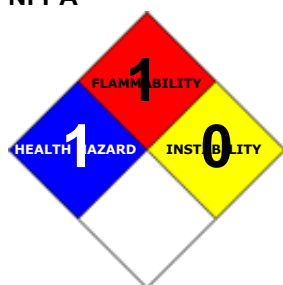
PRODUCT NAME

Irinotecan, Hydrochloride, Trihydrate

STATEMENT OF HAZARDOUS NATURE

CONSIDERED A HAZARDOUS SUBSTANCE ACCORDING TO OSHA 29 CFR 1910.1200.

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

Antineoplastic agent of the topoisomerase I inhibitor class; a derivative of camptothecin, an alkaloid extract from plants such as *Camptotheca acuminata*. For the treatment of metastatic tumours of the colon or rectum. Given by intravenous infusion. Camptothecins interact specifically with the enzyme topoisomerase I which relieves torsional strain in DNA by inducing reversible single strand breaks. Irinotecan and its active metabolite SN-38 bind to the topoisomerase I-DNA complex and prevent religation of these single strand breaks. It is thought that the cytotoxicity of irinotecan is due to double-strand DNA damage produced during synthesis when replication enzymes interact with the ternary complex formed by topoisomerase I, DNA and either irinotecan or SN-38. Mammalian cells cannot efficiently repair these double strand breaks. Irinotecan is a water-soluble precursor of the lipophilic metabolite SN-36 which is formed following carboxylesterase-mediated cleavage of the carbamate bond between camptothecin and the dipiperidino side chain. The metabolite is approximately 1000 times more potent than the parent as an inhibitor of topoisomerase I. Both irinotecan and SN-38 exist in an active lactone form and an inactive hydroxy acid anion form. A pH-dependent equilibrium exists between the two forms such that acid pH promotes the formation of the lactone.

SYNONYMS

C33-H38-N4-O6.HCl, "(1, 4' -bipiperidine)-1' -carboxylic acid, ", "(1, 4' -bipiperidine)-1' -carboxylic acid, ", "3, 4, 12, 14-tetrahydro-4, 11-diethyl-4-hydroxy-, 3, 4-dioxo-1H-", "pyrano(3' , 4' , 6' :6, 7)indolizino[1, 2-b]quinolin-9-yl ester, ", monohydrochloride, "3, 4, 12, 14-tetrahydro-4, 11-diethyl-4-hydroxy-, 3, 4-dioxo-1H-", "pyrano(3' , 4' , 6' :6, 7)indolizino[1, 2-b]quinolin-9-yl ester, ", monohydrochloride, "camptothecin 11 hydrochloride", 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyl, 7-ethyl-10-[4-(1-piperidino)-1-piperidino]carbonyl, "oxy camptothecin", hydrochloride), "(+)-7-ethyl-10-hydroxycamptothecin 10-[1, 4' -bipiperidine-1-", "carboxylate, monohydrochloride, trihydrate (CAS 136572-09-3)", "(+)-7-ethyl-10-hydroxycamptothecin 10-[1, 4' -bipiperidine-1-", "carboxylate, monohydrochloride, trihydrate (CAS 136572-09-3)", Campto, Camptosar, CPT-11, Topotecan, U-10144OE, "antineoplastic/ cytotoxic/ topoisomerase I inhibitor", "antineoplastic/ cytotoxic/ topoisomerase I inhibitor"

Section 2 - HAZARDS IDENTIFICATION

CANADIAN WHMIS SYMBOLS



EMERGENCY OVERVIEW

RISK

Possible risk of harm to the unborn child.

Possible risk of irreversible effects.

Harmful by inhalation, in contact with skin and if swallowed.

POTENTIAL HEALTH EFFECTS

ACUTE HEALTH EFFECTS

SWALLOWED

■ Accidental ingestion of the material may be harmful; animal experiments indicate that ingestion of less than 150 gram may be fatal or may produce serious damage to the health of the individual.

■ The killing action of antineoplastic drugs used for cancer chemotherapy is not selective for cancerous cells alone but affect all dividing cells. Acute side effects include loss of appetite, nausea and vomiting, allergic reaction (skin rash, itch, redness, low blood pressure, unwellness and anaphylactic shock) and local irritation. Gout and renal failure can occur.

EYE

■ Although the material is not thought to be an irritant, direct contact with the eye may cause transient discomfort characterized by tearing or conjunctival redness (as with windburn). Slight abrasive damage may also result. The material may produce foreign body irritation in certain individuals.

SKIN

■ Skin contact with the material may be harmful; systemic effects may result following absorption.

