

Laboratory Guidelines for the Safe Use of Chemical Carcinogens and Toxins

The National Institutes of Health (NIH) Guidelines for the Laboratory use of Chemical Carcinogens provide recommendations and requirements governing the use of chemical carcinogens in the NIH intramural programs.

The Department of Environmental Health and Safety (EHS) and the Laboratory Safety Committee (LSC) of Thomas Jefferson University has received permission from the NIH to modify the guidelines so that they may be adopted for use in the laboratories conducting research involving chemical carcinogens and toxins. The principle purpose of these guidelines is to assist the laboratory investigator in the selection and use of safeguards that will serve to ensure a safe and healthful environment in the use of chemical carcinogens and toxins at Thomas Jefferson University. The guidelines are designed to permit the necessary beneficial use of such compounds with minimum exposure to University personnel. The recommendations are based on established principles of laboratory safety.

The modified NIH Guidelines along with the Thomas Jefferson University Guide to Laboratory Safety should be followed in dealing safely with chemical carcinogens and/or toxins in research laboratories.

I. Introduction

The NIH Guidelines for the Laboratory Use of Chemical Carcinogens recommend procedures and safeguards that are applicable to the laboratory workplace for minimizing exposure of laboratory personnel to chemical substances that pose a carcinogenic or toxin risk. They apply to the use of chemical substances for which standards have been promulgated by the Occupational Safety and Health Administration (OSHA) as 29CFR 1910.1450, occupational exposure to hazardous chemicals in laboratories, and other chemical substances which in the judgment of Thomas Jefferson University Laboratory Safety Committee pose a carcinogenic or toxin risk to laboratory personnel.

The safeguards recommended in the guidelines consist of good laboratory practices and engineering controls that are useful in minimizing exposures to personnel and the environment from carcinogens and that are used in the laboratory. Their application to a specific laboratory activity must be based on the judgment of the principal investigator who is responsible for the safety of operations involving chemical carcinogens or toxins under his or her supervision. In selecting appropriate safeguards, the principal investigator must give specific attention to (I) the quantity of the chemical carcinogen or toxin to be used, (II) the physical and chemical properties of the agent, (III) the comparative carcinogenic potency, (IV) the type of experimental procedures that will be involved in the proposed use of chemical carcinogens, and (V) the engineering controls available in the laboratory.

Safety Data Sheets which provide specific technical and safety information pertaining to the use of individual chemical carcinogens/toxins can be obtained from the Environmental Health and Safety. This information can assist the user in making informed judgments as to the selection of appropriate safeguards for the conduct of work involving chemical carcinogens. In addition, a course in the recognition and control of chemical hazards in the laboratory is available from Environmental Health and Safety.

There are some chemical carcinogens and/or toxins that, if not adequately controlled may pose a significant risk to employees. The principal investigator who may wish to conduct a potential high risk operation must obtain permission from the Department of Environmental Health and Safety and the Laboratory Safety Committee prior to initiating the operation.

II. Policy

The use of chemical carcinogens and/or toxins within Thomas Jefferson University shall be planned and performed in a manner to ensure that a safe and healthful environment is maintained. The objective of this policy is to reduce employee and environmental exposures to chemical carcinogens and/or toxins used in Thomas Jefferson University laboratories to the lowest practicable level within permissible exposure limits.

1. Thomas Jefferson University Laboratory Safety Committee

The Laboratory Safety Committee is responsible for: (1) promulgating policies that provide for the safe conduct of work involving chemical carcinogens; (2) identifying chemical substances used in Thomas Jefferson University laboratories which may pose a carcinogenic or toxin risk; (3) developing and instituting procedures for approving high risk operations involving chemical carcinogens and/or toxins.

