

The Natural Resources Defense Council, a leading environmental nongovernmental organization in the area of toxic substances control, has used IARC cancer evaluations in many of its efforts to reduce the threat of environmental and industrial hazards. The NRDC is concerned that IARC statements not be used as obstacles to protecting public health. This letter demonstrates the importance of the message in the preceding Commentary by Lorenzo Tomatis. —EDITOR-IN-CHIEF

**NRDC**  
THE EARTH'S BEST DEFENSE

NATURAL RESOURCES DEFENSE COUNCIL

February 12, 2002

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Re: Concern that Working Group members who will be assessing styrene have financial conflicts of interest

The Natural Resources Defense Council (NRDC) is a non-profit public interest group using the law, science, and the support of more than 500,000 members nationwide to work towards a healthier environment. We are writing to express our concern regarding the current meeting of the *IARC Monographs Working Group on the Evaluation of Carcinogenic Risks to Humans, Vol. 82: Some traditional herbal medicines, some mycotoxins, naphthalene and styrene*, in Lyon on February 12-19, 2002. Our concerns stem from the evident conflict of interest surrounding the toxicologists who will provide opinion on styrene. The three toxicologists, James A. Bond, Gary P. Carlson, and George Cruzan each have financial relationships with groups representing the interests of the styrene manufacturers. Both Carlson and Cruzan are paid scientific consultants for SIRC, the Styrene Information and Research Center. Bond was employed by CIIT (Chemical Industry Institute of Toxicology), representing chemical manufacturers. The evident conflicts of these three experts is likely to undermine the credibility of the IARC work product on styrene.

Dr. Marcia Angell, senior lecturer at Harvard Medical School, and former editor-in-chief of the *New England Journal of Medicine*, defines a financial conflict as any financial association that may cause a researcher to prefer one outcome over another<sup>1</sup>. Financial conflict, Dr. Angell points out, is a function of the situation, not the investigator's response to it; there is nothing "potential" about it. Angell has spear-headed an important reform movement in medical journals that addresses conflict of interest issues, and her working definition of financial conflict is as applicable to IARC as to other scientific research.

The IARC Monographs are one of the most valuable assessments available to risk assessors and government policy-makers world-wide. NRDC has often cited and quoted the Monographs, and considers IARC a leader in cancer assessment. However, we note that all deliberations of the IARC Working Group are made "behind closed doors", and that no transcripts of the deliberations are publicly available. Most significant, the voting of the Working Group members is never made public. This lack of transparency, and lack of public oversight makes peer-review impossible. This situation would be intolerable except for the respect, credibility, and scientific integrity which has characterized the IARC...until recent times.

Recently, scientists with tremendous credibility have begun to question the scientific integrity of IARC decision-making frameworks as well as the outcomes of particular deliberations. A recent article by Dr. Lorenzo Tomatis, former Director of IARC, suggests that IARC has begun a new trend, towards downgrading carcinogens as follows:

Additional criteria for evaluating carcinogenicity which are related to mechanism(s) of action were originally introduced [by IARC] with the aim of further strengthening the scientific solidity of the evaluations. Unfortunately, such information has not been necessarily used to ensure better protection of public health. During the past few years, atrazine, saccharin, d-(2-ethylhexyl)phthalate, glasswool, rockwool and slagwool were downgraded from "possibly carcinogenic to humans" (group 2B of the IARC classification) to "not classifiable as to its carcinogenicity to humans (group 3 of the IARC classification), and 1,3-butadiene was classified as "probably carcinogenic to humans" (group 2A of the IARC classification), while the National Toxicologic Program of the USA has classified it as a recognized human carcinogen. Evidence for carcinogenicity provided by the results of experimental bioassays has been disregarded on the basis of unproven mechanistic hypotheses. If those hypotheses are shown to be incorrect once they have been tested experimentally, or if they do not account adequately for the wide range of susceptibility that is known to exist in human populations, very serious consequences for public health may follow.<sup>ii</sup>

This new trend towards downgrading carcinogens, coupled with Working Group members with obvious financial conflicts of interest, and the overall lack of transparency in the decision-making and voting processes, threatens to rob IARC of its credibility as an impartial and expert scientific agency.

IARC's recent deliberations on butadiene have also raised controversy. Dr. Benedetto Terracini, was Chair of the IARC 1998 Working Group in which Butadiene was classified as a Group 2A carcinogen. This classification was decided in a very unusual second vote, in which the final count was 14 votes for Group 1 v. 15 votes for Group 2A. Dr. Terracini points out, in a letter to Administrator Christine Whitman, US Environmental Protection Agency, that:

"Multidisciplinary groups of experts are a vital and irreplaceable tool in the exercise of evaluating scientific data (such as that undertaken by IARC, which remains a unique worldwide reference for scientists and public health authorities). Nevertheless, it must be acknowledged that occasionally the end point reflects their composition and the criteria for selecting its members."<sup>iii</sup>

Dr. Terracini's statement captures a fact that IARC does not seem to officially recognize; the composition of the panel members will affect the outcome of the decision. By choosing panel members whose financial ties with the industry are obvious, it is just as obvious that the decision will be biased towards favoring industry interests. Is IARC allowing the styrene industry to assess its own product, using the good name of IARC to lend credibility to the affair?

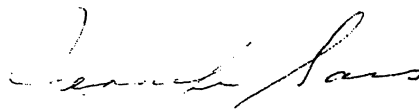
A consortium of a dozen prominent medical journals, including Lancet, the New England Journal of Medicine, JAMA, and others have recently responded to the problems of conflict of interest in medical research with progressive policies that will minimize undue influence of sponsorship on research agendas and results. These efforts include a new policy prohibiting researchers with financial conflicts of interest from authoring review articles, which, like IARC reviews, pick and choose among research findings for salient results for policy-making. In addition, the US EPA Science Advisory Board, which has been widely criticized for undue industry influence in its external reviews of EPA science, is currently addressing the problems of having industry scientists and industry-paid consultants acting as "independent" scientific reviewers. The results of financially conflicted scientific advisors is widely recognized to create undue bias and industry favoritism.

The WHO/IARC have now issued guidelines for disclosure of potential conflicts of interest by scientific experts selected to serve on task groups. Those who worked for adoption of these guidelines hope that they will be fully applied, and that to the extent possible panel members will be chosen who do not have financial conflicts of interest of any kind (particularly with the chemical industry and other business interests). It is hoped that efforts will also be made to assure that, to the extent that biases exist in panels, there will be an attempt by IARC to assure that there is a balance of viewpoints.

NRDC requests that IARC, in the interests of preserving the credibility and scientific integrity of the premiere international body of cancer assessment, remove from its Working Group any members with a financial conflict of interest. We appeal to the IARC as scientists, as persons of integrity, and as protectors of public health.

Respectfully,

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<sup>i</sup> Marcia Angell. Remarks delivered at the HHS conference on financial conflicts of interest. August 16, 2000. Available electronically at <http://ohrp.osophs.dhhs.gov/coi/angell.htm>

<sup>ii</sup> Lorenzo Tomatis. The IARC Monographs Programme: Changing attitudes towards public health. Int J Occup Environ Health, in press. 2002

<sup>iii</sup> Benedetto Terracini. Letter to Administrator Christine Whitman, US Environmental Protection Agency. August 10, 2001.