■ The material is not thought to be a skin irritant (as classified using animal models). Abrasive damage however, may result from prolonged exposures. Good hygiene practice requires that exposure be kept to a minimum and that suitable gloves be used in an occupational setting.

■ Open cuts, abraded or irritated skin should not be exposed to this material.

■ Entry into the blood-stream, through, for example, cuts, abrasions or lesions, may produce systemic injury with harmful effects. Examine the skin prior to the use of the material and ensure that any external damage is suitably protected.

INHALED

■ Inhalation of dusts, generated by the material, during the course of normal handling, may be harmful.

■ The material is not thought to produce respiratory irritation (as classified using animal models). Nevertheless inhalation of dusts, or fume, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress.

■ Side effects of topoisomerase I and II inhibitors (acting as antineoplastics/ cytotoxics) include early diarrhoea which may occur within 24 hours of exposure to the drug; this may be accompanied by symptoms including runny nose, increased salivation, watery eyes, sweating, flushing, abdominal cramping. Late diarrhoea may occur after 24 hours and usually peaks at about 11 days after treatment. Because of concerns of dehydration and electrolyte imbalances with diarrhoea it is important to be in contact with health care professionals for monitoring, and for medication and diet modifications advice.

Other common side-effects of therapy may include nausea and vomiting may also occur; low red and white blood cell counts may also result; anaemia may follow. Hair loss, poor appetite, fever and weight loss may also ensue. Less common symptoms include constipation, shortness of breath, insomnia, cough, headache, dehydration, chills, skin rash, flatulence, flushing of the face, mouth sores, heartburn and swelling of the feet and ankles.

■ Persons with impaired respiratory function, airway diseases and conditions such as emphysema or chronic bronchitis, may incur further disability if excessive concentrations of particulate are inhaled.

■ Clinical signs of quinoline intoxication include lethargy, respiratory distress and prostration leading to coma.

CHRONIC HEALTH EFFECTS

■ Strong evidence exists that the substance may cause irreversible but non-lethal mutagenic effects following a single exposure.

Results in experiments suggest that this material may cause disorders in the development of the embryo or fetus, even when no signs of poisoning show in the mother.

Limited evidence suggests that repeated or long-term occupational exposure may produce cumulative health effects involving organs or biochemical systems.

Anti-cancer drugs used for chemotherapy can depress the bone marrow with reduction in the number of white blood cells and platelets and bleeding. Susceptibility to infections and bleeding is increased, which can be life-threatening. Digestive system effects may include inflammation of the mouth cavity, mouth ulcers, esophagus inflammation, abdominal pain and bleeds, diarrhea, bowel ulcers and perforation. Reversible hair loss can result and wound healing may be delayed. Long-term effects on the gonads may cause periods to stop and inhibit sperm production. Most anti-cancer drugs can potentially cause mutations and birth defects, and coupled with the effects of the suppression of the immune system, may also cause cancer.

Quinoline is a metabolite of this material and in mammals has been shown to cause cancers of the liver and blood vessels. Adequate data in humans is not available.

There has been some concern that this material can cause cancer or mutations but there is not enough data to make an assessment.






Topoisomerase inhibitors represent a subgroup of plant alkaloids, which also encompasses the vinca alkaloids such as vincristine and vinblastine, taxanes and podophyllotoxin derivatives. Topoisomerase inhibitors act by preventing the unpackaging of DNA that must occur prior to transcription and replication. The earliest drugs in this class were inhibitors of topoisomerase II, however topoisomerase I inhibitors such as topotecan started entering the market in the mid-1990's. DNA topoisomerase II inhibitors are among the most efficacious drugs for the treatment of cancer. Despite their widespread use, the use of topoisomerase II inhibitors is limited by severe adverse effects to normal tissues, including cardiotoxicity.

In addition to problems associated with toxicity, sensitivity of cancer cells to topoisomerase II targeting agents is also, like many other cancer therapeutics susceptible to resistance. The efficacy of this class is thought to depend on the expression of the topoisomerase II alpha isoform, and drug resistance is often associated with loss or mutation of this isoform.

Irinotecan was clastogenic both in vitro (chromosome aberrations in Chinese ovary hamster cells) and in vivo (micronucleus test in mice). Atrophy of male reproductive organs was observed after intravenous administration of multiple daily dose in rats and rabbits. When administered intravenously to rats, at 1.3 times and 7 times the value given to patients, Irinotecan produced uterine horn endometrial stromal polyps and endometrial stromal sarcomas which showed a significant linear trend with dose.

