MINUTES

Subcommittee on Environmental Carcinogenesis

National Cancer Advisory Board

November 15, 1982

The Subcommittee on Environmental Carcinogenesis, National Cancer Advisory Board (NCAB), met on November 15, 1982 in Conference Room 11A10, Building 31, National Institutes of Health, Bethesda, Maryland.

Members Present

Mr. Sheldon Samuels (Chairman), AFL-CIO
Mrs. Angel Bradley, NCAB
Dr. Tim Lee Carter (ex-officio), Carter Clinic
Dr. William Powers, Harper Grace Hospital
Dr. Peter Pruess, Consumer Product Safety Commission
Dr. Janet Rowley, University of Chicago
Dr. Gerald Wogan, MIT

Dr. Richard H. Adamson (Exec. Sec.), NCI

Members Absent

Dr. Elliott Harris, NIOSH
Dr. Allen Heim, FDA
Dr. David Rall, NIEHS
Dr. Irving Selikoff, Mt. Sinai School of Medicine
Dr. John Todhunter, EPA

Invited Guests

Dr. Donald Barnes, EPA
Dr. Robert Brandt, OSHA
Dr. Charles Brown, NCI
Dr. William Nicholson, Mt. Sinai School of Medicine

Others Present

Mr. Jerry Boyd, The Cancer Letter
Mr. Jeff Christy, The Blue Sheet
Dr. John Festa, American Paper Institute
Dr. David Howell, NCI
Ms. Inga Park, Department of Energy
Ms. Harriet Stern, Geomet Technologies

Opening the meeting, Mr. Samuels expressed the opinion that the subcommittee's work to date has been very fruitful. He said that the subcommittee has received documents from the American Petroleum Institute, among which is an excellent paper by Dr. Lester Lave. Mr. Samuels also mentioned that at the last meeting of the subcommittee, Dr. Lamb, an unscheduled speaker, had been permitted to deliver a talk whose duration was as long or longer than those which were on the agenda. However, there was a subsequent telephone call to Dr. Adamson from Mr. O'Leary of the Chemical Manufacturers Association, who felt that insufficient time had been provided for presentation of his organization's viewpoint. Dr. Adamson pointed out to Mr. O'Leary that, in his opinion, Dr. Lamb had been given ample opportunity to speak, even though he was an unscheduled speaker. Moreover, Dr. Adamson added that members of the public present at the meeting were free to express their views in writing to him as Executive Secretary within ten days, and that this time limit would be extended as necessary to permit Mr. O'Leary such an opportunity. Although Mr. O'Leary did not subsequently submit a written complaint, Drs. Powers and Wogan suggested that Dr. Adamson write Mr. O'Leary asking him if he wishes to make a formal complaint or if he considers the matter closed.

Mr. Samuels then summarized the accomplishments of the subcommittee's first two meetings, pointing out that a main theme has been that NIH should not be doing risk assessment with regulation in mind. He added that after the present meeting, he, Dr. Adamson, and any other members who wished to participate would develop a draft paper summarizing the subcommittee's findings and suggestions. He suggested that this paper be given to the members of the subcommittee for their comments and then submitted at the January meeting of the NCAB for the Board's consideration, after which the paper could be reworked and resubmitted to the NCAB for approval as a policy paper of the NCI.

Since there was general agreement with this plan, Mr. Samuels next introduced Dr. Charles Brown, who presented a preliminary definition of quantitative risk assessment that was developed as a result of the subcommittee's first two meetings. After extensive discussion, during which several modifications were made, the subcommittee agreed on the following definition:

> Quantitative Risk Assessment. The assessment of both hazard and exposure information for purposes of estimating the likelihood that hazards associated with the substance will be realized in exposed individuals or populations. This assessment involves two steps:
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> (1) HAZARD IDENTIFICATION/CHARACTERIZATION (QUALITATIVE RISK ASSESSMENT)
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> The characterization of toxicity to humans as determined from observations on human populations and/or from experimental systems;
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> (2) QUANTITATIVE RISK ESTIMATION
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> The process by which the risk of disease or death in a population exposed to a toxic agent is related quantitatively to the pattern

of exposure, including factors such as the intensity and duration of exposure. The quantitative process includes an estimation of uncertainties.

