CHAPTER 1. INTRODUCTION

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People take thousands of breaths daily, leading to a total intake of about 10 000 litres of air per day. Consequently, the lung receives significant doses of many air contaminants, even those present at seemingly low and trivial concentrations. Around the world, people spend time in many different kinds of places, often referred to as microenvironments: their homes, workplaces, public places, other indoor environments, transportation, and outdoors. In all of these locations there are sources that emit airborne carcinogens that can be readily detected in indoor and outdoor air. Globally, combustion of fuels for heating, cooking, power generation, and industrial processes is a ubiquitous source. Combustion sources range from the burning of dung in open fires to highly sophisticated, massive combustion sources, such as coal-fired power plants, that may be equipped with control technology for particles and gases. Combustion engines, particularly for motor vehicles, are another worldwide source. Indoors there are carcinogens from tobacco smoking, building materials, and furnishings, as well as the naturally occurring carcinogen radon.

The extent of exposures to indoor and outdoor air pollution is well recognized. There has long been concern that airborne carcinogens contribute to the global burden of cancer, especially of the lung, which receives the most substantial inhaled doses. However, the topic of air pollution and cancer has not been reviewed systematically, particularly in its global dimensions. There is a rationale for undertaking such a comprehensive review: the more than 1.3 million new cases of lung cancer per year worldwide. Even a small contribution from air pollution to this number would strengthen the justification for implementing tighter control measures. In fact, several specific carcinogens or sources of carcinogens in indoor and outdoor air have already been the focus of substantial research and targeted control initiatives (e.g. diesel engines and exhaust, and radon and second-hand smoke indoors). In developing countries, high-level exposures to smoke from biomass fuels occur for billions of children and adults.

Estimates have been made of the burden of cancer attributable to environmental factors and of the contribution of air pollution to lung cancer specifically. Estimates have also been made for specific carcinogens, including radon and lung cancer. These estimates have been in the range of 3–5% for the fraction of lung cancer cases attributable to ambient air pollution. The 2004 estimates of the World Health Organization's Global Burden of Disease programme covered both outdoor and indoor air pollution. For ambient air pollution, the estimated number of lung cancer deaths worldwide was 62 000 per year (Cohen *et al.*, 2004). Indoor air pollution from solid fuel combustion was estimated to cause 16 000 lung

Table 1.1 Agents of high priority for evaluation or re-evaluation

Agent (overall evaluation of carcinogenicity to humans)[a]	Priority	Rationale for evaluation or re-evaluation
Carbon black (Group 2B)	High	New epidemiological studies New animal carcinogenicity data Mechanistic discussion (ultrafine particles)
Titanium dioxide (Group 3)	High	New epidemiological studies Mechanistic discussion (ultrafine particles)
Bitumen (USA: asphalt) (Group 2B/3)	High	Several ongoing epidemiological and animal carcinogenicity studies
Diesel engine exhaust (Group 2A)	High	New epidemiological studies
Gasoline engine exhaust (Group 2B)	Low	Few epidemiological studies specifically addressing gasoline engine exhaust No animal carcinogenicity data
	High	In combination with diesel engine exhaust
Air pollution, outdoor and indoor	High	New epidemiological studies
Sulfur dioxide (Group 3)	Low	New epidemiological studies
	High	In combination with air pollution

[a] Group 1, carcinogenic to humans; Group 2A, probably carcinogenic to humans; Group 2B, possibly carcinogenic to humans; Group 3, not classifiable as to its carcinogenicity to humans; Group 4, probably not carcinogenic to humans.
Adapted from IARC (2003).

cancer deaths per year, but estimates could not be made for all subregions (Smith *et al.*, 2004).

Workshop summary

To develop an approach for evaluating the carcinogenicity of air pollution, the International Agency for Research on Cancer (IARC) convened a multidisciplinary panel that included epidemiologists, toxicologists, atmospheric scientists, cancer biologists, and regulators. The group was charged with planning a series of Monographs on air pollution and constituents of air pollution, including several agents and mixtures that had been proposed by an ad hoc IARC Monographs Advisory Group on Priorities for Future Evaluations (Table 1.1). Implicit in convening the panel was an assumption that one or more Monographs on air pollution would benefit public health and that sufficient evidence was available to lead to an informative classification. The panel concurred with this general assessment.