Section 3 - COMPOSITION / INFORMATION ON INGREDIENTS

HAZARD RATINGS

	Min	Max	
Flammability:	1		
Toxicity:	2		
Body Contact:	2		
Reactivity:	1		
Chronic:	3		

Min/Nil=0
Low=1
Moderate=2
High=3
Extreme=4



NAME	CAS RN	%
irinotecan hydrochloride	100286-90-6	>98

Section 4 - FIRST AID MEASURES

SWALLOWED

- IF SWALLOWED, REFER FOR MEDICAL ATTENTION, WHERE POSSIBLE, WITHOUT DELAY.
- Where Medical attention is not immediately available or where the patient is more than 15 minutes from a hospital or unless instructed otherwise:
- For advice, contact a Poisons Information Center or a doctor.
- Urgent hospital treatment is likely to be needed.
- If conscious, give water to drink.
- INDUCE vomiting with fingers down the back of the throat, ONLY IF CONSCIOUS. Lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.

NOTE: Wear a protective glove when inducing vomiting by mechanical means.

- In the mean time, qualified first-aid personnel should treat the patient following observation and employing supportive measures as indicated by the patient's condition.
- If the services of a medical officer or medical doctor are readily available, the patient should be placed in his/her care and a copy of the MSDS should be provided. Further action will be the responsibility of the medical specialist.
- If medical attention is not available on the worksite or surroundings send the patient to a hospital together with a copy of the MSDS.

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 fumes or combustion products are inhaled remove from contaminated area.
- Lay patient down. Keep warm and rested.
- Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures.
- Apply artificial respiration if not breathing, preferably with a demand valve resuscitator, bag-valve mask device, or pocket mask as trained. Perform CPR if necessary.
- Transport to hospital, or doctor.

NOTES TO PHYSICIAN

- Treat symptomatically.

For employees potentially exposed to antineoplastic and/ or cytotoxic agents on a regular basis, a preplacement physical examination and history (noting risk factors) is recommended. Periodic follow-up examinations should also be undertaken and should be overseen by a physician familiar with the toxic effects of the substance and full details of the nature of work undertaken by the employee. Following administration of antineoplastics, control of nausea and vomiting may be attempted by giving phenothiazines such as perphenazine, prochlorperazine, promethazine or thiethylperazine before antineoplastic agents are administered. In bone-marrow depression, transfusion of blood or platelets reduces the risk of life-threatening hemorrhage. Granulocyte transfusions and injection of antibiotics may be necessary to combat infection in the neutropenic patient. Hyperuricemia is avoided by the addition of allopurinol to treatment schedules and measures such as alkalization of the urine and hydration may be adopted. MARTINDALE: The Extra Pharmacopoeia, 28th Edition.

Section 5 - FIRE FIGHTING MEASURES

Vapour Pressure (mmHG):	Negligible
Upper Explosive Limit (%):	Not available.
Specific Gravity (water=1):	Not available

Lower Explosive Limit (%): Not available

EXTINGUISHING MEDIA

■

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

FIRE FIGHTING

■

- Alert Emergency Responders and tell them location and nature of hazard.
- Wear breathing apparatus plus protective gloves.
- Prevent, by any means available, spillage from entering drains or water course.
- Use water delivered as a fine spray to control fire and cool adjacent area.
- DO NOT approach containers suspected to be hot.
- Cool fire exposed containers with water spray from a protected location.
- If safe to do so, remove containers from path of fire.
- Equipment should be thoroughly decontaminated after use.

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), hydrogen chloride, phosgene, nitrogen oxides (NO_x), other pyrolysis products typical of burning organic material.

May emit poisonous 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:

Gloves:

Respirator:

Particulate

Section 6 - ACCIDENTAL RELEASE MEASURES

MINOR SPILLS

■ It is recommended that areas handling final finished product have cytotoxic spill kits available.

Spill kits should include:

- impermeable body covering,
- shoe covers,
- latex and utility latex gloves,
- goggles,
- approved HEPA respirator,
- disposable dust pan and scoop,
- absorbent towels,
- spill control pillows,
- disposable sponges,
- sharps container,
- disposable garbage bag and
- hazardous waste label

To avoid accidental exposure due to waste handling of cytotoxics:

- Place waste residue in a segregated sealed plastic container.
- Used syringes, needles and sharps should not be crushed, clipped, recapped, but placed directly into an approved sharps container.
- Dispose of any cleanup materials and waste residue according to all applicable laws and regulations e.g. secure chemical landfill disposal.
- 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.

