I. Background and Purpose

Streptozotocin (Streptozotocin, Streptozocin, STZ, Zanosar®, CAS No. 18883-66-4) is a naturally occurring chemical derived from *Streptomyces achromogenes*. Originally developed as a broad-spectrum antibiotic, it was found to be selectively toxic to the beta cells of the pancreatic islets. Thus, it has been extensively utilized as a method to induce diabetes for use in various animal model systems.

Streptozotocin is considered to be a highly hazardous chemical. Because of this, guidelines have been developed by the Scott & White Office of Biosafety (in conjunction with the Central Texas Veterans Health Care System (CTVHCS) and the Texas A&M Health Science Center (TAMHSC)) for the preparation and use of streptozotocin for use in the laboratory or in animal experiments.

II. Scope

This document will apply to all Scott & White researchers utilizing streptozotocin in their laboratories and will apply to all researchers using Scott & White animal facilities and having an IACUC protocol that utilizes streptozotocin in animal research.

III. Exposure Hazards

Routes of exposure to streptozotocin include inhalation, ingestion, accidental ingestion and absorption (Sigma MSDS). Acute exposure to streptozotocin can induce irritation and can be toxic.

Chronic exposure to streptozotocin could lead to a number of health effects including:

A. Carcinogenicity—STZ is classified as a possible carcinogen for humans (2B by the IARC; 2 by the NTP).

B. Mutagenicity—STZ has been shown to be mutagenic for mammalian somatic cells.

C. Cytotoxicity—STZ has been shown to be cytotoxic, specifically for the pancreatic β-cells and the oxyntic mucosal cells of the stomach.

D. Teratogenicity—Reproductive studies have shown that STZ is teratogenic and has been associated with embryonic and neonatal developmental delays.

E. Reproductive Toxin—STZ has been shown to affect fertility when administered to both male and female rats.

IV. Risk Assessment and Exposure Controls

Because of the hazards associated with streptozotocin, it is incumbent upon the principal investigator to perform a thorough risk assessment when considering use of this chemical. The PI must also adhere to this SOP when developing laboratory-specific protocols. The following controls should be considered:

A. Administrative Controls

1. Use of STZ in the laboratory should be detailed in the laboratory safety manual.
2. Laboratory workers should receive specific training regarding the proper handling of STZ, which should be documented in the laboratory safety manual.

3. When planning in vivo use of STZ, PIs must fill out the appropriate hazard form for the IACUC.

4. All personnel involved in the use of STZ should be enrolled in an appropriate Occupational Health Program.

5. Any exposure to STZ should be immediately evaluated by Employee Health. An incident report should be filed with the Biosafety Office within 24 hours.

B. Engineering Controls

1. Because of the risk of inhalation exposures with powder forms of STZ, it is imperative that PIs make use of the chemical fume hood for measuring and reconstitution of STZ. This is the most practical solution for this.

2. When preparing solutions for in vivo use in animals, it is imperative that the biological safety cabinets (BSC) are utilized for maintaining sterility as required by the IACUC. Additionally, injections into animals should be performed within a BSC to control any aerosols that are generated during these procedures.

C. Personal Protective Equipment

1. Gloves: Standard powder-free latex or, more preferably, nitrile gloves are required for working with STZ.

2. Lab coats: Lab coats or disposable gowns are required for working with STZ. The benefit of disposable gowns (with cuffs) is the ability to ensure that all skin of the forearm and wrist is protected. It is advisable if lab coats are used, to supplement them with disposable sleeves.

3. Eye protection: Chemical safety glasses (ANSI Z-87 approved) are required for minimal protection when working with STZ.

4. Laboratory attire: As with all work in laboratories where hazardous chemicals/biologicals are stored/utilized, clothing should be appropriate and afford coverage of the entire body. No short pants/dresses and no open shoes are to be worn.

V. Procedures for working with streptozotocin for in vivo use in animals (Work Practices)

A. If STZ is obtained as a powdered chemical, it should be weighed and initially resuspended into solution within a chemical fume hood. All PPE should be donned prior to performing any work with STZ. Once resuspended, the material should be transferred to a biological safety cabinet (BSC) where it should be sterile filtered (0.2 μ). The PI needs to follow IACUC guidelines for use of non-pharmaceutical grade chemicals in animals. Such chemicals need to be prepared fresh on a daily basis. (If there is a problem with using a chemical fume hood for measurement, contact the Biosafety Officer to work out other alternatives).
B. If STZ is obtained in ampoules, it can be measured as above in A, within a chemical fume hood. Alternatively, it can be resuspended with sterile diluent in a biological safety cabinet (BSC), using aseptic techniques. The PI should then refer to the manufacturer’s instructions regarding storage and expiration of such reconstituted chemicals.

C. Disposables that come into contact with STZ should be either disposed of as chemical waste or, if they are sharps, should be discarded into approved sharps containers and disposed of as biohazardous (regulated medical) waste.

D. Injections of animals with STZ must be performed within a BSC whenever possible so that aerosols associated with injections may be contained.

E. Animals injected with STZ excrete STZ and its metabolites primarily through urine (and to a lesser extent through feces) usually within 72 hours of administration. Therefore, the bedding of these animals that is collected within that time period should be treated as hazardous material. Bedding from small animal cages should be dumped into biohazard bags using a BSC to control aerosol exposures. Bedding from larger animals (dogs, pigs, etc) should be collected by personnel wearing respiratory and mucosal protection (PAPR or full-face respirator with an N-100 cartridge; please note that medical clearance and fit-testing are required).

F. STZ itself is an RCRA-listed hazardous waste material. Surplus stocks and other waste materials must be disposed of as hazardous waste. Contact the Biosafety Office for disposal options.

G. All laboratories using STZ should have a spill kit on hand to assist in cleaning up minor spills. For minor spills:
   1. Notify everyone in the lab that a spill has occurred and clear the area.
   2. Remove any contaminated PPE or clothing and dispose of properly.
   3. Inform the laboratory supervisor that a spill has occurred.
   4. Put on fresh PPE.
   5. Let any aerosols settle for 30 minutes.
   6. Make sure you have another person to assist.
   7. Cover the area with disinfectant (10% dilution of household bleach is recommended)-soaked absorbent material (paper towels, etc).
   8. Apply more disinfectant in a circular pattern to enclose the spill and allow it to work for at least 10 minutes.
   9. Using tongs (or other mechanical aid), recover absorbent material and place into a hazardous waste container. Use additional absorbent material to recover remaining disinfectant and discard in hazardous waste.
   10. Clean the area a second time with disinfectant and absorbent material, paying careful attention to any splashes outside of the primary spill area.
   11. Close up the hazardous waste and dispose of properly.
12. File an incident report with the Biosafety Office.

For large spills, please contact the Biosafety Office for assistance.

H. Emergency contact information

Should you have an emergency situation develop, please use your institutional contact information listed below:

Scott & White Healthcare:
Biosafety: (254)771-4804 or (254)771-4833 (during business hours)
        (404)661-2647 (after business hours)

General Emergency: 24-2000

Texas A&M HSC:
Biosafety: (979)862-4549 (during business hours)
         (979)845-4311 (after business hours)

CTVHCS:
Safety Officer: (254)743-1110 (during business hours)
            (254)598-8356 (after business hours)

General Emergency: 4-4911