Identifying Chemicals with High Acute Toxicity
and DRI Requirements for their Use

INTRODUCTION

The toxicity of chemicals is assessed by their Lethal Dose or LD. An LD_{50} is the amount of a material, given all at once, which causes the death of 50% (one half) of a group of test animals. The LD_{50} is one way to measure the short-term poisoning potential (acute toxicity) of a material. Lethal doses may occur via different routes of exposure. The most common lethal dose notations on Safety Data Sheet (SDS) are the $LD_{50\ oral}$,defined as the oral dose at which 50 percent of the exposed test animals (rats or mice) died, usually within 1-2 hours and LC_{50}, defined as the concentration in air at which 50 percent of the test animals (rats or mice) died, usually within 1 hour. Some chemicals may also have an associated $LD_{50\ dermal}$, which is reflective of the amount of chemical in mg/Kg applied to the skin that caused 50% of the test animals to die. Not all chemicals have been tested and animal testing has fallen out of favor, so it is important to remember lack of this information on an SDS does not necessarily mean the chemical has no toxic properties.

OSHA, in the lab standard, considers an acutely toxic material (substances that have a high degree of acute toxicity) as those that "may be fatal or cause damage to target organs as the result of a single exposure or exposures of short duration." Various toxicological publications and agencies have defined the toxicity of a chemical as fitting into one of five to six categories. Generally speaking all models define a chemical with an oral LD_{50} of $\leq$ 50 mg/ Kg body weight as acute toxins and this is the number cited in the DRI Chemical Hygiene Plan. There were variations in interpretation, however, when it comes to skin and inhalation exposures. With the incorporation of the definitions from the Global Harmonization System of Chemical Classification into the OSHA Hazard Communication Standard, how toxicity is communicated on an SDS has been standardized[1] into toxic categories 1 (extreme) to 5 (practically non-toxic), defined in the table below.

Classification Summary for GHS

Acute toxicity hazard classification and Hazard Statements

Generally LD/LC50	Category 1	Category 2	Category 3	Category 4	Category 5 *
Oral (mg/kg)	≤5	>5 - ≤50	>50 - ≤300	>300 - ≤2000	>2000 - 5000
Dermal (mg/kg)	≤50	>50 - ≤200	>200 - ≤1000	>1000 - ≤2000	>2000 - 5000
Gases (ppm)	≤100	>100 - ≤500	>500 - ≤2500	>2500 - ≤20000	**
Vapours (mg/l)	≤0.5	>0.5 - ≤2.0	>2.0 - ≤10	>10 - ≤20	**
Dusts and Mists (mg/l)	≤0.05	>0.05 - ≤0.5	>0.5 - ≤1.0	>1.0 - ≤5	**
Symbol	Skull	Skull	Skull	Exclamation	No Symbol
Signal Word	Danger	Danger	Danger	Warning	Warning
Hazard Statement (oral)	H300 Fatal if swallowed	H300 Fatal if swallowed	H301 Toxic if swallowed	H302 Harmful if swallowed	H303 May be harmful if swallowed
Hazard Statement (dermal)	H310 Fatal in contact with skin	H310 Fatal in contact with skin	H311 Toxic in contact with skin	H312 Harmful in contact with skin	H313 May be harmful in contact with skin.
Hazard Statement (inhalation)	H330 Fatal if inhaled	H330 Fatal if inhaled	H331 Toxic if inhaled	H332 Harmful if inhaled	H333 May be harmful if inhaled

* Not all counties, including the U.S., will adopt category 5 into their regulations.

[1] Note: This change to the OSHA Hazard Communication Standard and the SDS toxicity language has caused some confusion because not only is the hazard numbering system is opposite that used in the NFPA fire diamond and HMIS classification systems, but unfortunately now many SDSs list acute toxicity as a hazard because many chemicals will fall into one of the GHS categories outlined in the table, and therefore the designation 'acute toxin' does not apply to just those materials that are extremely or highly toxic.

DRI DEFINITION OF HIGH ACUTE TOXICITY MATERIALS

The DRI Chemical Hygiene Plan has established high acute toxicity compounds as those with an oral LD_{50} of $\leq$ 50 mg/ Kg body weight. (This was based on the former OSHA hazard communication standard and is still correct for oral exposures in the revised standard.) The current OSHA definitions for LD_{50} dermal, LC_{50} gases, LC_{50} vapors and LC_{50} dusts and mists are $\leq$ 200 mg/Kg, $\leq$ 500ppm, $\leq$ 2 mg/l and $\leq$ 0.5 mg/l respectively. OSHA does not define extremely toxic chemicals, but based on the published models of toxicity, these would likely be chemicals with an oral LD_{50} $\leq$ 5 mg/Kg (GHS category 1acute toxins).

