

February 25, 2002

Dr. Gro Harlem Brundtland
Director-General
World Health Organization
20 Avenue Appia
CH 1211 Geneva 27
SWITZERLAND

**Re: Implementation of WHO Guidelines on Disclosure of Interest by Members of WHO
Expert Panels**

Dear Dr. Brundtland,

We are concerned about the problems of corporate influence and undisclosed conflicts of interest in the development of documents by WHO agencies, particularly regarding the cancer-causing properties of major industrial products and pollutants. There are two WHO agencies involved in this area about whom serious questions of scientific objectivity have been raised. The WHO's recent development of Disclosure of Interest Guidelines in the selection of outside experts was an important step in the right direction, but the implementation of these Guidelines will make all the difference in determining whether the problems will be properly handled.

Problems in evaluation of carcinogenicity of chemicals have been recently identified at a WHO organization, the International Agency for Research on Cancer (IARC) in Lyon. Dr. Lorenzo Tomatis, former Director of IARC, suggests that IARC has begun a new trend towards downgrading carcinogen classifications of chemicals on which there were positive results in experimental bioassays (1): "Evidence for carcinogenicity provided by the results of experimental bioassays has been disregarded on the basis of unproven mechanistic hypotheses." Dr. Tomatis warns that if those hypotheses are shown to be incorrect once they have been tested, very serious consequences for public health may follow. Newly released data on cancer in workers at a U.S. plant making one of the chemicals whose carcinogenic rating was downgraded by IARC, the herbicide atrazine, suggests that positive experimental cancer findings were indeed predictive of carcinogenicity in humans (2).

Experimental findings in cancer bioassays have an extremely high correlation with human carcinogenicity in the substances on which relatively complete information exists. All human carcinogens that have been tested in animals are likewise significantly carcinogenic experimentally. Equally important, nearly one-third of the known human carcinogens were first discovered in animals and only subsequently in humans. An improved understanding of mechanism(s) of action of carcinogens may indeed contribute to strengthen the evaluation of cancer risks. However, toxicological research openly or surreptitiously sponsored by industrial concerns should not lead to hastily reached conclusions, largely based on unproven hypotheses championed as being either correct or exclusive in explaining the complex critical effects of toxic substances on experimental animals, let alone on humans.

Another UN agency, the International Program on Chemical Safety (IPCS), is also now set to embark on a scientific analysis of mechanistic hypotheses of interpretation of the human relevance of positive experimental findings in cancer bioassays. If IPCS gets into this area, it should be done by an impeccable panel of independent experts whose qualifications and scientific objectivity are beyond question, given the recent pattern of these theories being used to undermine regulation of major industrial chemicals. It was a protest by 81 scientists over corporate influence at IPCS that led WHO to develop its Disclosure Guidelines (3).

The Natural Resources Defense Council (NRDC) and the California Environmental Protection Agency wrote earlier this year to IARC, protesting the presence of at least 3 scientists closely allied with the styrene industry on a Task Group who had been invited by IARC to serve on a Task Group that will this month be evaluating the carcinogenic potential of chemicals including styrene. NRDC is the leading environmental non-governmental organization (NGO) in the U.S. in the field of toxic substances control. IARC official J. Rice would not consider removing the styrene industry related scientists from the panel. He suggested that IARC *might* permit a scientist from NRDC or some other NGO to come as a nonvoting observer, at NRDC's expense, to a future IARC panel meeting.

We are also concerned about the role of "observers" at meetings of WHO agency scientific expert groups. At the IARC Task Group meeting where the carcinogenic evaluation of 1,3-butadiene was made in 1998, there was a highly unusual second vote conducted the day after the group had voted 17-13 to classify butadiene as a human carcinogen. One of the scientists who voted in the majority left the meeting that day and thus did not return the next day. Observers and panel members allied with the oil and rubber industries were that evening able to persuade two others to reverse their votes, and without any discussion of why such re-voting was justified, a second vote was allowed the next day, with the result that butadiene was downgraded to *probable* human carcinogen by a vote of 15-14. The panel chairman, Benedetto Terracini, requested IARC to disclose in the "monograph" that the vote had been so close and later complained to IARC for not having made such disclosure (4). There have been other expressions of concern over the participation of observers affiliated with financially interested parties (1). We feel that limiting who can come as observers has in practice limited participation to corporate representatives. Allowing observers to sit at the table with members of the IARC Task Groups, unidentified (with different-colored tags) as observers, and participating in the meetings as equals has exacerbated this problem. WHO expert meetings should be open to the public or closed; and if open, there should be an effort by WHO to financially assist the participation of scientists representing environmental NGOs and trade unions.

