6.0 Evaluation of Special Chemical Hazards

6.1 Background. The purpose of this chapter is to provide information to Principal Investigators regarding special chemical hazards. Most laboratories work with hazardous chemicals and the activities are performed in accordance with institutional policies. The Environmental Health & Safety office provides support to the research staff for establishing safe work practices in the laboratory. To cover the specific needs of a particular laboratory, the principal investigator is responsible for preparing a safety protocol for the proposed research program involving highly hazardous chemicals prior to its beginning. These protocols should be reviewed with laboratory personnel on an annual basis. In addition, the Environmental Health & Safety Office, in conjunction with the Chemical Safety Committee will review all protocols involving work with carcinogenic, highly toxic, or acutely hazardous chemicals every three years to determine whether the principal investigator is required to submit any changes regarding research activities. Environmental Health & Safety personnel are available to provide information and assistance in preparing these safety protocols.

6.2 Special Hazards.

6.2.1 Carcinogens. OSHA publishes a list of known carcinogens that are strictly regulated. The regulations on each are specific and detailed. Their use involves a long list of requirements concerning recordkeeping, posting, monitoring, facilities, training, contamination control and medical surveillance. The following chemicals are on OSHA's list:

1. 1,2-Dibromo-3-chloropropane
2. 1,3-Butadiene
3. 2-Acetylaminofluorene
4. 3,3’-Dichlorobenzidine
5. 4-Aminodiphenyl
6. 4-Dimethylaminobenzene
7. 4-Nitrobiphenyl
8. Acrylonitrile
9. Alpha-Naphthylamine
10. Asbestos
11. Benzidine
12. Beta-Naphthylamine
13. Beta-Propiolactone
14. Bis-Chloromethyl Ether
15. Cadmium
16. Coke oven emissions
17. Ethylene Oxide
18. Ethyleneimine
19. Formaldehyde
20. Inorganic Arsenic
21. Methyl Chloromethyl Ether
22. Methylene Chloride
23. Methylenedianiline
24. N-Nitrosodimethylamine
25. Vinyl Chloride
Although only a limited number of chemicals are carcinogens, they are found among all chemical classes and may present a number of hazards separate from their toxicity. Thus in any research laboratory where workers handle a wide variety of chemicals some are likely to be carcinogenic. The complexity of research at UT Health Science Center precludes establishing a single set of safety rules for working with carcinogens under all laboratory conditions. Institutional policies take cognizance of the following considerations:

(1) Carcinogens can be controlled using established laboratory procedures.

(2) Emphasis should be placed on engineering controls and good work practices.

(3) Carcinogens must be viewed individually and the biological, chemical and physical properties of each compound must be considered.

These guidelines below should be taken into consideration for all laboratories using carcinogens and other highly toxic chemicals:

1. Access to laboratories is limited to technical staff assigned to the research program and the necessary support staff.

2. Work should be performed in a suitable safety cabinet or other containment device depending on the nature of the experiment.
   a. A glove box, Class II biological safety cabinet or chemical fume hood should be used for handling pure carcinogens, including the preparation of stock solutions for in vitro procedures or for work with concentrated carcinogen solutions.
   b. Work with organic solvents and toxic or corrosive chemicals, including neutralization procedures should be done in a fume hood.

3. A hand washing facility must be available.

4. Vacuum service must be protected with an absorbent trap to prevent accidental contamination of the system.

5. Carcinogens should be stored in a clearly posted storage area preferably separated from other laboratory chemicals.

6. Stock bottles should be labeled with the full chemical name or a widely recognized substitute and should bear the warning “Potential Cancer Hazard” (NIH Guidelines), “Cancer Suspect Agent” (29CFR1910.1017, (l)) or “Chemical Carcinogen”.

7. Work surfaces should be protected with absorbent, plastic-backed bench paper.
6.2.2 Asphyxiants. Chemical asphyxiants prevent or interfere with the uptake and transformation of oxygen. Examples include carbon monoxide which prevents oxygen transportation, and hydrogen cyanide which inhibits enzyme systems and interferes with the transportation of oxygen to the tissues. At sufficiently high concentrations, both chemicals can result in immediate collapse and death.

6.2.3 Narcotics. Narcotics affect the central nervous system causing symptoms that range from mild anesthesia reactions to loss of consciousness and death at high doses. Examples include acetone, methyl ethyl ketone, and chloroform.

