GUIDE FOR DEVELOPING IACUC PROTOCOLS INVOLVING HAZARDOUS CHEMICALS

November 4, 2008

I. INTRODUCTION

A. Purpose: This guide has been developed by the **Institutional Biosafety Committee** (IBC) to assist PIs in determining reporting requirements for *in vivo* chemical hazards during preparation protocols for submission to the **Institutional Animal Use and Care Committee** (IACUC). This reference should be used in conjunction with the regularly updated **IACUC Hazardous Chemical Index** spreadsheet, if agents are not listed on the **IACUC Hazardous Chemical Index**, PIs should refer to criteria outlined below to determine if IBC registration (reporting) is required via completion of Appendix C of the IACUC protocol.

B. Primary Standards/References: The IBC criteria for determining "reportable chemicals" are consistent with the following sources:

1. The Occupational Safety and Hazard Administration (OSHA): **"Laboratory Safety Standard"** (29 CFR 1910.1450)

2. **"Prudent Practices in the Laboratory: Handling and Disposal of Chemicals"***:* National Research Council, 1995.

3. *Sax's Dangerous Properties of Industrial Materials, 11th Edition,* edited by Richard J. Lewis, Sr.

4. Sigma-Aldrich Inc.: **Material Safety Data Sheets** (MSDSs), and product-specific MSDSs provided by chemical vendors.

5. Physicians Desk Reference 61st edition, copyright 2007, Tomson PDR

II. REPORTABLE CHEMICALS: All *in vivo* use of chemicals meeting the following criteria must be reported on Appendix C of IACUC protocol (unless exempted under Section IV):

A. Agents identified as reportable ("Y") on most recent version of the **IACUC Hazardous Chemical Index**.

B. Carcinogens:

1. Identified on product MSDS as having known or suspected human carcinogenicity.

2. **OSHA "Select Carcinogens"** Note: if protocol involves *in vivo* use of formaldehyde refer to section II. I. for special considerations.

3. National Toxicology Program (NTP) – "11th Annual Report on Carcinogens" chemicals identified in most recent revision as:

a. **"Known to be Human Carcinogens"**

b. **"Reasonably Anticipated to be Human Carcinogens"**

4. **International Agency for Research on Cancer (IARC) - Cancer Monographs (March 30, 2007)**

a. Group 1 ("Carcinogenic to Humans") agents

b. Group 2A ("Probably Carcinogenic to Humans") agents

c. Group 2B ("Possibly Carcinogenic to Humans") agents

C. Hazardous Drugs:

1. All agents listed on the NIOSH publication: "Preventing Occupational Exposure to Antineoplastic and other Hazardous Drugs in Health Care Settings, **Appendix A: "Drugs Considered Hazardous."**

2. All agents listed on the OSHA Technical Manual: "Controlling Exposure to Hazardous Drugs, **Appendix VI, 2-1 "Some Common Drugs that are Considered to be Hazardous"**

Note: The IBC Biosafety Office has developed resource ("working with") pages to aid researchers in developing SOPs for managing hazards associated with a number of hazardous drugs, these references may be accessed at the **OEHS Chemical/Biological Safety Section Webpage**

D. Reproductive Toxins:

1. All agents with MSDS and/or other product information indicating that human reproductive toxin properties have been confirmed or are suspected (unless exempted under Section IV).

2. Agents listed on Sax's Guide and/or **Material Safety Data Sheets** (product specific or Sigma-Aldrich, Inc.) with human test data available indicative of known or suspected human reproductive toxicity (unless exempted under Section IV or "Guide to Chemical Classifications").

E. Acute Toxins: The National Research Council's "Prudent Practices" manual identifies acute toxicants as chemicals with the capability of inducing harmful effects (local and/or systemic) after a single exposure. Determination of acute toxicity can be made by comparing the LD_{50} of a compound (provided on product MSDS) to the values listed in the tables below:

1. *High-Hazard Acute Toxicants*: Any chemical that falls within the "HIGH" hazard level on Table 1. (below) is considered an acute toxicant and must be reported via hazardous chemical form (unless exempted under Section IV or "Guide to Chemical Classifications").

2. *Extremely Toxic Chemicals*: Chemicals falling within the "EXTREMELY and HIGHLY TOXIC" toxicity ratings on Table 2. (below) are acute toxicants and must be reported via hazardous chemical form (unless exempted under Section IV or "Guide to Chemical Classifications").

TABLE 1. Acute Toxicity Hazard Level

Hazard Level	Toxicity Rating	Oral LD_{50} (Rats, per kg)	Skin Contact LD_{50} (Rabbits, per kg)	Inhalation LC_{50} (Rats, ppm for 1 h)	Inhalation LC_{50} (Rats, mg/m^3 for 1 h)
High	Highly toxic	<50 mg	<200 mg	<200	<2,000
Medium	Moderately toxic	50 to 500 mg	200 mg to 1 g	200 to 2,000	2,000 to 20,000
Low	Slightly toxic	500 mg to 5 g	1 to 5 g	2,000 to 20,000	20,000 to 200,000

TABLE 2. Probable Lethal Dose for Humans

Toxicity Rating	Animal LD_{50} (per kg)	Lethal Dose When Ingested by 70-kg (150-lb) Human
Extremely toxic	Less than 5 mg	A taste (less than 7 drops)
Highly toxic	5 to 50 mg	Between 7 drops and 1 teaspoonful
Moderately toxic	50 to 500 mg	Between 1 teaspoonful and 1 ounce
Slightly toxic	500 mg to 5 g	Between 1 ounce and 1 pint
Practically nontoxic	Above 5 g	Above 1 pint

SOURCE: Modified, by permission, from Gosselin et al. (1984). Copyright 1984 by Williams & Wilkins, Baltimore.

