



**Info Sheet # 7 Carcinogenicity**

May 2011

**How does the GHS define carcinogenicity?**

A carcinogen is a chemical substance or a mixture of chemical substances that induces cancer or increases its incidence. Substances that have induced cancer in experimental animal studies are considered to be




presumed or suspected human carcinogens unless there is strong evidence to indicate the mechanism of tumor formation is not relevant to humans.

**How are carcinogens classified under GHS?**

Carcinogen classification involves two interrelated determinations: evaluation of strength of evidence and consideration of all other relevant information (weight of evidence analysis). Under GHS, carcinogens are categorized as either known/presumed carcinogens (Category 1) or suspected carcinogens (Category 2).

Category 1 is subdivided further based on whether the evidence for classification is mostly from human or animal data. See Table 1 below for hazard categories and hazard communication elements for carcinogens.

**Table 1: Carcinogen Classification and Hazard Communication Elements**

	<b>Category 1A</b>	<b>Category 1B</b>	<b>Category 2</b>
<b>Definition/criteria/description</b>	Known or presumed human carcinogens	Presumed to have carcinogenic potential for humans – largely based on animal evidence	Suspected human carcinogen
	Known to have carcinogenic potential for humans – largely based on human evidence	Presumed to have carcinogenic potential for humans – largely based on animal evidence	Evidence from animal and/or human studies is limited
<b>Symbol</b>	 Health Hazard	 Health Hazard	 Health Hazard
<b>Signal word</b>	Danger	Danger	Warning
<b>Hazard statement</b>	May cause cancer (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	May cause cancer (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)	Suspected of causing cancer (state route of exposure if it is conclusively proven that no other routes of exposure cause the hazard)

## Some Important Considerations in Carcinogen Classification

The information in this section is based on the official GHS text (3<sup>rd</sup> revised edition, Section 3.6.1 – 3.6.4) and the accompanying GHS decision logic/guidance (Section 3.6.5). Classification should be based on studies using reliable and acceptable methods. All peer-reviewed published studies and additional data accepted by regulatory authorities should be reviewed. Human evidence, animal studies, as well as other factors that may increase or decrease the level of concern should be considered. Carcinogen classification is based on strength of evidence and other considerations (e.g., weight of evidence). Expert judgment is necessary in applying the classification criteria; the GHS provides an approach to analysis rather than hard and fast rules for the evaluation of carcinogenicity data.

- Strength of evidence:
  - Sufficient evidence → causality (cause and effect relationship) between human exposure and development of cancer, or a causal relationship between the substance and increased tumor incidence in animal studies
    - May lead to Category 1A or Category 1B classification
  - Limited evidence → A positive association between exposure and cancer in humans, without demonstration of a causal relationship, or data from animal studies suggesting a carcinogenic effect, without demonstration of a causal relationship
    - May lead to Category 2 classification (Note: Limited evidence from both human and animal studies may result in a Category 1B classification on a case-by-case basis)
- Other considerations (weight of evidence analysis) – Beyond strength of evidence, a number of other factors should be considered that may influence the likelihood an agent may present a carcinogenic risk. The following are examples of factors that may increase or decrease the overall level of concern:
  - Tumor response factors: tumor incidence and tumor type, number of sites, progression to malignancy, latency, background incidence
  - Experimental study considerations: route of exposure; number of independent studies; adequacy of study design, conduct or interpretation
  - Additional factors: number of species or strains responding, gender specificity, relevant structure-activity relationships, toxicokinetics/toxicodynamics and mode of action and its relevance to humans (for example, mutagenicity, immunosuppression, etc.)

## How is classification applied to mixtures?

Mixtures are classified based on available data on the individual ingredients using cut-off values/concentration limits for those ingredients (See Table 2). Data on a mixture itself may be used on a case-by-case basis when such data is conclusive and accounts for factors including dose, duration of study, observations, and analysis of the test system (e.g. statistical analysis, test sensitivity). Bridging principles set forth in the GHS for carcinogens are appropriate for classifying mixtures. These include: dilution, batching, and substantially similar mixtures.

Table 2: Cut-off values/Concentration Limits Triggering Classification of Mixtures

Ingredient Classified as:	Cut-off/concentration limits triggering classification of a mixture as:	
	Category 1 carcinogen	Category 2 carcinogen
Category 1 carcinogen	≥ 0.1%	-
Category 2 carcinogen	-	≥ 0.1% (Note 1)
		≥ 1.0% (Note 2)

For complete text of these notes, refer to official GHS text:

Note 1: Not all regulatory authorities will require a label warning for Category 2 carcinogens present between 0.1 and 1.0%.

Note 2: Both an SDS and a label would generally be expected when a Category 2 carcinogen is present in a mixture at ≥ 1.0%.

## To learn more ...

- Electronic images of GHS pictograms may be downloaded from the United Nation's GHS website at <http://www.unece.org/trans/danger/publi/ghs/pictograms.html>

- The GHS, in its entirety (including classification criteria and label and MSDS requirements), can be downloaded at [http://www.unece.org/trans/danger/publi/ghs/ghs\\_rev03/03files\\_e.html](http://www.unece.org/trans/danger/publi/ghs/ghs_rev03/03files_e.html)
- OSHA Rulemaking and Information
  - Advanced Notice of Proposed Rulemaking at [http://www.osha.gov/pls/oshaweb/owadisp.show\\_document?p\\_table=FEDERAL\\_REGISTER&p\\_id=18890](http://www.osha.gov/pls/oshaweb/owadisp.show_document?p_table=FEDERAL_REGISTER&p_id=18890)
  - Notice of Proposed Rulemaking at [http://www.osha.gov/FedReg\\_oshapdf/FED20090930.pdf](http://www.osha.gov/FedReg_oshapdf/FED20090930.pdf)
  - Guide to the Globally Harmonized System for Classification and Labels is available at <http://www.osha.gov/dsg/hazcom/ghs.html>
  - OSHA GHS Web Page: <http://www.osha.gov/dsg/hazcom/global.html>
- For additional GHS information sheets developed through the OSHA-SCHC Alliance:
  - OSHA site: <http://www.osha.gov/dcsp/alliances/schc/schc.html#products>
  - SCHC site: <http://www.schc.org/committee/oshalliance/>
- A 16-hour training course on the GHS is offered by the Society for Chemical Hazard Communication (SCHC). [http://www.schc.org/schcnewsite/committee.php?page=profdev/courses/course\\_list.html](http://www.schc.org/schcnewsite/committee.php?page=profdev/courses/course_list.html)

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