The following information applies to chemicals that meet the definition of acute toxicity listed in the paragraph above.

PURCHASING PROCEDURE

Before you purchase or start working with any chemical read the Safety Data Sheet (SDS). If the material you are planning to purchase is extremely or highly toxic (or a known or suspect human carcinogen or reproductive toxin), you need to complete a particularly hazardous substance (PHS) registration and submit it to EH&S for approval **BEFORE** you order the chemical. If you are unsure about the level of toxicity, call EH&S and request a Hazard Assessment (HA). As part of the HA and PHS approval process, EH&S will review

- ✓ the toxicological data available for the material,
- ✓ your work area for the proper engineering controls needed to work with the material,
- ✓ your standard operating procedures for working with extremely and highly toxic compounds,
- ✓ training records of all persons in the lab

and will

- ✓ provide recommendations for additional engineering controls and PPE appropriate for working with the material, and
- ✓ determine if medical surveillance of affected employees will be required.

WORKING WITH EXTREMELY AND HIGHLY TOXIC MATERIALS

- Exposure limits

  Often times toxic chemicals will have an exposure limit listed on the SDS (in Sections V, 8 or 11 on older versions of MSDSs, in Section 11 of the new SDS (GHS) format). Permissible exposure limits (PELs) are set by the Occupational Safety and Health Administration (OSHA) and are published in Title 29 *Code of Federal Regulations* 1910.1000. The threshold limit value (TLV) is established by the American Conference of Governmental Hygienists (ACGIH). TLVs are typically more protective because ACGIH assesses the data about the hazards of occupational exposure to chemicals more frequently and updates their list on a regular basis. The ACGIH list is published annually in the *TLVs® and BIEs® booklet*.

  While exposure limits are important to take into consideration when assessing the hazards, especially via inhalation, of a chemical and choosing controls for using that material, it imperative to understand that an exposure limit may not be directly related to a material's LD_{50} where the method of exposure and ease of absorption (especially through the skin) are also considered. Equally important is the fact that not all chemicals have an assigned TLV or PEL or even an LD listed. This does not necessarily mean these materials are 'safe' because many chemicals have just not been thoroughly tested.

- Facility Requirements for working with extremely or highly toxic materials

  Requirements for engineering controls for working with acute toxins may vary depending on the specific chemical properties, such as physical state at room temperature or volatility of the compound. Some common requirements are

- Lab hood tested at least annually for an average face velocity of between 80 and 100 lfpm. (Note: Manipulations of highly toxic powders should be done in a powder's weighing hood or glove box if losses due to air flow in a lab hood are a concern.)

- Vented gas cabinets for all new processes involving highly toxic gases.

- Eyewash station and emergency shower no less than 10 seconds from point of use with path of travel free of obstructions that may inhibit immediate use

- Vinyl floor covering (with coving to contain spills) may be required.

- Surfaces/lab furnishings should be easily cleanable and lab stools/chairs should not have fabric seats or backs.

- Appropriate spill kits specific to the hazard must be kept in the lab in a location prominently displayed with signage.

- Fire extinguisher rated for the types of chemicals in the lab (for example a pyrophoric chemical will need special equipment).

▪ Work Practices and Procedures (also known as Administrative Controls)

- Best Practices

  - Substitute a less toxic alternative when at all possible

  - Always read the SDS for all chemicals involved in the process before purchasing them to ensure you have any special equipment for handling and storage required to safely use the chemical**. If any of the chemicals are particularly hazardous substances, complete the PHS registration form and obtain approval for purchase before placing the order**

  - At all times practices strict chemical hygiene in the lab
    - Do not eat, drink, smoke, chew gum or apply cosmetics in the lab
    - Do not store food in laboratory refrigerators
    - Do not store chemicals in break room refrigerators
    - Avoid skin and eye contact—do not touch your face or rub your eyes in the lab
    - Remove lab coat and leave in the lab before taking breaks, going to meetings, etc.
    - Wash hands when you remove gloves and before leaving the lab

  - Dress appropriately to work in the lab-long pants, closed, low heeled shoes (no open toes, no canvas), no bare midriffs

