

GENERAL REMARKS

This one-hundred-and-ninth Volume of the *IARC Monographs* presents evaluations of the carcinogenic hazards to humans arising from exposure to outdoor air pollution and particulate matter (PM) contained in polluted outdoor air. A summary of the findings has been published in *The Lancet Oncology* ([Loomis et al., 2013](#)).

Outdoor air pollution has myriad sources, both natural and anthropogenic. It is a mixture of mixtures, and the mix of contaminants in outdoor air varies widely in space and time, reflecting variation in its sources, weather, atmospheric transformations, and other factors. In any particular place, the pollution in outdoor air comes not only from local sources but also from sources that affect air quality regionally and even globally.

The complex mixture of air pollution has not previously been evaluated, as such, in the *IARC Monographs*. However, this Volume is the culmination of a series that has examined individual pollutants that are found in outdoor air. The heterogeneity of air pollution was an acknowledged challenge in planning this series of *Monographs*. Consequently, the International Agency for Research on Cancer (IARC) convened a special Advisory Group in 2004 to provide guidance on how to address air pollution and cancer. This Advisory Group recommended a sequence of reviews that would begin with specific combustion products and sources and culminate with a *Monograph* on outdoor air pollution ([Straif et al., 2013](#)). With respect to the final *Monograph*, the Advisory Group noted that

because outdoor air pollution cannot be readily defined, the final *Monograph* “should focus on those pollutants generated by human activities, particularly those entailing combustion and industrial processes” and should consider air pollution in rural as well as urban environments. Evaluations of a number of important air pollutants have been published in *IARC Monographs* Volumes 92, 93, 95, 100C, 100E, 103, and 105. The current Volume completes that planned sequence.

The nature of the evidence available to the Working Group differed across the sections of the *Monograph*. Exposure data were available on outdoor air pollution and in relation to mixtures associated with particular sources. Epidemiological studies that addressed the outdoor air pollution mixture and commonly measured indicators of exposure to it, notably including PM, were reviewed. Some studies of cancer in laboratory animals also assessed real-world outdoor air pollution mixtures, but most examined PM collected from outdoor air or organic matter extracted from outdoor air particles. Mechanistic studies also assessed effects related to a wide spectrum of exposure indicators, ranging from studies in exposed humans to experimental studies focusing on particular components of the mixture, such as PM, or samples derived from PM.

There is a substantial body of scientific literature on various sources of air pollution and on environmental concentrations of particular pollutants. The Working Group sought

representative data on air pollution worldwide, but as such data are often presented in government reports and online databases, this evidence could not be systematically reviewed. A systematic review of relevant epidemiological studies was conducted, and the evidence from animal carcinogenicity studies was systematically updated. Some of the same evidence was also considered in previous *IARC Monographs*. The Working Group cites the findings of these *Monographs* and of particular studies where they are informative with regard to the outdoor air pollution mixture.

The accumulated scientific evidence is notably consistent across studies of cancer in humans, cancer in animals, and mechanisms of carcinogenesis. The Working Group found that there is *sufficient evidence* in humans and in experimental animals for the carcinogenicity of outdoor air pollution in general and of PM in outdoor air pollution more specifically. These findings are supported by *strong mechanistic evidence* in exposed humans, including studies showing increased frequencies of micronuclei and chromosomal aberrations in individuals occupationally or residentially exposed to polluted air, as well as by studies showing genetic and related effects in animals and diverse experimental systems. A wide range of other effects related to carcinogenesis, including oxidative stress, inflammation, and epigenetic alterations, have also been observed in exposed humans and animals and in diverse experimental systems.

Given the variability of outdoor air pollution in space and time, the extent to which any classification of the cancer risk from outdoor air pollution can be generalized needs consideration. The Working Group acknowledged that the mix of pollution sources ranges widely and the exposures of any given population may be dominated by particular sources. Nonetheless, the exposure data document the presence of key mixture components, specifically particles, across diverse locations, and mechanisms of carcinogenicity apply across components and

locations. Consequently, the Working Group concluded that its classification for outdoor air pollution has general applicability.

The Working Group also noted that much of the world's population is exposed to air pollution at levels substantially above those at which associations with lung cancer have been demonstrated. Thus, the findings of the epidemiological studies of outdoor air pollution and cancer need to be generalized both to levels comparable to those at which the studies were carried out and to levels well above those spanned in currently available epidemiological studies.

The classification of outdoor air pollution and PM as *carcinogenic to humans (Group 1)* raises questions regarding the extent of the cancer burden attributable to these exposures. Using PM with particles of aerodynamic diameter less than 2.5 µm (PM_{2.5}) as an indicator of population exposure to outdoor air pollution, the Global Burden of Disease Project has made estimates of the global burden of lung cancer associated with outdoor air pollution. According to these estimates, 223 000 deaths per year worldwide (about 15% of all deaths from lung cancer) are attributable to outdoor air pollution ([Lim et al., 2012](#); [Straif et al., 2013](#)).

References

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