Working with Bromo-Deoxyuridine (BrDu)

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BACKGROUND

Bromo-Deoxyuridine (BrDu) is a white crystalline water-soluble compound that is frequently used in cancer treatment/research for inducing increased susceptibility to radiation therapy, and as a topical anti-viral treatment (Chaube, Murphy 1968). Its major vehicle of action involves incorporation ("binding") into tissue DNA through acting as a thymine analogue (Matsuoka et al., 1990). The same DNA-binding characteristics that provide BrDu its medicinal benefits are also attributable to an array of associated significant health and safety threats. Research has indicated that Bromo-Deoxyuridine has cytotoxic, strongly teratogenic, and mutagenic properties (Russo et al., 1984, Nakaguchi et al., 1971). These potentially severe side effects make BrDu exposure a significant health and safety threat to laboratory staff, animal handlers and other personnel who may be accidentally exposed to BrDu. Due to this health and safety threat the Institutional Biosafety Committee (IBC) has classified BrDu as a reportable hazardous chemical that must be reported on all Institutional Animal Care and Use Committee (IACUC) protocols.

PURPOSE

The purpose of this page is to provide the research community sufficient information regarding specific health threats/exposure routes, implementation of proper work methods, and provision of suitable personal protective equipment for development of research protocols that include measures for effectively reducing risk of occupational exposure to BrDu.

OCCUPATIONAL EXPOSURE HAZARDS

Primary routes of occupational exposure to BrDu include: aerosol exposure, ingestion, accidental injection, and tissue/transplancental absorption (National Institutes of Health 1988). Available industrial hygiene and epidemiology case studies are quite limited. The available scientific literature indicates the following potential consequences in relation to acute and chronic occupational exposure.

1. Cytotoxic Effects: While acute toxic effects appear to be limited, exposure via aerosol inhalation, ingestion, skin absorption, or accidental injection may produce serious subacute and chronic effects including: skin lesions, anemia, leukocytopenia,

thrombocytopenia and inhibition of cell growth (Naguchi et al., 1971, Matsuoka et al., 1990).

2. Teratogenic and Mutagenic Effects: Strong teratogen: exposure may induce abnormalities in micronucleus and sperm nuclei (Bruce and Heddle 1979). Strong teratogenic effects in mice, rats and other mammalian species (National Institutes of Health 1988, Ashman and Davidson 1981) have also been noted. Potential for producing birth defects and other heritable genetics mutations is strongly suspected (Rocchi 2005).

SAFE WORK METHODS

The list of potential BrDu related health hazards identified above make it imperative that PIs conduct thorough risk assessments and prepare protocols which include standard operating procedures (SOPs) which identify appropriate administrative controls, personal protective equipment (PPE), work methods, engineering controls, and waste disposal procedures for eliminating or sufficiently reducing exposure threat to all staff involved in the affected research.

1. Administrative Controls

a. Management considerations for BrDu and other potentially hazardous chemicals must be included in the laboratory Chemical Hygiene Plan.

b. Protocols involving use of BrDu must include completion of reportable hazardous chemical form and approval through the IACUC.

c. Principal investigators will develop and implement SOPs by which laboratory staff will prepare/administer BrDu with minimal potential for exposure.

d. All tasks having potential for occupational BrDu exposure (mixing of doses, dose preparation, administering of injections, etc.) will only be conducted by competent staff whom have received appropriate training (OSHA: “Worker Right to Know”) regarding the specific BrDu-related health and safety risks, SOPs, and procedures to be followed in event of an exposure incident.

e. All staff engaging in processes identified above are also required to complete

applicable modules of the VCU Laboratory Safety Training Modules.

2. Personal Protective Equipment: Staff involved with any tasks where potential for BrDu exposure exists must don the following PPE:

a. Examination gloves.

b. Safety glasses or safety goggles (ANSI Z-87 approved).

c. Lab coat.

d. Appropriate laboratory attire.

e. If aerosol exposure threat exists suitable respiratory protection must be provided. Prior to instituting respiratory protection to personnel, the laboratory must participate in the university Respiratory Protection Program.

3. Work Methods

a. Whenever feasible, procedures with the potential for producing BrDu aerosols should be conducted with a certified Class II biological safety cabinet (BSC) or chemical fume hood.

b. Needles used for BrDu injection will be disposed of in approved sharps containers immediately following use.

c. Needles used for BrDu injection should never be bent, sheared, or recapped. If recapping is absolutely necessary, a "Needle Recapping Waiver" must be submitted for IBC review/approval prior to proceeding.

d. Areas where BrDu is prepared and/or administered should be cleaned immediately following each task completion utilizing a 5% to 10% bleach/water solution (prepare fresh stock every 7 – 10 days).

4. Engineering controls

a. In cases where the recommended level of PPE does not provide sufficient protection (e.g.: splash potential, aerosolization potential) tasks should be conducted within a certified Class II BSC or chemical fume hood utilizing sash for added protection.

b. Syringes used for BrDu injection must be safety engineered (self-sheathing syringes, luer-lock syringes, etc.).

c. Animals should be appropriately restrained and/or sedated prior to administering injections and other dosing methods.

5. Waste Disposal

a. Surplus BrDu must be disposed of as a hazardous chemical through the OEHS Chemical Waste Management Program.

b. The limited available research has not concluded how extensively BrDu is metabolized making it imperative that all potentially contaminated carcasses, bedding, and other nonsharps materials be disposed of as Regulated Medical Waste (RMW) through incineration (National Institutes of Health 1988).

c. All contaminated sharps waste materials must be placed in proper sharps container and disposed of as RMW.

6. Spills: Small spills of BrDu should be cleaned with absorbent paper and soap and water. Don appropriate PPE during clean-up, dispose of all waste generated through OEHS. For larger spills of BrDu contact the OEHS emergency line (828-9834) for assistance.

LITERATURE CITED

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