

Standard Operating Procedure for Etoposide in Animals

1. Health hazards

Etoposide is a chemotherapy drug mainly used to treat lung cancer and testicular cancer, stomach cancer and non Hodgkin lymphoma. Etoposide is made from the mandrake plant.

Etoposide is an antineoplastic agents which target the DNA unwinding enzyme, topoisomerase II (DNA topoisomerases are essential for DNA replication, transcription, chromosomal segregation and DNA recombination).

Etoposide blocks the cell cycle in in S-phase and G2-phase of the cell cycle; induces apoptosis in normal and tumor cell lines; inhibits synthesis of the oncoprotein Mdm2 and induces apoptosis in tumor lines that overexpress Mdm2.

It is very soluble in methanol and chloroform, slightly soluble in ethanol, and sparingly soluble in water and ether.

Statement of Hazard:

Flammable liquid and vapor.

Based on animal data, Etoposide, is considered a potential developmental and reproductive toxicant.

May cause harm to the unborn child.

May cause genetic defects.

Suspected of causing cancer.

Contact with Skin or Eyes: Contact may cause irritation. Effects may include stinging, watering, redness and swelling of the eyes and redness, itching, burning and skin damage. May cause an allergic reaction on the skin.

	<p><u>Injection:</u> Local redness and pain are the primary symptoms of accidental injection in an occupational setting. Personnel are not anticipated to experience over-exposures to the therapeutic doses of this product. However, effects including bone marrow suppression with decreased blood cells, chills, fever, nausea, vomiting, severe gastrointestinal distress, liver disorders, unusual bleeding, severe loss of blood pressure, cardiac irregularities, breathing difficulties and hair loss may occur.</p> <p>As a precautionary measure, keep away from strong oxidizers (such as bleach) Strong acids, Strong bases and Strong reducing agents.</p> <p>*Pregnant women, breast feeding, or planning pregnancy, should not be exposed to or handle this cytotoxic in any form.*</p>
<p>2. Designated Area</p>	<p>ABSL-2 facility.</p>
<p>3.Training</p>	<p>Hazardous cytotoxic training and training on this SOP is required before working with Etoposide. This should include but is not limited to reviewing the MSDS, training on the physical hazards of the cytotoxics, symptoms of exposure, appropriate work practices, and proper use of PPE.</p>
<p>4. Personal Protective Equipment (PPE)</p>	<p>Double nitrile gloves or compatible cytotoxic-resistant gloves, Cytotoxic safety goggles, Lab coat and mask. Appropriate PPE should also be used for lower arms such as sleeve covers or securing gloves over the sleeves of laboratory coat.</p> <p>There are no established safe levels of exposure to cytotoxic drugs. Medical opinion is that even small quantities of cytotoxic drugs and their metabolites should be avoided as much as possible.</p> <p>The safest approach therefore is to reduce occupational exposure to levels as low as reasonably achievable.</p> <p><i>Pregnant women should not be exposed to or handle this cytotoxic in any form.</i></p>
<p>5.General Precautions for use of</p>	<p>The main routes of exposure to cytotoxic drugs are through the inhalation of drug particles or aerosols, skin absorption, inadvertent ingestion through contact with contaminated food or cigarettes, and needle stick injuries.</p>

<p>cytotoxic drug on Animal</p>	<p>Exposure may occur during preparation and administration of the drugs, handling of body fluids from animals receiving cytotoxic drugs, handling and disposal of cytotoxic wastes and related trace contaminated material, and transportation of cytotoxic drugs.</p> <p>Some cytotoxic drugs have a direct irritant effect on the mucous membranes, eyes and skin. Spills onto skin surfaces that have cuts or abrasions and punctures of the skin with a contaminated needle or broken glass can lead to severe soft tissue injury. They should be treated immediately and observed for potential problems.</p> <p>Tools (as, syringe, blades and safety needles where possible) should be adapted for BSL-2. Have a sharps container in close vicinity.</p> <p>Animals should be restrained or anesthetized during injection.</p> <p>Etoposide excreted by the animals, post injection, therefore the bedding is considered as contaminated.</p>
<p>6. Environmental / Ventilation Controls</p>	<p>The preparation of Etoposide including reconstitution, weighing, and diluting should be performed in a fume hood or biological safety cabinet (class II Type B). Work should be done over absorbent pads.</p> <p>Following preparation of Etoposide, the work area should be thoroughly cleaned with soap and water or with virusolve.</p> <p>Work should be conducted in ABSL-2 facility, <u>over absorbent pads</u> in a class II type A1 or A2 biological cabinet.</p>
<p>7. Special Handling Procedures & Storage Requirements</p>	<p>Handling:</p> <p>Etoposide should be handled in containment and done over absorbent pads.</p> <p>Any visible contamination or spills should be cleaned with virusolve and then washed with water. Any wipes contaminated with Etoposide must be disposed as Cytotoxic hazardous waste.</p> <p>Releases of Etoposide to the environment should be avoided.</p> <p>Utilize safe sharps procedures (i.e. sharps container in the immediate vicinity, Leurlock syringes are recommended). The fume hood or other approved containment must be cleaned upon completion of tasks.</p> <p>Any laboratory equipment or surfaces that have come in contact with Etoposide must be disposed of (cytotoxic cytotoxic waste) or decontaminated (wipe with virusolve follow by water soaked paper towels) Non-porous material (e.g. glassware) can be</p>

