IARC MONOGRAPHS

RADIATION

VOLUME 100 D
A REVIEW OF HUMAN CARCINOGENS

RADIOACTIVE MATERIAL

This publication represents the views and expert opinions of an IARC Working Group on the Evaluation of Carcinogenic Risks to Humans, which met in Lyon, 2-9 June 2009

LYON, FRANCE - 2012

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ON THE EVALUATION
OF CARCINOGENIC RISKS
TO HUMANS

International Agency for Research on Cancer
World Health Organization

GENERAL REMARKS

Part D of Volume 100 of the *IARC Monographs on the Evaluation of Carcinogenic Risks to Humans* considers all forms of radiation that were classified as *carcinogenic to humans (Group 1)* in Volumes 1–99.

Volume 100 – General Information

About half of the agents classified in Group 1 were last reviewed more than 20 years ago, before mechanistic studies became prominent in evaluations of carcinogenicity. In addition, more recent epidemiological studies and animal cancer bioassays have demonstrated that many cancer hazards reported in earlier studies were later observed in other organs or through different exposure scenarios. Much can be learned by updating the assessments of agents that are known to cause cancer in humans. Accordingly, IARC has selected *A Review of Human Carcinogens* to be the topic for Volume 100. It is hoped that this volume, by compiling the knowledge accumulated through several decades of cancer research, will stimulate cancer prevention activities worldwide, and will be a valued resource for future research to identify other agents suspected of causing cancer in humans.

Volume 100 was developed by six separate Working Groups:

Pharmaceuticals
Biological agents
Arsenic, metals, fibres, and dusts
Radiation
Personal habits and indoor combustions
Chemical agents and related occupations

Because the scope of Volume 100 is so broad, its *Monographs* are focused on key information. Each *Monograph* presents a description of a carcinogenic agent and how people are exposed, critical overviews of the epidemiological studies and animal cancer bioassays, and a concise review of the toxicokinetic properties of the agent, plausible mechanisms of carcinogenesis, and potentially susceptible populations, and life-stages. Details of the design and results of individual epidemiological studies and animal cancer bioassays are summarized in tables. Short tables that highlight key results appear in the printed version of Volume 100, and more extensive tables that include all studies appear on the website of the *IARC Monographs* programme (http://monographs.iarc.fr). For a few well-established associations (for example, tobacco smoke and human lung cancer), it was impractical to

include all studies, even in the website tables. In those instances, the rationale for inclusion or exclusion of sets of studies is given.

Each section of Volume 100 was reviewed by a subgroup of the Working Group with appropriate subject expertise; then all sections of each *Monograph* were discussed together in a plenary session of the full Working Group. As a result, the evaluation statements and other conclusions reflect the views of the Working Group as a whole.

Volume 100 compiles information on tumour sites and mechanisms of carcinogenesis. This information will be used in two scientific publications that may be considered as annexes to this volume. One publication, *Tumour Site Concordance between Humans and Experimental Animals*, will analyse the correspondence of tumour sites among humans and different animal species. It will discuss the predictive value of different animal tumours for cancer in humans, and perhaps identify human tumour sites for which there are no good animal models. Another publication, *Mechanisms Involved in Human Carcinogenesis*, will describe mechanisms known to or likely to cause cancer in humans. Joint consideration of multiple agents that act through similar mechanisms should facilitate the development of a more comprehensive discussion of these mechanisms. Because susceptibility often has its basis in a mechanism, this could also facilitate a more confident and precise description of populations that may be susceptible to agents acting through each mechanism. This publication will also suggest biomarkers that could render future research more informative. In this way, IARC hopes that Volume 100 will serve to improve the design of future cancer studies.

Specific remarks about the review of radiation in this volume

Solar radiation was classified as Group 1 in Volume 55 (IARC, 1992). At that time, some individual components of solar radiation, ultraviolet radiation A, B, and C, were classified as *probably carcinogenic to humans (Group 2A)*, along with sunlamps and sunbeds, which act as artificial sources of ultraviolet radiation. These agents are also reviewed in this volume to evaluate whether the epidemiological and mechanistic studies available today provide sufficient evidence to identify specific components of solar radiation as carcinogenic to humans. In Volume 75 (IARC, 2000), X-radiation and γ-radiation were classified as Group 1, along with neutrons. Internalized radionuclides that emit α particles or β particles were classified as Group 1 in Volume 78 (IARC, 2001). That volume also listed individually in Group 1 specific radionuclides for which there was sufficient evidence in humans. Of these, radon-222 and its decay products had been classified earlier as Group 1 in Volume 43 (IARC, 1988). One occupation involving radiation exposure, underground haematite mining with exposure to radon, was reviewed in Volume 1 (IARC, 1972) and classified as Group 1 in Supplement 7 (IARC, 1987).

In conducting this combined review of different types of ionizing radiation from various sources – resulting in a separate Group-1 classification for each of these types – the Working Group discussed the suggestion to arrive at a generic evaluation of the cancer hazards from exposure to radiation in the high-energy region of the electromagnetic spectrum (wavelength, <10 nm).

The Working Group considered that all types of ionising radiation, including the neutron particle, transfer their energy to biological material as either separate or clustered ionization and excitation events, primarily through a free–electron-mediated mechanism. Furthermore, the deposition

of energy from all types of ionizing radiation results in a wide variety of molecular damage in the cell, including base damage and single- and double-strand breaks in DNA, some of which may be clustered and form complex lesions. Subsequent processing of these lesions may lead to chromosomal aberrations and mutations. And finally, there is ample evidence that damage to DNA is indeed of primary importance in the biological outcome of exposure to ionising radiation. On the basis of these considerations, the Working Group reached the final evaluation that "All types of ionizing radiation are *carcinogenic to humans (Group 1)*"

In reviewing studies on occupational exposures to ultraviolet radiation, the Working Group found strong evidence of ocular melanoma in welders. After a literature search for other studies of welders and a review of this information, the Working Group concluded that these studies provide sufficient evidence of carcinogenicity. Welding fumes had been classified as *possibly carcinogenic to humans (Group 2B)* in Volume 49 (IARC, 1990) and this was not scheduled for update in this volume. A full review of welding was considered to be outside the scope of this meeting, as concern about welding has generally focused on exposures to mixtures of metal and chemical fumes (IARC, 1990). Welders and people who work with them may also be exposed to fumes of thorium-232, which is used in tungsten welding rods (NCRP, 1988; Nuclear Regulatory Commission, 2001). Although it is not possible without a full review to attribute the occurrence of ocular melanoma to ultraviolet radiation specifically, the review of ocular melanoma in this volume was thorough and the findings are expected to remain after a full review of welding in a subsequent *Monograph*. Accordingly, the Working Group made an evaluation that there is *sufficient evidence* in humans for the carcinogenicity of welding.

A summary of the findings of this volume appears in The Lancet Oncology (El Ghissassi *et al.*, 2009).

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