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

# Specific Target Organ Toxicity – Single Exposure March 2017

## *How does OSHA's Hazard Communication Standard (HCS 2012) define specific target organ toxicity – single exposure (STOT-SE)?*

Specific target organ toxicity (single exposure) (STOT-SE) means specific non-lethal effects on organs or organ systems in the body following single exposure to a chemical. All significant health effects that can impair function, whether reversible or irreversible, occurring immediately after exposure or following a delay, are included in this category of hazard. This category does not include effects specifically addressed elsewhere in HCS 2012. These include: acute toxicity, skin corrosion/irritation, serious eye damage/ eye irritation, respiratory or skin sensitization, germ cell mutagenicity, carcinogenicity, reproductive toxicity, and aspiration hazard.

## *How does HCS 2012 classify specific target organ toxicity – single exposure?*

A substance is classified under STOT-SE on the basis of the weight of all of the human and animal evidence. Human evidence indicating that a substance has produced a consistent and identifiable toxic effect leads to classification in this category. While human evidence is the primary source of information used for classification, data in experimental animals is also evaluated. Toxicologically significant effects in experimental animals which have affected the function or structure of a tissue/organ, or have produced serious changes in clinical biochemistry, blood or urine of the animals may also lead to classification under STOT-SE. Changes observed in animals are only used for classification under STOT-SE when they are relevant for human health. Specific organ toxicity can occur by any route of exposure that is relevant to humans, usually by swallowing, by absorption through the skin, or by breathing the substance.

Table 1: Classification Criteria

| Category | Category 1 | Category 2 | Category 3 |
|---|---|---|---|
| Description | Substances that have produced significant toxicity in humans, or that, on the basis of evidence from studies in experimental animals can be presumed to have the potential to produce significant toxicity in humans following single exposure.<br><br>Substances are classified in Category 1 for STOT-SE on the basis of:<br>(a) Reliable and good quality human evidence (cases studies or epidemiology studies); or<br>(b) Experimental animal studies that demonstrate significant and/or severe toxic effects that are relevant to human health and are produced at generally low exposure concentrations. | Substances that, on the basis of evidence from studies in experimental animals, can be presumed to have the potential to be harmful to human health following single exposure.<br><br>Experimental animal studies that demonstrate significant toxic effects that are relevant to human health and are produced at generally moderate exposure concentrations. (In exceptional cases, human evidence can be used to place a substance in this category.) | Transient target organ effects.<br><br>This category only includes narcotic effects (dizziness, drowsiness) and respiratory tract irritation (sore throat, cough). These effects, while adversely altering human function, are of short duration after exposure, and do not result in significant alterations of structure or function following recovery. |

Note: The specific target organ/organ system that has been primarily affected by the classified substance shall be identified, where possible, and where this is not possible, the substance shall be identified as a general toxicant.

Table 2 shows some of the label elements for STOT-SE. The precautionary statements are not included due to space limitations of this fact sheet. See §1910.1200 for complete classification and labelling information.

Table 2: Label Elements

| Category | Category 1 | Category 2 | Category 3 |
|---|---|---|---|
| Pictogram |  |  |  |
| Signal Word | Danger | Warning | Warning |
| Hazard Statement | Causes damage to organs (or state all organs affected, if known) (state route of exposure if no other routes of exposure cause the hazard)) | May cause damage to organs (or state all organs affected, if known) (state route of exposure if no other routes of exposure cause the hazard) | May cause respiratory irritation;<br>Or<br>May cause drowsiness or dizziness |

## *Important considerations in classifying a substance as a STOT-SE:*

Data should be carefully evaluated and, where possible, should not include secondary effects. A substance that causes liver damage, for example, can also result in effects on other organs/tissues as a result of the damage to the liver, and thus, should not be classified as toxic to these other organs. The relevant route(s) of exposure by which the substance produces damage should be identified.

A weight of evidence approach is used to classify substances under STOT-SE. This can include human incidents (case studies), epidemiological studies, and acute toxicity studies in experimental animals. In exceptional cases, it may be appropriate to classify a substance in Category 2 on the basis of human evidence when the weight of all evidence, including animal, does not support a Category 1 classification.

