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The first step in cancer prevention is to identify the causes of human cancer. The IARC Monographs Programme (http://monographs.iarc.fr/) is an international, interdisciplinary approach to carcinogenic hazard identification. Its principal product is the serial publication of the IARC Monographs on the Evaluation of Carcinogenic Risks to Humans, which began in 1971 in accordance with one of the fundamental missions of the Agency: to prepare and distribute authoritative information on human cancer and especially on its causes and prevention.

Each Monograph consists of a comprehensive, critical summary and review of the published scientific literature and an evaluation of the overall evidence of carcinogenicity to humans. The IARC Monographs are a worldwide endeavour that has involved more than 1300 scientists from more than 50 countries. Reviews and evaluations of nominated agents and exposures are carried out by Working Groups of scientific experts who are invited to participate on the basis of their expertise in the topic. Since 1971, more than 950 chemicals, complex mixtures, occupational exposures, physical agents, biological agents, personal habits, and household exposures have been reviewed, some of them several times as new information has become available. More than 100 of these agents have been identified as carcinogenic to humans (Group 1), and

more than 350 as probably carcinogenic or possibly carcinogenic to humans (Groups 2A and 2B).

The IARC Monographs have evolved into the World Health Organization's encyclopaedia on the roles of environmental agents in human cancer causation. National and international health agencies use the Monographs as a source of scientific information, and as scientific support for their actions to prevent exposure to these agents. A recent example was the reference to the Monographs in developing the fourth edition of the European Code Against Cancer. Individuals, too, use the conclusions from the Monographs to inform their choices to reduce their exposure to potential carcinogens. In this way, the IARC Monographs contribute to cancer prevention and the improvement of public health.

In 1995, the IARC Handbooks of Cancer Prevention were launched to complement the IARC Monographs by providing evaluations of approaches to cancer prevention. The same rigorous procedures of critical review and evaluation as for the IARC Monographs are used. Evaluations have included chemopreventive agents, preventive actions, effectiveness of screening, and effectiveness of tobacco control. The IARC Handbooks of Cancer Prevention programme has now been relaunched, with a focus on primary and secondary prevention.

Advisory Group to Recommend Priorities for the IARC Monographs during 2015–2019 (7–9 April 2014)

An Advisory Group of 21 scientists from 13 countries met at IARC in April 2014 to recommend evaluation topics for 2015–2019 and to discuss strategic matters for the IARC Monographs Programme. The Advisory Group considered responses to a call for nominations on the IARC website and recommended a broad range of agents and exposures with high or medium priority (Table 1); IARC will use this advice in making decisions on agents for future evaluations.

Table 1. Agents recommended for evaluation by the IARC Advisory Group with high priority

Acrylamide, Furan, 5-Hydroxymethyl-2-furfural
2-Amino-4-chlorophenol, 2-Chloronitrobenzene, 4-Chloronitrobenzene, 1,4-Dichloro-2-nitrobenzene, 2,4-Dichloro-1-nitrobenzene
Aspartame and sucralose
Bisphenol A
1-Bromopropane
Carbon nanotubes, multi-walled
Beta-carotene
3-Chloro-2-methylpropene
Coffee
Dietary iron and iron used as supplements or for medical purposes
Dimethylformamide
N,*N*-Dimethyl-*p*-toluidine
Disinfected water used for drinking, showering, bathing, or swimming
Electronic cigarettes and nicotine
Ethyl acrylate
Ethyl tertiary butyl ether (ETBE), Methyl tertiary butyl ether (MTBE), *tert*-Butyl alcohol (TBA)
Hot mate drinking
Human cytomegalovirus (HCMV)
Indium-tin oxide
Isobutyl nitrite
2-Mercaptobenzothiazole
Obesity and overweight
Opium
Pesticides (including Carbaryl, Diazinon, Lindane, Malathion, Pendimethalin, Permethrin)
Phenyl and octyl tin compounds
ortho-Phenylenediamine dihydrochloride
Physical inactivity and sedentary work
Red and processed meats
Shiftwork
Styrene
Tetrabromobisphenol A (TBBPA)
Tungsten
Welding and welding fumes

In addition, the Advisory Group endorsed the current system of expert reviews with strict management of conflict of interests; encouraged the Secretariat to explore the use of systematic review tools to further increase transparency and efficiency; supported recent recommendations of a separate Advisory Group on Quantitative Risk Characterization that the Monographs could progressively include exposure–response relationships, particularly from epidemiological studies, as a basis for estimates of global cancer burden by IARC; recognized the need for systematic identification of mechanistic data, with transparent selection of publications and inclusion of high-throughput and high-content data streams, to focus on clear elucidation of mechanistic processes; and recommended exploration of additional opportunities to address cancer risk in low- and middle-income countries, including enhanced retrieval of relevant exposure data for Monographs and increased dissemination of pertinent evaluations (Straif et al., 2014).