All personnel likely to be involved in an antineoplastic (cytotoxic) spill must receive practical training in:

- the correct procedures for handling cytotoxic drugs or waste in order to prevent and minimize the risk of spills
- the location of the spill kit in the area
- the arrangements for medical treatment of any affected personnel

- the procedure for containment of the spill, and decontamination of personnel and the environment, including the different procedures for major and minor spills
- the procedure for waste disposal according to the nature and extent of the spill

MAJOR SPILLS

- Moderate hazard.
- CAUTION: Advise personnel in area.
- Alert Emergency Responders and tell them location and nature of hazard.
- Control personal contact by wearing protective clothing.
- Prevent, by any means available, spillage from entering drains or water courses.
- Recover product wherever possible.
- IF DRY: Use dry clean up procedures and avoid generating dust. Collect residues and place in sealed plastic bags or other containers for disposal. IF WET: Vacuum/shovel up and place in labelled containers for disposal.
- ALWAYS: Wash area down with large amounts of water and prevent runoff into drains.
- If contamination of drains or waterways occurs, advise emergency services.

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

■ The National Institute of Health (USA) recommends that the preparation of injectable antineoplastic drugs should be performed in a Class II laminar flow biological safety cabinet and that personnel preparing drugs of this class should wear appropriate personal protective gear. Emphasise controls on containment.

- 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.
- Atmosphere should be regularly checked against established exposure standards to ensure safe working conditions are maintained.

Empty containers may contain residual dust which has the potential to accumulate following settling. Such dusts may explode in the presence of an appropriate ignition source.

- Do NOT cut, drill, grind or weld such containers
- In addition ensure such activity is not performed near full, partially empty or empty containers without appropriate workplace safety authorisation or permit.

RECOMMENDED STORAGE METHODS

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

STORAGE REQUIREMENTS

- Antineoplastics (cytotoxics):
- should be clearly identifiable to all personnel involved in their handling
- should be stored in impervious break-resistant containers
- should be stored in separate, clearly marked storage areas to minimize the risk of breakage, and to limit contamination in the event of leakage.

Spill kits should be available in storage areas.

- 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: Must not be stored together

O: May be stored together with specific preventions

+: May be stored together

Section 8 - EXPOSURE CONTROLS / PERSONAL PROTECTION

EXPOSURE CONTROLS

The following materials had no OELs on our records

- irinotecan hydrochloride: CAS:100286-90-6 CAS:111348-33-5 CAS:136572-09-3

MATERIAL DATA

IRINOTECAN HYDROCHLORIDE:

■ 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.

CEL TWA: 0.001 mg/m³.

PERSONAL PROTECTION



Consult your EHS staff for recommendations

EYE

■

- Chemical protective goggles with full seal
- Shielded mask (gas-type)
- Contact lenses may pose a special hazard; soft contact lenses may absorb and concentrate irritants. A written policy document, describing the wearing of lens or restrictions on use, should be created for each workplace or task. This should include a review of lens absorption and adsorption for the class of chemicals in use and an account of injury experience. Medical and first-aid personnel should be trained in their removal and suitable equipment should be readily available. In the event of chemical exposure, begin eye irrigation immediately and remove contact lens as soon as practicable. Lens should be removed at the first signs of eye redness or irritation - lens should be removed in a clean environment only after workers have washed hands thoroughly. [CDC NIOSH Current Intelligence Bulletin 59]

HANDS/FEET

■ 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.

- Rubber gloves (nitrile or low-protein, powder-free latex). Employees allergic to latex gloves should use nitrile gloves in preference.
- Double gloving should be considered.
- PVC gloves.
- Protective shoe covers.
- Head covering.

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
- fluorocautchouc
- polyvinyl chloride

Gloves should be examined for wear and/ or degradation constantly.

OTHER

-
- When handling antineoplastic materials, it is recommended that a disposal work-uniform (such as Tyvek or closed front surgical-type gown with knit cuffs) is worn.
- For quantities up to 500 grams a laboratory coat may be suitable.
- For quantities up to 1 kilogram a disposable laboratory coat or coverall of low permeability is recommended. Coveralls should be buttoned at collar and cuffs.
- For quantities over 1 kilogram and manufacturing operations, wear disposable coverall of low permeability and disposable shoe covers.
- For manufacturing operations, air-supplied full body suits may be required for the provision of advanced respiratory protection.
- Eye wash unit.
- Ensure there is ready access to an emergency shower.
- For Emergencies: Vinyl suit
-
- 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.

RESPIRATOR

Protection Factor	Half-Face Respirator	Full-Face Respirator	Powered Air Respirator
10 x PEL	P1	-	PAPR-P1
	Air-line*	-	-
50 x PEL	Air-line**	P2	PAPR-P2
100 x PEL	-	P3	-
		Air-line*	-
100+ x PEL	-	Air-line**	PAPR-P3

* - 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 65°C).

