UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

February 25, 1987

SAB-EC-87-023

The Honorable Lee M. Thomas
Administrator
U. S. Environmental Protection Agency
401 M Street, S.W.
Washington, D.C. 20460

OFFICE OF
THE ADMINISTRATOR

Dear Mr. Thomas:

As part of an ongoing series of research-in-progress reviews, the Science Advisory Board has reviewed the Office of Research and Development's Integrated Air Cancer Project.

The Integrated Air Cancer Project views air pollution from the standpoint of the receptor and tries to address these issues: (1) what components of polluted air pose the greatest potential cancer risk, and what are the sources of those components; and (2) how are primary emissions dispersed, transported and transformed in the atmosphere, and what are humans actually exposed to in the ambient environment?

The Agency requested that the Science Advisory Board address eight specific questions in three broad areas of strategy and approach, relevance to risk assessment, and determination of health effects. To address these questions, the Science Advisory Board formed the Integrated Air Cancer Project Research Review Subcommittee.

After reviewing a written description of the program and the results of previous technical peer reviews, the Subcommittee heard briefings on the program September 16 at the Health Effects Research Laboratory in Research Triangle Park, North Carolina. The following day, the Subcommittee asked additional questions of the researchers, prepared a draft report, and provided an oral summary of its findings to the researchers and the laboratory management.

In general, the Subcommittee finds the Integrated Air Cancer Project to be scientifically well-founded. The project represents a logical and appropriately innovative approach that can achieve its long-range goals of addressing these complex environmental health issues. The project effectively exploits some of the research tools and results developed in the past decade and presents an example of

effective multi-laboratory research management within the Agency. For the first time, the Agency is addressing the carcinogenic potency of mixtures of materials in the air. This approach is a critical step to characterizing the exposure of humans to a complex environment.

The attached report details the Subcommittee's findings. The Subcommittee concludes that this project is well planned, organized and executed. The project could be improved by considering three highlighted recommendations. First, to obtain the greatest short-term benefit from the work done in this program, the Subcommittee recommends that EPA give increased attention to both data presentation and exploratory data analysis used to discover new relationships or confirm certain hypotheses. Second, the Subcommittee believes that chemical compound identification ought to proceed more quickly. The importance of compound identification to the project's first objective of carcinogen designation merits additional effort. Finally, the Subcommittee recommends that an epidemiological perspective could aid in developing the link of the chemical studies to cancer risk in human populations.

Through the efforts of the project's leaders, and the cooperation and support of the laboratory directors, an extensive multi-laboratory team has been asssembled which is actively and effectively working together to accomplish the goals of this long-range and complex project. Since its inception, the project has been productive and has achieved important new results. It promises to remain productive. The Subcommittee commends the project managers, the project task leaders, the researchers, the laboratory directors, and the Agency for the success of this project to date.

The Subcommittee strongly supports continuation of this project. This recommendation is based on the scientific merit of the work undertaken and its potential use as a training ground for Agency scientists undertaking multidisciplinary environmental research.

The Subcommittee appreciates the opportunity to conduct this review and would be pleased to discuss it further with you. We would appreciate a formal response to the conclusions and recommendations presented in the report.

Sincerely,

George M. Hidy
Chair, Integrated Air Cancer Project
Research Review Subcommittee
Science Advisory Board

Norton Nelson
Chair, Executive Committee
Science Advisory Board

REVIEW OF THE OFFICE OF RESEARCH AND DEVELOPMENT'S

INTEGRATED AIR CANCER PROJECT

REPORT OF THE INTEGRATED AIR CANCER PROJECT

RESEARCH REVIEW SUBCOMMITTEE

SCIENCE ADVISORY BOARD

February 1987

U. S. ENVIRONMENTAL PROTECTION AGENCY

NOTICE

This report has been written as a part of the activities of the Science Advisory Board, a public advisory group providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide a balanced expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency, and hence the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute endorsement of recommendation for use.

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EXECUTIVE SUMMARY

The Subcommittee finds that the Integrated Air Cancer Project (IACP) is a scientifically well-founded initiative that has effectively applied current knowledge of field sampling, chemical analysis, source-receptor linkage methods and mutagenic testing. It has also systematically addressed the carcinogenicity of mixtures in ambient air. Four important achievements have occurred in its early stages. These include: (a) developing methods for sampling and testing organic mixtures for mutagenicity; (b) segregating non-volatile and volatile organic fractions contributing to mutagenicity; (c) demonstrating mutagenicity in organic products of atmospheric reactions; and (d) applying receptor modeling to estimate source contributions to airborne organic mutagens.

