

IARC Monographs Volume 125: Some Industrial Chemical Intermediates and Solvents

Questions and Answers

In November 2019, a Working Group of 13 scientists from eight countries met at the International Agency for Research on Cancer (IARC) in Lyon, France, to finalize their evaluation of the carcinogenicity of five High Production Volume chemicals: glycidyl methacrylate, 1-butyl glycidyl ether, 1-bromo-3-chloropropane, 4-chlorobenzotrifluoride, and allyl chloride. These assessments will be published in Volume 125 of the *IARC Monographs*.

What are the results of the evaluation?

Glycidyl methacrylate was classified as *probably carcinogenic to humans* (Group 2A), on the basis of *sufficient evidence* of carcinogenicity in experimental animals and *strong* mechanistic evidence. There is *strong evidence* that glycidyl methacrylate, based on mechanistic considerations, belongs to a class of reactive glycidyl epoxides, for which one member (glycidol) has been classified as *probably carcinogenic to humans*, and *strong evidence* that glycidyl methacrylate exhibits key characteristics of carcinogens in human primary cells.

1-Butyl glycidyl ether and **1-bromo-3-chloropropane** were classified as *possibly carcinogenic to humans* (Group 2B), on the basis of *sufficient evidence* of carcinogenicity in experimental animals and *strong* mechanistic evidence that these chemicals exhibit key characteristics of carcinogens in experimental systems.

4-Chlorobenzotrifluoride was classified as *possibly carcinogenic to humans* (Group 2B), on the basis of *sufficient evidence* of carcinogenicity in experimental animals.

For **allyl chloride**, overall, the Working Group confirmed the previous evaluation of *not classifiable as to its carcinogenicity to humans* (Group 3).

For all five agents, the evidence from studies of cancer in humans was *inadequate*.

What does the classification mean in terms of risk?

The classification indicates the strength of the evidence that a substance or agent causes cancer. The *IARC Monographs* programme seeks to identify cancer hazards, meaning the potential for the exposure to cause cancer. However, it does not indicate the level of cancer risk associated with exposure at different levels. The cancer risk associated with substances or agents that are assigned the same classification may be very different, depending on factors such as the type and extent of exposure and the size of the effect of the agent at a given exposure level.

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What are the different strength-of-evidence evaluation groups?

Evidence of Cancer in Humans	Evidence of Cancer in Experimental Animals	Mechanistic Evidence	Evaluation
Sufficient			Carcinogenic (Group 1)
	Sufficient	Strong (exposed humans)	
Limited	Sufficient		Probably carcinogenic (Group 2A)
Limited		Strong	
	Sufficient	Strong (human cells or tissues)	
		Strong (mechanistic class)	Possibly carcinogenic (Group 2B)
Limited			
	Sufficient		Not classifiable (Group 3)
		Strong (experimental systems)	
	Sufficient	Strong (does not operate in humans)	Not classifiable (Group 3)
All other situations not listed above			

How was the evidence reviewed?

During an *IARC Monographs* evaluation, experts critically review the scientific evidence according to strict criteria, which focus on determining the strength of the available evidence that the agent causes cancer. These criteria are described in the Preamble to the *IARC Monographs*, which is available here: <https://monographs.iarc.fr/wp-content/uploads/2019/07/Preamble-2019.pdf>.

Experts critically review four types of data:

- the situations in which people are exposed to the agent;
- epidemiological studies of cancer in humans exposed to the agent (scientific evidence of carcinogenicity in humans);
- experimental studies of cancer in laboratory animals treated with the agent (scientific evidence of carcinogenicity in experimental animals); and
- studies of how cancer develops in response to the agent (scientific evidence on carcinogen mechanisms).

For all the agents considered in Volume 125, the evidence from studies of cancer in humans was *inadequate*. The only available study of cancer in humans, on allyl chloride workers, was considered uninformative because of its small size and potential co-exposures. No studies in humans were available on absorption, distribution, metabolism, or excretion. Mechanistic studies and exposure data for humans were sparse.

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Who is exposed to these agents and how?

Glycidyl methacrylate is used mainly in the production of epoxy polymers and vinyl and acrylic resins. These polymers are subsequently used in dental sealants, composites and adhesives, bone composite materials, powder coatings, hydrogel lenses, and food contact material.

Exposure to glycidyl methacrylate as a monomer is not expected from use of the polymerized products. Occupational exposures by inhalation and dermal contact have been reported for chemical production workers in one study. Potential short-term exposure may occur during the preparation of dental or bone composite materials, but no exposure data were available in these settings.

1-Butyl glycidyl ether is a reactive intermediate and viscosity-reducing solvent used in the manufacture of epoxy resins. It is also used as a surface modifier in the dyeing of cotton and wool. Occupational exposure is possible at workplaces where 1-butyl glycidyl ether is produced or used, but exposure of the general population is not expected from use of the polymerized products.

1-Bromo-3-chloropropane is an intermediate in the manufacture of a wide range of pharmaceuticals, some pesticides, and other chemicals. Occupational exposure is possible at workplaces where 1-bromo-3-chloropropane is produced or used, but exposure of the general population is unlikely.

4-Chlorobenzotrifluoride is widely used as a solvent and diluent for inks, paints, toners, and coatings and in dispersive applications in the automotive industry. It is also a major component in industrial and consumer formulations such as cleaners, degreasers, stain removers, and sealants. One study reported occupational exposures in paint- and vehicle-manufacturing facilities. The general population may be exposed via consumer products and contaminated water and fish. However, no studies measuring exposure of the general population were available.

What are IARC's recommendations based on these results?

IARC is a research organization that evaluates the evidence on the causes of cancer but does not make health recommendations. However, the evaluations made by the *IARC Monographs* are often used as a basis for national and international policies, guidelines, and recommendations to minimize cancer risks.