Volume 110: Perfluoro-octanoic acid, tetrafluoroethylene, dichloromethane, 1,2-dichloropropane, and 1,3-propane sultone (3–10 June 2014)

In June 2014, a Working Group assessed the carcinogenicity of perfluoro-octanoic acid (PFOA), tetrafluoroethylene (TFE), dichloromethane (DCM), 1,2-dichloropropane (1,2-DCP), and 1,3-propane sultone (1,3-PS). 1,2-DCP was classified as *carcinogenic to humans* (Group 1), based on *sufficient evidence* that exposure causes cancer of the biliary tract. The most important human evidence came from studies of workers in a small offset printing plant in Osaka, Japan, with a very high risk of cholangiocarcinoma. The Working Group classified DCM as *probably carcinogenic to humans* (Group 2A), based on *limited evidence* in humans for biliary tract cancer and non-Hodgkin lymphoma and *sufficient evidence* in experimental animals. TFE was upgraded from *possibly carcinogenic to humans* (Group 2B) to *probably carcinogenic to humans* (Group 2A), based on *inadequate evidence* in humans and *sufficient evidence* in experimental animals with unusual results (neoplasms at multiple sites and with very high incidence observed in exposed rodents of both sexes, including liver haemangiosarcoma, hepatocellular carcinoma, and histiocytic sarcoma in mice, and renal cell adenoma or carcinoma [combined], hepatocellular carcinoma, mononuclear cell leukaemia, and the rare liver haemangiosarcoma in female rats). 1,3-PS was classified as *probably carcinogenic to humans* (Group 2A), based on *inadequate evidence* in humans and *sufficient evidence* in experimental animals with a mechanistic upgrade supported by strong evidence for genotoxicity. PFOA was classified as *possibly carcinogenic to humans* (Group 2B), based on *limited evidence* in humans for testicular and kidney cancer and *limited evidence* in experimental animals (Benbrahim-Tallaa et al., 2014).

Volume 111: Fluoro-edenite, silicon carbide fibres and whiskers, and carbon nanotubes (30 September–7 October 2014)

In October 2014, a Working Group reviewed the carcinogenicity of fluoro-edenite, silicon carbide (SiC) fibres and whiskers, and carbon nanotubes (CNTs), including single-walled and multi-walled types (SWCNTs and MWCNTs). Fluoro-edenite fibrous amphibole was classified as *carcinogenic to humans* (Group 1), based on *sufficient evidence* in humans that it causes mesothelioma and *sufficient evidence* in experimental animals. SiC fibres are by-products of the manufacture of SiC particles by the Acheson process; SiC whiskers are produced by other processes. Occupational exposures associated with the Acheson process were classified as *carcinogenic to humans* (Group 1), based on *sufficient evidence* in humans that they cause lung cancer. Fibrous SiC was classified as *possibly carcinogenic to humans* (Group 2B), based on *limited evidence* in humans that it causes lung cancer and *inadequate evidence* in experimental animals. SiC whiskers were upgraded from *possibly carcinogenic to humans* (Group 2B) to *probably carcinogenic to humans* (Group 2A), based on *inadequate evidence* in humans, *sufficient evidence* in experimental animals, and consideration of their physical properties.

There was no epidemiological study on CNTs. Regarding carcinogenicity in experimental animals, there was *sufficient evidence* for MWCNT-7, *limited evidence* for two types of MWCNTs with dimensions similar to MWCNT-7, and *inadequate evidence* for SWCNTs. MWCNT-7 was classified as *possibly carcinogenic to humans* (Group 2B), and SWCNTs and MWCNTs excluding MWCNT-7 were categorized as *not classifiable as to their carcinogenicity to humans* (Group 3) (Grosse et al., 2014).

Handbook Volume 15: Breast cancer screening (11–18 November 2014)

Breast cancer is the leading cancer in women worldwide, and the potential role of primary prevention is limited because most risk factors are directly linked with endogenous hormone levels and reproductive factors. Therefore, secondary prevention is a priority. In addition to breast cancer screening by mammography, clinical examination, and self-examination, which were already evaluated in 2002, the Working Group for this Handbook extended its review to non-mammographic imaging techniques such as magnetic resonance imaging (MRI), digital breast tomosynthesis (or 3D mammography), breast-specific positron emission tomography, ultrasound as an adjunct to mammography for women with dense breasts, and computer-assisted diagnosis in combination with digital mammography; also, the effectiveness of screening high-risk women was evaluated.

Based on available data, there is sufficient evidence for the effectiveness of mammography screening in women aged 50–74 years. While the evidence for overdiagnosis is also sufficient, overall the Working Group concluded that there is a net benefit in screening women aged 50–69 years. Data on breast self-examination remain unconvincing. In contrast, clinical breast examination showed sufficient evidence for shifting the stage distribution of tumours detected towards a lower stage. Of all the new technologies considered, sufficient evidence was reached only for an increased detection rate, mostly of invasive tumours, with adjunct tomosynthesis compared with mammography alone. MRI as an adjunct to mammography in high-risk women with a *BRCA1* or *BRCA2* mutation provided an increased sensitivity but decreased specificity (Lauby-Secretan et al., 2015a).

