OHS Registration #: _____

Expiration Date: _____

STANDARD OPERATING PROCEDURE/APPROVAL FORM
FOR CARCINOGENS AND HIGHLY TOXIC MATERIALS

Instructions: Please complete this form to request approval to use and possess highly toxic or carcinogenic material from the University Chemical Hygiene Committee as required by Chapter 12 of the University Chemical Hygiene Plan and University Policy 7-37.

Submit a separate form for each chemical. Copies of the current guidelines and Chemical Hygiene Plan are available at the DOHS web site: http://www.udel.edu/OHS/. For questions, please contact the University Chemical Hygiene Officer at 831-2103.

Form Updated: January 2007

Please attach a detailed synopsis of how this material will be used in your research.

Section I – Information

1. Principal Investigator(s): _____
2. E-Mail Address: _____
3. Department: _____
4. Address: _____
5. Phone Number: _____ 6. Fax Number: _____
7. Lab(s) to be Used: _____
8. Chemical: Actinomycin including 23-21, C, D, S and S3

Section II – Use and Storage

A. Purchasing

All purchases of this material must have approval from the Principal Investigator (PI) or authorized personnel before ordering. The user is responsible to ensure that a current Material Safety Data Sheet (MSDS) is obtained unless a current one is already available within the laboratory. Quantities of this material will be limited to _____, and/or the smallest amount necessary to complete the experiment.

B. Authorized personnel

Please select the general categories of personnel who could obtain approval to use this material:

1. ☐ Principal Investigator 2. ☐ Graduate Students 3. ☐ Undergraduates
4. ☐ Technical Staff 5. ☐ Post Doctoral Employees
6. ☐ Other (Describe): _____

Please list the specific personnel and their approval level (Attach an addendum to this form for additional personnel):

NOTE: The Principal Investigator must be aware of all purchases of this material. The Principal Investigator must assure the there is not an exceedance of the quantity limits.

1. _____	☐ Purchase	☐ Use the Material
2. _____	☐ Purchase	☐ Use the Material
3. _____	☐ Purchase	☐ Use the Material
4. _____	☐ Purchase	☐ Use the Material
5. _____	☐ Purchase	☐ Use the Material

The Principal Investigator will update this section when any personnel changes occur. If changes occur, document the changes (include the record of training of additional personnel) in the laboratory's files and submit an addendum to the University Chemical Hygiene Officer with all training documentation.

C. Storage

Materials will be stored according to compatibility and label recommendations in a designated area.

1. Please list compounds that this chemical is incompatible with: _____
2. Please list special storage requirements (I.E.: Refrigerated, Inert Atmosphere, Desiccated, etc.): _____
3. Please list specific storage area (This Area Must be Marked and Labeled): _____

Storage areas will be inspected by laboratory personnel on a regular basis. Personnel will check for safety concerns such as improper storage, leaking/damaged container(s), damaged labels, quantities in excess of approved limits, theft/disappearance of material, etc. The inspector will also determine if an inventory reduction is possible. The Principal Investigator will designate one individual to complete this inspection.

4. Please select an inspection frequency:

☐ Weekly ☐ Biweekly

☐ Bimonthly ☐ Monthly

D. Use location:

Materials shall be used only in the following designated areas.

Check all that apply:

1. ☐ Demarcated Area in Lab (Describe): _____
2. ☒ Fume Hood
3. ☐ Glove Box
4. ☐ Other (Describe): _____

Section III – Personnel Safety and Protection

A. Training requirements:

All users must demonstrate competency and familiarity regarding the safe handling and use of this material prior to purchase. The Principal Investigator is responsible for maintaining the training records for each user of this material. Training should include the following:

1. Review of current MSDS
2. Chemical Hygiene/Right-To-Know
3. Chemical Waste Management
4. Review of the OSHA Lab Standard
5. Review of the Chemical Hygiene Plan
6. Special training provided by the department/supervisor
7. Review of the departmental safety manual if applicable
8. Safety meetings and seminars
9. One-on-One hands-on training with the Principal Investigator or other knowledgeable laboratory personnel.
10. Other: _____

B. Personal Protective Equipment:

All personnel are required to wear the following personal protective equipment whenever handling this material:

1. Proper Laboratory Attire (Pants or dresses/shorts below the knees, sleeved shirt, close-toe shoes)
2. Safety Glasses – **Researchers must upgrade to chemical safety splash goggles if a splash, spray or mist hazard exists. In general, safety glasses can be worn if the fume hood sash is properly positioned to provide the splash, spray and mist protection, otherwise indirect venting chemical safety splash goggles must be worn.**
3. Lab Coat
4. Chemical Protective Gloves: PVC or Nitrile