6.2.4 Heavy metals and their compounds. Heavy metals are relatively harmless in the metallic state, but their fumes, dust, and soluble compounds are well-known toxins. Some are carcinogenic. Others are nephrotoxins, hepatotoxins, or neurotoxins. The most common heavy metals are arsenic, beryllium, cadmium, chromium, lead, mercury, nickel, and silver. Acute toxic effects from exposure to heavy metals result from inhalation and ingestion of dusts or inhalation of fumes. Metal fumes are generally more hazardous than dusts because the particles in fumes can enter the bloodstream easier. Bronchitis, chemical pneumonia, and pulmonary edema may result. Beryllium and cadmium are two of the most toxic metals when inhaled. Symptoms include nausea, vomiting, abdominal pain, and diarrhea. Chronic exposure to heavy metals may lead to long-term effects. For example, chronic exposure to lead may damage the nervous system, brain and kidneys. Exposure to mercury over a long period can permanently damage the liver, kidney, and brain. Chronic inhalation of cadmium can cause emphysema and kidney damage. Carcinogenic effects have been shown from exposure to chromium, nickel, arsenic, cadmium, and beryllium. Prenatal effects have been observed from exposure to methyl mercury. In addition, some lead compounds are embryotoxic. Some metals and their compounds can be absorbed through the skin. Mercury metal, and tetraethyl lead for example can enter the bloodstream through this route. Nickel, arsenic, chromium, and beryllium cannot penetrate the skin but they can damage the skin or cause allergic-type reactions.

6.2.5 Cyanides. The simple metallic cyanides are highly toxic by ingestion. Cyanides are readily absorbed through the skin, mucous membranes, and by inhalation. Alkali salts are toxic by ingestion. Even small amounts of sodium and potassium cyanide are highly toxic and death may occur within minutes from ingestion. Inhalation of toxic fumes from hydrogen cyanide gas may result in death in a few seconds. Symptoms of poisoning include dizziness, headaches, tightness in the chest, palpitation of the heart, and difficulty in breathing.

6.2.6 Nerve Agents. Nerve agents are the most toxic of the known chemical agents. They are hazards in their liquid and vapor states and can cause death within minutes after exposure. Nerve agents inhibit acetyl cholinesterase in tissue, and their effects are caused by the resulting excess acetylcholine. Nerve agents are considered major military threat agents.

6.3 Application for Approval to Work with Carcinogenic, Highly Toxic, or Acutely Hazardous Chemicals. The UTHSCSA Chemical Safety Committee established a peer-review approval process for carcinogenic and other highly toxic or acutely hazardous chemicals that can present a risk to human health. One of the charges of this Committee is to review procedures including the safe use, storage and disposal of hazardous chemicals, as a mechanism to ensure proper safeguards are being practiced in the laboratory, and thereby,
reducing occupational exposures to these chemicals. All Principal Investigators who wish to work with chemical carcinogens, highly toxic, or acutely hazardous chemicals at the Health Science Center usually do so as part of work on a grant or contract. All research protocols involving the use of chemical carcinogens, highly toxic, or acutely hazardous chemicals must complete the following:

1. Application for Approval to Work with Carcinogenic, Highly Toxic, or Acutely Hazardous Chemicals - for submittal to the Chemical Safety Committee through the Environmental Health & Safety Office. The Principal Investigator is responsible for completing the application in its entirety and providing the most accurate information. If the project or grant involves using chemical carcinogens in live animals, Appendix A: Application to Use Chemical Carcinogens with Live Animals must be completed.

Classes of Chemicals Requiring Chemical Safety Approval

A. Carcinogens – any chemical which meets one of the following criteria:

   a. Listed under Group 1 (carcinogenic to humans) or Group 2A (probably carcinogenic to humans) by the International Agency for Research on Cancer Monographs (IARC).
   b. Listed as "Known to be Human Carcinogens" in the Annual Report on Carcinogens published by the National Toxicology Program (NTP).
   c. Listed under the Occupational Safety & Health Administration (OSHA), 29 CFR 1910.1003.

   Examples include, but not limited to Streptozotocin, DMBA, 12-0-Tetradecanoyl-phorbol-13-acetate (TPA), and 3-methylcholanthracene. For the complete lists from IARC, NTP and OSHA, please refer to the Chemical Safety Handbook, Appendix C, C-1, and C-2 (http://research.uthscsa.edu/safety/Chemical/2007ChemicalSafetyHandbook.pdf).

B. Antineoplastic Agents – chemotherapy and cytotoxic drugs used in cancer therapy. Examples include Cyclophosphamide, Tamoxifen, Cisplatin, Daunorubicin, and Doxorubicin Hydrochloride.

C. Mutagens – chemical agents that alter DNA. Mutagens are also typically carcinogens. Examples include Urethane, Ethyl methanesulfonate, and Bromodeoxyuridine (BRDU).

