**** MATERIAL SAFETY DATA SHEET ****

1. CHEMICAL PRODUCT AND COMPANY IDENTIFICATION

COMMON NAME: CAMPTOSAR(TM) INJECTION

SYNONYMS: Irinotecan hydrochloride injection
MOLECULAR FORMULA: Mixture
MANUFACTURER/SUPPLIER: PHARMACIA & UPJOHN
7171 PORTAGE RD
KALAMAZOO, MI 49001-0199

TELEPHONE NUMBERS: (616) 833-5122 - (24 HOURS)
(616) 833-7555 - (8:00 a.m. - 4:30 p.m.)

2. COMPOSITION/INFORMATION ON INGREDIENTS

INGREDIENT 1
COMMON NAME: Water
% BY WEIGHT: < 94 %
CAS NUMBER: 7732-18-5
EXPOSURE LIMIT(S): Not established.

INGREDIENT 2
COMMON NAME: D-sorbitol
% BY WEIGHT: < 5 %
CAS NUMBER: 50-70-4
EXPOSURE LIMIT(S): Not established.

INGREDIENT 3
COMMON NAME: Irinotecan hydrochloride trihydrate
CHEMICAL NAME: (4S)-4,11-diethyl-4-hydroxy-9-{(4-piperidinopiperidino) carbonyloxy}-1H-pyrano{3',4':6,7}indolizino{1,2-b}quinoline-3,14(4H,12H)dione hydrochloride
% BY WEIGHT: 2 %
CAS NUMBER: 100286-90-6
EXPOSURE LIMIT(S):
UPJOHN EXPOSURE LIMIT-TWA: 0.4 UG/M3

INGREDIENT 4
COMMON NAME: Lactic acid
% BY WEIGHT: < 0.1 %
CAS NUMBER: 50-21-5
EXPOSURE LIMIT(S): Not established.

EXPOSURE LIMIT(S) FOR THE MATERIAL:
UPJOHN EXPOSURE LIMIT-TWA: 0.4 UG/M3

3. HAZARDS IDENTIFICATION

PRIMARY ROUTE(S) OF EXPOSURE: Skin contact, eye contact, ingestion and inhalation.
EFFECTS OF OVEREXPOSURE: The active ingredient, irinotecan hydrochloride trihydrate, is cytotoxic and will produce severe toxic effects to rapidly dividing tissues upon overexposure. When administered clinically by intravenous injection, adverse events such as weakness, nausea, vomiting, diarrhea, anorexia and alopecia (hair loss) are commonly reported. The main toxic effects are severe myelosuppression (reduction in the number of white blood cells in the blood that could increase the risk of infection) and early and late forms of diarrhea that

may also be severe.
TARGET ORGANS: Blood. Gastrointestinal system.
MEDICAL CONDITIONS AGGRAVATED BY EXPOSURE: Not established.

4. FIRST AID MEASURES

EYES: Flush with water for 15 minutes. Hold eyelids open to assure complete contact with water.
SKIN: Wash with soap and water. Remove contaminated clothing.
INHALATION: Remove from exposure.
INGESTION: Contact a physician or poison control center.

5. FIRE FIGHTING MEASURES

FLASH POINT: Nonflammable.
LOWER EXPLOSION LIMIT (LEL): Not applicable.
UPPER EXPLOSION LIMIT (UEL): Not applicable.
EXTINGUISHING MEDIA: Water, carbon dioxide, or dry chemical.
FIRE-FIGHTING PROCEDURES: Wear self-contained breathing apparatus and full body protective equipment.
UNUSUAL FIRE OR EXPLOSION HAZARDS: None known.
HAZARDOUS COMBUSTION PRODUCTS: Carbon monoxide. Carbon dioxide. Nitrogen oxides

6. ACCIDENTAL RELEASE MEASURES

STEPS TO BE TAKEN IN CASE MATERIAL IS RELEASED OR SPILLED: Spills should be cleaned-up by experienced personnel wearing appropiate protective gear. For large spills, a Saranex coated Tyvek suit (or equivalent) should be worn with rubber boots, nitrile gloves, chemical goggles, and an approved respirator. For small spills (single vial), skin coverings, nitrile gloves, goggles and respiratory protection should be used. Keep out of drains; prevent entry to surface water, groundwater and soil. Contain and mop up liquid spills with absorbant material. Clean area with water, detergent or an acidified detergent solution. Solutions of CAMPTOSAR will fluoresce blue/white under an ultraviolet (UV) light set at a wavelength of 365 nm and is easily removed from most surfaces using the above cleaning agents. Clean the area until fluorescent areas which are water soluble have been eliminated. Monitoring the clean-up process using the UV light should avoid unintentionally spreading the contamination by the use of an inappropriate cleaning technique (such as the use of copious volumes of cleaning solution). Note: many materials, other than CAMPTOSAR fluoresce (e.g., cellulose). However, if the fluorescent material is suspected to be CAMPTOSAR and is spread by wetting, it should be treated as drug. All clothing, personal protective equipment, and towels should be UV inspected and if contaminated with CAMPTOSAR should be cleaned or bagged and incinerated.