	<p>decontaminated by soaking in virusolve for 24 hours.</p> <p>Upon completion, soak all surgical equipment in 80%(v/v) ethanol for at least one hour before washing with soap and water and autoclaving.</p> <p>When transporting Etoposide, the vials should be placed in secondary, sealed, plastic, labeled, non-breakable containers.</p> <p>All equipment must be decontaminated prior to removal from the room housing the infected animals.</p> <p>DO NOT use bleach for disinfection of work surfaces where Etoposide has been used.</p> <p>Hands must be washed upon exiting animal room.</p>
<p>8. Precautions for Animal Use</p>	<p>No recapping needles. Have a sharps container in close vicinity. Animals should be restrained or anesthetized during injection. Once Etoposide is injected, animals , animal waste and cages are considered hazardous.</p> <p>Hands must be washed upon exiting animal room.</p>
<p>9. Animal handling practices</p>	<ol style="list-style-type: none"> 1. Animals must be housed in filter top cages marked as biohazards (including the name of the pathogen/biohazard). Handling the cages (including bedding) will be done only by the researchers. 2. Use a class II Biological Safety Cabinet at all times (especially during injection or any surgical procedure), when performing work on these animals and/or when moving animals from dirty to clean cages. 3. Injecting animals with Etoposide: Animals will be injected IP with Etoposide within Class II Biosafety cabinet or designated cytotoxic fume hood. All needles will be disposed of in sharps container – do not recap or bend needles. 4. Infected animals considered hazardous; take precautions to avoid the creation of aerosols when changing or washing cages, or cleaning the room. A respirator is recommended for personnel that are immunocompromised and for healthy personnel if work is done outside the ventilated cabinet. 5. Care should be taken to avoid exposure to bedding dust when handling exposed animals and their waste materials during this time. 6. Dead animals must be placed in primary plastic bags, which are then placed in biosafety bags for infectious waste incineration. 7. All surfaces and racks that may be contaminated will be decontaminated with virusolve followed by water ASAP.

	<p>8. The bedding is considered contaminated and requires special handling.</p> <p><u>When changing cages, use the following technique:</u></p> <ul style="list-style-type: none"> • Transfer the animals to clean cages . • Decontaminate the used cages with virusolve. • Insert the used cages in a plastic bag . • Twist the ends of full bags, and seal with tape. Label with wide tape or other type of label marked “toxin- Etoposide. • Transport the bags of cages to a HEPA filtered dumping station that draws air away from the use (or BSC Type II), it is recommended to use a fume hood. • If local ventilation controls are not available for opening cages or dumping bedding, an N-99 respirator and safety goggles must be worn. • All contaminated bedding will be labeled as hazardous materials and handled accordingly: incinerated or placed in cytotoxic waste bags for disposal. • Use virusolve to decontaminate the cages, then put in plastic bags (marked “toxin- Etoposide) and sealed for transport to the washroom. • In the washroom ,cages should be unloaded from the bags with the appropriate PPE as mentioned above and run through the cage wash in the conventional manner. Note- cage wash personnel that meet the criteria for extra precautions above (pregnant exc.) should take extra precautions (additional PPE) when handling cages that may have Etoposide contamination.
<p>10. Spill and Accident Procedures</p>	<ol style="list-style-type: none"> 1. Spills must be cleaned immediately by properly protected trained personnel wearing a gown, goggles, two pairs of gloves (nitrile) and respirator mask covering the mouth and nose . 2. Minor Liquid Spills: should be cleaned immediately by personnel wearing a PPE. Use absorbent pads to wipe liquid. The spill area should then be cleaned thoroughly with virusolve (<i>allow at least 15 minutes</i>) and then wash the area with soap and water. Place waste in plastic bag and then in the cytotoxic waste container. 3. Powder/Major Spills: should be cleaned immediately by personnel wearing a PPE. For powder or major liquid spills outside of a fume hood or approved containment, personnel should be instructed to leave the laboratory and

	<p>entrance should be restricted for at least 30 min. In addition to the above specified PPE, a respirator and safety goggles, should also be worn. Contain or absorb spill with absorbent material, it may be helpful to lightly wet the absorbent material. Wipe the area with virusolve 1-2 times (<i>allow at least 15 minutes</i>) and then wash the area with soap and water.</p> <p>Collect and place waste in plastic bag and then in the cytotoxic waste container.</p> <p>**Prevent, by any means available, spillage from entering drains or water courses.**</p> <p><u>Exposure:</u></p> <p>4. In case of injection with Etoposide, wash the affected area with soap and water for at least 15 minutes. Consult with Employee Health Center.</p> <p>5. Eye Contact: Immediately flush eyes with water for at least 15 minutes. If irritation occurs or persists, get medical attention.</p> <p>Skin Contact: Remove clothing and wash affected skin with soap and water. This material may not be completely removed by conventional laundering. Consult professional laundry service. Do not home launder. If irritation occurs or persists, get medical attention.</p> <p>Inhalation: Remove to fresh air and keep patient at rest. Seek medical attention immediately.</p> <p>Report the accident/injury to the Biosafety Unit.</p>
<p>11. Waste Disposal</p>	<p>Dispose all waste material in the appropriate cytotoxic waste container.</p> <p>Unused solutions of Etoposide and contaminated solid waste will be disposed of as hazardous cytotoxic material.</p> <p>Releases of Etoposide to the environment should be avoided.</p>
<p>I hereby confirm that I have read the SOP (Standard Operating Procedure) for Working with Etoposide in Animals, and agree to follow these procedures.</p>	
<p>Name:</p>	<p>Title:</p>
<p>Signature:</p>	<p>Date:</p>

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