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

- For potent pharmacological agents:

Powders

To prevent contamination and overexposure, no open handling of powder should be allowed.

- Powder handling operations are to be done in a powders weighing hood, a glove box, or other equivalent ventilated containment system.
- In situations where these ventilated containment hoods have not been installed, a non-ventilated enclosed containment hood should be used.
- Pending changes resulting from additional air monitoring data, up to 300 mg can be handled outside of an enclosure provided that no grinding, crushing or other dust-generating process occurs.
- An air-purifying respirator should be worn by all personnel in the immediate area in cases where non-ventilated containment is used, where significant amounts of material (e.g., more than 2 grams) are used, or where the material may become airborne (as through grinding, etc.).
- Powder should be put into solution or a closed or covered container after handling.
- If using a ventilated enclosure that has not been validated, wear a half-mask respirator equipped with HEPA cartridges until the enclosure is validated for use.

Solutions Handling:

- Solutions can be handled outside a containment system or without local exhaust ventilation during procedures with no potential for aerosolisation. If the procedures have a potential for aerosolisation, an air-purifying respirator is to be worn by all personnel in the immediate area.
- Solutions used for procedures where aerosolisation may occur (e.g., vortexing, pumping) are to be handled within a containment system or with local exhaust ventilation.
- In situations where this is not feasible (may include animal dosing), an air-purifying respirator is to be worn by all personnel

in the immediate area. If using a ventilated enclosure that has not been validated, wear a half-mask respirator equipped with HEPA cartridges until the enclosure is validated for use.

- Ensure gloves are protective against solvents in use.

Unless written procedures, specific to the workplace are available, the following is intended as a guide:

- For Laboratory-scale handling of Substances assessed to be toxic by inhalation. Quantities of up to 25 grams may be handled in Class II biological safety cabinets*; Quantities of 25 grams to 1 kilogram may be handled in Class II biological safety cabinets* or equivalent containment systems. Quantities exceeding 1 kg may be handled either using specific containment, a hood or Class II biological safety cabinet*.
- HEPA terminated local exhaust ventilation should be considered at point of generation of dust, fumes or vapors.
- The need for respiratory protection should also be assessed where incidental or accidental exposure is anticipated. Dependent on levels of contamination, PAPR, full face air purifying devices with P2 or P3 filters or air supplied respirators should be evaluated. When handling: Quantities of up to 25 grams, an approved respirator with HEPA filters or cartridges should be considered. Quantities of 25 grams to 1 kilogram, a half-face negative pressure, full negative pressure, or powered helmet-type air purifying respirator should be considered. Quantities in excess of 1 kilogram, a full face negative pressure, helmet-type air purifying, or supplied air respirator should be considered.

Written procedures, specific to a particular work-place, may replace these recommendations

* For Class II Biological Safety Cabinets, Types B2 or B3 should be considered. Where only Class I, open fronted Cabinets are available, glove panels may be added, Laminar flow cabinets do not provide sufficient protection when handling these materials unless especially designed to do so.

Section 9 - PHYSICAL AND CHEMICAL PROPERTIES

PHYSICAL PROPERTIES

Solid.

Does not mix with water.

State	Divided solid	Molecular Weight	162.19
Melting Range (°F)	384.8- 388.4	Viscosity	Not Applicable
Boiling Range (°F)	Not available	Solubility in water (g/L)	Partly miscible
Flash Point (°F)	Not available	pH (1% solution)	Not applicable
Decomposition Temp (°F)	Not available.	pH (as supplied)	Not applicable
Autoignition Temp (°F)	Not available	Vapour Pressure (mmHG)	Negligible
Upper Explosive Limit (%)	Not available.	Specific Gravity (water=1)	Not available
Lower Explosive Limit (%)	Not available	Relative Vapor Density (air=1)	>1
Volatile Component (%vol)	Negligible	Evaporation Rate	Not available

APPEARANCE

Pale yellow to yellow crystalline powder; does not mix well with water.

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

irinotecan hydrochloride

TOXICITY AND IRRITATION

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

TOXICITY	IRRITATION
Oral (rat) LD50: 867 mg/kg	Nil Reported
Intravenous (rat) LD50: 83.6 mg/kg	
Oral (mouse) LD50: 765 mg/kg	
Intraperitoneal (mouse) LD50: 177 mg/kg	
Intravenous (mouse) LD50: 132 mg/kg	
Intravenous (dog) LD50: 40 mg/kg	

■ Camptothecin (CPT) is a cytotoxic quinoline alkaloid which inhibits the DNA enzyme topoisomerase I (topo I). Studies have shown that substitution at position 7, 9, 10 and 11 can have positive effect on CPT activity and physical properties, e.g. potency and metabolic stability. Enlargement of the lactone ring by one methylene unit also enhances its abilities, as in homocamptothecin. Substitution at position 12 and 14 leads to inactive derivative.

