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Misconceptions and Misuse of International Agency for Research on Cancer 'Classification of Carcinogenic Substances': The Case of Asbestos

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Abstract
In their work on human cancer, the International Agency for Research on Cancer have run a programme of «monographs» that evaluate carcinogenic risk of chemicals to man. The data collected provide considerable information on the risk from substances identified as carcinogens. However, this is largely unused in the IARC classification scheme in spite of the use of the term 'risk' in the title and text of the monographs. Consequently, some governments and pressure groups use hazard identification to advance the cause for banning agents without conducting a risk assessment. Confusion and indiscriminate use of 'hazard' and 'risk' mean that the hazard data are commonly misrepresented as risk data. A common political response is to push regulatory action to extremes, citing the Precautionary Principle. Unfortunately, eliminating substances on the grounds of inherent hazard can deny major benefits to societies and undermine the sustainable developments. This is nowhere better illustrated than in the case of the minerals known collectively as asbestos. Evidence available clearly differentiates the hazards of chrysotile and amphibole asbestos, yet the current IARC classification does not make this distinction. This is in spite of the fact that amphibole asbestos produces orders of magnitude more diseases than chrysotile when used in the same way. The overwhelming weight of evidence available indicates that chrysotile can be used safely with low risk. Cement products such as water pipes and boards for housing provide are versatile products made at affordable cost for the developing countries which if not available would cost rather than save lives.

Introduction

The International Agency for Research on Cancer (IARC) is the World Health Organization (WHO)

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sponsored agency whose mission is to co-ordinate and conduct research on the causes of human cancer, mechanisms of carcinogenesis, and to develop scientific strategies for cancer control. In 1970, the IARC Governing Council adopted a resolution concerning the role of IARC in providing government authorities with expert, independent, and scientific opinion on environmental carcinogenesis. As one means to that end, the Governing Council recommended that IARC should prepare a programme of 'monographs' on the evaluation of carcinogenic risk of chemicals to man, which became the initial title of the series. Since its inception in the early 1970s, the 'Programme' has reviewed more than 885 agents, and IARC Monographs have become well known for their thoroughness, accuracy, and integrity. With these data, there is ample opportunity to provide meaningful information for nations to use in gauging the extent of risk to their populations, regarding a substance identified as a hazard. Information concerning route of exposure to humans, actual conditions during use, cumulative exposure to the agent, pharmacokinetics regarding its fate in the human host, and so on, are in many cases available for complete hazard characterization. However, this information is largely unused in the IARC classification scheme. Indeed, one has to ask why does IARC persist in using the term 'risk' in the title and text of their monographs when, in fact, they agree that they do not perform risk assessment. The preamble to the IARC Monographs states that '*The Monographs represent the first step in carcinogenic risk assessment, which involves examination of all relevant information in order to assess the strength of the available evidence that certain exposures could alter the incidence of cancer in humans. The second step is quantitative risk estimation*' [1]. However, this second step of quantitative risk estimation is rarely performed. Ignoring risk assessment, some governments and pressure groups (often non-governmental organizations or NGOs) simply use hazard identification to advance the cause for banning an agent. There is no attempt to conduct the appropriate quantitative risk assessment to prevent unintended consequences.

Misconception of Terminology

The compounds or materials evaluated in the *IARC Monographs* Volumes 1–94, have been compiled into a list that contains all agents, mixtures, and exposure circumstances evaluated to date and classified as 'Group 1', that is - carcinogenic to humans [2].

This list was last updated in September 2006. It now contains some 99 agents, mixtures, and activities. The 99 entries are divided into three sections : 'Agents and groups of agents'; 'Mixtures'; 'Exposure circumstances'. Examples from each of these three sections are given for illustrative purposes in Table 1.

We may pose the question: does the presence on the IARC list of 'Group 1 - Agents, Mixtures and Activities' imply that these must be banned? The answer is obviously No! The reason is because the IARC classification covers only the identification and characterization (hazard) of these agents, mixtures, and activities. It does not include the *assessment of risk*, in other words the probability of toxic manifestations under actual conditions of use today and resulting exposure circumstances. This is an important distinction: 'hazard' is not 'risk' (Table 2). The IARC classification is about hazard, not risk. Indeed, characterizing a substance as hazardous only implies hazard identification.