2. Department of Environmental Health and Safety

The Department of Environmental Health and Safety is responsible for: (1) assisting the principal investigator in the selection of appropriate personal protective equipment, laboratory practices and engineering controls; (2) providing technical guidance to personnel at all levels of responsibility on matters pertaining to laboratory safety; (3) inspecting laboratories at least annually to assess compliance with policies for the safe conduct of work involving chemical carcinogens and/or toxins; (4) investigating all reported accidents which result in the exposure of personnel of the environment to a chemical carcinogen and/or toxin and recommending corrective action to reduce the potential for recurrence; (5) supervising decontamination operations where accidents have resulted in significant contamination of laboratory areas; and (6) developing and conducting appropriate training and information programs to promote methods for the safe handling of chemical carcinogens and/or toxins.

3. Principal Investigator

The principal investigator has the primary responsibility for (1) acquiring the knowledge and information needed to recognize and control chemical hazards in the laboratory; (2) selecting and employing laboratory practices and engineering controls that reduce the potential for exposure to chemical carcinogens to the lowest practicable level; (3) obtaining approval when required from the Laboratory Safety Committee to conduct a high risk operation involving chemical carcinogens; (4) informing those employees, for whom the investigator is responsible, of the potential hazards associated with the use of chemical carcinogens or toxins and instructing them in the use of laboratory practices, engineering controls, and procedures for dealing with accidents involving such compounds; (5) supervising the safety performance of his or her staff to ensure that the required laboratory practices and engineering controls are employed; (6) arranging for immediate medical attention and reporting to the Department of Environmental Health and Safety any accident that results in (a) inoculation of chemical carcinogens or toxins through cutaneous penetration, (b) ingestion of chemical carcinogens or toxins, (c) inhalation of chemical carcinogens or toxins, or (d) any incident resulting in overt exposure to personnel or danger of environmental contamination by chemical carcinogens or toxins; (7) assisting representatives of the Department of Environmental Health and Safety with any problems pertaining to operation and implementation of laboratory practices and engineering controls; (8) informing each laboratory worker about the OSHA Standard, 29CFR 1910.1450, "Occupational Exposure to Hazardous Chemicals in Laboratories" and ensuring compliance with this safety standard.

4. Employee

Each employee is responsible for (1) knowing and complying with safety guidelines, regulations and procedures required for the task assigned; (2) reporting unsafe conditions to the principal investigator, immediate supervisor or Environmental Health and Safety and (3) reporting to the principal investigator or immediate supervisor all facts pertaining to every accident resulting in exposure to chemical carcinogens.

III. Medical Surveillance

Where practical methods are available, consideration should be given to employing these methods for surveillance of those employees who use the particular carcinogen on a regular basis. The Laboratory Safety Committee and/or Environmental Health and Safety should consult with the medical director of University Health Services, and with knowledgeable scientists who have broad experience in chemical carcinogenesis or toxins to determine whether such surveillance should be implemented for detecting evidence of employee exposure. Evidence of employee exposure is a clear signal calling for examination, identification and possible revision of the laboratory practices that may have contributed to employee exposure.

The University Health Services should ensure that the following information is included in each employee's medical record; (a) reports of accidents that have resulted in i) inoculation of chemical carcinogens or toxins through cutaneous penetration, ii) ingestion of chemical carcinogens or toxins, iii) inhalation of chemical carcinogens or toxins, and iv) any incident resulting in overt exposure of the employee to chemical carcinogens or toxins (b) results in any surveillance procedures employed; and (c) results of environmental measurements of chemical carcinogens or toxins that may have been made within the employees work environment.

IV. Employee Education

All employees working with, or who may be potentially exposed to, chemical carcinogens or toxins should receive sufficient information and training that will enable them to work safely and to understand the relative significance of the potential hazards as they relate to them personally. All employees directly involved or associated with areas in which chemical carcinogens or toxins are used should be periodically advised about (1) the possible sources of exposure, (2) adverse health effects (carcinogenic and other) associated with exposure, (3) laboratory practices and engineering controls in use to limit exposure, (4) the use and purpose of any recommended environmental and medical monitoring procedures, and (5) their responsibilities for following proper laboratory practices to help protect their health and provide for the safety of themselves and fellow employees. This information should be provided by persons qualified by training and experience, including their supervisors, principal investigator(s) and representatives of the Department of Environmental Health and Safety.