In rabbits and dogs, quinoline and its metabolites are excreted in the urine. Urinary excretion of quinoline and its metabolites was nearly complete 24 hours after i.v. dosing of dogs with 20 or 25 mg/kg. Less than 0.5% of the administered quinoline was

excreted unchanged. Approximately 29%-32% of the administered quinoline was recovered from the urine as 3-hydroxyquinoline (free and conjugated forms). Approximately 0.4%-0.8% of free quinoline was detected in rabbit urine collected 24 hours after administration of an oral dose of 250 mg/kg. Approximately 6.7%-11.0 % of the quinoline was determined to be excreted as a labile compound that yields quinoline on heating with acid. About 3%-4% of quinoline was excreted as the metabolite 5,6-dihydroxyquinoline.

Repeat dose toxicity: Groups of 20 male Sprague-Dawley rats were fed a diet containing 0.05% (low-dose), 0.10% (mid-dose), or 0.25% (high-dose) quinoline for approximately 16-40 weeks. Absolute and relative liver weights were significantly increased in all treatment groups, and the difference between initial and final mean body weights decreased with increasing dose. Histological examination of the liver revealed fatty change, bile duct proliferation, and oval cells in treated animals. Also, nodular hyperplasia was seen in the mid- and high-dose animals.

Carcinogenicity: No reliable human epidemiological studies are available that address the potential carcinogenicity of quinoline. However, laboratory studies have shown that quinoline is mitogenic and mutagenic in vitro and in vivo, and that humans and rats share a common quinoline-metabolizing P450 enzyme. Liver tumors have been observed in rats and mice exposed to quinoline via oral and i.p. routes of exposure, but not in rats exposed subcutaneously, despite the fact that the s.c. injections resulted in maximally tolerated doses more than 40 times higher than i.p. doses given to mice. The observation of skin tumors on mice dermally exposed to quinoline and tumor promoter tetradecanoyl phorbol acetate suggests that quinoline can initiate skin tumors (no other tumor types were reported) without first-pass metabolism in the liver, but the question of whether inhaled quinoline would have such effects without promotion remains.

Several animal studies report hepatocarcinogenicity (hepatocellular carcinomas and haemangioendotheliomas or haemangiosarcomas, a vascular tumor) in rats and mice following oral dosing with quinoline. Quinoline has also been reported to be a hepatocarcinogen in newborn mice following intraperitoneal exposure. Metastatic changes, arising from these tumors, were detected in the lungs of some of the rats. Hepatic tumours (carcinomas, adenomas, and basophilic altered foci) were observed in male newborn mice, but not male or female newborn rats. No tumors, but basophilic altered foci, were observed in female newborn mice.

Quinoline initiated skin tumors in female SENCAR mice following dermal application

Important aspects of the hepatocarcinogenicity of quinoline are the relatively short latency period (as low as 12 weeks) for tumor formation, and the fact that one of the tumor types observed, haemangioendotheliomas, is uncommon in rats and mice.

Other studies indicate species differences in regard to liver tumorigenesis by quinoline; mice and rats are most susceptible and hamsters and guinea pigs appear to be resistant.

Quinoline is considered likely to be carcinogenic in humans in accordance with proposed EPA carcinogen risk assessment guidelines (U.S. EPA, 1996) on the basis of observations of exposure-related increased incidence of an unusual malignant tumor in multiple strains of rats and mice, in multiple experiments using oral, dermal, i.p., and s.c. dosing, and at an early age. This determination is supported by studies that demonstrate that quinoline is genotoxic.

Quinoline can apparently act as a promoter of liver carcinogenicity as well. Quinoline, 3-fluoroquinone (3-FQ), or 5-fluoroquinone (5-FQ) were fed to F344 male rats in their diet (0.1% and 0.05%) for a period of 6 weeks following a single, 200 mg/kg i.p. injection of the liver carcinogen diethylnitrosamine (DEN). The number and areas of GST-P (placental glutathione S10 transferase)-positive foci induced in the liver increased significantly as a result of treatment with 0.1% but not 0.05% quinoline.

