Produced by SCHC-OSHA Alliance
GHS Information Sheet Workgroup

Respiratory Sensitization

September 2025

What is Respiratory Sensitization?

Respiratory sensitization refers to hypersensitivity of the airways occurring after inhalation of a substance or mixture. (See 29 CFR 1910.1200, Appendix A.4). In contrast to respiratory irritation, respiratory sensitization is an immunological response to previous exposure to a chemical. Hypersensitivity is normally seen as asthma, but other hypersensitivity reactions involving the nose (rhinitis), eyes (conjunctivitis), or lungs (alveolitis) are also considered.

Previous exposure to a specific substance is necessary for respiratory sensitization. The first phase is induction (or sensitization) and the second phase is elicitation. Upon induction/sensitization, development of specialized memory cells in the immune system of an individual occurs following the initial exposure to a respiratory sensitizer. During elicitation, an allergic respiratory reaction is produced following exposure to a respiratory sensitizer. The specialized memory cells produced in the individual's immune system following the initial exposure respond to the subsequent exposure, e.g., an allergic reaction takes place.

How to classify for Respiratory Sensitization

Substance Classification

A chemical is classified as a respiratory sensitizer if there is evidence in humans that the substance can lead to specific respiratory hypersensitivity and/or there are positive results from an appropriate animal test. The classification of a material as a respiratory sensitizer is typically based on human experience, as validated animal testing models for sensitization are unavailable. However, data from other animal studies that measure Immunoglobulin E (IgE) or pulmonary responses may provide information in a weight of evidence assessment. If it can be demonstrated that a substance induces symptoms of asthma by irritation only in people with bronchial hyperactivity, the substance should not be considered a respiratory sensitizer.

Respiratory sensitizers should be classified as Category 1, or as sub-categories 1A or 1B. When data are sufficient, Category 1A is assigned to chemicals with a high potential to cause respiratory sensitization in humans and Category 1B is assigned to chemicals with a low to moderate potential to cause respiratory sensitization in humans. When data are not sufficient for sub-categorization, respiratory sensitizers shall be classified as Category 1. (see Table 1 below)

Table 1: Classification Criteria

Category 1	Sub-Category 1A	Sub-Category 1B
Effects seen in either humans or animals will normally justify classification in a weight of evidence approach for respiratory sensitizers. Substances shall be classified as Category 1 where data are insufficient for sub-categorization with these criteria: a) evidence in humans that the substance can lead to specific respiratory hypersensitivity; and/or b) positive results from an animal test.	Substances showing a high frequency of occurrence in humans; or a probability of occurrence of a high sensitization rate in humans based on animal or other tests. Severity of reaction may also be considered.	Substances showing a low to moderate frequency of occurrence in humans; or a probability of occurrence of a low to moderate sensitization rate in humans based on animal or other tests. Severity of reaction may also be considered

Mixture Classification

A mixture is classified when there is sufficient data on the mixture as a whole, otherwise, it is classified using one of two methods based on available ingredient data.

- When reliable and good quality evidence from human experience or appropriate studies in experimental animals is available for the mixture, then use a weight of evidence evaluation of these data.
- When the mixture itself has not been tested but there are sufficient data on both the individual ingredients and similar tested mixtures to adequately characterize the hazards of the mixture, use of bridging principles (dilution, batching, concentration, interpolation, and substantially similar mixtures and aerosols). (See Appendix A.0.5 to 1910.1200 Health Hazard Criteria for detailed guidance.
- When data are only available for at least one ingredient that has been classified and is present at or above the appropriate cut-off value/concentration limit for the specific endpoint as shown Table 2.

