International Agency for Research on Cancer

World Health Organization

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IARC Monographs evaluate the carcinogenicity of butyl benzyl phthalate, dibutyl phthalate, and diisononyl phthalate

IARC Monographs Volume 142

Questions and Answers (Q&A)

The meeting for *IARC Monographs* Volume 142, Butyl benzyl phthalate, dibutyl phthalate, and diisononyl phthalate, was convened by the International Agency for Research on Cancer (IARC) in Lyon, France, and took place on 9–16 June 2026.

At the meeting, the Working Group of 23 international experts from 13 countries evaluated the carcinogenicity of three phthalates: butyl benzyl phthalate, dibutyl phthalate, and diisononyl phthalate.

More information about Meeting 142 is available on the *IARC Monographs* website: https://monographs.iarc.who.int/iarc-monographs-volume-142/.

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 142 of the *IARC Monographs*, to be published in 2027.

1. What agents were evaluated in *IARC Monographs* Meeting 142?

The Working Group for *IARC Monographs* Volume 142 evaluated the carcinogenicity of three chemicals: butyl benzyl phthalate (BBzP), dibutyl phthalate (DBP), and diisononyl phthalate (DINP).

BBzP is a high-production-volume chemical that has been used as a plasticizer in polyvinyl chloride (PVC) and other plastics. Products include floor tiles, vinyl foam and carpet backing, and cellulosic resins. Other uses include personal care products, adhesives, and paints.

DBP is a high-production-volume chemical that has been used as a plasticizer in PVC and other plastic products. Other uses include personal care products, adhesives, and paints. It is also used in some pharmaceutical capsules.

[1] Sun M, Glass DG, Josephy PD, Mancini FR, Ogawa K, Blanc EB, et al. Carcinogenicity of butyl benzyl phthalate, dibutyl phthalate, and diisononyl phthalate *Lancet Oncol*. Published online 3 July 2026; https://doi.org/10.1016/S1470-2045(26)00334-7.

The use of BBzP and DBP has declined in recent decades, and their use is restricted in several products such as children's toys and food contact material in some countries.

DINP is a "high-molecular-weight" phthalate, used as a plasticizer in PVC and other plastics, e.g. in vinyl flooring and cables. Other uses include sealants, adhesives, and paints. It is a widely used replacement for some other plasticizers that have been phased out.

2. Who is most likely to be exposed to butyl benzyl phthalate, dibutyl phthalate, and diisononyl phthalate?

Exposure occurs in workers who produce phthalates or in the production, use, and disposal of products containing phthalates. Highest exposure has been shown in settings where phthalates, rubber, and plastics are manufactured, but exposure also occurs in other occupations, including those in nail salons, waste-related activities, and retail.

The general population is exposed mainly via the diet but also via personal care products, indoor air and dust, and (for DBP) some pharmaceuticals. Metabolites of the three phthalates have commonly been detected in the urine, including in children and adolescents, indicating ubiquitous exposure in the general population.

3. Have these agents been previously evaluated by the *IARC Monographs* programme? What was the result of the previous evaluation?

BBzP has been previously evaluated by the *IARC Monographs* programme in 1998 in Volume 73[2] as *not classifiable as to its carcinogenicity to humans* (Group 3).

DBP and DINP have not been previously evaluated by the *IARC Monographs* programme.

4. Has the *IARC Monographs* programme previously evaluated other phthalates?

The *IARC Monographs* programme has evaluated di(2-ethylhexyl)phthalate (DEHP), most recently in Volume 101[3] in 2011, when it was evaluated as *possibly carcinogenic to humans* (Group 2B).

[2] IARC (1999). Some chemicals that cause tumours of the kidney or urinary bladder in rodents and some other substances. *IARC Monogr Eval Carcinog Risks Hum*. 73:1–674. Available from: https://publications.iarc.who.int/91.

[3] IARC (2013). Some chemicals present in industrial and consumer products, food and drinking-water. *IARC Monogr Eval Carcinog Risks Hum*. 101:1–553. Available from: https://publications.iarc.who.int/125. PMID:24772663.

5. What are the results of the evaluation?

Table 1. Summary of classifications in *IARC Monographs* Volume 142

Agent	Evidence stream			Overall evaluation
	Cancer in humans	Cancer in experimental animals	Mechanistic evidence	
Butyl benzyl phthalate (BBzP)	*Inadequate*	*Sufficient*	*Strong* in experimental systems (KC6, KC8, KC10)	**Group 2B**
Dibutyl phthalate (DBP)	*Inadequate*	*Limited*	*Strong* in experimental systems (KC4, KC5, KC6, KC8, KC10)	**Group 2B**
Diisononyl phthalate (DINP)	*Inadequate*	*Sufficient*	*Strong* in experimental systems (KC8)	**Group 2B**

KC, key characteristic of carcinogens; KC4, alters epigenetic alterations; KC5, induces oxidative stress; KC6, induces chronic inflammation; KC8, modulates receptor-mediated effects; KC10, alters cell proliferation, cell death, or nutrient supply.