The Subcommittee attributes the early achievements of the IACP to its leadership and the cooperation of participating staff. To date, the leadership has successfully resolved the potential difficulties in merging skills from four different laboratories,* and have produced a relatively stable funding base, and reinforced the need for cooperation at the staff level.

The Subcommittee suggests that IACP can further its results by aggressively conducting chemical analysis for mutagenic compound identification. The project should present the data in a uniform framework applying statistical methods. The Subcommittee encourages exploratory data analysis to seek important interrelationships in the data set. The project also would benefit by the participation of an epidemiologist. Through this interaction, the project can collaborate more closely with EPA's expanding risk assessment capability.

At the request of EPA, the subcommittee evaluated three groups of eight specific issues. These include:

Strategy and Approach

1. What is the role of IACP in Clean Air Act (Section 112) strategy development?

   Subcommittee response: The results of the project will assist EPA in addressing the nature, potency and origins of organic air toxicants. It will also provide sampling test methods and guidance on control priorities.

* These are the Air and Energy Research Laboratory (AERL), the Atmospheric Sciences Research Laboratory (ASRL), the Environmental Monitoring Systems Laboratory (EMSL), and the Health Effects Research Laboratory (HERL).

2. Does IACP provide a new means to understand the behavior of airborne toxics?

   Subcommittee response: By integrating chemical identification, mutagenic activity and source contributions, the IACP will improve our understanding of the behavior of airborne toxics.

3. Does IACP assist in developing risk assessment methods?

   Subcommittee response: Although the project does not address risk assessment per se, IACP will stimulate methods development.

4. Should IACP address control technology?

   Subcommittee response: It is premature to factor emission controls into the current research design.

Relevance to Risk Assessment

1. Does IACP have a suitable approach for its goals?

   Subcommittee response: The methods are carefully considered and use accepted chemistry and bioassay measures. The risk evaluation aspects could be improved by adding personal diaries to the Boise study.

2. Should more emphasis be placed on personal or microenvironmental monitoring?

   Subcommittee response: Incorporating personal monitoring should be a low priority. The ambient and indoor measurements are suitable for the present program.

Bioassay Methods and Health Endpoints

1. Are additional bioassays warranted?

   Subcommittee response: Not at the present time, because the bioassays now in the program are practical and appropriately selected.

2. Should non-cancer endpoints be included?

   Subcommittee response: Given the available resources, this extension would dilute the focus of the project: it is not recommended.

The Subcommittee provides additional recommendations which include: (1) in describing the project, the investigators should make it clear that the project addresses only organics resulting from incomplete fuel combustion and not all airborne toxics; (2) the EPA/Chinese cooperative study of airborne materials (Lung Cancer and Air Pollution Study-Xuan Wei County, Yunan Province, China) may well provide a valuable comparison for the IACP findings; (These two programs should be closely coordinated.) (3) because the IACP's success will depend on long-term, sustained support and funding, EPA should provide this support to ensure that it obtains the full benefit from the work undertaken; and (4) the project has a strong early record of achievement through management and staff focus on its objectives and this focus should be sustained--temptations to expand or dilute the project with additional goals should be resisted at the present time.

INTRODUCTION

At the request of the Office of Research and Development (ORD), the Science Advisory Board agreed to conduct a series of reviews on a number of ongoing research programs within the Agency. Committees of recognized experts have conducted the peer reviews of ongoing research programs to communicate to the Agency the progress being made in meeting research needs pertinent to the development of regulations and policy. One of the reviews requested for FY 1986 was a review of the Integrated Air Cancer Project. ORD's requests to the Science Advisory Board are presented in Appendix 1.

To conduct this review, the Science Advisory Board formed the Integrated Air Cancer Project Research Review Subcommittee, which reviewed documents describing the study, including the results of three previous technical peer reviews. The Subcommittee held a public meeting in Research Triangle Park, North Carolina on September 16-17, 1986, and prepared a draft of this report on-site. Subsequent revisions of the report were handled by mail and telephone conversations. The Executive Committee of the Science Advisory Board reviewed and accepted the report.

The Subcommittee was chaired by Dr. George Hidy of the Desert Research Institute and included two members of the technical peer review panel which reviewed the program in its earlier stages. These members were Dr. Joan Daisey of Lawrence Berkeley Laboratory (previously affiliated with New York University) who chaired the technical peer review panel, and Dr. Dennis Schuetzle of Ford Motor Company. The Subcommittee (Appendix 2) represented a wide range of disciplines both in the health and measurement areas.

