Guidelines for Use of Cytotoxic Agents

I. Purpose:
The purpose of this document is to establish guidelines for the safe handling and disposal of cytotoxic agents that will minimize the risk of the inadvertent exposure to Research personnel.

II. Introduction:
Cytotoxic agents are pharmaceutical agents primarily used to treat malignant neoplasms, certain inflammatory conditions and certain viral infections. They are potentially dangerous because of their genotoxic, oncogenic, mutagenic or teratogenic effects as well as their ability to elicit local and systemic hypersensitivity reactions. Examples of these agents include paclitaxel (taxol), doxorubicin (adriamycin), 5-fluorouracil (5-FU), and streptozotocin (STZ).

The routes of exposure include:
- Inhalation of drug dusts or droplets
- Absorption via skin or mucous membranes
- Injection
- Ingestion via contact with contaminated items that are placed in one's mouth

III. Personal Protective Equipment (PPE)
The following PPE should be worn when handling cytotoxic agents:

a. Disposable, powder-free gloves with permeation resistance to specific hazardous drugs must be worn for all procedures involving cytotoxic agents.
   - Double gloving is required.
   - Reminder that the outer glove should be removed if punctured, torn or contaminated.
   - When removing gloves, dispose in proper hazardous waste container for disposal.
   - Hands must be washed thoroughly before and after gloving. Gloves are not a substitute for hand washing.

b. Disposable, protective, lint-free gowns of low-permeability must be worn.
   - Potentially contaminated gowns will not be worn outside of the work area.
   - Potentially contaminated gowns will be disposed in the proper hazardous waste container (See Section VI below).

c. Safety goggles

d. Respiratory Protection
   - N95 HEPA respirator when local exhaust ventilation is not available. *Note: You must be fit-tested by the Industrial Hygienist to wear an N95 respirator.

 e. If the work occurs within an ABLS-2 housing room, then all of the required PPE must also be worn (bonnet, face shield, two pair of booties). *Please note that the two pairs of “chemo” gloves can replace the nitrile gloves and the chemo gown can replace the disposable gown or Tyvek suit.
IV. Safe Work Practices
   a. Administration of cytotoxic agent(s) must be performed either in a biosafety cabinet or chemical fume hood. Preparation of the agents must be performed within a chemical fume hood.
   b. No eating or drinking.
   c. Store all waste in covered receptacles.
   d. Minimize aerosols by taking care when:
      o Withdrawing needles from drug vials
      o Transferring drugs via needles/syringes
      o Expelling drugs from needles
   e. Use a plastic lined absorbent pad to cover work area.
   f. Clean all surfaces including containers with appropriate detergent when complete.

V. Use of Cytotoxic Agents in Animals
   a. All work with cytotoxic drugs in animals must be approved by the VA Pittsburgh Healthcare System (VAPHS) Institute Animal Care and Use Committee (IACUC).
   b. Procedures cannot start until the Animal Research Facility (ARF) Supervisor is notified of the use of the cytotoxic agent in advance (recommended 30 days, if possible).
   c. When animals are administered cytotoxic drugs, Research personnel must do the following:
      o Post-procedure cards must list the full name of the cytotoxic agent at least once. After that, abbreviations can be used.
      o A blue chemical hazard sticker must be placed on the white cage card.
      o A yellow door sign listing the agent in use and the hazards caused by the agent must be posted on the entrance to the housing room.
   d. Handling of the animal or opening of the cage must be performed under a chemical fume hood or biosafety cabinet until at least one cage has occurred (minimum time 72 hours, maximum time 1 week).
   e. Dirty bedding must be placed in a yellow trace chemotherapeutic waste bag for disposal. If the waste is placed in a red biohazard bag, the biohazard box must be marked as chemotherapeutic waste.

VI. Disposal Guidelines
Wastes from cytotoxic agents include spent or excess compounds generated from treatment preparation and administration, liquid and solid wastes from cell cultures treated with the agents, expended personal protective equipment, and spill cleanup materials. Cytotoxic wastes which are biohazardous are classified as chemotherapeutic waste and must be managed as such.

