

IARC Monographs evaluate the carcinogenicity of 1,1,1-trichloroethane and four other industrial chemicals

Questions and Answers (Q&A)

The meeting for *IARC Monographs* Volume 130: 1,1,1-Trichloroethane and Four Other Industrial Chemicals, convened by the International Agency for Research on Cancer (IARC) and held remotely due to the coronavirus disease (COVID-19) pandemic, took place on 7–22 October 2021.

The Working Group of [international experts](#), including 20 scientists from 12 countries, evaluated the carcinogenicity of five agents: 1,1,1-trichloroethane, 1,2-diphenylhydrazine, diphenylamine, *N*-methylolacrylamide, and isophorone.

More information about the meeting is available on the *IARC Monographs* website: <https://monographs.iarc.who.int/iarc-monographs-volume-130/>.

The outcome of the assessment has been published in a summary article in *The Lancet Oncology*¹ and will be described in detail in Volume 130 of the [IARC Monographs](#), to be published in 2022.

What are the results of the evaluation?

1,1,1-Trichloroethane was classified as *probably carcinogenic to humans (Group 2A)* on the basis of *limited* evidence of carcinogenicity in humans (specifically, for multiple myeloma) and *sufficient* evidence of carcinogenicity in experimental animals.

1,2-Diphenylhydrazine, diphenylamine, N-methylolacrylamide, and isophorone were classified as *possibly carcinogenic to humans (Group 2B)* on the basis of *sufficient* evidence of carcinogenicity in experimental animals.

What are these chemicals used for, and who is exposed to them?

1,1,1-Trichloroethane (CAS No. 71-55-6) was used extensively until the 1990s as a solvent, metal degreaser, and chemical intermediate, and in numerous other applications. Although it is listed as a High Production Volume (HPV) chemical, production and use have greatly decreased since the implementation of the [Montreal Protocol on Substances that Deplete the Ozone Layer](#). 1,1,1-Trichloroethane is now mostly used as a chemical feedstock in closed systems and for essential purposes, such as for medical devices and aviation safety. Poorly documented non-essential uses may occur in low- and middle-income countries.

¹ *IARC Monographs* Volume 130 Working Group (2021). Carcinogenicity of 1,1,1-trichloroethane and four other industrial chemicals. *Lancet Oncol*, Published online 11 November 2021; [https://doi.org/10.1016/S1470-2045\(21\)00659-8](https://doi.org/10.1016/S1470-2045(21)00659-8)

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1,2-Diphenylhydrazine (CAS No. 122-66-7) has been used as an industrial intermediate, primarily in the manufacture of benzidine dyes. Benzidine dyes have not been produced for several decades in the USA and the European Union (EU), although they may still be used in other countries. 1,2-Diphenylhydrazine is also used as an intermediate in the manufacture of certain drugs. Sparse exposure data are available.

Diphenylamine (CAS No. 122-39-4) is an HPV chemical. It is used in lubricants and greases, hydraulic fluids, metal-working fluids, dyes, and textile-treatment products, and to produce industrial antioxidants. It is used in agriculture to prevent scalding on apples and pears (although it is prohibited in the EU, it is frequently applied to post-harvest fruit in agricultural markets in the USA). Occupational exposures probably occur during synthesis and agricultural application, and exposure of the general population occurs through fruit consumption in certain countries. Sparse exposure data are available.

N-Methylolacrylamide (CAS No. 924-42-5) is an HPV chemical. It is used as an intermediate in the manufacture of chemicals and polymers for adhesives, sealants, inks, resins, paints, plastics, and paper and textile finishes. Documented worker exposure events involved the use of a grout containing N-methylolacrylamide in the construction of tunnels (one in Norway and one in Sweden) and as a sealant in window manufacture. Sparse exposure data are available.

Isophorone (CAS No. 78-59-1) is an HPV chemical. It is widely used as a solvent and chemical intermediate in the manufacture of lacquers and vinyl/acetate-based polymers, inks and paints, agrochemicals, nitrocellulose finishes, and washing and cleaning products. It has been measured in numerous polymer-based products, including food packaging and inflatable swimming-pool toys and other aquatic inflatables. It has also been detected in several food items, possibly because of agrochemical contamination or migration from packaging. Sparse exposure data are available.

Have these agents previously been evaluated by the IARC Monographs programme?

1,1,1-Trichloroethane was evaluated in 1999 by the IARC Monographs programme and at that time was classified in Group 3 (*not classifiable as to its carcinogenicity to humans*). It is also listed as a food additive by the Joint Expert Committee on Food Additives (JECFA) of the Food and Agriculture Organization of the United Nations (FAO) and the World Health Organization (WHO), [with no Acceptable Daily Intake \(ADI\) allocated](#).

N-Methylolacrylamide was evaluated in 1994 by the IARC Monographs programme and at that time was classified in Group 3 (*not classifiable as to its carcinogenicity to humans*). N-Methylolacrylamide has not been evaluated by other WHO programmes.

The IARC Monographs programme has not previously evaluated 1,2-diphenylhydrazine, diphenylamine, or isophorone. However, diphenylamine was evaluated by the Joint FAO/WHO Meeting on Pesticide Residues (JMPR) in 1998, and [an ADI was established](#). 1,2-Diphenylhydrazine and isophorone have not been evaluated by other WHO programmes.

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How was the evidence reviewed in the *IARC Monographs* evaluation?

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

What are the different strength-of-evidence evaluation groups used by the *IARC Monographs*?

The strength-of-evidence groups that contribute to each evaluation are summarized in the following table.

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	
	Sufficient	Strong (does not operate in humans)	Not classifiable (Group 3)
All other situations not listed above			

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What does the *IARC Monographs* classification mean in terms of risk?

The *IARC Monographs* classification indicates the strength of the evidence that a substance or agent can cause 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 or in different scenarios. 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.

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.

You can find more information on the *IARC Monographs* evaluation process here:

https://monographs.iarc.who.int/wp-content/uploads/2018/07/QA_ENG.pdf.

For more information, please contact

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The International Agency for Research on Cancer (IARC) is part of the World Health Organization. Its mission is to coordinate and conduct research on the causes of human cancer and the mechanisms of carcinogenesis, and to develop scientific strategies for cancer control. The Agency is involved in both epidemiological and laboratory research and disseminates scientific information through publications, meetings, courses, and fellowships. If you wish your name to be removed from our press release emailing list, please write to com@iarc.fr.