Since the definition of quantitative risk assessment was the first item on the subcommittee's draft paper, Dr. Nicholson suggested that the second item be the purposes beyond regulatory action for which quantitative risk assessment could be used. As an example, he pointed out that the apparent imminence of increased abestos-related cancer, and the potential litigation associated with it, place quantitative risk assessment in a social/economic role. Furthermore, this is a situation in which risk assessment also focuses attention on needs for research, surveillance, possible intervention, and treatment.

Mr. Samuels then suggested that the third item be consideration of the institutional arrangements of quantitative risk assessment: i.e., who is to do the work and what safeguards will surround the effort. He felt that there should be a separation between research and regulation, and that quantitative risk assessment should initially be done by a research establishment that has no regulatory function. He added that this does not preclude replication of this work by regulatory agencies.

In response to a question from Dr. Powers concerning risk assessment of low-level radiation, Dr. Adamson explained that the NIH was directed by Dr. Brandt, Assistant Secretary for Health, to consider how best to proceed with the development of radioepidemiologic tables that would enable a calculation to be made of the likelihood that a paticular cancer was caused by exposure to low-level radiation from fallout from U.S. weapons tests in the 1950s and early 1960s. A subcommittee of the DCCP Board of Scientific Counselors was subsequently appointed by NCI at the request of the Director, NIH, to develop the necessary plans to prepare the tables, but not to prepare the tables themselves. Dr. Adamson added that the tables will probably be developed by a group outside the NIH and will then be peer reviewed by another, independent organization.

Dr. Carter pointed out that the Centers for Disease Control (CDC) is a non-regulatory agency well-equipped to conduct risk assessment. Mr. Samuels agreed that CDC might be appropriate in many instances, but suggested that in a larger sense, the Surgeon General might marshal whatever resources available to him on an ad hoc basis to do risk assessment. In situations where originators of data are outside the research establishment, the Surgeon General might create a special committee to evaluate the data. All deliberations of this kind would be conducted as peer reviews and would take place at open meetings.

Dr. Powers noted that it is part of the purview of the National Cancer Advisory Board to recommend to the National Cancer Program such activities as the unbiased accumulation of data and other resources for use in cancer risk assessment, and that this information might eventually be made available as a resource to the public.

Mr. Samuels next suggested that the fourth item on the paper be the application and validity of research models with respect to human cancer, and that it include consideration of the nature, limitations, and role of scientific models used in risk estimation.

For the fifth item, Mr. Samuels proposed a reaffirmation that the terms "safe" and "safety" not be used in risk assessment, since they have no scientifically demonstrable basis. Dr. Powers suggested that the term "tolerable" might be more appropriate under certain circumstances.

Dr. Wogan recommended that the sixth item be a positive statement of the contribution of NCI research to risk assessment. Dr. Rowley felt that this should be expanded to include all research institutions which use such techniques as chromosomal aberrations, DNA-adduct formation, sister chromatid exchange, and analysis of urinary mutagens to contribute to risk assessment. Dr. Wogan also suggested that the contribution of such research initiatives as biochemical epidemiology be mentioned.

For the seventh item, it was suggested that the draft document reaffirm the NCI role in environmental carcinogenesis, including selection of compounds and methods of testing through NCI's representation on the Executive Committee of the NTP.

Dr. Nicholson proposed that the eighth and last item be a statement concerning the uncertainties of quantitative risk assessment, including the influence of the quality of underlying data and the power of negative studies. He also felt that any risk estimate should specify its meaningful biological limits: i.e., the range of biological consequences of a given risk.

Mr. Samuels added that while the draft document focuses specifically on the problems of assessing risks from carcinogens and carcinogenic processes, there should be no implication that the principles articulated in the document are limited only to risk assessment of carcinogens. To emphasize this point, Mr. Samuels suggested that the presentation to the subcommittee by Dr. Robert Tardiff on risk assessment activities at the National Academy of Sciences be referenced in the document, as well as a paper by Dr. DeNevers on setting exposure standards in various parts of the U.S. Government.

Finally, at Mrs. Bradley's urging, the subcommittee agreed that the draft document should be entitled "Policy of Risk Assessment of the Health Effects of Hazardous Exposures to Populations."

Since there was no further business to conduct, Mr. Samuels thanked the members of the subcommittee for their efforts and adjourned the meeting.

Richard H. Adamson, Ph.D.
Executive Secretary

Executive Secretary's Note: The following documents were provided at this meeting:

Agenda
Definition for Quantitative Risk Assessment