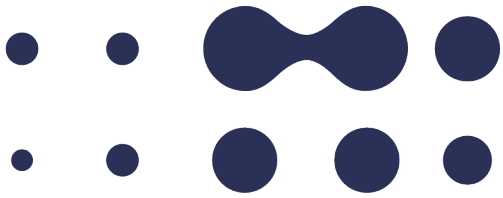
6. How did the Working Group reach these results?

BBzP was classified as *possibly carcinogenic to humans* (Group 2B) in two ways: (i) via *sufficient* evidence for cancer in experimental animals; and (ii) via *strong* mechanistic evidence of the key characteristics of carcinogens in experimental systems. For BBzP, the evidence regarding cancer in humans was *inadequate*.

> BBzP, in Fischer 344/N rats, caused an increase in the incidence of mononuclear cell leukaemia in males and females, and benign or malignant pheochromocytoma (combined) of the adrenal medulla in males, as reported in two well-conducted studies, one complying with Good Laboratory Practice (GLP) (NTP, 1982; 1997; see also Q14). BBzP exhibits the key characteristics of carcinogens: it induces chronic inflammation; modulates receptor-mediated effects; and alters cell proliferation, cell death, or nutrient supply in experimental systems.

DBP was classified as *possibly carcinogenic to humans* (Group 2B) on the basis of *strong* mechanistic evidence of the key characteristics of carcinogens in experimental systems. For DBP, the evidence for cancer in experimental animals was *limited*, and the evidence regarding cancer in humans was *inadequate*

> DBP exhibits the key characteristics of carcinogens: it induces epigenetic alterations; induces oxidative stress; induces chronic inflammation; modulates receptor-mediated effects; and alters cell proliferation, cell death, or nutrient supply. The evidence for cancer in experimental animals was *limited*, because



only benign tumours were observed in male and female Sprague-Dawley (SD) rats (NTP, 2021; see also Q14).

DINP was classified as *possibly carcinogenic to humans* (Group 2B) in two ways: (i) via *sufficient* evidence for cancer in experimental animals; and (ii) via *strong* mechanistic evidence of the key characteristics of carcinogens in experimental systems. For DINP, the evidence regarding cancer in humans was *inadequate*.

DINP caused, in multiple studies that complied with GLP, an increase in the incidence of hepatocellular carcinoma and hepatocellular adenoma or carcinoma (combined) in male and female B6C3F$_1$/CrlBR mice (US EPA, 1998a) and in male and female Fischer rats (US EPA, 1998b); and hepatocellular carcinoma in female Sprague-Dawley CD rats (US EPA, 1987). It also caused renal tubule cell carcinoma in male and mononuclear cell leukaemia in male and female F344N rats (US EPA, 1986; 1998b) (see Q14). DINP exhibits the key characteristics of carcinogens: it modulates receptor-mediated effects.

7. What types of exposure did the *IARC Monographs* Working Group review?

The *IARC Monographs* programme performs hazard identification that includes the review of evidence from all potential exposure sources. The available evidence on cancer in humans came mainly from studies that were performed in the general population assessing exposure via the measurement of phthalate metabolites in urine. This method assesses recent exposure to phthalates via all sources. In the general population, the most important source is diet, followed by consumer products including personal care products, the indoor environment, and, in some cases, pharmaceuticals. A small number of studies on cancer in humans also assessed exposure via specific routes, such as pharmaceuticals or indoor dust. For mechanistic studies in exposed humans, most studies also used urine biomonitoring. However, there were several studies that assessed exposure to phthalates via the estimation of phthalate exposure via indoor dust.

8. Why did IARC decide to evaluate these three agents?

BBzP, DBP, and DINP were each accorded high priority by the most recent *IARC Monographs* Advisory Group to Recommend Priorities for the *IARC Monographs* (2024).[4]

The agents were all listed as high-production-volume chemicals by the Organisation for Economic Co-operation and Development (OECD) (for the year 2007) and the United States Environmental Protection Agency (US EPA) (for the year 2024). These are ubiquitous plasticizers used mainly in PVC production for their softening properties, and they are present in a multitude of consumer products.

Notably, phthalates have shown endocrine-disrupting properties. Concerns regarding potential health impacts (e.g. toxicity to reproduction, development, and the endocrine system; and also obesity and obesity-related

[4] IARC (2024). Report of the Advisory Group to Recommend Priorities for the *IARC Monographs* during 2025–2029. Lyon, France: International Agency for Research on Cancer. Available from: https://monographs.iarc.who.int/wp-content/uploads/2024/11/AGP_Report_2025-2029.pdf.

health effects) have been raised in recent decades, such that in many countries, restrictions on use and specific regulations are being established or have already been implemented, including removal from products for infants, such as food contact materials, baby bottles, and toys.