Genotoxicity: Quinoline is a mutagen in *Salmonella typhimurium* in the presence of metabolic activation. Quinoline has also been shown to induce chromosome aberrations and sister chromatid exchanges in the rat liver and micronucleus formation in the bone marrow of CD1 male mice. Although a predominance of data suggest that quinoline is genotoxic, the results of at least one study indicate that a nongenotoxic (i.e., mitogenic) mechanism of action may play a role in its hepatocarcinogenicity (Quinoline was found to have significant activity in the *Salmonella typhimurium* strain TA100, but generally not in strains TA1537 and TA1538, nor TA98, suggesting that it may be acting via base-pair substitution).

3-Fluoro- and 2- and 3-chloroquinolines were less mutagenic than all other fluoro- and chloro-substituted derivatives of quinoline. The 3-fluoro derivative of quinoline completely blocks the mutagenic activity of quinoline. Substitutions at other locations do not reduce quinoline's mutagenicity, and in some cases enhance it (presumably by inhibiting detoxification pathways).

Studies suggest that the 2,3-epoxide is the active metabolic mutagen based on the fact that the 4-chloro isomer is weakly mutagenic (presumably no mutagenicity would be observed if a 3,4-epoxide were necessary), the 4-methyl isomer is strongly mutagenic (suggested to be because of suppression of detoxification of the 2,3-epoxide), and the 2-methyl isomer is weakly mutagenic (the authors report that methyl substitution at the site of epoxide formation is known to partially reduce mutagenicity).

Exposure to the material for prolonged periods may cause physical defects in the developing embryo (teratogenesis).

NOTE: Substance has been shown to be mutagenic in at least one assay, or belongs to a family of chemicals producing damage or change to cellular DNA.

Convulsions, respiratory tract changes, diarrhoea, nausea, vomiting, endocrine changes, changes in serum composition, changes in blood cell count, changes in thymus weight, pigmented or nucleated red blood cells, gastrointestinal ulceration, changes in spleen weight, foetotoxicity, foetolethality, specific developmental abnormalities (central nervous system, eye/ ear, craniofacial, skin and appendages, musculoskeletal, cardiovascular), effects on newborn recorded.

Hypersensitivity reactions including severe anaphylactic or anaphylactoid reactions have been observed following therapy. Cases of colitis complicated by ulceration, bleeding, ileus, and infection have been observed. Rare cases of renal impairment and acute renal failure have been identified, usually in patients who became volume depleted from severe vomiting and/or diarrhea.

The drug may cause foetal harm when administered to a pregnant woman. Irinotecan was teratogenic in rats at doses greater than 1.2 mg/kg/day. Teratogenic effects included a variety of external, visceral, and skeletal abnormalities. Irinotecan administered to rat dams for the period following organogenesis through weaning at doses of 6 mg/kg/day caused decreased learning ability and decreased female body weights in the offspring.

Section 12 - ECOLOGICAL INFORMATION

Refer to data for ingredients, which follows:

IRINOTECAN HYDROCHLORIDE:

■ For antineoplastics:

Ecotoxicity:

Because antineoplastics are genotoxic, mutagenic and carcinogenic concerns are warranted for their potential effect in the environment. There are a number of known mammalian toxic and nausea effects associated with antineoplastic treatment, which could indicate that similar effects, might be expected in non-target mammals, and possibly also in non-target species other than mammals. Total dosage over a whole therapy protocol is approximately 150 mg /kg body weight. Approximately 14-53% of the administered pharmaceutical is excreted unmetabolised into urine.

Antineoplastics as a class of drugs are of potential concern for environmental impacts, not just for their acute toxicity but perhaps more for their ability to effect subtle genetic changes, the cumulative impact of which over time can lead to more profound ecologic change. Hospitals are the major source of genotoxic drugs. publicly-owned waste-water treatment works (POTWs) that service hospitals, especially multiple hospitals, are likely candidates for releasing these chemicals into surface

waters.

Antineoplastics are highly [geno]toxic compounds, primarily from hospitals, with poor removal from sewage treatment plants (STWs). Antineoplastic agents, antitumour agents primarily used only within hospitals for chemotherapy, are found sporadically and in a range of concentrations, probably because only small amounts are introduced to STWs via domestic sewage because of their long-lived physiologic retention.

These compounds act as nonspecific alkylating agents (i.e., specific receptors are not involved) and therefore have the potential to act as either acute or long-term stressors (mutagens carcinogens/ teratogens/ embryotoxins) in any organism.

Using well-established QSAR modelling techniques almost 1/5 of the commonly used antineoplastics were predicted to be very toxic to algae, and close to 1/3 were predicted to be non-toxic to plants. A third of the compounds were predicted to be very toxic to daphnids, and almost half were predicted to be non-toxic to daphnids. Slightly more than 1/5 were predicted to be very toxic to fish, and 47% were predicted to be non-toxic to fish.