OVERVIEW

General Comments

The Subcommittee commends the efforts of the Integrated Air Cancer Project and the team which has undertaken it. The project plan is both scientifically well founded and appropriately innovative in applying

current knowledge. The project is adequately funded in relation to EPA's research priorities. The researchers are highly motivated, and realistic about what their efforts will yield and logical in their approach to this important environmental issue. The team is especially important to the Agency because of its integrated interdisciplinary and multi-laboratory nature and its coordinated approach to the investigation of a complex problem. The management team should be commended and encouraged to continue its efforts.

The Project made early and extensive use of a technical peer review panel chaired by Dr. Joan Daisey. It is important to note that the IACP addressed the recommendations of this earlier review panel and used the panel as part of the planning effort. Indeed, the panel monitored the progress of IACP in implementing its study design. The IACP research team was responsive to the recommendations of the technial peer review panel to improve the project.

Major Project Strengths

The major strengths include the following:

1. Strengthening the program by establishing a technical peer review and advisory panel and being responsive to that panel's recommendations. The panel, which was established in 1984 and chaired by Dr. Joan Dasiey, consisted of outside experts from each of the disciplines represented in the project who were also experienced in interdisciplinary environmental studies.

2. Focusing the program by setting achievable short-term objectives which are targeted to and compatible with its long-term goals.

3. Developing a cost-effective and efficient approach to characterize urban air chemistry and to identify fractions and individual compounds with high mutagenic activity that are good candidates for cancer testing in animals.

4. Developing bioassay directed fractionation and compound identification methods to identify important mutagens and characterize complex mixtures of airborne organic substances.

5. Appropriate selection of practical mutagenic and carcinogenic assays.

6. Developing unique and innovative methodology to detect vapor phase mutagens in primary emissions and their demonstration in laboratory experiments.

7. Identifying mutagens and potential carcinogens originating from atmospheric transformations of primary source materials.

8. Making an innovative use of receptor modeling to understand the contribution of sources of mutagenic compounds in the ambient air.

9. Establishing an effective and committed interdisciplinary research team supported by four laboratory directors who have marshalled sufficient resources to implement IACP.

Major Project Weaknesses

1. Data Analysis

The IACP, at this stage of development, would benefit from increased attention to an in-depth analysis of data, particularly in exposure assessment. The Subcommittee perceived an uneven application of statistical methods to the data representation in the poster presentations and in some of the briefings. "Level A" statistics, the basic statistical representation, should be uniformly applied and complete for the data. Application of "Level B" statistics, or exploratory data analysis, is presently needed. Both elements of this analysis would profit from having someone with oversight responsibility for data analysis. Such oversight in data management and analysis would ensure that the data set is treated statistically in an uniform manner. Exploratory analysis would be used to discover new relationships or confirm certain hypotheses in this large data base that may not be apparent from simpler analyses. Successful completion of "Level B" could require one or two individuals who could work full time on data analysis. The perspective on the IACP results as a whole should profit from this approach.

2. Compound Identification

Carcinogen compound identification merits increased attention. This area is proceeding more slowly than warranted when compared to its importance to the fulfilling the IACP's first objective. This component is essential to addressing the objectives of the study.

3. Epidemiological Input

The involvement of an epidemiologist with the IACP, without converting the project into an epidemiological study per se, would be advantageous because of the additional perspective the epidemiologist and the IACP will provide each other for risk assessment, and the identification of possible opportunities for related studies.

ISSUES

The Agency submitted three groups of issues for the Subcommittee's evaluation. These included the project's overall strategy and approach, its relevance to risk assessment, and bioassay methods and other health endpoints.

Strategy and Approach

1. What role could this research program play in developing the strategies and data necessary for understanding, prioritizing, and regulating pollutants and sources which constitute the most serious risk under the Clean Air Act (e.g., Section 112)?

From the regulatory point of view, the IACP makes three significant contributions. First, the IACP improves EPA's understanding of sources of airborne mutagens; the contribution of atmospheric transformations to the presence of mutagens in ambient air; complex organic mixtures in the atmosphere; and human exposure to and risk from these mixtures. These improvements should lead the Agency to develop a broader perspective on air toxics and different approaches to regulate toxic air pollutants.

Second, the IACP determines the relative contribution of semi-volatile and particulate material to the total burden of mutagenic material in ambient air. Finally, the IACP provides a basis for standardizing methods that define exposure and those inputs to risk analysis which the Agency needs to recognize.