Cytotoxic wastes must be disposed separately from biohazardous or regular municipal waste according to state regulations. Liquid cytotoxic wastes cannot be disposed down the drain or sanitary sewer. Solid cytotoxic wastes cannot be disposed in the regular trash or in red biohazard bags.

   a. Unused portions of cytotoxic agents must be disposed through the chemical waste disposal program.
      • A hazardous waste label must be completed and placed on the container.
      • Contact the GEMS/Environmental Protection Specialist to pick up the waste (412-822-3197).
b. Used liquid cytotoxic wastes should be collected in leak proof containers which are constructed from glass or plastic with tight fitting lids (e.g., cell culture media bottles).
   - Liquid waste includes spent cytotoxic waste as well as liquid cell culture waste from cells treated with cytotoxic agents.
   - The waste container (e.g., cell culture media bottle) should be capped and placed in a separate yellow chemotherapeutic waste container.

c. Solid cytotoxic wastes, including items such as personal protective equipment that comes in contact with a cytotoxic agent during administration into an animal and contaminated plastic ware from cell cultures treated with cytotoxic agents are considered to have trace amounts and should be collected in yellow plastic bags and then placed in the yellow waste container that is labeled as “chemotherapeutic waste”.

d. Sharps disposal - Needles that are used for injection of cytotoxic agents into animals must be disposed in a yellow and white Sharps container. This Sharps container must be dedicated to disposal of only Sharps that come into contact with cytotoxic agents. Other solid and liquid wastes that are created should be disposed in larger yellow waste containers as described in sections b and c above. Sharps waste containers used to collect cytotoxic wastes are yellow and white, puncture-proof and leak-proof, and are labeled “Chemotherapeutic Waste”. Contact the Environmental Management Service (EMS) to pick up the waste (412-360-3685).

e. Bulk cytotoxic agents include drug vials, ampules, or other containers filled to a weight greater than 3% of the capacity of the container. These “bulk” items must be disposed in the designated black plastic container. U-Listed wastes (i.e., streptozotocin) must also be disposed in the black containers. All bulk cytotoxic agents are disposed through the hazardous waste disposal program. Contact the GEMS/Environmental Protection Specialist to pick up the waste (412-822-3197).

VII. Spill Clean-Up

a. Spill kits should be kept in all areas where cytotoxic agents are routinely used.
b. A spill kit should contain the following:
   - Two (2) pairs of disposable “chemotherapeutic” gloves
   - Low-permeability protective garments (gown, shoe covers)
   - Safety glasses or splash goggles
   - N95 Respirator
   - Absorbent plastic-backed spill pads
   - Disposable towels
   - Two (2) hazardous waste disposal bags (yellow)
   - Disposable scoop
   - Warning sign
c. Spill must be cleaned up immediately.
d. Spills should be cleaned according to the following procedures:
   - Identify that a spill has occurred and warn others by placing specific warning signs around the contaminated area to prevent approaching traffic.
   - Don appropriate PPE from the spill kit.
   - If applicable, remove glass fragments using enclosed scoop and dispose of in puncture-resistant container.
- Wipe liquids with enclosed absorbent spill pad; remove powder with dampened gauze or absorbent spill pad
- Proceed from areas of lesser to greater contamination when cleaning.
- The contaminated surface should be washed with detergent, then several times with water.
- All contaminated materials should be placed in the enclosed disposal bags, sealed and then placed in the designated yellow waste container.
- Spills within the biosafety cabinet should be cleaned immediately.
  - A spill kit should be used if the spill volume exceeds 150 milliliters.
  - Spills should be cleaned first with water, then a disinfectant.
  - The biosafety cabinet should be thoroughly cleaned after spill cleanup.

  e. For large spills (spill amounts larger than 5 milliliters or 5 grams), contact the Spill Response Team at 412-360-3705 during normal business hours or dial the Boiler Plant at 412-360-6139 during non-business hours.

Refer to Medical Center Memorandum (MCM) TX-035 Handling of Cytotoxic Agents and EC-046 Exposure to Hazardous Drugs for additional information on the use of cytotoxic drugs within the VAPHS.