■ For quinoline:

Henry's Law constant: 2.49×10^{-7} atm-m³mol⁻²

Koc 79-205

Bioconcentration factor 21

log Kow 2.03

Environmental fate:

When released to aquatic systems, quinoline will biodegrade. The rate depends upon temperature and microbial conditions, with complete degradation occurring within 5 days. Quinoline is also likely to be photolysed at rates that depend on pH, depth of water, season, and presence of humic acids. Photolytic half-lives range from 21 days during the summer to 160 days during the winter. A low Henry's Law constant predicts little volatilisation.

Given a bioconcentration factor (BCF) of 21 and a Koc of 79-205, sorption to suspended sediments and bioaccumulation are likely to be responsible for a moderate-to-low level of removal from aquatic systems.

When released to soil, quinoline is likely to leach quickly into groundwater. It is predicted that less than 0.5% of quinoline released would sorb to sediments and particulates, and quinoline is likely to partition into water, given its moderate water solubility and low Kow. Once quinoline partitions to water, it is not likely to volatilise to air because of its low Henry's Law constant. There was no relation between adsorption and soil carbon content.

Biodegradation is likely to take place but, on the basis of information available for quinoline in water, hydrolysis, oxidation, and volatilisation should not be significant.

Quinoline released to the atmosphere is likely to react with hydroxyl radicals, with an estimated reaction half-life of 2.51 days. Because of its strong absorption of light wavelengths >290 nm, quinoline has the potential for direct photolysis in the atmosphere. Removal from the atmosphere can occur via wet and dry deposition.

■ DO NOT discharge into sewer or waterways.

Section 13 - DISPOSAL CONSIDERATIONS

Disposal Instructions

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

! 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.

- Antineoplastic (cytotoxic) wastes must be packed directly, ready for incineration, into color-coded, secure, labelled, leak-proof containers sufficiently robust to withstand handling without breaking, bursting or leaking.
- Containers of special design are available for particular needs (such as disposal of sharps) and should be used.
- Once filled and closed, such containers must never be re-opened.
- Immediate containers must bear a nationally accepted symbol or device depicting cytotoxic substances and be labelled with the words: CYTOTOXIC WASTE - INCINERATE in a style of lettering approved by the national/ state authority.
- Where policies and procedures permit the merging of cytotoxic wastes with medical waste in an outer container used for medical waste, cytotoxic waste must first be placed in identifiable color-coded/ labelled cytotoxic containers prior to merging.
- Management procedures must ensure that merged medical and cytotoxic waste is subjected to the incineration requirements appropriate for the total destruction of the cytotoxic waste.

WASTE STORAGE OF CYTOTOXIC WASTES For the storage of cytotoxic waste, segregated or merged with medical waste, provide:

- special storage areas with adequate lighting.
- waste security and restriction of access to authorized persons.
- storage areas designed to facilitate easy routine cleaning and maintenance to hygienic standards, or post-spill decontamination.
- storage of cytotoxic waste in standard, identifying bins or other appropriate containers.

COLLECTION OF CYTOTOXIC WASTES

- Procedures for the collection of cytotoxic wastes, which are compatible with existing operational needs, and which protect workers, other people and the environment, must be developed.
- Waste must be removed from the site by contractors whose workers have been instructed in the protective methods to be used against the hazards involved, and who comply with the safe work practices established by internal and/or national/ state policies. Contractors must instruct, train and direct their personnel in the safe and legal handling of cytotoxic wastes. Contractor's personnel should observe the operating procedures of the waste-generator.
- Transport of cytotoxic wastes, through the community, must comply with the appropriate national/ state codes.

DESTRUCTION OF CYTOTOXIC WASTES

- Destruction of cytotoxic wastes should be carried out in multi-chambered incinerators, licenced for this purpose, operating at 1100 deg. C. or more, with a residence time of at least 1 second.
- Operators must be trained in handling procedures and hazards involved with handling the waste.
- Waste which arrives at the incinerator inappropriately packaged should NOT be returned to the waste generator. An authorized representative of the waste generator must attend the incinerator site to rectify the situation.

Section 14 - TRANSPORTATION INFORMATION

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

Section 15 - REGULATORY INFORMATION

No data for irinotecan hydrochloride (CAS: , 100286-90-6, 111348-33-5, 136572-09-3)

Section 16 - OTHER INFORMATION

LIMITED EVIDENCE

- Cumulative effects may result following exposure*.
- Limited evidence of a carcinogenic effect*.

* (limited evidence).

Ingredients with multiple CAS Nos

Ingredient Name	CAS
irinotecan hydrochloride	100286-90-6, 111348-33-5, 136572-09-3

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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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