The basis of the re-evaluation of all three agents, as reported in the *IARC Monographs* Advisory Group Report (2024)[4], was the availability of new evidence of cancer in experimental animals, and mechanistic evidence of several of the key characteristics of carcinogens. In addition, there was some evidence of breast cancer suggested in a few studies among women exposed to some of the phthalates.

9. Why is the *IARC Monographs* programme evaluation important?

The evaluation carried out by the *IARC Monographs* programme is a rigorous and comprehensive review, synthesis, and integration of all the available scientific evidence of cancer in humans and experimental animals and of mechanistic evidence related to carcinogenicity. In addition, exposure is characterized globally in a wide variety of settings (e.g. occupational and general population).

10. What does the *IARC Monographs* classification indicate?

The *IARC Monographs* classifications reflect the strength of the scientific evidence as to whether an agent can cause cancer in humans, but they do not indicate the degree of risk of developing cancer at a given exposure level or for a given route or type of exposure. The types of exposure, the extent of risk, the people who may be at risk, and the cancer types linked with the agent can be very different across agents with the same classification.

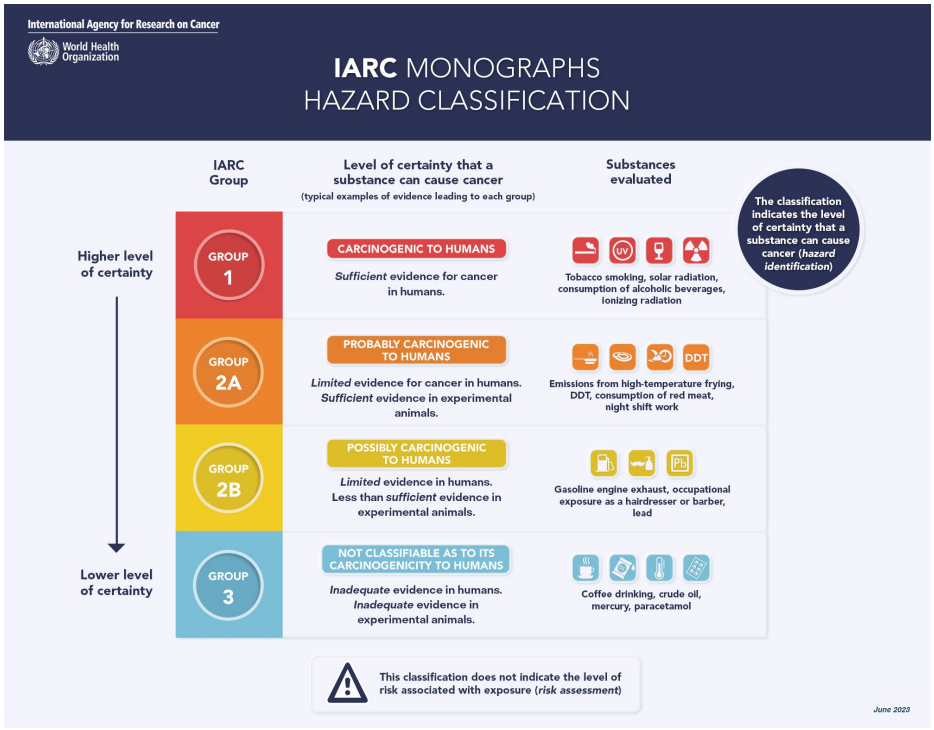


Fig. 2. Summary of *IARC Monographs* hazard classification

Since the IARC Group indicates the strength of the evidence regarding a cancer hazard and not the cancer risk at a given level of exposure, the cancer risk (at typical exposure levels) associated with two agents classified in the same IARC Group may be very different.

11. 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.

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 three 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 is also 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 or *strong* mechanistic evidence.

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.

12. How are the *IARC Monographs* classifications used?

IARC is a research organization that evaluates evidence on the causes of cancer but does not make health recommendations. Health and regulatory agencies may include *IARC Monographs* evaluations when considering actions to prevent exposure to potential carcinogens. IARC does not recommend regulations, legislation, or public health interventions, which remain the responsibility of individual national governments and other international organizations.

13. What types of study were eligible for review by the IARC Working Group and where did they come from?

As described in the current Preamble to the *IARC Monographs*[5], the Working Group reviews publicly available scientific data, such as peer-reviewed papers in the scientific literature, and may also review unpublished

[5] IARC (2019). Preamble to the *IARC Monographs* (amended January 2019). Lyon, France: International Agency for Research on Cancer. Available from: https://monographs.iarc.who.int/iarc-monographs-preamble-preamble-to-the-iarc-monographs/.

reports, if made available in their final form by governmental agencies and if they contain enough detail for critical review.