Personnel may be required to wear other Personal Protective Equipment when working with this material. The Principal Investigator should contact the University Chemical Hygiene Officer to discuss the selection of chemical protective clothing (aprons, suits and gloves) and respirators. Please check all that apply:

1. ☐ Chemical Safety Splash Goggles	2. ☐ Face Shield
3. ☐ Chemical Protective Clothing (Describe): _____	
4. ☐ Chemical Protective Splash Apron (Describe): _____	
5. ☐ Respirator (Type): _____	
6. ☐ Other (Describe): _____	

C. Safe Work Practices

The following safe work practices should be employed when using this material:

1. Wear all required personal protective equipment
2. Cover open wounds
3. Wash hands thoroughly when work with the material is completed
4. No mouth pipetting
5. Use of sharps, such as glass Pasteur pipettes, needles, razor blades, etc. should be avoided or minimized
6. Must not work alone in the laboratory
7. Please list any other safe work practices: _____

D. Personnel Decontamination and Emergency Actions

For most exposures, decontamination should occur as follows:

1. Small Skin Exposures –

    a. Wash contaminated skin in sink with tepid water for 15 minutes
    b. Have buddy locate the MSDS
    c. Wash with soap and water
    d. Contact Occupational Health and Safety at 831-8475 for further direction

2. Eye Exposure –

    a. Locate the emergency eye wash
    b. Turn eye wash on and open eyelids with fingers
    c. Rinse eyes for 15 minutes
    d. Have buddy contact 911 for the Newark Campus, 9-911 for all others and locate the MSDS
    e. Notify OHS

3. Large Body Area Exposure –

    a. Locate the emergency safety shower
    b. Stand under shower and turn it on
    c. Rinse whole body while removing all contaminated clothing
    d. Have buddy contact 911 for the Newark Campus, 9-911 for all others and locate the MSDS
    e. Rinse body for 15 minutes
    f. Notify OHS

1. Ingestion Emergencies –

    a. If swallowed do NOT induce vomiting.
    b. If vomiting occurs, lean patient forward or place on left side (head-down position, if possible) to maintain open airway and prevent aspiration.
    c. Never give liquid to a person showing signs of being sleepy or with reduced awareness; i.e. becoming unconscious
    d. Have buddy contact 911 for the Newark Campus, 9-911 for all others and locate the MSDS

e. Notify OHS

2. Inhalation Emergencies –

    a. If fumes or combustion products are inhaled remove from contaminated area.
    b. Lay patient down. Keep warm and rested.
    c. Prostheses such as false teeth, which may block airway, should be removed, where possible, prior to initiating first aid procedures.
    d. 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.
    e. Have buddy contact 911 for the Newark Campus, 9-911 for all others and locate the MSDS
    f. Notify OHS

3. Injection Emergencies –

    a. Clean the areas with soap and water
    b. Allow the wound to bleed
    c. Have buddy contact 911 for the Newark Campus, 9-911 for all others and locate the MSDS
    d. Notify OHS

Please list any special decontamination procedures: For every vial spilled (assuming 0.5 mg active ingredient), apply 2.2 ml of trisodium phosphate (TSP). A contact time of 30 minutes with TSP is recommended. Soak equipment/ utensils in an excess of 5% trisodium phosphate for 30 minutes to destroy any remaining trace amounts of active compound. The solution is then considered to be no longer genotoxic and may be disposed of.

E. Exposure Symptoms and Treatment

Please list the emergency procedures to be followed in the event of an exposure. These will be found in the MSDS for the compounds:

1. **Skin Contact Symptoms:** The material is not thought to produce adverse health effects or skin irritation following contact (as classified using animal models). Nevertheless, 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

2. **Eye Contact Symptoms:** This material can cause eye irritation and damage in some persons.

3. **Ingestion Symptoms:** Severely toxic effects may result from the accidental ingestion of the material; animal experiments indicate that ingestion of less than 5 gram may be fatal or may produce serious damage to the health of the individual.

4. **Inhalation Symptoms:** The material is not thought to produce respiratory irritation (as classified using animal models). Nevertheless inhalation of the material, especially for prolonged periods, may produce respiratory discomfort and occasionally, distress. 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.

