IARC Monographs evaluate the carcinogenicity of talc and acrylonitrile
IARC Monographs Volume 136

Lyon, France, 5 July 2024 – The International Agency for Research on Cancer (IARC), the cancer agency of the World Health Organization (WHO), has evaluated the carcinogenicity of talc and acrylonitrile. The outcome of the assessment has been published in a summary article in The Lancet Oncology and will be described in detail in Volume 136 of the IARC Monographs, to be published in 2025.

Acrylonitrile

Acrylonitrile is a volatile organic compound that is mainly used in the production of polymers. These include polyacrylonitrile, styrene–acrylonitrile, acrylonitrile butadiene styrene, and other synthetic rubbers such as acrylonitrile butadiene. Uses of these polymers include fibres for clothing, carpets, and other textiles, as well as plastics for consumer products, automotive parts, and construction.

Exposure to acrylonitrile

Occupational exposure may occur during the production of acrylonitrile and its use in polymer production. Acrylonitrile is present in cigarette smoke. The general population is exposed to acrylonitrile mainly via inhalation of cigarette smoke (including second-hand smoke). Another source of exposure is air pollution. Several acrylonitrile metabolites and adducts have been measured as biomarkers of exposure to acrylonitrile.

Results of the evaluation of acrylonitrile

The Working Group classified acrylonitrile as carcinogenic to humans (Group 1) on the basis of sufficient evidence for cancer in humans for lung cancer. There was also limited evidence in humans for bladder cancer. The evidence was mainly from studies in workers producing or using acrylonitrile. In addition, there was sufficient evidence for cancer in experimental animals and strong mechanistic evidence of key characteristics of carcinogens in experimental systems.

Strength-of-evidence determinations for acrylonitrile

Classification in Group 1 indicates the highest level of certainty that a substance can cause cancer.

The strongest evidence came from a large cohort study of workers in different industries producing or using acrylonitrile. In this study, workers with higher exposure to acrylonitrile had a higher rate of lung cancer mortality compared with workers with lower exposures.

In this study, several additional analyses were performed to rule out biases; an increased rate of lung cancer was observed in all of these analyses.

There was also a large case–control study reporting a higher chance of prior exposure to acrylonitrile in lung cancer cases than in controls who did not have lung cancer. Several other smaller cohort studies also provided evidence indicating a higher rate of lung cancer in workers with higher exposure to acrylonitrile. For bladder cancer, the increased rate was observed only in some of the analyses in the large study, and the body of evidence was less consistent.

There was also sufficient evidence for cancer in experimental animals. Acrylonitrile caused an increase in the incidence of malignant neoplasms in both sexes of two species in multiple studies.

Finally, the IARC Monographs use key characteristics of carcinogens (KCs) to systematically evaluate the mechanistic evidence of carcinogenicity of substances. There was strong mechanistic evidence that acrylonitrile exhibits KCs in experimental systems. Acrylonitrile is electrophilic or can be metabolically activated to an electrophile (KC1), is genotoxic (KC2), induces oxidative stress (KC5), causes immortalization (KC9), and alters cell proliferation, cell death, or nutrient supply (KC10).

Talc

Talc, a naturally occurring mineral, is mined in many regions worldwide. Exposure to talc occurs in occupational settings during the mining and milling or processing of talc, or during the production of talc-containing products. General population exposure through the use of talc-containing cosmetics and body powders is best documented; however, exposure through food, drugs, and other consumer products is likely, although less well documented.

Because of the challenges of accurate measurement, contamination of talc with asbestos may still be a concern and may lead to exposure of workers and the general population to asbestos (e.g. via contaminated talc-based make-up and body powder).

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Results of the evaluation of talc

After thoroughly reviewing the available scientific literature, the Working Group of 29 international experts classified talc as probably carcinogenic to humans (Group 2A) on the basis of a combination of limited evidence for cancer in humans (for ovarian cancer), sufficient evidence for cancer in experimental animals, and strong mechanistic evidence that talc exhibits key characteristics of carcinogens in human primary cells and experimental systems.

Strength-of-evidence determinations for talc

The Group 2A classification is the second highest level of certainty that a substance can cause cancer.

There were numerous studies that consistently showed an increase in the incidence of ovarian cancer in humans self-reporting the use of body powder in the perineal region. Although the evaluation focused on talc not containing asbestos, contamination of talc with asbestos could not be excluded in most of the studies of exposed humans.

In addition, biases in how talc use was reported in the epidemiological studies could not be ruled out with reasonable confidence. As a result, a causal role for talc could not be fully established. An increased rate of ovarian cancer was also observed in studies looking at occupational exposure of women exposed to talc in the pulp and paper industry. However, confounding by co-exposure to asbestos could not be excluded, and the increased rate was based on small numbers of ovarian cancers in those occupational studies.

In experimental animals, treatment with talc caused an increase in the incidence of malignant neoplasms in females (adrenal medulla and lung) and a combination of benign and malignant neoplasms in males (adrenal medulla) of a single species (rat).

Finally, the IARC Monographs use key characteristics of carcinogens (KCs) to systematically evaluate the mechanistic evidence of carcinogenicity of substances. There was strong mechanistic evidence that talc exhibits KCs, including inducing chronic inflammation (KC6) and altering cell proliferation, cell death, or nutrient supply (KC10). In reviewing the experimental evidence, the Working Group included only studies in which contamination of the talc with asbestos was highly unlikely.

Note to Editors

“Talc containing asbestos” remains a part of the definition of asbestos (classified as carcinogenic to humans, Group 1, by the IARC Monographs programme in 2009 in Volume 100C3) and was not included in the present evaluation (Volume 136). There is sufficient evidence that asbestos causes mesothelioma and cancers of the

lung, larynx, and ovary in humans. There is limited evidence that asbestos causes cancers of the pharynx, stomach, and colorectum.

This new evaluation of “talc” supersedes the previous evaluations of “talc not containing asbestos or asbestiform fibres” and “perineal use of talc-based body powder”.

Perineal use of talc-based body powder was evaluated by the IARC Monographs programme in 2006 in Volume 93 as possibly carcinogenic to humans (Group 2B) on the basis of limited evidence for ovarian cancer. Inhaled talc not containing asbestos or asbestiform fibres was not classifiable as to its carcinogenicity to humans (Group 3).

IARC Monographs classification

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.

More information about Meeting 136 is available on the IARC Monographs website: https://monographs.iarc.who.int/iarc-monographs-volume-136/.

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