

1 December 2023

IARC Monographs evaluate the carcinogenicity of perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS)

Questions and Answers (Q&A)

The meeting for *IARC Monographs* Volume 135: Perfluorooctanoic acid (PFOA) and Perfluorooctanesulfonic acid (PFOS), convened by the International Agency for Research on Cancer (IARC) in Lyon, France, took place on 7–14 November 2023.

The Working Group of 30 [international experts](#) from 11 countries evaluated the carcinogenicity of perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS).

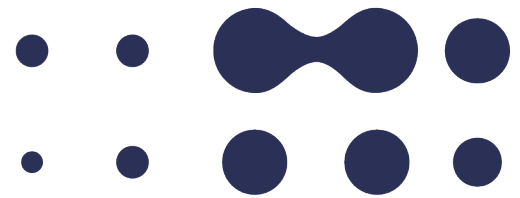
More information about the meeting is available on the *IARC Monographs* website: <https://monographs.iarc.who.int/iarc-monographs-volume-135/>.

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 135 of the *IARC Monographs*, to be published in 2024.

1. What are PFOA and PFOS?

Perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS) have been the most widely used chemicals in a large group of fluorinated compounds called per- and polyfluoroalkyl substances (PFAS). PFOA and PFOS have been used in a wide range of applications, such as fluoropolymer production; aerosol propellants; solvents; pesticides; antifoaming agents; surface treatments for household products, textiles, leather, masonry, and paper and board, including food packaging; levelling agents in paints, coatings, and waxes; plastics; lubricants and greases; and firefighting foams. Depending on the country, the use of PFOA and PFOS has decreased or been completely phased out in the past decades because of agreements and regulations such as the Stockholm Convention. However, exposure continues via products made before the regulations came into effect and via the environment, because of the extreme persistence of these chemicals. They can also be formed by precursors, which are other PFAS chemicals that can transform into PFOA and PFOS; thus, even if direct production of PFOA and PFOS ceases, they may still occur in the environment.

¹ Zahm S, Bonde JP, Chiu WA, Hoppin J, Kanno J, Abdallah M, et al. (2023). Carcinogenicity of perfluorooctanoic acid (PFOA) and perfluorooctanesulfonic acid (PFOS). *Lancet Oncol*, Published online 30 November 2023; [https://doi.org/10.1016/S1470-2045\(23\)00622-8](https://doi.org/10.1016/S1470-2045(23)00622-8)



2. What are the results of the evaluation?

The results of the evaluation are summarized in Table 1.

Table 1. Summary of classifications in IARC Monographs Volume 135

Agent	Evidence stream			Overall evaluation
	Cancer in humans	Cancer in experimental animals	Mechanistic evidence (key characteristics of carcinogens)	
Perfluorooctanoic acid (PFOA)	<i>Limited</i> (renal cell carcinoma and testicular cancer)	<i>Sufficient</i>	<i>Strong</i> in exposed humans (KCs 4, 7), human primary cells (KCs 5, 7, 8), experimental systems (KCs 4, 5, 7, 8, 10)	Group 1
Perfluorooctanesulfonic acid (PFOS)	<i>Inadequate</i>	<i>Limited</i>	<i>Strong</i> in exposed humans (KCs 4, 7), human primary cells (KCs 5, 7, 8), experimental systems (KCs 4, 5, 7, 8, 10)	Group 2B

KCs, key characteristics of carcinogens; KC4, induces epigenetic alterations; KC5, induces oxidative stress; KC7, is immunosuppressive; KC8, modulates receptor-mediated effects; KC10, alters cell proliferation, cell death, or nutrient supply.

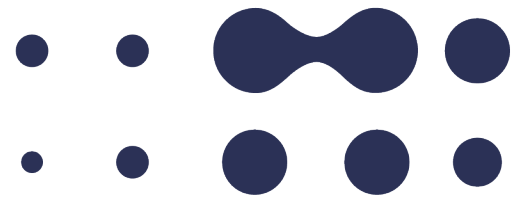
3. How did the Working Group arrive at these classifications?

PFOA is *carcinogenic to humans* (Group 1). The Group 1 evaluation for PFOA was based on the combination of *sufficient* evidence for cancer in experimental animals and *strong* mechanistic evidence (for epigenetic alterations and immunosuppression) in exposed humans. In addition, there was *limited* evidence for cancer in humans (for renal cell carcinoma and testicular cancer).

PFOS is *possibly carcinogenic to humans* (Group 2B). The Group 2B evaluation for PFOS was based on *strong* mechanistic evidence across test systems, including in exposed humans.