The ChemWatch MSDS, which is available at http://www.udel.edu/OHS/ oftentimes, has treatment information for Emergency Room Personnel and Doctors to follow. Please list any information that can be provided to assist with the treatment:

NOTES TO PHYSICIAN

Control of nausea and vomiting may attempted by giving phenothiazones such as perphenazine, prochlorperazine, promethazine or thiethylperazine before antineoplastic agents are administered. In bone-marrow depression, transfusion of blood or platelets are given to reduce the risk of life-threatening haemorrhage. Granulocyte transfusions and injection of antibiotics may be necessary to combat infection in the neutropenic patient. Hyperuricaemia is avoided by the addition of allopurinol to treatment schedules and measures such as alkanisation of the urine and hydration may be adopted.
If conscious, give water or a suspension of activated charcoal. Azide ingestions are potentially dangerous to health care providers. In the acid stomach, volatile and toxic hydrazoic acid is formed. Isolate vomitus, gastric washings, dispose of azide residues promptly and safely. Keep patient in well ventilated area.

MARTINDALE: The Extra Pharmacopoeia, 27th Ed.

F. Spills

The laboratory should be prepared to clean up minor spills (25 ml/25 g or less) of highly toxic/carcinogenic materials should they occur in a properly operating fume hood. Chemical spill clean up guidance can be found at http://www.udel.edu/OHS/chemspillkit/chemspillkit.html. Laboratory personnel cleaning up a spill will wear all personal protective equipment listed above and manage all cleanup debris according the waste disposal section. Notify OHS of any spills, even if the lab staff handled the clean-up.

Please list the following:

1. Location of Spill Cleanup Materials for a small spill: _____

2. Any special measures/cleanup material required to cleanup a spill: Remove all ignition sources. Clean up all spills immediately. Avoid contact with skin and eyes. Control personal contact by using protective equipment. Use dry clean up procedures and avoid generating dust. Contain or absorb spill with sand, earth or vermiculite. Place in a suitable labeled container for waste disposal. For every vial spilled (assuming 0.5 mg active ingredient), apply 2.2 ml of trisodium phosphate (TSP). A contact time of 30 minutes with TSP is recommended. Soak equipment/ utensils in an excess of 5% trisodium phosphate for 30 minutes to destroy any remaining trace amounts of active compound. The solution is then considered to be no longer genotoxic and may be disposed of through the hazardous waste program.

If a spill is large or occurs outside of a fume hood, the laboratory occupants should immediately vacate the laboratory, close all doors and contact Occupational Health & Safety at 831-8475 during working hours or 911 after hours. If the laboratory personnel determine that the spill is not contained to the lab or could cause harm to people outside the laboratory, they should pull the building fire alarm and go to the Emergency Gathering Point to await the University Police and Emergency Responders. The responsible/knowledgeable person should provide the University Police and the Emergency Responders with the following:

1. Common Name of the Material Involved

2. A copy of a MSDS, if possible

3. Any pertinent information related to the emergency, such as location in the lab, other hazards in the lab, etc.

G. Emergency Phone Numbers:

Below are a list of emergency numbers to contact in the event of an emergency:

1. Police, Fire or Medical Emergency, call – 911 on the Newark Campus, 9-911 for all others

2. Occupational Health & Safety – X8475

Please provide a list of other emergency phone numbers, such as after hour contacts for laboratory personnel or any other important phone number, to be used in the event of an emergency: _____

H. Other Special precautions

Please list any other special precautions or procedures not listed in the above sections. Please be as specific as possible: _____

I. Chronic Health Effects

There has been some concern that this material can cause cancer or mutations but there is not enough data to make an assessment. Principal routes of exposure are by accidental skin and eye contact and inhalation of generated dusts. The drug is given in short courses because of its potential for severe toxicity. Apart from nausea and vomiting adverse effects are often delayed, occurring days or weeks after the completion of the course of treatment. In clinical use 10-15 ug/kg (500 ug) is administered intravenously for 5 days. Serious toxic side-effects usually appear 10-14 days after therapy has been initiated. These include erythema, stomatitis (inflammations of the mouth), fever, hypocalcaemia, myalgia (muscle pains), gastro-intestinal effects, hair loss, and kidney and liver abnormalities. Bone-marrow depression is apparent 1-7 days after therapy. In subacute animals studies (5 to 30 days), anorexia, gastrointestinal effects (including haemorrhaging and ulceration), testicular abnormalities, and haematological and lymphoidal alterations were reported at dosages as low as 10 ug/kg/day. Actinomycin forms stable complexes with DNA and interferes with DNA dependent RNA synthesis. It may also enhance the cytotoxic effects of radiotherapy. In addition it possesses immunosuppressive properties. The material is mutagenic is several assay systems and produced local sarcomas in mice and rats receiving intermittent subcutaneous or intraperitoneal injections at dosages as low as 10 ug/kg. It was also embryotoxic and teratogenic in rats and mice given intraperitoneal injections of 25 ug/kg/day or more. Medical conditions which may be aggravated by exposure to the drug include pre-existing blood, gastrointestinal, skin or testicular disorders, chicken pox, herpes zoster and pregnancy. 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.