Dr. Rice commented on how IARC has applied the WHO Disclosure Guidelines in a recent message to Dr. B. Castleman. "Each case of a declared interest is decided on its own merits. In any case, declared interests (if any) are stated by each person at the opening session of the meeting. If we decide that some one with essential expertise has too close a tie to industry, we either decline his/her participation with thanks; or offer him/her observer (non-voting) status; or require that they recuse themselves from an evaluation that involves a conflict. We have 'disinvited' individuals, yes, after receiving their statement of interests." We have not heard of any participants with vested interests recusing themselves from voting.

Dr. Rice offered to meet with NRDC when he returns to Washington at the end of February, and NRDC in response asked to be provided with the following in advance of the meeting:

-- recent figures on how many Working Group members had financial conflicts-of-interest, how many were asked not to take part, how many recused themselves, and how many had conflicts but were allowed to participate

-- copies of the declarations by participants in the Monographs for which there have been "apparent" conflicts of interest (e.g., for styrene, butadiene, saccharin, atrazine, methyl t-butyl ether, glass wool).

Under the WHO Guidelines, the experts' declarations may be made publicly available in cases where the objectivity of the meeting is being questioned.

In his message this month to Dr. Castleman, Dr. Rice wrote, "It is getting very difficult to find individuals who have contributed significantly to the scientific literature on specific chemicals and who have no research funding or other connection with industry." While we share the concern that the high scientific quality that characterized the IARC Monographs in the past should be preserved, we feel that there are sufficient independent scientists with expertise in carcinogenesis available in governments and academia; and we see this attitude at IARC as a capitulation to corporate influence rather than a proper implementation of the WHO Guidelines.

We feel that it is very important that the WHO Director-General's Office establish implementation procedures for the Guidelines at all WHO institutions. In order to protect the integrity of WHO institutions, it is necessary that genuine efforts be made to assure that financial conflicts of interest are fully disclosed and analyzed. If an individual has such a conflict of interest, it should be presumed that s/he cannot be totally objective and therefore should not be a member of the scientific panel. While it is appropriate to open Task Group meetings with discussions of potential conflicts and biases of panel members, we feel that it is also important to exercise judgment in the selection of panel members, based on their disclosure forms and relevant information on the chemicals to be studied and related business interests, in selecting who is invited to participate in the first place.

Transparency is essential to the process, as WHO clearly realized in establishing the Guidelines. There should not be a high threshold for the release of disclosure forms by WHO and WHO agencies, when questions of scientific objectivity and balance of expert groups are raised. We accordingly request that, first of all, IARC be instructed to comply with the above-mentioned request from NRDC for declaration forms immediately.

These matters may be properly taken up by the World Health Assembly and at the next meeting of the IARC Governing Council.

We look forward to hearing from you soon. Please respond to Dr. Barry Castleman.

Sincerely,

Olav Axelson, M.D., Sweden, Division of Occupational and Environmental Medicine, Linkoping University <olav.axelson@ymk.liu.se>

Barry Castleman, Sc.D., USA, Environmental Consultant <bcastle@bcpl.net>

Jayshree Chander, M.D., USA, Department Community and Family Medicine, University of California-San Francisco. <jypsyjays@hotmail.com>

Annette M. David, MD, Philippines, Clinical Associate Professor, Pulmonary Medicine University of the Philippines <am david@ite.net>

Samuel Epstein, M.D., USA, Professor Emeritus, Environmental and Occupational Medicine, University of Illinois epstein@uic.edu

G Franco, MD, Italy, Chair Occupational Medicine, University of Modena <franco@unimo.it>