2. Do the strategy and approach taken by this project provide a new avenue to understanding part of the air toxics problem?

Yes. While several approaches (source characterization, source apportionment) used in this study are not new in themselves, the integration of these techniques with mutagenic assessment is unique. The method yields results on the primary sources of ambient airborne mutagens, the identification of compounds accountable for this mutagenic activity, and the importance of atmospheric conversion to the presence of mutagens. The project is unique in its approach to addressing exposure to complex organic mixtures. However, the IACP should be careful in describing its efforts to clarify that its scope is limited to organic products of incomplete combustion and does not include airborne carcinogens, such as asbestos, heavy metals and radon.

3. Does this project represent a useful step forward in developing methods and data for the risk assessment of complex mixtures?

Yes. The study provides an important way to address human exposure to airborne organic species and provides an approach to generating inputs for risk assessment. The IACP wisely has not attempted to address new methods for risk assessment, per se. The IACP should serve as a catalyst for such efforts. Three areas where the IACP might inspire creative related or complementary work are adding an epidemiological perspective to assist in relating to human risk, personal monitoring to develop an exposure estimate, and clinical studies of the effects of respiratory irritants.

4. Should we be considering a research component which would address the effects of emerging control technologies, e.g., catalysts on wood stoves and diesels, on the emissions from sources?

No. The Subcommittee believes it is premature for IACP to be concerned with control technology. First, it is necessary to determine which specific chemical compounds need to be controlled and which sources contribute to the presence of these compounds in the atmosphere. Engineers can then effectively use this information to develop and optimize control devices for these specific pollutants. Scientists have learned that developing "generic" emission control devices may be ineffective. For example, certain emission control devices for diesel engines effectively reduce the mass of particulates but increase the mutagenic potential of the remaining particulate mass in the air.

Relevance to Risk Assessment

1. Does the SAB agree with this strategy and approach to exposure assessment, or do you consider a change in emphasis important to the accomplishment of the project goals?

At the present time, the IACP should emphasize the development of exposure assessment methodology, using bioassay-directed compound identification and the fixed location monitoring at outdoor sites, and secondarily at indoor microenvironmental sites. The Project should consider only limited exploratory work on personal monitoring. As a third priority, IACP also should direct some effort toward identifying tracers in support of the source apportionment studies. IACP could introduce inexpensive daily personal diaries for its study in Boise as a first step towards bringing exposed individuals into the scope of the project. Further thought on how to approach risk assessment and epidemiology could be initiated, but active field work should be deferred to later project stages.

The Subcommittee emphasizes that while certain additional activities (such as some limited personal monitoring for lead, an auto exhaust tracer, and potassium, a wood burning tracer, in Boise) may be of some value, the SAB strongly recommends that the present IACP core program be maintained.

2. In particular, what emphasis should be placed on personal exposure monitoring, microenvironmental monitoring (e.g., indoor), and ambient monitoring at this stage and in the future stages of the IACP?

In order of decreasing importance, the emphasis should be on ambient, microenvironmental, and personal monitoring. The ambient monitoring is important to EPA's present mission and, together with the microenvironmental monitoring, will help EPA address the issue of whether indoor and ambient air contribute significantly to cancer risk. The importance of personal monitoring may increase as the IACP progresses. Until analytical techniques are advanced or new samplers developed, they will not provide the necessary degree of compound speciation and bioassay reliability that can be derived from either ambient or microenvironmental monitoring.

Bioassay Methods and Other Health Endpoints

1. Since bioassay techniques are assumed to be imperfect predictors of human carcinogens, does the SAB feel that additional bioassays should be included at this time?

For the purposes of the IACP, the staff have selected the best available practical methods. The Subcommittee does not recommend inhalation testing at this stage because of the large expense and high uncertainties associated with interpretation. Possibly at a later stage in the project, data will be sufficient to support the design of inhalation studies.

2. EPA's air toxics health research program does address non-cancer health effects. However, these studies are generally oriented toward specific compounds of concern rather than complex mixtures of ambient air. Should health endpoints other than cancer be studied as part of the IACP?

No, because such expansion will dilute the project's current direction, given the available resources. As the IACP progresses in identifying various gaseous and particulate components in wood stove effluents and its atmospheric transformations, other EPA research groups can review these chemicals and determine whether any of them pose non-cancerous respiratory disease hazards. The IACP should not alter its focus to include non-cancer endpoints.