Section VI – Waste Disposal

The authorized person using this material is responsible for the safe collection, preparation and proper disposal of waste unless otherwise stated below. Waste shall be disposed of as soon as possible and in accordance with all laboratory and University procedures. All personal must obtain chemical waste disposal training via DOHS.

Specific instructions:

Collect solid waste material in a 7mil polyethylene bag and label with an orange chemical waste label. Collect liquid waste in a "Justrite" container provided by DOHS. Label with a hazardous waste label. Use proper laboratory ventilation such as a fume hood to manage both liquid and solid wastes. Contact DOHS for removal. Do not put in the normal trash or pour any solutions down the drain.

Section V – Signature and Verification

Your signature below indicates that you have completed this form accurately to the best of your knowledge, you acknowledge all requirements and restrictions of this form and that you accept responsibility for the safe use of the material.

1. Prepared By: _____ Date: _____

   Signature: _____

2. Principal Investigator: _____ Date: _____

   Signature: _____

Section VI – Approval Process

A. University Chemical Hygiene Officer Approval

The Principal Investigator should have this form completed as accurately as possible. Please e-mail or fax this form to the University Chemical Hygiene Officer at eich@udel.edu or 831-1528. The Chemical Hygiene Officer will review and verify the form and make any necessary changes or updates.

1. University CHO: _____ Date: _____

Signature: _____

B. Conditional Approval to Purchase and Use

This form will then be e-mailed or faxed to a member of the University Chemical Hygiene Committee (CHC), usually from the same department as the requesting PI. The Committee Member will meet with the Principal Investigator or designee and discuss the form and the use of the material. If the Committee Member finds the procedure acceptable, they can offer a conditional approval for purchase and use of this material.

2. CHC Member: _____ Date: _____

Signature: _____

C. Full Approval

A signed copy of the form will be sent, via campus mail, to the University Chemical Hygiene Officer, who will bring it up at the next Chemical Hygiene Committee Meeting for full approval. All approvals will be good for two years. The complete, signed approval form will kept on file with Occupational Health & Safety and a copy will be sent to the Principal Investigator to keep on file.

3. Acceptance: _____ Date: _____

CHC Chair: _____

Signature: _____

D. Approval Expiration

The approval for use and purchase of this material will expire should any of the approved information change, with the exception of Section II, B and C, Authorized Personnel and Storage Location, or two years after CHC approval. If, at the end of two years, the procedure is substantially the same, the Principal Investigator can complete a renewal form and send it to the University CHO, who can approve the renewal for an additional two years.

CHECKLIST FOR POSSESSION AND USE OF CARCINOGENS AND HIGHLY TOXIC MATERIALS

The checklist is provided to assist a researcher with the approval process for possession and use of carcinogens and highly toxic materials. This form may be kept on file in the laboratory with the SOP to serve as documentation. The complete procedure can be found in the University Chemical Hygiene Plan in Chapter 12.

Date and Initial	
_____	1. Complete a Standard Operating Procedure/Approval Form For Carcinogens and Highly Toxic Materials and submit this form to OHS for review
_____	2. Review and make OHS's changes and recommendations
_____	3. Meet with a member of the University Chemical Hygiene Committee to review the approval form and the use of the material.
_____	4. Submit (via campus mail) the completed and signed form back to the University Chemical Hygiene Officer for conditional approval to purchase and use the material. The University Chemical Hygiene Committee will review this form at the next scheduled meeting for full approval.
_____	5. Complete a Job Hazard Analysis (JHA) for each experiment in which this compound is used. These JHAs must be kept on file in the laboratory and updated every 5 years or when a process changes.
_____	6. Provide and document training for every worker who will use the material. Training shall include hands-on instruction as well as review of the JHA, SOP and the University Chemical Hygiene Plan; specifically Chapter 12.
_____	7. Conduct a trial run with OHS present.
_____	8. Have OHS present the first time a process using this material occurs.