

The following Safety Short is a guide on the safe handling practices that should be used when using BRdU as a biomarker for cell division. Because of the safety concerns associated with the toxic properties of BRdU many researchers are switching to a safer biomarker, Ki-67. Ki-67 is a nuclear protein produced in all phases of cell division except the resting phase. This may prove to be a safe and non-toxic substitute for BRdU for many applications.

Use and Safe Handling of Bromodeoxyuridine (BrdU) in Research

- I. **Purpose and Scope:** The purpose and scope of this document to review the use of Bromodeoxyuridine (BrdU) in research and to discuss the associated hazards and safe handling practices. The following is a link to the Safety Data Sheet.
<http://fscimage.fishersci.com/msds/91378.htm>.

- II. Bromodeoxyuridine (BrdU) is a water soluble synthetic thymidine analog that is used to identify actively growing cells. The chemical becomes incorporated into a cell's DNA when the cell is dividing by substituting BrdU for thymidine during the S-phase or synthetic phase of cell division. Antibodies specific for BrdU can then be used to detect the incorporated chemical indicating which cells are actively replicating DNA.

It is generally administered to animals in small amounts by injection either shortly before they are sacrificed or by chronic administration. Administration is usually IV, IP or by way of the drinking water.

- III. **Definitions:**
Cytotoxic-something that is toxic to cells causing cell killing
Mutagenic- a physical or chemical agent that changes the genetic information (usually DNA) of an organism and thus increases the frequency of mutations above background
Teratogenic- able to disturb the growth and development of an embryo or fetus

- IV. **Potential Hazards:** BrdU in and of itself is moderately toxic with an LD50 well over 500 mg/kg in the mouse with some reports indicating as much as 8,000 mg/kg. According to the Hazardous Substances Data Bank, BrdU is degraded at a fairly rapid rate following injection in mice and rats by two metabolic pathways; hydrolysis at the glycosidic bond to yield bromouracil and 2-deoxyribose which is then presumably further metabolized. The other is debromination which is evidenced by liberation of bromide ion. The further fate of the remainder of the molecule has not been studied.

Employees may be exposed to BrdU through bedding, dusts, cages or excretion of animals administered the chemical however risks are believed to be negligible because of the low

doses that are administered and the fact that virtually all of the drug should be bound to cellular nucleic acids or be metabolized. Since BrdU becomes incorporated into DNA it is classified as cytotoxic, mutagenic and teratogenic. Safety precautions are warranted when handling or administering the chemical in the research setting.

V. Personal Protective Equipment: The primary route of exposure is through the generation of aerosols, ingestion, or accidental injection. Staff involved with any tasks where exposure to BrdU is possible must don the following PPE at a minimum:

- a. Nitrile exam gloves
- b. ANSI approved safety glasses or goggles (where splash is possible)
- c. Lab coat or disposable closed front gown
- d. Other appropriate lab attire
- e. An approved and fitted half face respirator if not working in a containment device such as a fume hood

BrdU Preparation: BrdU solutions must be prepared in a certified chemical fume hood while wearing PPE. Work surfaces should be covered with absorbent plastic-backed disposable bench paper for weighing or manipulating solutions. Label all solutions with the contents, concentration, hazard warnings (teratogen, mutagen, cytotoxic), date prepared, expiration etc. Store in appropriate leak proof container and transport in a secondary container such as zip lock bag.

BrdU Administration: Administration to rodents must be conducted in a certified chemical fume hood or certified biological safety cabinet by properly trained staff. Animals should be chemically or physically restrained prior to starting the procedure. Cover all work surfaces with absorbent plastic-backed, disposable bench paper. Both personnel administering and in the immediate area should wear appropriate PPE including chemical resistant nitrile gloves, disposable lab coat or gown, and mucous membrane protection (including chemical goggles, face shield and surgical mask) before commencing the task.

Acute administration with sacrifice outside Animal Facilities - Where BrdU is administered acutely and the animal sacrificed within a few hours without returning to an ARP Facility

1. No AUSI is needed on the cage.
2. No special treatment of the waste is required.
3. Sharps must be disposed of in an approved sharps container.
4. Remaining BrdU solution, contaminated bench paper, gloves, etc should be disposed of through the OH&S Support Facility by incineration.

Chronic administration - BrdU may be administered to animals on a chronic basis by IV or IP injection, by osmotic pump or in their drinking water.

1. You must follow ARP safety precautions and have an AUSI for animal cages for chronic administration of BrdU.
2. If administering in drinking water prepare BrdU water bottles in a certified fume hood wearing appropriate PPE listed above.
3. Waste drinking water should be diluted to 10% with bleach and disposed of down the drain with running water.
4. Dispose of bedding through standard ARP protocol.
5. All animal carcasses are disposed of as regulated medical waste.