A course in the recognition and control of chemical hazards in the laboratory will be offered by the Department of Environmental Health and Safety. This course will provide specific information on the safe handling of chemical carcinogens or toxins. Principal investigators who successfully complete this course will be authorized to use most chemical carcinogens or toxins without further approval. The course is open to all investigators and technicians who may come in contact with hazardous chemicals.

V. Laboratory Practices and Engineering Controls

The laboratory practices and engineering controls recommended in this section detail general safeguards that should be observed when working with chemical carcinogens in the laboratory. These safeguards will provide protection to the laboratory worker from exposure to chemical carcinogens or toxins in the majority of situations. There are instances, however, when the physical and chemical properties, the proposed use, the quantity of chemical carcinogens or toxins needed for a particular use, or the carcinogenic or other toxic hazard of a chemical carcinogen or toxin will be such that either additional or fewer controls might be needed to protect the laboratory worker. Professional judgment is, therefore, essential in the interpretation of these recommendations.

1. Personnel Practices

Protective Clothing. Laboratory clothing that protects street clothing, such as a fully fastened laboratory coat or a disposable jumpsuit, should be worn when chemical carcinogens are being used. Laboratory clothing used for this purpose should not be worn outside the laboratory area. Clothing overtly contaminated by chemical carcinogens should be removed immediately and disposed of or decontaminated prior to laundering. Home laundering of laboratory coats is prohibited. When methods for decontaminating clothing are unknown or not applicable, disposable protective clothing should be worn. Gloves which are appropriate to the task and chemicals in use should be worn when handling a chemical carcinogen. Disposable gloves should be discarded after each use and immediately after overt visible contact with a chemical carcinogen or toxin.

Eye Protection. Devices to provide appropriate eye protection should be available and used in the laboratory work area. The type of device used will depend upon the hazard presented by the operation and chemical in use.

Eating, Drinking and Smoking. There should be no eating, drinking, smoking, chewing of gum or tobacco, application of cosmetics or storage of utensils, food or food containers in laboratory areas where chemical carcinogens are used or stored.

Pipetting. Mechanical pipetting aids should always be used for all pipetting procedures.

Personal Hygiene. All personnel should wash their hands immediately after the completion of any procedure in which a chemical carcinogen has been used and when they leave the laboratory. Immediately following any contact with a carcinogen or toxin, personnel should wash, or if appropriate, shower the affected area.

2. Operational Practices

Work Area Identification. Each entrance to a work area, where chemical carcinogens are being used or stored, should have affixed to it a sign with the following warning:

CAUTION - POTENTIAL HAZARD (define hazard) Authorized Personnel Only

Access Control. Work areas where chemical carcinogens or toxins may be entered only by persons authorized by the principal investigator or his / her designee. Maintenance, custodial and emergency personnel should be advised of the hazards that they may encounter before they are called on to enter

the laboratory. Access doors to work areas should be kept closed while experiments involving chemical carcinogens or toxins are in progress.

Work Surfaces. All work surfaces on which chemical carcinogens or toxins are used should be covered with stainless steel or plastic trays, dry absorbent plastic backed paper, or other impervious material. The protective surfaces should be decontaminated or disposed of after the procedure involving a chemical carcinogen or toxin has been completed.

Use of Primary Containment Equipment. Procedures involving volatile chemical carcinogens or toxins and solid or liquid chemical carcinogens or toxins that may result in the generation of aerosols should not be conducted on the open bench; they should only be conducted in a chemical fume hood, or a glove box. Examples of aerosol producing procedures are: Sonication; the opening of closed vessels; transfer operations; preparation of feed mixtures; blending; open vessel centrifugation; and the application, injection or intubation of a chemical carcinogen or toxin into experimental animals. Tissue culture and other biological procedures involving chemical carcinogens may be conducted in a Class II type B Biological Safety Cabinet. The principal investigator should obtain guidance from Environmental Health and Safety on the selection and use of containment equipment.