Table 2: Cut-off values/concentration limits triggering classification of mixtures:

Ingredient Classified as:	Cut-off/concentration limits triggering classification of a mixture as:	
	Solid/Liquid	Gas
Category 1 Classification	≥ 0.1%	≥ 0.1%
Category 1A Classification	≥ 0.1%	≥ 0.1%
Category 1B Classification	≥ 1.0%	≥ 0.2%

Label Elements for Respiratory Sensitization

Table 3: Hazard Communication Label Elements for Respiratory Sensitization (29CFR 1910.1200, Appendix C)

Category		Category 1	Category 1A	Category 1B
Pictogram				
Signal Word		**Danger**	**Danger**	**Danger**
Hazard Statement		May cause allergy or asthma symptoms or breathing difficulties if inhaled	May cause allergy or asthma symptoms or breathing difficulties if inhaled.	May cause allergy or asthma symptoms or breathing difficulties if inhaled
Precautionary Statements	Prevention	**Avoid breathing dust/fume/gas/mist/vapors/spray.** Chemical manufacturer, importer, or distributor to specify applicable conditions. **[In case of inadequate ventilation] wear respiratory protection.** Chemical manufacturer, importer, or distributor to specify equipment. *- Text in square brackets may be used if additional information is provided with the chemical at the point of use that explains what type of ventilation would be adequate for safe use.*		
	Response	**If inhaled: If breathing is difficult, remove person to fresh air and keep comfortable for breathing.** **If experiencing respiratory symptoms: Call a poison center/doctor/...** ... Chemical manufacturer, importer, or distributor to specify the appropriate source of emergency medical advice.		
	Storage	Not required.		
	Disposal	**Dispose of contents/container to...** ... in accordance with local/regional/national/international regulations (to be specified). Chemical manufacturer, importer, or distributor to specify whether disposal requirements apply to contents, container, or both.		

Important considerations during classification

When considering human evidence, it is necessary that the size of the population exposed, and the extent of exposure be taken into consideration. Human evidence includes:

- Clinical history and data from appropriate lung function tests confirmed by:
  - *in vivo* immunological testing (skin prick test); or
  - *in vitro* immunological testing (serological analysis); or
  - studies that may indicate other specific hypersensitivity reactions where immunological mechanisms of action have not been proven (repeated low-level irritation, pharmacologically mediated effects); or
  - A chemical structure related to chemicals known to cause respiratory hypersensitivity.
- Data from positive bronchial challenge tests with the substance conducted according to accepted guidelines for the determination of a specific hypersensitivity reaction.

Data from appropriate animal studies include information which may indicate the potential of a chemical to cause sensitization by inhalation in humans. As stated above, recognized and validated animal models to predict the potential for a chemical to induce respiratory sensitization are not available. Animal evidence includes:

- Measurements of Immunoglobulin E (IgE) and other specific immunological parameters in animals
- Specific pulmonary response in guinea pigs

To learn more…

- **OSHA: Hazard Communication Safety and Health Topics Page**. Available at: https://www.osha.gov/hazcom
  View the HCS 2012 standard, the HCS 2024 standard, the compliance directive, the Hazard Classification Guidance, the *Small Entity Compliance Guide*, , briefs, pictograms, QuickCards™, Frequently Asked Questions, and other resources.

- **UNECE: About the Globally Harmonized System of Classification and Labelling of Chemicals (GHS) (from the UN).** Available at: https://unece.org/about-ghs

- ***Globally Harmonized System of Classification and Labelling of Chemicals (GHS):*** *Revision 3 and Revision 7* (also known as "The Purple Book.")
  - **Revision 3:** https://unece.org/ghs-rev3-2009
  - ***Revision 7:*** *https://unece.org/ghs-rev7-2017*

  Note: Newer revisions of the "Purple Book" have been developed; however, HCS 2012 follows GHS Revision 3, and the HCS 2024 follows GHS Revision 7 and parts of Revision 8. In some instances, conforming to different revisions may render the user out of compliance with the HCS.

- **OSHA/SCHC Alliance Information Sheets**. Available at:
  - OSHA site: https://www.osha.gov/alliances/schc/schc
  - SCHC site: https://www.schc.org/osha-alliance