Obtained from "Prudent Practices in the Laboratory" (1995). National Academy of Science.

F. Mutagens:

1. All agents with MSDS and/or other product information indicating that human mutagenic properties have been confirmed or are suspected (unless exempted under Section IV).

2. Agents listed on Sax's Guide and/or **Material Safety Data Sheets** (product specific or Sigma-Aldrich, Inc.) with human test data available indicative of known or suspected human mutagenicity (unless exempted under Section IV).

G Teratogens:

1. All agents with MSDS and/or other product information indicating that human teratogenic properties have been confirmed or are suspected (unless exempted under Section IV).

2. Agents listed on Sax's Guide and/or **Material Safety Data Sheets** (product specific or Sigma-Aldrich, Inc.) with human test data available indicative of known or suspected human Teratogenicity (unless exempted under Section IV).

H. Other Reportable Chemicals: Due to special health and safety concerns, a limited number of chemicals that may not otherwise fall within the reportable categories listed above must also be reported via hazardous chemical form. The current list of special chemicals includes:

1. **5-bromo-2-deoxyuridine (BrDu)**: Refer to OEHS information page: **"Working with Bromo-Deoxyuridine"** for details regarding the special health and safety concerns and reporting requirements for BrDu.

2. **Complete Freund's Adjuvant (CFA)**: Refer to OEHS information page: **"Working with Complete Freund's Adjuvant (CFA)"** for details regarding the special health and safety concerns and reporting requirements for CFA.

3. Centers for Disease Control **"Select Agents":** Refer to OEHS **"Select Agent Information Page"** for details regarding the special health and safety concerns and reporting requirements for select agents.

I. Formaldehyde, Special Conditions:

1. When used in conjunction with perfusion procedures: concentrations ≤ 37%: Solutions containing ≤ 37% formaldehyde are exempt from IACUC reporting requirements, provided that the laboratory maintains an up-to-date **Chemical Hygiene Plan** participates in applicable **University Laboratory Safety Training Modules**, and meets other general program requirements of the **Office of Environmental Health and Safety - Chemical/Biological Safety Section**.

2. All other *in vivo* use of formaldehyde will be reported on the "Animal Experimentation Involving Chemical Hazards" form provided in Appendix C.

J. Glutaraldehyde, Special Considerations

1. When used in conjunction with perfusion procedures glutaraldehyde is exempt from IACUC reporting requirements, provided that the laboratory maintains an up-to-date **Chemical Hygiene Plan** participates in applicable **Laboratory Safety Training**

Modules, and meets other general program requirements of the **Office of Environmental Health and Safety - Chemical/Biological Safety Section**.

2. All other *in vivo* use of glutaraldehyde will be reported on the "Animal Experimentation Involving Chemical Hazards" form provided in Appendix C.

III. NOVEL CHEMICALS WITH UNKNOWN OR LIMITED AVAILABLE TOXICOLOGICAL DATA:

1. Compounds with limited hazard information will be considered hazardous and reported on Appendix C until sufficient toxicological data becomes available for making a hazard assessment.

2. Test compounds with unknown identities/toxicological properties will be considered hazardous chemicals and reported in Appendix C (a generic header: "unknown test compounds" may be utilized). PIs will provide a list of all compounds tested along with a brief description of any noted note toxicological properties to the **Biosafety Office** at the time of the IACUC annual review.

IV. EXEMPTIONS

A. Routinely Administered Pre/Post Operational Drugs: Analgesics, anesthetics, antibiotics, perfusates, and euthanasia agents do not require reporting on Appendix C provided they are addressed in the laboratory chemical hygiene plan and meet the following criteria:

1. Agents are <u>not</u> listed IARC 1, 2A, or 2B or NTP "Known" or "Suspected" carcinogens, NIOSH and/or OSHA "hazardous drugs," OSHA select carcinogens, and are not listed in Section II.H. ("Other Reportable Chemicals) of this text.

2. Euthanasia agents manufactured under the label "Euthasol®" (or similar preparations) do not require reporting on Appendix C.

3. Agents must be addressed in laboratory chemical hygiene plan.

4. New or novel pre/post operational drugs will be addressed on a case-by-case basis, contact the **Biosafety Office** to initiate a product review.

5. Formaldehyde and/or Glutaraldehyde used in perfusion procedures under conditions established in sections II. I. and J. do not require reporting on Appendix C.

B. USDEA Schedule I and II Controlled Substances: Drugs listed under **Schedule I and II of the U.S. Drug Enforcement Agency Controlled Substance Act** are not required to be reported on Appendix C provided the agents are addressed in laboratory chemical hygiene plan.