Use of Analytical Instrumentation. Vapors or aerosols produced by analytical instruments, when used with chemical carcinogens, should be captured through local exhaust ventilation at the site of their production or be vented into a chemical fume hood. When a sample containing a chemical carcinogen or toxins is removed from an analytical instrument, it should be placed in a tightly stoppered sample tube or otherwise safeguarded from contaminating the laboratory. Analytical equipment that becomes overtly contaminated should not be used until it has been decontaminated.

Storage and Identification of Stock Quantities. Stock quantities of chemical carcinogens and or toxins should be stored in a designated storage area or cabinet. Such a storage area or cabinet should be located within the laboratory work area. The storage area or cabinet should have affixed to it a sign with the following warning:

CAUTION - POTENTIAL HAZARD (define hazards)

The person responsible for the storage area should maintain a listing of stock quantities of chemical carcinogens or toxins that are stored within the storage area. The inventory should include the quantities of chemical carcinogens or toxins acquired and the dates of acquisition. Storage vessels containing stock quantities should be labeled with the following warning:

CAUTION - POTENTIAL HAZARD (define hazards)

Additional storage precautions may be required for certain compounds based upon other properties (i.e., flammability, radioactivity, etc.).

Working quantities. Working quantities of chemical carcinogens or toxins present in the work area should be kept to a minimum. Quantities should not normally exceed the amounts required for use in 1 week. This does not include amounts stored in a designated chemical carcinogen or toxin storage area or cabinet that is located within the laboratory work area. Storage vessels containing working quantities should have affixed to them labels with the following warning:

CAUTION - POTENTIAL HAZARD (define hazard)

Laboratory Transport. Storage vessels containing chemical carcinogens or toxins that are to be moved from one site to another (e.g., storage area to work area) should first be placed in a durable outer container. Contaminated materials which are to be transferred from work areas to disposal areas should be placed in a closed plastic bag or other suitable impermeable and sealed primary container. The primary container should be placed in a durable outer container before being transported. The outer container should be labeled with both the name of the chemical carcinogen or toxin and the following warning:

CAUTION - POTENTIAL HAZARD (define hazard)

Housekeeping. General housekeeping procedures which suppress the formation of aerosols such as the use of a wet mop or a vacuum cleaner equipped with a high efficiency particulate air (HEPA filter) to remove particulates should be used. Dry sweeping and dry mopping should not be used because of the hazard of aerosol formation. In those instances where a chemical carcinogen or contaminated material is spilled, special cleanup procedures developed for the individual compound should be employed.

Protection of Vacuum Lines. Each vacuum service including water aspirators, should be protected (e.g., with an absorbent or liquid trap and a HEPA filter) prevent entry of any chemical carcinogen into the system. When using a volatile carcinogen or toxin, a separate vacuum pump should be used. This device should be placed within or vented into an appropriate laboratory-type hood.

Packaging and Shipping. Chemical carcinogens or toxins should be securely packaged to withstand shocks, pressure changes, and any other conditions which might cause the leakage of contents incident to ordinary handling during transportation. Information concerning the proper methods for packaging and shipping of hazardous materials is detailed in Department of Transportation regulations 49 CFR Parts 170-178. Material Safety Data Sheets (MSDS must accompany chemicals that are shipped from laboratories).

Decontamination. Contaminated materials should either be decontaminated by approved procedures that decompose the chemical to produce a safe product or be removed for subsequent disposal.

Disposal. Prior to the start of any laboratory activity involving a chemical carcinogen or toxin, plans for the handling and ultimate disposal of contaminated wastes and surplus amounts of the carcinogen should be completed. The principal investigator should obtain guidance from the Department of Environmental Health and Safety in selecting the best methods available that are in compliance with Federal, State and local regulations.

3. Faculty Recommendations

Handwashing Facility. A handwashing facility should be available within the work area. This need not be a facility used exclusively for handwashing. The use of liquid soap is recommended. When new facilities are installed, foot- or elbow operated faucets should be provided.

Eye Wash Facility. An ANSI approved emergency eye wash facility should be located in each laboratory. It should be designed to wash both eyes at the same time with a continuous stream of water. Environmental Health and Safety can provide assistance in the selection of appropriate eyewash equipment.

