IARC Monographs

Head
Dr Vincent Cogliano

Scientists
Dr Robert Baan
Dr Lamia Benbrahim-Tallaa
Dr Véronique Bouvard
Dr Fatiha El Ghissassi
Dr Crystal Freeman
Dr Yann Grosse
Ms Neela Guha
Dr Béatrice Secretan
Dr Kurt Straif

Editor
Laurent Galichet

Technical Assistants
Sandrine Égraz
Ms Anne-Sophie Hameau
Ms Dorothy Russell

Secretary
Helene Lorenzen-Augros

Website: http://monographs.iarc.fr/

The first step in cancer prevention is to identify the causes of human cancer. The *IARC Monographs* are a series of scientific reviews that identify environmental factors that can increase the risk of cancer in humans.

Each *Monograph* includes a critical review of the pertinent scientific studies on a known or suspected carcinogen, followed by an evaluation of the overall weight of the evidence that the agent can alter the risk of cancer in humans. It is written by an international, interdisciplinary Working Group of expert scientists. Since 1971, *Monographs* have been developed for more than 900 agents, 400 of which have been identified as carcinogenic, probably *carcinogenic, or possibly carcinogenic* to humans. These include chemicals, complex mixtures, occupational exposures, physical agents, biological agents, and personal habits and household exposures.

The *IARC Monographs* are a worldwide endeavour that has involved more than 1200 scientists from 53 countries. The *Monographs* are unique in that the critical reviews and evaluations are developed by experts who conducted the original research.

National and international health agencies use the *Monographs* as a source of scientific information on known or suspected carcinogens and as scientific support for their actions to prevent exposure to these agents. Individuals, too, use the information and conclusions from the *Monographs* to make better choices that reduce their exposure to potential carcinogens and their risk of developing cancer. In this way, the *IARC Monographs* contribute to cancer prevention and the improvement of public health. The 2008–2009 biennium saw the publication of Volume 97 of the Monographs, *1,3-Butadiene, Ethylene Oxide, and Vinyl Halides (Vinyl Fluoride, Vinyl Chloride and Vinyl Bromide).*

Updating the assessments of human carcinogens

The programme's principal activity during the 2008–2009 biennium has been a special review of known human carcinogens, which will be published as Volume 100 of the *IARC Monographs*. This volume is updating IARC's assessments of the more than 100 agents that had been classified as *carcinogenic to humans* (Group 1) in Volumes 1–99. This volume is being developed in six parts that span the diversity of carcinogenic agents:

A. *Pharmaceuticals* (Oct 2008)
B. *Biological Agents* (Feb 2009)
C. *Metals, Arsenic, Dusts and Fibres* (Mar 2009)
D. *Radiation* (June 2009)
E. *Personal Habits and Household Exposures* (Sept 2009)
F. *Chemical Agents and Related Occupations* (Oct 2009)

Volume 100 has shown that there is stronger evidence of carcinogenicity for most of these agents, identified some new human carcinogens (Table 1) and extended earlier findings to include additional target sites. For example, estrogen-only menopausal therapy is now causally associated with ovarian cancer, asbestos is also causally associated with ovarian cancer, hepatitis C virus with non-Hodgkin lymphoma, formaldehyde with leukaemia, ultraviolet-emitting tanning devices with ocular melanoma,

Table 1. Human carcinogens that were newly identified in Volume 100

Pharmaceuticals
- Aristolochic acid
- Etoposide
- Phenacetin
Biological Agents
- Kaposi sarcoma herpes virus
- *Clonorchis sinensis*
Dusts
- Leather dust
Radiation
- Ultraviolet radiation (including UVA, UVB, UVC)
- Ultraviolet-emitting tanning devices
Personal Habits and Household Exposures
- Acetaldehyde associated with alcohol consumption
Chemical Agents
- 3,3',4,4',5-Pentachlorobiphenyl (PCB-126)
- 2,3,4,7,8-Pentachlorodibenzofuran

welding with ocular melanoma, and parental smoking with hepatoblastoma in the smokers' children, among many other similar findings.

Volume 100 is highlighting the contribution of mechanistic information to the identification of carcinogenic agents. Some examples:

Aristolochic acid: within 6 years after plants of the genus *Aristolochia* were classified as carcinogenic, mechanistic studies were able to attribute this risk to aristolochic acid, which could lead to a practical means of testing herbal preparations for this cancer hazard.

Formaldehyde: Within 5 years after the previous *Monograph* on formaldehyde, mechanistic studies have replaced previous assertions of biological implausibility with new evidence that formaldehyde can cause blood-cell abnormalities that are consistent with leukaemia development.

Alcohol consumption: Genetic epidemiology studies provided evidence that alcohol consumption poses particularly high risks of oesophageal and other cancers based on a genetic polymorphism of metabolic activity that occurs in a large proportion of people of eastern Asian origin.