Volume 112: Tetrachlorvinphos, parathion, malathion, diazinon, and glyphosate (3–10 March 2015)

In March 2015, a Working Group of 17 experts from 11 countries reviewed the carcinogenicity of five organophosphate pesticides. Four insecticides (tetrachlorvinphos, parathion, malathion, and diazinon) and glyphosate, the most widely used herbicide worldwide, were evaluated. The insecticides tetrachlorvinphos and parathion were classified as *possibly carcinogenic to humans* (Group 2B), based on *sufficient evidence* in experimental animals. The insecticides malathion and diazinon and the herbicide glyphosate were classified as *probably carcinogenic to humans* (Group 2A). For malathion and glyphosate, the evidence in experimental animals was *sufficient* and the evidence in humans was *limited*. For diazinon, *limited evidence* was found in both experimental animals and humans. The

limited evidence in humans supporting these three Group 2A classifications comprised reports of increased cancer risks from occupational cohort and case–control studies in Canada, Sweden, and the USA. The large Agricultural Health Study reported positive associations for malathion (prostate cancer) and diazinon (non-Hodgkin lymphoma subtypes, leukaemia, and lung cancer). An increased risk of non-Hodgkin lymphoma with glyphosate use was reported in multiple case–control studies but was not seen in the Agricultural Health Study. Strong mechanistic evidence, particularly for genotoxicity and oxidative stress, was found for malathion, diazinon, and glyphosate. Together with the *limited evidence* of human carcinogenicity for diazinon, this strong mechanistic evidence formed the basis for the Group 2A classification. The mechanistic evidence independently supported the Group 2A classifications of malathion and glyphosate (Guyton et al., 2015).

Volume 113: DDT, lindane, and 2,4-D (2–9 June 2015)

In June 2015, a Working Group of 26 experts from 13 countries evaluated the carcinogenicity of the insecticides dichlorodiphenyltrichloroethane (DDT) and lindane and the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D). DDT was heavily used for insect control in agriculture and public health, but current use is largely restricted to malaria control. DDT was classified as *probably carcinogenic to humans* (Group 2A), based on *limited evidence* in humans and *sufficient evidence* in experimental animals. Epidemiological studies found positive associations between exposure to DDT and non-Hodgkin lymphoma, testicular cancer, and liver cancer. Lindane was formerly used for insect control, but its use is now largely banned. Lindane was classified as *carcinogenic to humans* (Group 1), based on *sufficient evidence* in both humans and experimental animals. Epidemiological studies of agricultural workers exposed to lindane showed a 60% increased risk of non-Hodgkin lymphoma. 2,4-D is a high production volume chemical that has been used since the 1940s to control weeds in agriculture, forestry, and urban settings. 2,4-D was classified as *possibly carcinogenic to humans* (Group 2B), based on *inadequate evidence* in humans and *limited evidence* in experimental animals. Experimental studies provided strong evidence that 2,4-D induces oxidative stress and moderate evidence that 2,4-D causes immunosuppression. However, epidemiological studies did not find strong or consistent increases in cancer risk in relation to 2,4-D exposure (Loomis et al., 2015).

Volume 114: Consumption of red meat and processed meat (6–13 October 2015)

In October 2015, a Working Group assessed the carcinogenicity of the consumption of red meat and processed meat. Red meat refers to unprocessed mammalian muscle meat (e.g. beef, veal, pork, and lamb), including that which may be minced or frozen. Processed meat refers to meat that has been transformed through salting, curing, fermentation, smoking, or other processes to enhance flavour or improve preservation. Meat curing and smoking can result in the formation of carcinogenic chemicals, including *N*-nitroso compounds (NOCs) and polycyclic aromatic hydrocarbons (PAHs). High-temperature cooking by pan-frying, grilling, or barbecuing produces high amounts of carcinogens, including heterocyclic aromatic amines (HAAs) and PAHs.

The Working Group assessed more than 800 epidemiological studies, including large cohorts in many countries on several continents and in populations with diverse ethnicities and diets. A meta-analysis of colorectal cancer in 10 cohort studies reported a statistically significant dose–response relationship with a 17% increased risk (95% confidence interval [CI], 1.05–1.31) per 100 g/day of red meat and an 18% increased risk (95% CI, 1.10–1.28) per 50 g/day of processed meat. The Working Group classified consumption of processed meat as *carcinogenic to humans* (Group 1), based on *sufficient evidence* for colorectal cancer. A positive association was found between consumption of processed meat and stomach cancer. Consumption of red meat was classified as *probably carcinogenic to humans* (Group 2A), based on substantial epidemiological data showing high *limited evidence* for colorectal cancer and on strong mechanistic evidence. Consumption of red meat was also positively associated with pancreatic cancer and with prostate cancer.

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