



## Hazard Communication Information Sheet reflecting the US OSHA Implementation of the *Globally Harmonized System of Classification and Labelling of Chemicals (GHS)*

Produced by the SCHC-OSHA Alliance  
GHS/HazCom Information Sheet Workgroup

### Reproductive Toxicity

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#### **How does OSHA's Hazard Communication Standard (HCS 2012) define 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. Adverse effects on sexual function and fertility include changes in the structure and function of the male and female reproductive systems and modifications in any other functions that are dependent upon the integrity of the reproductive systems. Under HCS 2012, 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. Adverse effects on or via lactation are also included in reproductive toxicity, although classified separately from other reproductive effects.

#### **How does HCS 2012 classify reproductive toxins?**

Classification as a reproductive toxin is determined based upon the total weight of evidence using expert judgment. Under HCS 2012, reproductive toxins are categorized as either known or presumed human reproductive toxicants (Category 1) or suspected human reproductive toxicants (Category 2).

Category 1 is subdivided based on whether the evidence for classification is mostly from human or animal data. Effects on or via lactation are classified in a single separate category. See Table 1 below for hazard categories and hazard communication elements for reproductive toxicants. The precautionary statements are not included due to space limitations of this fact sheet. See §1910.1200 for complete classification and labelling information.

**Table 1: Classification Criteria**

Category	Category 1A	Category 1B	Category 2	Effects on or via lactation
	Known or presumed human reproductive toxicant		Suspected human reproductive toxicant	
Description	Known human reproductive toxicant – largely based on human evidence	Presumed human reproductive toxicant – largely based on animal evidence	Evidence from animal and/or human studies is limited	Toxicants which may interfere with lactation or which may be present in breast milk and may cause harm to breast-fed children
Pictogram				No pictogram
Signal Word	Danger	Danger	Warning	No signal word
Hazard Statement	May damage fertility or the unborn child (state specific effect if known)(state route of exposure if no other routes of exposure cause the hazard)	May damage fertility or the unborn child (state specific effect if known) (state route of exposure if no other routes of exposure cause the hazard)	Suspected of damaging fertility or the unborn child (state specific effect if known) (state route of exposure if no other routes of exposure cause the hazard)	May cause harm to breast-fed children.

### ***Important considerations in classifying a substance as a reproductive toxin:***

Classification as a reproductive toxicant applies to those chemicals that have an intrinsic ability to produce an adverse effect on reproduction based on the total weight of evidence. Chemicals should not be classified as reproductive toxicants if such an effect is produced solely as a non-specific secondary consequence of other toxic effects.

The term "weight of evidence" means that all the available information on the potential of a chemical to cause an adverse reproductive effect is considered together. This information may include results from epidemiological studies and case reports in humans and specific animal reproduction studies, along with sub-chronic, chronic and special studies in animals that provide information regarding toxicity to reproductive and related endocrine organs. Consideration may also be given to data for chemically related substances. The weight given to the available studies may be influenced by the following factors:

- Quality of studies
- Consistency of results
- Nature and severity of effects
- Level of statistical significance for intergroup differences
- Number of endpoints affected
- Relevance of route of administration to humans
- Freedom from bias

Both positive and negative results should be considered together when making a weight of evidence determination. However, a single, positive study performed according to good scientific principles and with statistically or biologically significant positive results may justify classification.

### ***Maternal toxicity***

Development of the offspring throughout gestation and during the early postnatal stages can be influenced by toxic effects in the mother either through non-specific mechanisms related to stress and the disruption of maternal homeostasis, or by specific maternally-mediated mechanisms. Ideally, data from animal studies should provide clear evidence of specific reproductive toxicity in the absence of other, systemic, toxic effects. However, if developmental toxicity occurs together with other toxic effects in the dam, the potential influence of the generalized adverse effects should be assessed to the extent possible. In some situations it is reasonable to assume that reproductive toxicity is due to a secondary consequence of maternal toxicity, e.g. when the dams fail to thrive or are incapable of nursing pups. However, the presence of maternal toxicity should not generally be used to negate findings of embryo/fetal effects unless it can be clearly demonstrated on a case-by-case basis that the effects are secondary non-specific effects; i.e. secondary to maternal toxicity. This is a complex issue because of uncertainties surrounding the relationship between maternal toxicity and developmental outcome; thus expert judgment and a weight of evidence approach should be used.

### ***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 reproduction test system (e.g. statistical analysis, test sensitivity). Bridging principles set forth in HCS 2012 for reproductive toxicants are appropriate for classifying mixtures and can be used when there are sufficient data on both the individual ingredients and similar tested mixtures to adequately characterize the mixture. 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 reproductive toxicant	Category 2 reproductive toxicant	Additional category for effects on or via lactation
Category 1 reproductive toxicant	≥ 0.1%		
Category 2 reproductive toxicant		≥ 0.1%	
Additional category for effects on or via lactation			≥ 0.1%

### To learn more...

- OSHA: Hazard Communication : <https://www.osha.gov/dsg/hazcom/index.html>
- SCHC site: <http://www.schc.org/osha-alliance>

*The information contained in this sheet is believed to accurately represent current OSHA HCS requirements. However, SCHC cannot guarantee the accuracy or completeness of this information. Users are responsible for determining the suitability and appropriateness of these materials for any particular application.*

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