D. Select Agent Toxins and other Toxins – Select Agent Toxins have the potential to pose a severe threat to animal health and safety, plant health and safety. Examples include tetrodotoxin and botulinum neurotoxin. Other toxins that would require CSC approval include cholera toxin (subunit A) and pertussis toxin.

E. Highly Toxic Chemicals – chemicals that have a high degree of acute toxicity. These agents meet the following criteria:

   a. Median lethal dose (LD₅₀) of 50 mg or less when administered orally to rats [LD₅₀ < 50 mg/kg].
b. Median lethal dose (LD$_{50}$) of 200 mg or less when administered by continuous dermal contact for 24 hours (or less if death occurs within 24 hours) to the skin of rabbits [LD$_{50}$ < 200 mg/kg].
c. Median lethal concentration (LC$_{50}$) in air of 200 parts per million by volume when administered by continuous inhalation for one hour (or less if death occurs within one hour) to rats [LC$_{50}$ < 200 ppm].
Examples include sodium arsenite, mercury, cadmium, and osmium tetroxide.

F. **Pesticides, Insecticides, Herbicides** – defined as “any substance or mixture of substances intended for preventing, destroying, repelling, or mitigating any pest” by the Federal Insecticide, Fungicide, and Rodenticide Act. Examples include Paraquat, Diquat, and Chlorpyrifos.

G. **Pyrophoric Chemicals** – substances that will ignite spontaneously upon contact with air. Examples include tertiary-butyl lithium, iron sulfide, and many reactive metals.

H. **Nanoparticles** – is defined as a small particles (1 - 100 nanometers) that behave as a whole unit in terms of its transport and properties. Some nanoparticles, such as Zinc Oxide, are thought to have cytotoxic properties.

I. **Neurotoxins** – chemical agents that can affect the transmission of signal between neurons. Examples include MPTP and snake venom.

For other highly hazardous chemicals that do not fall under these categories, please contact Chemical Safety Manager, at 567-2955 for assistance or to verify if a specific chemical requires CSC approval.

**Protocol Submission and Review Process:** Chemical Protocols are reviewed on a continuous basis by the Committee. It is highly recommended that protocols are submitted well in advance of any funding or other agency deadlines. Principal Investigators must submit chemical protocols through the online E-Protocol system (https://uthscsa.keyusa.net/). After the application is received in the Environmental Health & Safety Office, the application will be reviewed for completeness prior to submitting to the Chemical Safety Committee. The Chemical Safety Committee will approve or disapprove each application usually within 30 days of receipt. An approval letter will be mailed to the Principal Investigator, and, if the project requires approval from the Institutional Animal Care and Use Committee (IACUC) approval, the Institutional Animal Care Program (IACP) office. If, for any reason, the application is not approved, the Principal Investigator will be notified as to the reason the application was not approved and will be given the opportunity to re-submit their application.

3. **Administrative Approval for Use of Routine Carcinogenic or Highly Toxic Chemicals** - Recently, the Chemical Safety Committee has revised the approval process for certain carcinogenic or highly toxic chemicals (see list below). The Committee acknowledges there are several carcinogens that are used routinely in labs, and when used in accordance to standard operating procedures (SOP), are relatively safe. So, instead of requiring Investigators to submit
a chemical safety application through eProtocol, the use of these chemicals is being approved administratively by Environmental Health & Safety. A written SOP is provided to the Investigator/lab, to be reviewed by lab workers using the chemical, and after receiving the PI Acknowledgement form, an approval letter is drafted and sent to the PI. One benefit to this modified review process is a reduction of paperwork for the Principal Investigator.

Administrative approval is granted to Principal Investigators who work with the following routine carcinogens or highly toxic chemicals:

- Acrylamide
- Acetonitrile
- Boric Acid
- Chloroform
- Chloramphenicol
- Ethidium Bromide
- Formaldehyde (including 10% formalin)
- Methylene Chloride
- Paraformaldehyde
- Phenol
- Phenylmethylsulfonyl fluoride (PMSF)
- Phorbol 12-myristate 13-acetate (PMA)
- Sodium Azide
- Trypan Blue

Environmental Health & Safety has developed written standard operating procedures (SOP) which contains useful safety information normally found on the SDS for each chemical listed as well as emergency response and first aid treatment for these specific chemicals, and is meant to be used as a reference source for laboratory personnel.

6.4 Chemical Carcinogens Lists. The International Agency for Research on Cancer (IARC), the National Toxicology Program (NTP), and the Occupational Safety and Health Administration (OSHA) each have compiled lists of carcinogenic chemicals. These lists are not meant to be all-inclusive but rather, serve as a source for principal investigators in determining which chemicals may require committee approval for use and storage in the laboratory. For your convenience, these lists are included in Appendix B, C, and D. Please refer to the websites for updated lists.