International Agency for Research on Cancer

World Health Organization

IARC Monographs Questions and Answers

What does the IARC Monographs Programme do?

The Monographs Programme identifies and evaluates environmental causes of cancer in humans. To date, more than 900 agents have been reviewed.

What types of agents or substances are evaluated?

The Monographs Programme evaluates chemicals (e.g. formaldehyde), complex mixtures (e.g. air pollution), occupational exposures (e.g. work in coke production), physical agents (e.g. solar radiation), biological agents (e.g. hepatitis B virus), and personal habits (e.g. tobacco smoking).

How does IARC choose which agents to evaluate?

IARC works with international experts to identify priorities from among agents suspected of causing cancer, based on the availability of scientific evidence of carcinogenicity and evidence that people may be exposed to the agent. Priority can be given to a wide variety of agents or substances with different impacts on public health. For example, air pollution has a high public health impact because everyone is exposed, even if exposure levels are generally low. On the other hand, occupational exposures, such as those involving vinyl chloride, may be very high and can therefore have a marked impact even if very few workers are exposed.

How is the evaluation carried out?

The evaluation is carried out by a Working Group of independent international experts. The experts prepare draft documents in advance, based on the available scientific evidence, and subsequently gather for eight days at IARC in Lyon to discuss and finalize their assessment of whether a specific agent causes cancer. They critically review the scientific evidence according to strict criteria, which focus on determining the strength of the available evidence that the agent causes cancer. First, the experts work in subgroups to 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 animals)
- Studies of how cancer develops in response to the agent (scientific evidence on cancer mechanisms).

During the second part of the meeting, the entire Working Group meets together to discuss the subgroup evaluations and to combine these into overall evaluations of carcinogenicity to humans.

IARC Monographs Questions and Answers

What are the different classifications?

IARC classifies carcinogens in five categories ranging from *carcinogenic to humans* (Group 1) to *probably not carcinogenic to humans* (Group 4). The classification indicates the weight of the evidence as to whether an agent is capable of causing cancer (technically called "hazard"), **but it does not measure the likelihood that cancer will occur (technically called "risk") as a result of exposure to the agent.**

How are these classifications used? Can IARC enforce regulations based on these classifications?

Health and regulatory agencies include IARC evaluations in their consideration of actions to prevent exposure to potential carcinogens. IARC does not recommend regulations, legislation, or public health interventions, which remain the responsibility of individual governments and other international organizations.

What are the different classifications of agents?

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

Group 2
This category includes agents with a range of evidence of carcinogenicity in humans and in experimental animals. At one extreme are agents with positive but not conclusive evidence in humans. At the other extreme are agents for which evidence in humans is not available but for which there is sufficient evidence of carcinogenicity in experimental animals. There are two subcategories, indicating different levels of evidence.

Group 2A: The agent is *probably carcinogenic to humans*.
This category is used when there is limited evidence of carcinogenicity in humans and sufficient evidence of carcinogenicity in experimental animals. Limited evidence 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.

Group 2B: The agent is *possibly carcinogenic to humans*.
This category is used when there is limited evidence of carcinogenicity in humans and less than sufficient evidence of carcinogenicity in experimental animals. It may also be used when the evidence of carcinogenicity in humans does not permit a conclusion to be drawn (referred to as "inadequate" evidence) but there is sufficient evidence of carcinogenicity in experimental animals.

IARC, 150 Cours Albert Thomas, 69372 Lyon CEDEX 08, France - Tel: +33 (0)4 72 73 84 85 - Fax: +33 (0)4 72 73 85 75

Group 3: The agent is *not classifiable as to its carcinogenicity to humans*.
This category is used most commonly when the evidence of carcinogenicity is inadequate in humans and inadequate or limited in experimental animals. Limited evidence in experimental animals means that the available information suggests a carcinogenic effect but is not conclusive.

Group 4: The agent is *probably not carcinogenic to humans.*
This category is used when there is evidence suggesting lack of carcinogenicity in humans and in experimental animals.

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 Monographs Programme seeks to identify cancer hazards, meaning the potential for the exposure to cause cancer. However, it does not indicate the level of risk associated with exposure. The cancer risk associated with substances or agents assigned the same classification may be very different, depending on factors such as the type and extent of exposure and the strength of the effect of the agent.

What is the difference between risk and hazard?

The IARC Monographs Programme evaluates **cancer hazards but not the risks associated with exposure.**

The distinction between *hazard* and *risk* is important. An agent is considered a cancer *hazard* if it is capable of causing cancer under some circumstances. *Risk* measures the probability that cancer will occur, taking into account the level of exposure to the agent. The Monographs Programme may identify cancer hazards even when risks are very low with known patterns of use or exposure. Recognition of such carcinogenic hazards is important because new uses or unforeseen exposures could lead to risks that are much higher than those currently seen.

What do classifications in Groups 2A and 2B mean?

Group 2A means that the agent is **probably** carcinogenic to humans. For agents in this category, there is usually convincing evidence that the agent causes cancer in laboratory animals and some evidence that it could cause cancer in humans, but the evidence in humans is not conclusive.

Group 2B means that the agent is **possibly** carcinogenic to humans. Agents can be classified in Group 2B in several different ways. Usually a classification of Group 2B means that there is convincing evidence that the agent causes cancer in experimental animals but little or no information about whether it causes cancer in humans. This category can also be used when there is some evidence that the agent could cause cancer in humans and in experimental animals but neither the evidence in humans nor the evidence in animals is convincing enough to permit a definite conclusion to be drawn.

For example, radiofrequency electromagnetic fields are classified in Group 2B because there is evidence that falls short of being conclusive that exposure may cause cancer in humans and in

animals. *Aloe vera* leaf extract is also classified in Group 2B, based on studies showing that it causes cancer in rats, but it has not been studied in humans.

Why should two substances or agents classified in the same Group not be compared?

The classifications reflect the strength of the scientific evidence as to whether an agent causes cancer in humans but do not reflect how strong the effect is on the risk of developing cancer. The types of exposures, 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. Therefore, comparisons within a category can be misleading. First, exposures may vary widely. For example, there is widespread exposure to the Group 1 agent air pollution, whereas far fewer people would be exposed to certain Group 1 chemicals, such as 1,2-dichloropropane. Second, the magnitude of risk associated with exposure to two agents may be very different. Active smoking carries a much higher risk of lung cancer than does air pollution, although both are categorized in Group 1. Third, the number of resulting cancers can be different; for example, tobacco smoking causes some common cancers, whereas 1,2-dichloropropane causes a rare bile duct cancer. This also applies to Group 2 agents. For example, radiofrequency electromagnetic fields and the prescription drug digoxin are each classified in Group 2B.

In other words, because the Groups indicate the strength of the evidence regarding a cancer hazard and not the risk, the risk associated with two agents classified in the same Group may be very different.

Where can I find the list of agents evaluated and their categories?

The list of agents classified by the Monographs Programme can be found on IARC's webpage:

http://monographs.iarc.fr/ENG/Classification/index.php

More information about the Monographs Programme is available at

http://monographs.iarc.fr/index.php

IARC, 150 Cours Albert Thomas, 69372 Lyon CEDEX 08, France - Tel: +33 (0)4 72 73 84 85 - Fax: +33 (0)4 72 73 85 75