14. What sources of information were considered by the Working Group in its evaluation of the evidence of cancer in experimental animals?

As described in the current Preamble to the *IARC Monographs* (last revised in 2019),[5] the Working Group reviews publicly available scientific data, including peer-reviewed papers in the scientific literature, and may also review unpublished reports, if made available in their final form by governmental agencies and if they contain enough detail for critical review by the Working Group. The available bioassay reports for BBzP, DBP, and DINP are listed below. For DINP, in addition to scientific research publications, the Working Group was able to retrieve and review several Data Evaluation Reports that were submitted for regulatory authorization to the United States Environmental Protection Agency (US EPA) and made available and accessible on the US EPA website (https://www.epa.gov/pesticides/) or by the National Technical Reported Library (https://ntrl.ntis.gov/NTRL/).

BBzP

NTP (1982). Carcinogenesis bioassay of butyl benzyl phthalate (CAS No. 85-68-7) in F344/N rats and B6C3F$_1$ mice (feed study). NTP-80-25. NIH Publ. No. 82-1769. Tech. Rep. Ser. No. 213. Research Triangle Park (NC), USA: National Toxicology Program. Available from: https://ntp.niehs.nih.gov/sites/default/files/ntp/htdocs/lt_rpts/tr213.pdf, accessed on 10 June 2026.

NTP (1997). Effect of dietary restriction on toxicology and carcinogenesis studies in F344/N rats and B6C3F$_1$ mice. NIH Publ. No. 97-3376. NTP TR 460. *Tech Rep Ser* No. 460. Research Triangle Park (NC), USA: National Toxicology Program. Available from: https://ntp.niehs.nih.gov/sites/default/files/ntp/htdocs/lt_rpts/tr460.pdf, accessed on 10 June 2026.

DBP

NTP (2021). NTP technical report on the toxicology and carcinogenesis studies of di-*n*-butyl phthalate (CASRN 84-74-2) administered in feed to Sprague Dawley (Hsd:Sprague Dawley SD) rats and B6C3F$_1$/N mice. NTP TR 600. Research Triangle Park (NC), USA: National Toxicology Program. Available from: https://ntp.niehs.nih.gov/publications/reports/tr/tr600, accessed on 10 June 2026.

DINP

US EPA (1986). Chronic toxicity/oncogenicity study in F-344 rats. Test material: MRD-83-260. Report prepared by Plutnick RT. Submitted by Exxon Chemical Americas. Project No. 326075. Available from: https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0510211.xhtml, accessed 10 June 2026.

US EPA (1987) A chronic toxicity carcinogenicity feeding study in rats with Santicizer 900. Submitted by Monsanto Co. Project No. 81-2572. Study No. BD-81-244. Available from: https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS0513172.xhtml, accessed 10 June 2026.

US EPA (1998a). Oncogenicity study in mice with di(isononyl)phthalate including ancillary hepatocellular proliferation and biochemical analyses. Report prepared by Moore MR. Submitted by Aristech Chemical Corporation. Study No. 2598-105. Available from: https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS05562833.xhtml, accessed 10 June 2026.

US EPA (1998b). Oncogenicity study in rats with di(isononyl)phthalate including ancillary hepatocellular proliferation and biochemical analyses. Report prepared by Moore MR. Submitted by Aristech Chemical Corporation. Study No. 2598-104. Available from: https://ntrl.ntis.gov/NTRL/dashboard/searchResults/titleDetail/OTS05562832.xhtml, accessed 10 June 2026.

15. How was the evidence reviewed in this 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.*[5]

The experts critically review four types of data:

- data on human exposure to the agent;
- epidemiological studies of 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 investigating the biological mechanisms by which the agent may cause cancer (mechanistic evidence).

16. What does the IARC evaluation mean?

The *IARC Monographs* programme identifies cancer hazards but does not evaluate the risks associated with specific levels or circumstances of exposure, nor the risk-to-benefit ratio for medical treatments. The distinction between hazard and risk is important. An agent is considered to be a cancer hazard if it is capable of causing cancer under some circumstances or exposure levels. “Risk” measures the probability that cancer will occur, taking into account the level of exposure to the agent.

17. What is the relationship between IARC and WHO?

IARC has a unique dual position as an independent international cancer research institute, and as the specialized cancer research agency of the World Health Organization within the United Nations system, established in May 1965 by a resolution of the World Health Assembly. IARC is governed by its Governing Council and Scientific Council; the former comprises representatives from each Participating State, plus the WHO Director-General. The *IARC Monographs* programme has its own defined scientific methods as set by the Preamble to the *IARC Monographs*.[5] More information about IARC governance can be found here: https://www.iarc.who.int/cards_page/organization-and-management/.

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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.