Evidence from human experience often contains uncertainties, particularly with regard to exposure conditions. Evidence from animal studies typically provides more detail that can be used to evaluate whether or not exposure to a given substance could result in functional impairment. Thus all available evidence is considered in the classification process. HCS 2012 provides examples of the types of toxic effects that are considered relevant to classification as STOT-SE (see A.8.2.1.7.3). For example, significant organ damage noted at animal autopsy and/or upon microscopic examination of tissue is considered to be a relevant toxic effect, whereas changes in organ weight with no accompanying evidence of organ dysfunction would not support classification as a Category 1 or Category 2 STOT-SE.

HCS 2012 provides guidance values that can be used to assist with STOT-SE classification in Categories 1 and 2 when using acute toxicity data from experimental animals in the weight of evidence assessment (See Table A.8.1). The principal reason for providing such values is the recognition that all chemicals are potentially toxic at high enough doses, thus it is important to consider the dose/concentration at which a toxic effect occurs. The guidance value ranges provided in HCS 2012 are not strict threshold values, but rather, should be used in an overall weight of evidence approach. It is important to remember that positive human data predominates over animal data.

STOT-SE Category 3 includes only respiratory tract irritation (sore throat, cough) and narcotic effects (dizziness, drowsiness).

Respiratory tract irritants

- Respiratory tract irritants are classified primarily using human data. Category 3 respiratory tract irritants cause irritant effects that impair function with symptoms such as cough, pain, choking, and breathing difficulties.
- Observations from animal inhalation studies may be used as part of the weight of evidence approach.

Narcotic effects

- Substances that cause central nervous system (CNS) depression are classified as STOT-SE Category 3 for narcotic effects. CNS depression in humans may cause such effects as: drowsiness, narcosis (a dazed or sluggish feeling), reduced alertness, loss of reflexes, lack of coordination, and vertigo. CNS depression can also cause: headache, nausea, reduced judgment, dizziness, irritability, fatigue, impaired memory function, deficits in perception and coordination, reaction time or sleepiness.
- Narcotic effects may also be observed in animal studies and can include: lethargy (drowsiness), lack of coordination of muscle movement, and others.
- Where CNS symptoms are not temporary in nature, classification in Category 1 or 2 should be considered.

## *How is classification applied to mixtures*

When data are available for a mixture, the mixture is classified using the same criteria as for substances, i.e. use of good quality evidence from human experience or appropriate animal studies by a weight of evidence evaluation of the data. When a mixture itself has not been tested, but there are sufficient data on both the individual ingredients and on similar mixtures, these data are used in accordance with bridging principles set forth in HCS 2012 for specific target organ toxicants. These include: dilution, batching, concentration of highly toxic mixtures (Category 1 ingredients), interpolation within one toxicity category, substantially similar mixtures, and aerosols. When there is no reliable evidence or test data for the mixture itself but where data is available for some or all of the ingredients of a mixture, the following cutoff values (see Table 2) are used to trigger classification of mixtures under STOT-SE.

There are no defined cut-offs for mixture classification as STOT-SE Category 3. A cut-off value /concentration limit of 20% is considered appropriate as an additive of all Category 3 ingredients for each endpoint, respiratory tract irritation and narcotic effects evaluated separately. Expert judgment must be exercised in recognizing that such effects may occur at higher or lower concentrations, depending upon the ingredient(s) being evaluated.

Table 3: Cut-off values/concentration limits triggering classification of mixtures:

| Ingredient Classified as: | Cut-off/concentration limits triggering classification of a mixture as: | |
|---|---|---|
| | Category 1 | Category 2 |
| Category 1 Target organ toxicant | ≥1.0% | |
| Category 2 Target organ toxicant | | ≥1.0% |

## *To learn more…*

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

Under the Occupational Safety and Health Act, employers are responsible for providing a safe and healthy workplace and workers have rights. OSHA can help answer questions or concerns from employers and workers. OSHA's On-site Consultation Program offers free and confidential advice to small and medium-sized businesses, with priority given to high-hazard worksites. For more information, contact your regional or area OSHA office, call 1-800-321-OSHA (6742), or visit www.osha.gov.