In the 'Preamble of the IARC Monographs on the Evaluation of Carcinogenic Risks to Humans' posted on the Internet in January 2006 [3], it is stated that '*A cancer hazard is an agent that is capable of causing cancer under some circumstances, while a cancer risk is an estimate of the carcinogenic effect expected from exposure to a cancer hazard. The Monographs are an exercise in evaluating*

Table 1. Group I: Agents, mixtures, and activities

Agents and groups of agents:
Asbestos
Benzene
Cadmium
Oestrogen therapy, post-menopausal
Oestrogens, both steroidal and non-steroidal
Oral contraceptives, sequential
Silica (crystalline, inhaled in the form of quartz or cristobalite)
Vinyl chloride
Tamoxifen
X-radiation and gamma radiation
Mixtures:
Alcoholic beverages
Analgesic mixtures containing phenacetin
Salted fish (Chinese-style)
Tobacco smoke
Wood dust
Exposure circumstances:
Aluminium production
Boot and shoe manufacture
Furniture and cabinet making
Iron and steel foundry
Painter (occupational exposure)
Rubber industry
Solar irradiation
Tobacco smoking

Table 2. Distinction between hazard and risk

Hazard identification: A source of risk that does not necessarily imply a potential for occurrence. A hazard produces risk only if an exposure pathway exists and if exposures create the possibility of adverse consequences.	
Risk Assessment: A process that involves the integration of data, hazard identification, exposure pathways, and dose-response relationships to estimate the nature and likelihood of adverse effects.	

cancer hazard, despite the historical presence of the word "risk" in the title. The distinction between hazard and risk is important, and the Monographs identify cancer hazard even when risks are very low at current exposure levels, because new uses or unforeseen exposures could engender risks that are significantly higher'.

It is thus recognized that hazard identification is an essential but insufficient component of risk assessment, which also comprises exposure data over time and estimation of the likely risk under actual conditions of use. Because of the conceptual confusion and indiscriminate use of the terms 'hazard' and 'risk', untoward fear of unwelcome end points such as cancer, in many sectors of the general public, is driven by the hazard data misrepresented as the risk data. This misconception often results in political response to perceived fear, sometimes nurtured by narrow or single-issue NGOs driving a media taste for sensationalism, pushing regulatory action to extremes. Some Governments and NGOs seek to ban all hazardous materials by citing the Precautionary Principle, and inferring that the outcome of such application is always benign, that is, better safe than sorry. However, eliminating substances merely on the grounds of inherent hazard denies major benefits to societies and can undermine sustainable development. If we look in other contexts it is readily seen that to ban significant hazards would lead to the elimination of household electricity on the grounds that its hazardous properties can make it lethal in a domestic environment.

Exceptions: Politics or Science

Consider, again, the 99 or so agents and exposure circumstances identified by IARC where exposure to complex mixtures are causally linked to cancer. Oestrogen therapy and of course the contraceptive pill, chemotherapeutic agents used in the treatment of some cancers, the production of rubber, boot, and shoe manufacturing, furniture and cabinet making, and the house painter's environment are among agents and places of work where excess cancers have been reported. Also, let us not forget that alcoholic beverages are class I carcinogens [4]. A ban of these agents and places of work would cause chaos globally. If only for these reasons, IARC could include additional pronouncements in their documents to warn of the potential unintended consequences that might follow extreme control or a ban.

When dealing with potentially harmful substances, that is, those whose hazardous properties could affect human health, the classical three-pronged approach is used:

- hazard identification (characterisation);
- risk assessment;
- risk management.

The IARC classification scheme refers only to the first of these: 'hazard identification'. It does not refer to 'risk assessment', which, as already mentioned, must include the various components of dose and duration of the exposure. In consequence, the IARC classification is not meant to be used as a 'risk management' instrument for regulatory action, and cannot be so used, without the proper risk assessment step.