  - Use appropriate Personal Protective Equipment (PPE)
    - Safety glasses with side shield or wrap around style or goggles must be worn by all persons, including those already wearing prescription glasses
    - Lab coat-knee length and buttoned
    - Gloves available that are appropriate for All chemicals you are using—not just the highly toxic ones. (Contact EH&S if you need help with glove selection)

    The PPE listed above is the minimally acceptable for working with hazardous materials. Additional or more stringent PPE requirements for working with extremely or highly toxic chemicals may be required depending on the amount of and how the chemical will be used. As part of the hazard assessment process and PHS and SOP development, the proper PPE for working with the chemical in a lab setting will be identified. Note this may be different from what is found on the material's SDS

because the safety data sheets are written to cover large scale use and chemical manufacturing operations. When in doubt, contact EH&S for assistance in PPE selection.

- Laboratories that have extremely or highly toxic compounds in inventory shall designate a use area within the lab with signage reflecting the wording found in the DRI Chemical Hygiene Plan, Section V.B. Work with extremely or highly toxic materials must be limited to the areas indicated on your SOP. In addition,
  - Compounds with an $LD_{50} \leq 50$ mg/Kg or $LC_{50} \leq 500$ ppm must be handled in a laboratory hood or other approved exhausted enclosure.
  - Compounds with an $LD_{50} \leq 50$ mg/Kg or $LC_{50} \leq 500$ ppm must be kept in a locked, restricted area, such as a lab that is locked when unattended. Additionally, those with an $LD_{50} \leq 5$ mg/Kg or $LC_{50} \leq 100$ ppm should be kept in a locked cabinet and it is recommended that a log be maintained to keep a record of who has used the material, in what quantity and when.

- Standard Operating Procedures (SOPs)

  In addition to the PHS, a written SOP is required for each extremely and highly toxic material used in the lab. It is the lab PI/manager's responsibility to ensure an SOP has been developed for each chemical classified as a high acute toxin before the chemical is used in lab procedures. The SOP will describe how the lab will handle a hazardous chemical safely, including the amount and concentration used, how to obtain or create the working solution, and special handling procedures, engineering controls, and personal protective equipment required. The SOP should also include information on the specific areas where the material may be used. The SOP can take any format, but must include pertinent information on the topics listed below.
  - Circumstances of Use
  - Potential Hazards
  - Engineering Controls
  - Work Practice Controls
  - Personal Protective Equipment
  - Transportation and Storage
  - Emergency procedures
    - Exposures/Unintended contact
    - Spill Procedures
  - Waste Disposal
  - Chemical specific training (Typically an SOP will include a sign off page that indicates by employee name, ID number, signature and date that the employee has reviewed the chemical's SDS and has read and understood the information on the chemical's SOP and agrees to fully adhere to the DOP requirements. Alternately a copy of the form in appendix D or the DRI Chemical Hygiene Plan can be stapled to each SOP to serve as the sign off page.)

  Incorporating safety procedures into experimental protocols is encouraged as long as the protocol includes all the same information required for development of a chemical specific SOP and there is documentation of training as noted in the last SOP bullet above.

- Training

  All employees who will be working in a laboratory at DRI are required to take the lab safety orientation online course upon hire and to attend an annual laboratory/hazardous waste generator training session provided by EH&S. In addition, laboratory PIs/Supervisors/Managers are responsible for providing lab specific training, which includes providing safety information such as PPE requirements, lab specific chemical hazard information, lab specific SOPs and spill procedures, emergency response procedures, etc. and to document this has occurred. (A form for documenting lab specific training is located in the DRI Chemical Hygiene Plan, Appendix D.)

- Medical Surveillance

  Generally speaking, medical surveillance is not usually required for working with chemicals in lab scale quantities in a laboratory environment. Upon receipt of the PHS registration, EH&S will evaluate the proposed use/operation, available engineering and administrative controls and PPE requirements and will determine the need for additional safety controls, including industrial hygiene monitoring or medical surveillance of workers with potential exposure to extremely/highly toxic materials. If it is determined that medical surveillance is required in order to conduct the work, the Division or project will be responsible for covering the costs incurred.

REFERENCES TBD

- 29 CFR 1910.1000; 1910.1200; 1910.1450
- ACGIH TLV/BIE booklet
- Prudent Practices in the Laboratory, Chapter 4
- ACS Handbook of Chemical Health and Safety, Chapter 20
- CRC Press- 1994
- DRI CHP