7. HANDLING AND STORAGE

PRECAUTIONS FOR HANDLING AND STORING: Irinotecan inhibits DNA replication. Solutions should be handled with extreme care to avoid personal exposure, either by skin contact, ingestion, inhalation or other means.
PRODUCT PREPARATION AND ADMINISTRATION: Hospital personnel preparing or administering CAMPTOSAR should wear nitrile gloves, safety glasses, a closed-front gown with knit cuffs and masks. Preparation of all antineoplastic agents should

be done in a class II laminar flow biological safety cabinet with exhaust air discharged external to the room environment. All needles, syringes, vials, ampules and other equipment or disposable clothing which have been in contact with CAMPTOSAR should be segregated and incinerated at a temperature not less than 1000 degrees celsius.

8. EXPOSURE CONTROLS/PERSONAL PROTECTION

RESPIRATORY PROTECTION: Approved respirator.
VENTILATION: Nonrecirculating local exhaust.
PROTECTIVE GLOVES: Nitrile.
EYE PROTECTION: Chemical goggles.
OTHER PROTECTIVE EQUIPMENT: Protective covering for exposed areas of skin.

9. PHYSICAL AND CHEMICAL PROPERTIES

APPEARANCE/PHYSICAL STATE: Pale yellow to slightly yellow liquid which fluoresces blue/white when exposed to ultraviolet (UV) light (365 nm).
MOLECULAR WEIGHT: Mixture.
PH: 3.5 (range 3.0 to 3.8)
SOLUBILITY IN WATER: Freely soluble.

10. STABILITY AND REACTIVITY

STABILITY: Stable. Stable for 18 months at room temperature when protected from light.
PHYSICAL CONDITIONS TO AVOID: Exposure to light. pH >10.
INCOMPATIBILITY WITH OTHER MATERIALS: None known. Other drugs should not be added to the infusion solution.
HAZARDOUS POLYMERIZATION: Does not occur.

11. TOXICOLOGICAL INFORMATION

ACUTE STUDIES: All information presented in Section 11 applies to irinotecan hydrochloride trihydrate:
EYE IRRITATION (RABBIT): Caused minimal and transient irritation to the eyes of rabbits.
SKIN IRRITATION (RABBIT): Not irritating to the intact skin of rabbits, but slightly irritating to the scratch marks (open wounds) of the abraded skin. Dermal absorption via intact skin was found to be slow and minimal and via the abraded skin it was found to be fast but minimal.
INTRAVENOUS LD50 (DOG): 40-80 mg/kg
INTRAVENOUS LD50 (RAT): 84 mg/kg
INTRAVENOUS LD50 (MOUSE): 133 mg/kg
ACUTE TOXICITY: Administration to female beagle dogs resulted in lethal toxicity attributed to immunosuppression, bone marrow suppression and gastrointestinal toxicity, after 5 consecutive daily intravenous doses of 7.5 mg/kg/day or after 4 consecutive daily oral doses of 18.75 mg/kg/day or greater.
ORAL LD50 (RAT): 867 mg/kg
ORAL LD50 (MOUSE): 1,064 mg/kg (approximately)
INTRAPERITONEAL LD50 (MOUSE): 177 mg/kg
SUBCHRONIC/CHRONIC STUDIES: A rat four week intravenous study had a no effect level of 0.8 mg/kg/day.

CHRONIC STUDIES: A rat six month IV study showed effects on blood at 0.0064 mg/kg/day, the lowest dose tested.
OTHER STUDIES: Antigenic potential in guinea pigs.
GENOTOXICITY:
Positive: In vitro - chromosomal aberration (Chinese Hamster Ovary cells) with and without activation.
Positive: In vivo - micronucleus test, i.p., mouse.
Negative: In vitro - Ames assay with and without metabolic activation.
REPRODUCTION/FERTILITY: No effects on fertility from IV doses up to 6.0 mg/kg/day in rats and rabbits. Maternal toxicity was observed at IV doses of 6.0 mg/kg/day.
TERATOGENICITY: Teratology studies showed that IV doses of 1.2 mg/kg/day in the rat depressed growth in the fetuses. At 6.0 mg/kg/day, external, visceral and skeletal abnormalities were noted. Teratogenic effects have been reported in rabbits at IV dosages of 0.06 mg/kg/day.
CARCINOGENICITY: Long-term carcinogenicity studies with irinotecan have not been conducted. Rats were, however, administered intravenous doses of 2 mg/kg or 25 mg/kg irintotecan once per week for 13 weeks and were then allowed to recover for 91 weeks. Under these condions, there was a significant linear trend with dose for the incidence of combined uterine horn endometrial stromal polyps and endometrial stromal sarcomas. Ingredient(s) are not listed as carcinogenic by IARC, NTP or OSHA.

12. DISPOSAL CONSIDERATIONS

WASTE DISPOSAL METHOD: Dispose of by incineration in accordance with applicable international, national, state, and/or local waste disposal regulations.

13. SHIPPING REGULATIONS

Not regulated for transportation by the United States Department of Transportation (DOT), International Maritime Organization (IMO), or International Air Transport Association (IATA). May be subject to state and/or local transportation requirements.

14. OTHER INFORMATION

REVIEWED BY: Environmental Health Sciences.
DISCLAIMER: The MSDS information is believed to be correct but should only be used as a guide. Pharmacia & Upjohn disclaims any express or implied warranty as to the accuracy of the MSDS information and shall not be held liable for any direct, incidental or consequential damages resulting from reliance on the information.

15. LABELING

This drug is subject to FDA labeling requirements; therefore, it is exempt from the labeling requirements of the OSHA Hazard Communication Standard.