In addition, epidemiological studies recently confirmed the carcinogenicity of 2.3.7.8-tetrachlorodibenzo-*para*-dioxin, which was classified in 1997 as *carcinogenic to humans* based on mechanistic information. This shows that mechanistic studies can provide robust evidence of carcinogenicity without waiting for the observation of tumours in exposed humans.

Volume 100 continues the international character of the *Monographs*. The experts who participated in its development numbered 160 scientists from 28 countries (Table 2). More importantly, these *Monographs* addressed several carcinogenic hazards that disproportionately affect developing countries. Some examples:

Hepatitis B and C viruses: these infect a half-billion people, mostly in Asia and Africa, and lead to high rates of liver cancer in these areas.

Aflatoxins: these fungal toxins are prevalent in humid tropical areas and cause liver cancer, particularly in people infected with hepatitis B virus.

Parasitic infections: *Schistosoma haematobium*, endemic in Africa and the eastern Mediterranean region, causes urinary bladder cancer; some liver flukes endemic in southeastern Asia cause cholangiocarcinoma.

Areca nut: chewed by 600 million people in southeastern Asia, especially India, and responsible for high incidences of cancers of the oral cavity and oesophagus in those areas.

Smokeless tobacco: used by hundreds of millions of people in southeastern Asia and responsible for cancers of the oral cavity, oesophagus, and pancreas.

Household use of coal: use of solid fuels for cooking and heating is highly prevalent in many developing countries and causes high rates of lung cancer, including in nonsmokers.

Table 2. Country of affiliation of the experts for Volume 100

Australia	5
Belgium	1
Brazil	1
Canada	7
China	2
Costa Rica	1
Czech Republic	1
Denmark	4
Finland	7
France	7
Germany	10
India	3
Iran	1
Italy	5
Japan	5
Mexico	1
Netherlands	1
New Zealand	1
Norway	2
Portugal	1
Republic of Korea	2
Russian Federation	1
South Africa	1
Spain	3
Sweden	2
Thailand	1
United Kingdom	13
USA	71
Total	*160*

In the future, cancer assessments will increasingly rely on molecular epidemiology and on information about mechanisms of carcinogenesis. To this end, Volume 100 is summarising currently available information on the multiple mechanisms of carcinogenesis for the agents known to cause cancer in humans. This will provide insight into how other agents might cause cancer in humans and will be particularly useful in future assessments of new and untested chemicals, for which 2-year bioassays and epidemiological studies of cancer are unlikely to be available. The *Monographs* developed for Volume 100 will provide information that will be synthesised in two future IARC Scientific Publications: *Tumour Concordance between Animals and Humans* and *Mechanisms Involved in Human Carcinogenesis.* These scientific publications will be initiated during the 2010–2011 biennium, after the results of Volume 100 have been published.

Priorities for future IARC Monographs

In June 2008 IARC convened an Advisory Group to identify high priorities for new *IARC Monographs* during the next 5 years. Before the Advisory Group met, IARC solicited nominations from the scientific community and the general public via the Internet. Seeking such input is meant to ensure that new *Monographs* reflect current research and public health priorities. Most of the Advisory Group's recommendations (Table 3) are new topics that have never before been reviewed by IARC or by other public health agencies. This indicates a high level of interest in the continued work of the *IARC Monographs* to provide authoritative evaluations of new or previously established cancer hazards.

In addition, other topics will be scheduled as significant new scientific information becomes available or as national health agencies identify an urgent public health need. Some additional topics (Table 3) have already arisen from discussions during the expert meetings for Volume 100.

Table 3. High priorities for future *IARC Monographs*

Most pressing priorities from the Advisory Group

- *Radiofrequency electromagnetic fields and radar (includes mobile telephones)
- Motor vehicle emissions (includes diesel, gasoline, biofuel exhausts)
- *Polyomaviruses (SV40, BK, JC, Merkel cell virus)
- Asphalt/bitumen
- Acrylamide, furan

Other high priorities from the Advisory Group

- Acetaldehyde
- *Carbon-based nanoparticles
- *Crystalline fibres other than asbestos
- *Growth hormone
- *Iron and iron oxides
- *Malaria
- Nucleoside-analogue antiviral drugs
- *Outdoor air pollution (includes sulfur oxides, nitrogen oxides, ozone, dusts)
- *Perfluorooctanoic acid (PFOA) and other perfluorinated compounds
- *Sedentary work
- *Statins
- *Stress
- Testosterone and other androgenic steroids
- *Ultrafine particles
- Welding
- Some agents recently tested in experimental animals

Additional high priorities arising from Volume 100

- Benzene
- Nickel metal
- Polyhalogenated dibenzo-para-dioxins, dibenzofurans, and biphenyls

*Never before reviewed by IARC

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