Exhaust Air from Primary Containment Equipment. The exhaust air from glove boxes should be treated by filtration, reaction, absorption, electrostatic precipitation or incineration. The need for and type of treatment of exhaust air from other primary containment equipment, including open face laboratory-type hoods should be determined by the Department of Environmental Health and Safety in consultation with the principal investigator. All exhaust air from primary containment equipment should be discharged to the outdoors so that the possibility of entry into the supply air intake of any building is minimized.

4. Additional Recommendations for Animal Experimentation

In selecting specific safeguards for animal experimentation involving chemical carcinogens or toxins, careful attention should be given to animal care and housing methods, bulk chemical storage and disbursement procedures, dosage preparation and challenge procedures, waste management and disposal practices, and personnel protection requirements.

Experimental animals should be housed so that potentially contaminated feed, feces, urine and bedding can be handled in a controlled fashion. Animal care personnel should wear a completely closed jumpsuit or its equivalent, laboratory issued shoes or booties, head cover, and gloves of suitable material. Clean clothing should be provided weekly or more frequently as the situation dictates. Personnel should be encouraged to shower when they leave the animal care or dosage preparation areas. Under no

circumstances should personal protective clothing or equipment be permitted beyond the boundary of the animal facility. Personnel working in animal rooms where exposure to potentially contaminated airborne particulate material or vapors exists should be provided suitable respiratory protection.

VI. Situations Requiring Special Consideration

The purpose of this section is to generally describe situations involving chemical carcinogens where either more or less stringent safeguards might be considered in providing protection to laboratory personnel. No specific definitions for such situations can be provided; an attempt to do so would be misleading. Any modification to the laboratory practices and engineering controls described in Section 5 should be carefully considered by the principal investigator.

The risk of exposure to a chemical carcinogen used in the laboratory is related among other things to the quantity and physical properties of material used and the nature and complexity of the experimental procedure. There is greater risk of exposure if, under the same procedural conditions, 100 mg of material is used than when 1 m g of material is used. Similarly when the same quantity of material is used, the potential for exposure is greater for operations such as blending, preparation of dry feed mixtures or the manipulation of powders than it is for operations such as the preparation of aliquots of stock solutions. Compounds with high vapor pressures generally present a greater risk of exposure than nonvolatile compounds. Also, the toxicity and carcinogenic potency of the material are important factors to consider when selecting safeguards.

1. Higher Risk Situations

Careful judgment must be given in the selection of safeguards for any proposed activity which involves known highly potent chemical carcinogens or toxins, operations that involve large quantities of chemical carcinogens or toxins, or complex procedures having a significant potential for producing aerosols or contamination. When these or similar situations exist, the principal investigator should obtain guidance from the Laboratory Safety Committee before initiating the proposed activity. The principal investigator should keep informed of approval requirements for certain high risk operations that are established by the Laboratory Safety Committee.

2. Lower Risk Situations

Where the principal investigator determines that less stringent safeguards can be used to provide protection, the safeguards selected should require at a minimum, strict adherence to good laboratory practices. Laboratory personnel should not eat, drink, smoke, chew gum or tobacco, apply cosmetics or store food in areas where chemical carcinogens are used or stored. Hands should be washed following the completion of a procedure in which chemical carcinogens are used.

The laboratory worker should develop the habit of keeping hands away from mouth, nose, eyes, and face. A fully fastened laboratory coat and gloves should be worn when handling chemical carcinogens. Mechanical pipetting aids should be used for all pipetting procedures.

Operations involving volatile chemical carcinogens or toxins or the removal of chemical carcinogens or toxins from stock quantities should always be performed with-in a laboratory-type hood, or other suitable containment equipment. The work surfaces on which chemical carcinogens or toxins are used should be covered with stainless steel or plastic trays, dry absorbent plastic-backed paper, or other impervious material.

Stock quantities of chemical carcinogens or toxins should be the minimum quantity required for efficient use. Storage vessels containing stock quantities should have affixed to them labels with the following warning:

CAUTION - POTENTIAL HAZARD (define hazard)

The stock quantities should be maintained in a designated storage area when not in use. The transport of stock quantities should be done in a manner as to prevent breakage or spillage.