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

PFOA was previously evaluated in 2014 and was classified in Group 2B (with *limited* evidence for cancer in humans). PFOS was evaluated for the first time.



5. Why was PFOA re-evaluated?

The Advisory Group to Recommend Priorities for the *IARC Monographs* during 2020–2024² recommended that PFOA should be re-evaluated with high priority by the *IARC Monographs* programme. This recommendation was based on the publication of new evidence coming from several studies on cancer in humans, an anticipated animal bioassay, and a large volume of scientific literature on mechanistic data.

6. Was there key new evidence that was used in the re-evaluation of PFOA?

Since the previous evaluation of PFOA, the interest in and scientific research on these compounds have surged. The number of animal bioassays has approximately doubled since the previous evaluation, and there has been a vast increase in the number of mechanistic studies, including studies in exposed humans. There has also been a large increase in the number of studies on cancer in humans, mainly in the general population with relatively low exposure to PFOA and PFOS. Exceptionally, the Working Group itself conducted an ecological analysis of rates of orchiectomy, an indicator of testicular cancer, in relation to average serum levels of PFOA by municipality in the Veneto Region of Italy.^{3,4}

7. Where can these chemicals be found?

Because of their chemical stability, PFOA and PFOS are ubiquitously present in the environment, even in remote locations. Increased concentrations have been measured at some contaminated sites because of industrial emissions and use in firefighting foams.

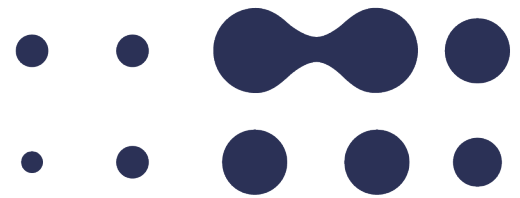
PFOA and PFOS have been found in food packaging, carpets, building materials, cosmetics, cookware, waterproof clothing, and firefighting foams. However, in most countries the use of PFOA and PFOS in these products was phased out in the past two decades, and exposure may occur due to legacy contamination. In countries where the use of PFOA and PFOS has not been phased out, there may be continuing exposure to these agents via consumer products.

In industry, PFOA and PFOS have been used for their surface-tension-lowering and stain-repellent properties, for example in plastic manufacturing or metal plating.

² IARC (2019). Report of the Advisory Group to Recommend Priorities for the *IARC Monographs* during 2020–2024. Lyon, France: International Agency for Research on Cancer. Available from: https://monographs.iarc.who.int/wp-content/uploads/2019/10/IARCMonographs-AGReport-Priorities_2020-2024.pdf.

³ Sistema Epidemiologico Regionale (2016). Ricognizione epidemiologica iniziale sulle orchiectomie per tumore del testicolo rilevate nell'area interessata dalla contaminazione idropotabile da PFAS. Padova, Italy: Sistema Epidemiologico Regionale. Available from: <https://sian.aulss9.veneto.it/index.cfm?method=mys.apridoc&iddoc=809> [Italian]

⁴ Pitter G, Da Re F, Canova C, Barbieri G, Zare Jeddì M, Daprà F, et al. (2020). Serum levels of perfluoroalkyl substances (PFAS) in adolescents and young adults exposed to contaminated drinking water in the Veneto Region, Italy: a cross-sectional study based on a health surveillance program. *Environ Health Perspect*. 128(2):27007. <https://doi.org/10.1289/EHP5337>



The use of these chemicals in fluoropolymer production and in firefighting foams has led to environmental contamination from industrial emissions and run-off from firefighter training activities. In addition, PFOA and PFOS may enter the environment via industrial and municipal waste disposal.

8. Who is exposed to these agents, and how?

Exposures are expected to be highest among workers involved in producing PFOA or PFOS or using these chemicals directly in the manufacture of other products. Inhalation is thought to be the main route of exposure for workers, although dermal exposure is possible. Since restrictions on the use of these agents came into effect, occupational exposure is likely to have decreased in some countries, although it is likely to be continuing in other countries. There is continuing exposure in waste management.

PFOA and, to a much larger extent, PFOS have been widely used in some firefighting foams (also known as aqueous film-forming foams, AFFFs), which are used particularly in airport and military firefighting operations as well as in training. The use of PFOA and PFOS in these applications has been banned in many countries, but exposure of firefighters to PFOA and PFOS is possible when old stocks of AFFFs are used.

The general population is exposed mainly via food and drinking-water, and potentially via consumer products. At contaminated sites, drinking-water is the main exposure source for the general population.