Planning the approach to developing the Monographs was complicated by the myriad sources of outdoor and indoor air pollution, the highly complex and variable nature of air pollution mixtures in indoor and outdoor places where people spend time, and the need to consider mixtures related to specific sources (e.g. tobacco smoke) along with mixtures of these mixtures (e.g. tobacco smoke and biomass fuel smoke). In addition, the panel was aware that the evidence base has gaps and that research in progress might influence timing of specific Monographs.

In previous Monographs, IARC had reviewed specific air pollutants as well as groups of air pollutants and source-related mixtures (Table 1.2). Dating back to 1983, some of these Monographs warrant updates that have not yet been carried out.

In formulating an approach to air pollution and cancer, the panel considered two possible sequences: building from evaluation of specific components to broad air pollution mixtures, and evaluating air pollution more generally first and then moving to identify those components requiring separate evaluation. The panel found reasons to consider both approaches appropriate.

Table 1.2 Some air pollutants, groups of air pollutants, and source-related mixtures previously reviewed by the IARC Monographs Programme

Agent	Overall evaluation of carcinogenicity to humans[a]	Reference
Polycyclic aromatic hydrocarbons	Group 2A/2B/3	IARC (1983)
Nitro-polycyclic aromatic hydrocarbons	Group 3	IARC (1984)
Bitumen (USA: asphalt)	Group 2B/3	IARC (1987)
Benzene	Group 1	IARC (1987)
Asbestos	Group 1	IARC (1987)
Radon	Group 1	IARC (1988)
Diesel engine exhaust	Group 2A	IARC (1989a)
Gasoline engine exhaust	Group 2B	IARC (1989a)
Titanium dioxide	Group 3	IARC (1989b)
Sulfur dioxide	Group 3	IARC (1992)
Trichloroethylene	Group 2A	IARC (1995)
Carbon black	Group 2B	IARC (1996)
1,3-Butadiene	Group 2A	IARC (1999)
Man-made vitreous fibres	Group 2B/3	IARC (2002a)
Styrene	Group 2B	IARC (2002b)
Involuntary smoking	Group 1	IARC (2004)
Formaldehyde	Group 1	IARC (2006)

[a] Group 1, carcinogenic to humans; Group 2A, probably carcinogenic to humans; Group 2B, possibly carcinogenic to humans; Group 3, not classifiable as to its carcinogenicity to humans; Group 4, probably not carcinogenic to humans.

After extensive discussion, the panel proposed a sequence that would begin with a volume on polycyclic aromatic hydrocarbons (PAHs), updating a topic last reviewed in 1983 (IARC, 1983). Because combustion of organic materials, which generates PAHs, figures prominently in producing much indoor and outdoor air pollution, the panel concluded that IARC should begin the sequence of Monographs by updating that volume.

It was decided that a subsequent volume would cover combustion-related contaminants in indoor air, including separate Monographs on biomass fuels, wood smoke, coal combustion, and cooking fuels and fumes. These contaminants represent major exposures for billions of people around the world. Because of the commonalities among these topics, they would best be reviewed by a single panel. The needed expertise would reflect that of the present planning panel but would also need to draw on researchers from developing countries.

Another proposed volume would cover the topic of outdoor air pollution. The panel noted that outdoor air pollution cannot be readily defined; therefore, the Monograph should focus on those pollutants generated by human activities, particularly those entailing combustion and industrial processes. While air pollution is most prominent in urban locations, coverage should extend to rural environments as well.

In addition, there would be a volume directed at engine emissions, including diesel and gasoline engines. Such emissions are, of course, contributors to urban and rural air pollution. They represent a critical source and are subject to control through various technical and regulatory mechanisms. The panel noted that several new studies would be providing evidence over the next several years.

Many specific components of air pollution might be considered as topics for further Monographs. The panel suggested several such groups (e.g. particulate matter, solvents) but

concluded that further decisions would be made as the Monograph series proceeded and new data were evaluated in the context of prior IARC Monographs.

There were other issues noted that merit attention in developing the Monographs. Outdoor and indoor air pollution are mixtures that contain specific carcinogens, some already classified as Group 1 by IARC. The planning panel noted that mixtures containing specific carcinogens should consequently be categorized as carcinogenic as well, unless there are unidentified interactions among the mixture components. There are analogies in prior reviews of mixtures including diesel engine exhaust and second-hand smoke. Within the guidance given by the Preamble to the IARC Monographs, the evaluation of a particular air pollution mixture will hinge on the toxicological and epidemiological evidence on the cancer risk associated with the mixture while also considering the carcinogenic activity of the individual mixture components.

