



Germ Cell Mutagenicity **March 2017**

How is germ cell mutagenicity defined under HazCom 2012?

A germ cell mutagen is a chemical that may cause mutations in the germ cells of humans that can be transmitted to the progeny. A mutation is defined as a permanent change in the amount or structure of the genetic material in a cell. The terms mutagenic or mutagen are used to refer to those agents giving rise to an increased occurrence of mutations in populations of cells and/or organisms. Genotoxic is a more general term that applies 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.

How is germ cell mutagenicity classified under HazCom 2012?

Under GHS, germ cell mutagens are classified in one of two categories based on the weight of evidence. Category 1 germ cell mutagens are those chemicals that are either known to induce or that should be regarded as if they induce heritable mutations in germ cells of humans. Category 2 germ cell mutagens are those that cause concern owing to the possibility that they may induce heritable mutations in germ cells of humans.

Category 1 is subdivided based on whether the evidence is from human epidemiological studies or from other types of mutagenicity data (e.g., *in vivo* mammalian mutagenicity tests in either heritable germ cells or somatic cells). See tables below for hazard categories and hazard communication elements for germ cell mutagens.

Table 1: Classification Criteria

Category	Category 1A	Category 1B	Category 2
Description	Chemicals known to induce heritable mutations in germ cells of humans	Chemicals regarded as if they induce heritable mutations in germ cells of humans	Chemicals which cause concern for humans owing to the possibility that they may induce heritable mutations in the germ cells of humans

Table 2 shows some of the label elements for classification category. 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: Hazard Communication Label Elements for Germ Cell Mutagenicity

Category	Category 1A	Category 1B	Category 2
Pictogram			
Signal Word	Danger	Danger	Warning
Hazard Statement	May cause genetic defects (state route of exposure if no other routes of exposure cause the hazard)	May cause genetic defects (state route of exposure if no other routes of exposure cause the hazard)	Suspected of causing genetic defects (state route of exposure if no other routes of exposure cause the hazard)

Important considerations in classifying a substance as a germ cell mutagen:

Classification should be based on the intrinsic ability of the chemical to induce mutations in germ cells based on the results of well conducted, scientifically validated tests. All available evidence should be reviewed and evaluated using expert judgment. Classification should be made based on the total weight of evidence. Both positive and negative results are considered together in the weight of evidence determination. However, a single positive study performed according to good scientific principles and with statistically and biologically significant positive results may justify classification (HCS 2012, §1910.1200 Appendix A, Section A.0.3.5). See Table 3 for examples of tests that may be considered when evaluating potential for germ cell mutagenicity.

Table 3: Examples of scientifically validated mutagenicity/genotoxicity tests

Type of Test	Examples
In vivo heritable germ cell mutagenicity tests	Rodent dominant lethal mutation test (OECD 478) Mouse heritable translocation assay (OECD 485) Mouse specific locus test
In vivo somatic cell mutagenicity tests	Mammalian bone marrow chromosome aberration test (OECD 475) Mouse spot test (OECD 484) Mammalian erythrocyte micronucleus test (OECD 474)
Mutagenicity tests in germ cells	Mammalian spermatogonial chromosome aberration test (OECD 483) Spermatid micronucleus assay
Genotoxicity tests in germ cells	Sister chromatid exchange analysis in spermatogonia Unscheduled DNA synthesis test (UDS) in testicular cells
Genotoxicity tests in somatic cells	Liver Unscheduled DNA Synthesis (UDS) <i>in vivo</i> (OECD 486) Mammalian bone marrow Sister Chromatid Exchange (SCE)
In vitro mutagenicity tests	<i>In vitro</i> mammalian chromosome aberration test (OECD 473) <i>In vitro</i> mammalian cell gene mutation test (OECD 476) Bacterial reverse mutation test (OECD 471)

How is germ cell mutagenicity applied to mixtures?

1. Classify based on reliable and good quality evidence on the mixture itself.
2. Use bridging principles (dilution, batching, and substantially similar mixtures). See Section A.0.5 of Appendix A to 1910.1200 Health Hazard Criteria for detailed guidance: (http://www.osha.gov/dsg/hazcom/appendix_a.pdf).
3. Classify based on cut-off values/concentration limits of the ingredients in a mixture (Table 3).

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 Mutagen	Category 2 Mutagen
Category 1 Classification	≥ 0.1%	-
Category 2 Classification	-	≥ 1.0%

To learn more...

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

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