ADDITIONAL SUBCOMMITTEE COMMENTS

Clarification of Objectives

The IACP should edit its written materials and provide status summaries to clarify its objectives and the reasons for selecting a particular subset of activities. In particular, it should emphasize that the IACP is addressing organic products of incomplete combustion and not the full range of air carcinogens that would include such pollutants as asbestos and radon. Such materials should directly state that risk assessment is not a major objective of the IACP. The Subcommittee considered whether the term cancer in the IACP's title could be misleading given the fact that most assays concern mutagenicity. It concluded that the title is appropriate, since ultimately the long-term goal of this project is to assess human exposure to carcinogens.

Extension of the Program

The meteorological measurements could be improved at Boise by including observations of the vertical temperature structure and acoustic sounder recordings, as well as appropriate measures of solar radiation.

EPA might have a research management analyst examine this program, not to change it, but instead to study its success. The results of this analysis then could be applied to other opportunities for collaborative work at EPA and possibly other government research programs.

Miscellaneous Remarks

Other miscellaneous points related to the study include the following:

The China study (Lung Cancer and Air Pollution Study-Xuan Wei County, Yunan Province, China) is an important related study, and the IACP management team should ensure that they are aware of its progress and results.

Because of the respect which the Subcommittee has for this project and the Subcommittee's concern for its future, the following three points are being repeated.

1. The IACP is a long-term project requiring long-term support. The Subcommittee strongly recommends that EPA provide the stable, long-term support needed to complete its program.

2. The IACP is a training ground for Agency scientists to learn to think more broadly and is, therefore, of great importance to EPA beyond the immediate utility of the research results.

3. The IACP needs to be vigilant if it is to maintain its focus over the length of this study. The techniques developed and peripheral results are interesting and valuable in themselves. However, if they are overemphasized within IACP resources, the project may be diluted and may not productively address its long-term goals.

APPENDIX 1

ISSUES FOR CONSIDERATION

The Office of Research and Development has described the Integrated Air Cancer Project (IACP) as a long-range interdisciplinary research program planned to identify principal airborne carcinogens, their sources, and to improve EPA's ability to assess human exposure and risk from these carcinogens. To accomplish these goals, an interdisciplinary team of scientists from four Agency research laboratories has designed a stepwise program of laboratory and field studies with short-term objectives that contribute to the long-range project goals.

The Office of Research and Development referred the following issues to the Science Advisory Board:

1. Air toxics are increasingly important to the Agency from the perspectives of source characterization, monitoring and modeling of exposure and health effects. In addition, complex mixtures in urban air have posed particularly difficult problems for the Agency.

   A. What role could this research program play in developing the strategies and data necessary for understanding, prioritizing, and regulating pollutants and sources which constitute the most serious risk under the Clean Air Act (e.g., Section 112)?

   B. Do the strategy and approach taken by this project provide a new avenue to understanding part of the air toxics problem?

   C. Does this project represent a useful step forward in developing methods and data for the risk assessment of complex mixtures?

   D. Should we be considering a research component that would address the effects of emerging control technologies, e.g., catalysts on wood stoves and diesels, on the emissions from sources?

2. The Agency's risk assessment process requires information from research in a number of areas, such as source characterization, transport and fate, exposure assessment, dose estimation, and health assessment. Exposure assessment has been considered an important component of the IACP program. Intensive chemical and bioassay characterization of specific microenvironments, however, is planned to precede the development of personal monitors for specific pollutants identified as either tracer chemicals or important carcinogens. At this stage of the project, extensive personal monitoring or large exposure monitoring surveys do not appear to be the appropriate approach to meeting the initial project goals.

A. Does the SAB agree with this strategy and approach to exposure assessment or do you consider a change in emphasis important to the accomplishment of the project goals?

B. In particular, what emphasis should be placed on personal exposure monitoring, microenvironmental monitoring (e.g., indoor) and ambient monitoring at this stage and in future stages of the IACP?

3. The IACP has used short-term mutagenesis and animal cancer bioassays as the most reasonable indicators of human cancer.

A. Since bioassay techniques are imperfect predictors of human carcinogens, does the SAB feel that additional bioassays should be included at this time?

B. EPA's air toxics health research program does address non-cancer health effects. However, these studies are generally oriented toward specific compounds of concern rather than complex mixtures of ambient air. Should health endpoints other than cancer be studied as part of the IACP?

APPENDIX 2

U.S. ENVIRONMENTAL PROTECTION AGENCY
SCIENCE ADVISORY BOARD
INTEGRATED AIR CANCER PROJECT RESEARCH REVIEW SUBCOMMITTEE

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