IARC evaluates overall carcinogenicity but does not specifically quantify risk at either the individual or population level. The panel noted that such quantification would be a necessary step in determining the implications of higher-level IARC designations for control strategies.

Going on the assumption that mixtures containing carcinogens are necessarily carcinogenic themselves, the panel noted that a lack of evidence of carcinogenicity from experimental and observational studies could result from inadequacies and difficulties of the research approaches on mixtures. In the chapters in this IARC Scientific Publication, these limitations are discussed in further detail.

References

Cohen AJ, Anderson HR, Ostro B *et al.* (2004). Urban air pollution. In: Ezzati M, Lopez A, Rodgers A, Murray C, eds. *Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors*, Vol. 2. Geneva: World Health Organization, pp. 1353–1433.

IARC (1983). Polynuclear aromatic compounds, Part 1, Chemical, environmental and experimental data. *IARC Monogr Eval Carcinog Risk Chem Hum*, 32: 1–453. PMID:6586639

IARC (1984). Polynuclear aromatic hydrocarbons, Part 2, Carbon blacks, mineral oils (lubricant base oils and derived products) and some nitroarenes. *IARC Monogr Eval Carcinog Risk Chem Hum*, 33: 1–222. PMID:6590450

IARC (1987). Overall evaluations of carcinogenicity: an updating of IARC Monographs volumes 1 to 42. *IARC Monogr Eval Carcinog Risks Hum Suppl*, 7: 1–440. PMID:3482203

IARC (1988). Man-made mineral fibres and radon. *IARC Monogr Eval Carcinog Risks Hum*, 43: 1–300.

IARC (1989a). Diesel and gasoline engine exhausts and some nitroarenes. *IARC Monogr Eval Carcinog Risks Hum*, 46: 1–458. PMID:2483415

IARC (1989b). Some organic solvents, resin monomers and related compounds, pigments and occupational exposures in paint manufacture and painting. *IARC Monogr Eval Carcinog Risks Hum*, 47: 1–442. PMID:2636273

IARC (1992). Occupational exposures to mists and vapours from strong inorganic acids and other industrial chemicals. *IARC Monogr Eval Carcinog Risks Hum*, 54: 1–310. PMID:1345371

IARC (1995). Dry cleaning, some chlorinated solvents and other industrial chemicals. *IARC Monogr Eval Carcinog Risks Hum*, 63: 1–551. PMID:9139128

IARC (1996). Printing processes and printing inks, carbon black and some nitro compounds. *IARC Monogr Eval Carcinog Risks Hum*, 65: 1–578. PMID:9148039

IARC (1999). Re-evaluation of some organic chemicals, hydrazine and hydrogen peroxide. *IARC Monogr Eval Carcinog Risks Hum*, 71: 1–315. PMID:10507919

IARC (2002a). Man-made vitreous fibres. *IARC Monogr Eval Carcinog Risks Hum*, 81: 1–381. PMID:12458547

IARC (2002b). Some traditional herbal medicines, some mycotoxins, naphthalene and styrene. *IARC Monogr Eval Carcinog Risks Hum*, 82: 1–556. PMID:12687954

IARC (2003). Report of an ad-hoc IARC Monographs Advisory Group on Priorities for Future Evaluations (IARC Internal Report No. 03/001).

IARC (2004). Tobacco smoke and involuntary smoking. *IARC Monogr Eval Carcinog Risks Hum*, 83: 1–1438. PMID:15285078

IARC (2006). Formaldehyde, 2-butoxyethanol and 1-tert-butoxypropan-2-ol. *IARC Monogr Eval Carcinog Risks Hum*, 88: 1–478. PMID:17366697

Smith KR, Mehta S, Maeusezahl-Feuz M (2004). Indoor air pollution from household use of solid fuels. In: Ezzati M, Lopez A, Rodgers A, Murray C, eds. *Comparative Quantification of Health Risks: Global and Regional Burden of Disease Attributable to Selected Major Risk Factors*, Vol. 2. Geneva: World Health Organization, pp. 1435–1493.