9. On the basis of this evaluation, what recommendations does IARC make?

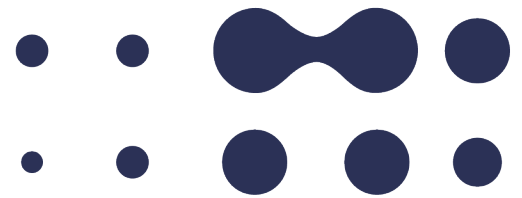
IARC is a research organization that generates and evaluates evidence related to the causes of cancer but does not make health recommendations. However, the evaluations made by the *IARC Monographs* programme are often used as a basis for national and international policies, guidelines, and recommendations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

10. 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, the classification 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.



11. 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 Table 2.

Table 2. Strength-of-evidence groups used by the IARC Monographs

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)	
Limited			Possibly carcinogenic (Group 2B)
	Sufficient	Strong	
	Sufficient	Strong (does not operate in humans)	Not classifiable (Group 3)
All other situations not listed above			

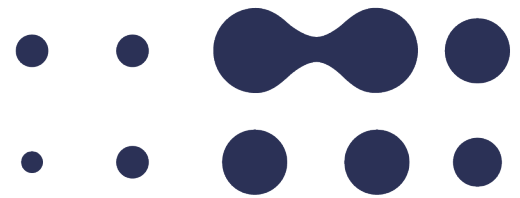
12. What are the four different categories into which agents are classified by the IARC Monographs?

Group 1: The agent is *carcinogenic to humans*.

This category is used when there is *sufficient* evidence for cancer in humans. In other words, there is convincing evidence that the agent causes cancer in humans. The evaluation is usually based on the results of epidemiological studies showing development of cancer in exposed humans. Agents can also be classified in Group 1 on the basis of *sufficient* evidence for cancer in experimental animals supported by *strong* evidence in exposed humans that the agent has mechanistic effects that are important for cancer development. This was the basis of the Group 1 evaluation for PFOA.

Group 2:

This category includes agents with a range of evidence regarding cancer in humans and in experimental animals. At one extreme of the range are agents with positive but not conclusive evidence regarding cancer in humans. At the other extreme are agents for which evidence in humans is not available but for which there is



sufficient evidence for cancer in experimental animals. There are two subcategories, which indicate different levels of evidence.

Group 2A: The agent is *probably carcinogenic to humans*.

This category is used in four different scenarios:

1. When there is *limited* evidence for cancer in humans and *sufficient* evidence for cancer in experimental animals (*“limited”* evidence for cancer in humans” means that a positive association has been observed between exposure to the agent and cancer but that other explanations for the observations, technically termed “chance”, “bias”, or “confounding”, could not be ruled out with reasonable confidence);
2. When there is *limited* evidence for cancer in humans and *strong* mechanistic evidence;
3. When there is *sufficient* evidence for cancer in experimental animals and *strong* mechanistic evidence in human primary cells or tissues;
4. When, based on mechanistic considerations, the agent belongs to a class of agents of which one or more is *probably carcinogenic to humans* (Group 2A) or *carcinogenic to humans* (Group 1).

These scenarios may also occur simultaneously within a Group 2A classification.

Group 2B: The agent is *possibly carcinogenic to humans*.

This category is used when there is *limited* evidence for cancer in humans and less-than-sufficient evidence for cancer in experimental animals. It may also be used when the evidence regarding cancer in humans does not permit a conclusion to be drawn (referred to as *inadequate* evidence) but there is *sufficient* evidence for cancer in experimental animals. It can also be used when there is *strong* mechanistic evidence, as was the case for PFOS.

Group 3: The agent is *not classifiable as to its carcinogenicity to humans*.

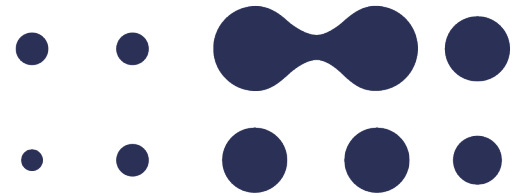
This category is used most commonly when the evidence is *inadequate* regarding cancer in humans and *inadequate* or *limited* for cancer in experimental animals, and mechanistic evidence is less than *strong*. *Limited* evidence for cancer in experimental animals means that the available information suggests a carcinogenic effect but is not conclusive.

13. 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 on the *IARC Monographs* website: <https://monographs.iarc.who.int/wp-content/uploads/2019/07/Preamble-2019.pdf>.

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

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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, 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.who.int.

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