Chemical Hygiene Plan – Appendix C: GHS Reference Materials

This appendix provides an overview of Globally Harmonized System (GHS) hazard classifications under the Hazard Communication Standard for highly toxic materials. This overview provides information about categories under the classification of acute toxicity, mutagens', reproductive and carcinogen hazards.

When chemicals are rated with one of the following GHS hazard classifications at the listed Category levels, then the Ch. 8 Form 1: Chemical Prior Approval Form must be completed:

- **Acute toxicity** – Category 1 and 2
- **Germ cell mutagenicity** – Category 1A Substances known to induce heritable mutations in germ cells of humans and Category 1B: Substances which should be regarded as if they induce heritable mutations in the germ cells of humans,
- **Reproductive Hazard** – Category 1: Known or presumed human reproductive toxicants and Category 2; suspected human reproductive toxicant.
- **Carcinogen** – Category 1 (includes 1A and 1B): Known or presumed human carcinogens, Category 2: Suspected human carcinogens.

Once the form is completed, Environmental Health & Safety will review the information and intended use location to determine if any special procedures or equipment are needed for handling and use.

Health Hazard Classifications

The following is from Or-OSHA's standard on the chemical classifications that PCC Laboratory instructional operations shall use for defining the prior approval hazards.

1. Acute Toxicity

Acute toxicity refers to those adverse effects that occur following oral or dermal administration of a single dose of a substance, or multiple doses given within 24 hours, or an inhalation exposure of 4 hours.

Substances can be allocated to one of four toxicity categories based on acute toxicity by the oral, dermal or inhalation route according to the numeric cut-off criteria as shown in Table A.1.1 in the standard. PCC shall only require prior approval based on acute toxicity for Category 1 and 2 listed chemicals.

Acute toxicity values are expressed as (approximate) LD50 (oral, dermal) or LC50 (inhalation) values or as acute toxicity estimates (ATE).

2. Germ Cell Mutagenicity

A mutation is defined as a permanent change in the amount or structure of the genetic material in a cell. The term mutation applies both to heritable genetic

changes that may be manifested at the phenotypic level and to the underlying DNA modifications when known (including, for example, specific base pair changes and chromosomal translocations). The term mutagenic and mutagen will be used for agents giving rise to an increased occurrence of mutations in populations of cells and/or organisms.

The more general terms genotoxic and genotoxicity apply to agents or processes which alter the structure, information content, or segregation of DNA, including those which cause DNA damage by interfering with normal replication processes, or which in a non-physiological manner (temporarily) alter its replication. Genotoxicity test results are usually taken as indicators for mutagenic effects.

This hazard class is primarily concerned with chemicals that may cause mutations in the germ cells of humans that can be transmitted to the progeny. However, mutagenicity/genotoxicity tests in vitro and in mammalian somatic cells in vivo are also considered in classifying substances and mixtures within this hazard class.

The classification system provides for two different categories of germ cell mutagens to accommodate the weight of evidence available. The two-category system is described in the Figure A.5.1 in the Or-OSHA standard but the following categories shall require prior approval process.

- **Category 1A**: Substances known to induce heritable mutations in germ cells of humans.
- **Category 1B**: Substances, which should be regarded as if they induce heritable mutations in the germ cells of humans

3. Carcinogenicity

Carcinogen means a substance or a mixture of substances, which induce cancer or increase its incidence. Substances and mixtures which have induced benign and malignant tumors in well- performed experimental studies on animals are considered also to be presumed or suspected human carcinogens unless there is strong evidence that the mechanism of tumor formation is not relevant for humans.

Classification of a substance or mixture as posing a carcinogenic hazard is based on its inherent properties and does not provide information on the level of the human cancer risk which the use of the substance or mixture may represent.

For the purpose of classification for carcinogenicity, substances are allocated to one of two categories based on strength of evidence and additional weight of evidence considerations. In certain instances, route-specific classification may be warranted. PCC shall require prior approval based on acute toxicity for Category 1A, 1B, and 2 listed chemicals.

- **Category 1A and 1B**: Known or presumed human carcinogens

  The classification of a substance as a Category 1 carcinogen is done on the basis of epidemiological and/or animal data. This classification is further distinguished on the basis of whether the evidence for classification is largely from human data (Category 1A) or from animal data (Category 1B)

- **Category 2**: Suspected human carcinogens

  The classification of a substance in Category 2 is done on the basis of evidence obtained from human and/or animal studies, but which is not sufficiently convincing to place the substance in Category 1A or B. This classification is based on strength of evidence together with weight of evidence considerations. Such evidence may be from either limited evidence of carcinogenicity in human studies or from limited evidence of carcinogenicity in animal studies.

Where the weight of evidence for the carcinogenicity of a substance does not meet the above criteria, any positive study conducted in accordance with established scientific principles, and which reports statistically significant findings regarding the carcinogenic potential of the substance, must be noted on the safety data sheet.

4. Reproductive Toxicity

Reproductive toxicity includes adverse effects on sexual function and fertility in adult males and females, as well as adverse effects on development of the offspring. Some reproductive toxic effects cannot be clearly assigned to either impairment of sexual function and fertility or to developmental toxicity. Nonetheless, chemicals with these effects shall be classified as reproductive toxicants.

Adverse effects on sexual function and fertility means any effect of chemicals that interferes with reproductive ability or sexual capacity. This includes, but is not limited to, alterations to the female and male reproductive system, adverse effects on onset of puberty, gamete production and transport, reproductive cycle normality, sexual behavior, fertility, parturition, pregnancy outcomes, premature reproductive senescence, or modifications in other functions that are dependent on the integrity of the reproductive systems.

Adverse effects on development of the offspring means any effect of chemicals which interferes with normal development of the conceptus either before or after birth, which is induced during pregnancy or results from parental exposure. These effects can be manifested at any point in the life span of the organism. The major manifestations of developmental toxicity include death of the developing organism, structural abnormality, altered growth and functional deficiency.

For the purpose of classification for reproductive toxicity, substances shall be classified in one of two categories based on the effects on sexual function and fertility, and on development.

- **Category 1**: Known (1A) or presumed human (1B) reproductive toxicant:
- **Category 2**: Suspected human reproductive toxicant.

Adverse effects on or via lactation are also included in reproductive toxicity, but for classification purposes, such effects are treated separately. Classifications are (a), (b) and (c).

The following link to a listing of Particularly Hazardous Substances that Carnegie Mellon University published with their Chemical Hygiene plan has been provided as a general reference. The list is useful to cross check with GHS listings to determine which materials require prior approval for use BUT NO LIST IS COMPLETE you must check the SDS for possible additional chemicals rated as highly toxic.

https://www.cmu.edu/ehs/Laboratory-Safety/chemical-safety/documents/cmuphstable.pdf