The Case of the Asbestos Minerals

It should be recognized that the word 'asbestos' is a generic, commercial term that is used to describe a group of six minerals from two very different families of fibrous silicates: the serpentines and the amphiboles. The only serpentine known as asbestos is chrysotile or 'white asbestos', whereas the five amphibole asbestos minerals include crocidolite or 'blue asbestos' and amosite or 'brown asbestos'. With the growing body of recent evidence regarding the distinct 'hazard characterization' of chrysotile versus that of the amphibole varieties of asbestos, the time has come to differentiate better between the characteristic hazards associated with the two types of asbestos. Although the current IARC classification does not make this distinction for the different varieties of asbestos, the various exercises of 'risk assessment' carried over several years of investigations between the two families of asbestos have confirmed that the risk associated with the use of chrysotile is quite different from that known for the amphiboles. In fact, the amphibole asbestos minerals crocidolite and amosite, the only two that are commercially important, have and continue to produce orders of magnitude more disease than does chrysotile asbestos when the fibres are used in the same way [5].

Finally, it is now generally accepted that the much longer residence time (bio-persistence) of inhaled amphibole fibres in the lung is one of the key factors for their much higher pathogenicity compared to chrysotile [6, 7]. Recent quantitative reviews that analysed data from available epidemiological surveys to determine potency of asbestos in relation to fibre types, confirmed the difference in risk between chrysotile and the amphiboles [5, 8]. Recently published experimental bio-persistence studies [9–12] provide strong support for the differences seen epidemiologically from exposure to either chrysotile or amphibole asbestos.

Additionally, many epidemiological studies [13] have shown no evidence of increased cancer risk from chrysotile exposure at presently regulated occupational exposure levels (~1 f/ml, 8-hour time-weighted average), as recommended by the Group of Experts convened by WHO in Oxford (1989). More recently, amulti-centre case-control study in Europe[14] has shown that occupational exposure to asbestos does not appear to contribute to the lung cancer burden in men in Central and Eastern Europe, whereas in contrast, the lung cancer risk in the UK is increased following exposure to asbestos. The authors suggest that differences in fibre types and circumstances of exposure may explain their results.

The methods in use today for controlling chrysotile exposures in the work place have been greatly improved over the years. Thus, instead of concentrations of 50 to 100 fibres/cm^3 that occurred in the past, currently typical exposures are below 1 fibre/cm^3, which carries a low to negligible risk of adverse health effects [5, 15]. Experience from over 50 years of use has shown that amphiboles should be avoided. However, the weight of evidence today indicates that chrysotile can be used relatively safely with low, and generally negligible, attendant risk. Chrysotile in cement products such as water pipes and cement boards for housing makes the products more versatile, enabling them to withstand extremes of temperatures and weather. These can also be produced at affordable cost for developing countries. If its use were proscribed the elimination would, without doubt, cost lives rather than save lives. In many developing countries around the world, there are still thousands of villages without adequate water distribution systems. In November 2006, the US National Academies stated that inadequate drinking water is a leading cause of death in children [16]. '*Inadequate drinking water is the second-leading cause of death among children world-wide, according to a new report from the United Nations Development Program. Almost 2 million children die from unsanitary water every year. Globally, about 1.1 billion people do not have access to clean water, and 2.6 billion lack adequate sanitation, according to the report. Although many countries are improving access to water, drainage systems and the number of households with toilets (these) are not keeping pace (with demand), leading to the spread of disease. In Peru, children in homes with toilets and clean water are 59% more likely to survive childhood than those without, and in Egypt, the number is 57%*'. In Egypt alone, there are presently some 2 400 villages without the infrastructure for adequate clean water distribution. Confronted with this problem, the Egyptian Scientific Research Academy has recently requested reopening and operating chrysotile plants and reintegrating a workforce of 3 500 workers and technicians, taking into account the fact that chrysotile is not dangerous, if the necessary health and industrial measures are applied in these installations. This illustrates the consequences and serious economic and developmental aspects being heaped on the developing world by the environmental imperialism of the pressure groups who perpetuate the misrepresentation of the concepts of hazard and risk.

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