Janvier Gasana, M.D., Ph.D., USA, Department of Public Health, Florida International University <gasanaj@fiu.edu>

Fernanda Giannasi, Brazil, Engineer at Labor Inspectorate Sao Paulo, Coordinator of Ban Asbestos Virtual Citizen Network of Latin America <giannasi@telnet.com.br>

Philippe Grandjean, MD, PhD, Denmark, University of Southern Denmark <pgrand@health.sdu.dk>

Morris Greenberg, M.D., United Kingdom, Former HM Inspector of Factories; Former Senior Medical Officer, Division of Toxicology and Environmental Health, Department of Health

Kim Hooper, Ph.D., Hazardous Materials Laboratory, California Environmental Protection Agency, USA <kim_hooper@hotmail.com>

James Huff, Ph.D., USA, National Institute of Environmental Health Sciences, former Chief of the IARC Monographs Programme <huff1@niehs.nih.gov>

Michael Jacobson, Ph.D., USA, Executive Director, Center for Science in the Public Interest <mjacobson@cspinet.org>

T. K. Joshi, M.D., India, Project Director, Centre for Occupational and Environmental Health, Lok Nayak Hospital <joshitk@vsnl.com>

Kulkarni G.K., M.D., India, President - Indian Association of Occupational Health (IAOH)

Joseph LaDou, M.D., USA, Director, International Center for Occupational Medicine, University of California School of Medicine <joeladou@aol.com>

Maria Mazaheri, M.D., Iran, Department of Occupational Medicine, Tehran University of Medical Sciences <maria_mazaheri@yahoo.com>

Yalemtsehay Mekonnen, Ph.D., Ethiopia, Addis Ababa University <yalemtsehay@yahoo.com>

Ronald Melnick, Ph.D., USA, National Institute of Environmental Health Sciences

Dario Mirabelli, M.D., Italy, Unit of Cancer Epidemiology, San Giovanni Battista Hospital and University of Turin

Roderico Ofrin, M.D., Philippines, Faculty of Health Sciences, University of the Philippines Open University

Timo Partanen, Ph.D., Costa Rica, Central American Institute for Studies on Toxic Substances, Universidad Nacional <timo_partanen@yahoo.com>

Friedrich Pott, M.D., Germany, former Head of the Department of Experimental Hygiene, Heinrich Heine University <0217153853-0001@t-online.de>

Joel Marc C. Rubio, MD, Guam, Chief of Medicine, Pacificare Asia-Pacific Health Center

Jennifer Sass, Ph.D., USA, Senior Scientist, Natural Resources Defense Council jsass@nrdc.org

Colin L. Soskolne, PhD, Canada, Department of Public Health Sciences, University of Alberta <colin.soskolne@ualberta.ca>

Maria Lurenda Suplido, M.D., Philippines, Associate Professor, Occupational Medicine University of the Philippines - Open University, Associate Member Philippine Society of Clinical and Occupational Toxicology

Benedetto Terracini, M.D., Italy, Department of Biomedical Science and Human Oncology, University of Torino

Lorenzo Tomatis, M.D., Italy, former Director of IARC <ltomatis@hotmail.com>

Andrew Watterson PhD, Scotland, Co-ordinator, Occupational and Environmental Health Research Group, Stirling University

Catharina Wesseling, M.D., Ph.D., Costa Rica, Central American Institute for Studies on Toxic Substances, Universidad Nacional

Note: Institutional affiliations of signatories are for identification purposes only.

REFERENCES

1. Tomatis L. The IARC Monographs Program: Changing Attitudes Towards Public Health. *Internat. J. Occ. Envir. Health* (in press, 2002).
2. Blair A. (U.S. National Cancer Institute) letter to J. Blondell (U.S. Environmental Protection Agency), Nov. 14, 2001.
3. Abrams H. et al. Letter to the World Health Organization, International Labor Office, United Nations Environment Program, and International Program on Chemical Safety. *Arch. Envir. Health* 51: 338-339 (1996).
4. Terracini B. letter to C. Whitman (Administrator, U.S. Environmental Protection Agency), Aug. 10, 2001.