Appendices: A. General References

American Conference of Government Industrial Hygienists. *Threshold Limit Values for Chemical Substances and Physical Agents in the Workroom Environment*. Cincinnati, 1980 (Issued annually)

Bretherick, L. *Handbook of Reactive Chemical Hazards*. 2nd ed. London-Boston: Butterworths, 1979.

Manufacturing Chemists Association. *Guide for Safety in the Chemical Laboratory*. 2nd ed. New York: Van Nostrand Reinhold Company, 1972.

National Research Council. *Prudent Practices for Handling Hazardous Chemicals in Laboratories*. Washington, DC: National Academy Press, 1981.

NIOSH/OSHA *Pocket Guide to Chemical Hazards*: Third printing. DHEW (NIOSH): Publ. No. 78-210. GPO Stock No. 017-003-00342-4 August, 1980.

Patty's Industrial Hygiene and Toxicology. 3rd revised ed. Volume 1 - General Principles. 1978: Volume II - Toxicology, 1980: Volume III - Theory and Rationale of Industrial Hygiene Practice. 1979. New York: Wiley-Interscience.

Steere, N.V., Ed. *CRC Handbook of Laboratory Safety*. 2nd ed. West Palm Beach, FL: CRC Press. 1971.

Thomas Jefferson University *Guide to Laboratory Safety*

World Health Organization. *Handling Chemical Carcinogens in the Laboratory Problems of Safety* IARC Scientific Publications No. 33. Lyon, France: International Agency for Research on Cancer. 1979. Single copies available through WHO Publications Centre USA. 49 Sheridan Avenue, Albany, NY 12210.

_____ IARC *Monograph Series: Evaluation of Carcinogenic Risk of Chemicals to Humans* Lyon, France: International Agency for Research on Cancer (IARC). Albany, NY: WHO Public. Centre USA.

B. Approval Procedures

Recognized Chemical Carcinogens and Toxins Carcinogens

Benzene	Carbon tetrachloride	Chloroform	1.2	7.12-Dimethylbenz[a] anthracene
Dibromo-3-chloropropane			1.1	4-Dimethylaminazo-benzene
Dimethylethylenimine	p-Dioxane	Ethylene		3,3'-Dimethylbenzidine
dibromide	Propylenimine	Ethionine	3/ methyl-4-	Dinitrosopiperazine
amino-azopenzene	Urethane	Bromoethyl		N-Hydroxy-2-acetyla-
methanesulfonate	Chloromethyl	methyl ether		minofluorene
Diepoxybutane	1,1 Dimethylhydrazine	1,2		3-Methylcholanthrene
Dimethylhydrazine	Ethylenimine	Ethyl		4.4/-Methylene
methanesulfonate	Hydrazine	Methylhydrazine		bis(2-chloraniline)
Methyl methanesulfonate	N-Nitrosodiethylamine			1-Methyl-3-nitro-
N-Nitrosodimethylamine	N-Nitrosodi-n-			1-ni-trosoguanidine
butuylamine	N-Nitrosodi-n-propylamine	N-		1-Naphthyamine
Nitroso-N-ethylurethane	N-Nitroso-N-			N-[4-5-Nitro-2-furyl)-
methylurethane	N-Nitrosopiperidine			2-thiazoyl]-formamide
Polychlorinated biphenyls	b-Propiolactone	N-		N-Nitroso-N-
Acetoxy-2-acetylamino	fluorene	2-		ethylurea
Acetylamino	fluorene			N-Nitroso-N-methylurea
				4-Nitroquinoline-1-oxide
				Procarbazine
				1.3-Propane sultone
				m-Toluenediamine
				Uracil
				mustard
				Vinyl chloride
				Bis(chloromethyl)ether
				4-
				Aminobiphenyl
				Benzidine
				3,3/-
				Dichlorobenzidine
				3,3/-
				Dimethoxybenzidine
				2-
				Naphthylamine
				4-Nitrobiphenyl