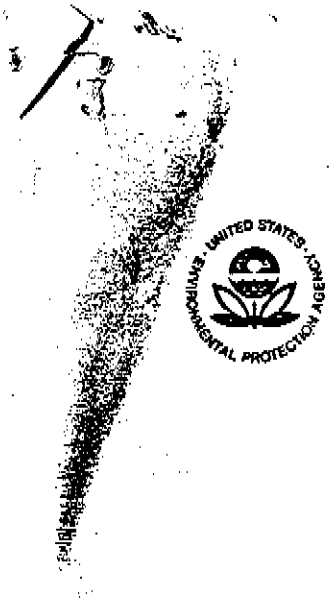

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
THE ADMINISTRATOR

April 26, 1985

Honorable Lee M. Thomas
Administrator
U.S. Environmental Protection Agency
401 M Street, SW
Washington, DC 20460

Dear Mr. Thomas:

The Science Advisory Board has completed its review of the Office of Research and Development's Total Human Exposure Research Program. The Board's review was carried out by a Review Panel of its Subcommittee on Strategic and Long-Term Research Planning. The Review Panel focused on five major topic areas including the development of measurement methods; microenvironmental field studies; total human exposure field studies; dosage research investigations; and statistical protocols, data-base development, and exposure models.

In general, the Review Panel was impressed with the quality of the scientific effort being expended by Agency staff scientists. It was clear to the Panel that, while certain dedicated professionals have recognized the importance of this issue and have carried out research of high scientific quality to improve our understanding of total human exposure, they have done so at a level of support far below what is required. In order to further increase our understanding of this critical issue, further emphasis should be given to this program. The Panel's major recommendations include identification of the issue of total human exposure as an emerging scientific issue of critical importance to the Agency's responsibilities; coordination of future research activities related to total human exposure at senior levels of the Agency; and basing future data collection activities on carefully developed experimental design and probability sampling protocols.

Thank you for the opportunity to present our evaluation of this program.

Sincerely,

Norton Nelson, Chairman
Executive Committee

James Ware, Chairman
Total Human Exposure Review Panel

cc: Mr. A. James Barnes
Dr. Bernard Goldstein
Dr. Terry Yosie

REPORT OF THE
REVIEW PANEL ON TOTAL HUMAN EXPOSURE

REVIEW OF THE AGENCY'S ONGOING RESEARCH IN UNDERSTANDING TOTAL HUMAN EXPOSURE TO INDOOR AND AMBIENT AIR POLLUTION

U.S. Environmental Protection Agency
Science Advisory Board
Washington, D.C. 20460

May 1985

NOTICE

This report has been written as part of the activities of the Environmental Protection Agency's Congressionally established Science Advisory Board, a public group providing extramural advice on scientific issues. The Board is structured to provide a balanced, independent, expert assessment of scientific issues it reviews, 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.

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Key to Acronyms

EMTS	-	Exposure Methods Test Site
EPA	-	Environmental Protection Agency
MEM	-	Microenvironmental Monitoring
NAAQS	-	National Ambient Air Quality Standards
NEM	-	NAAQS Exposure Model
NO_2	-	Nitrogen Dioxide
OAQPS	-	Office of Air Quality Planning and Standards
ORD	-	Office of Research and Development
PEM	-	Personal Exposure Monitoring
SAB	-	Science Advisory Board
SALTRP	-	Strategic and Long-Term Research Planning (Subcommittee)
SHAPE	-	Simulated Human Air Pollution Exposure
TEAM	-	Total Exposure Assessment Methodology
VOC	-	Volatile Organic Compound

I. EXECUTIVE SUMMARY

This is the report of the Science Advisory Board's (SAB) Total Human Exposure Review Panel. The Panel met on February 25-26, 1985 at EPA's Environmental Research Center, Research Triangle Park, NC, in order to review the Agency's research program on total human exposure to indoor and ambient air pollution.

The Review Panel focused on five major topic areas described in the program document prepared by the Office of Research and Development: 1) development of measurement methods; 2) statistical protocols, data-base development, and exposure models; 3) microenvironmental field studies; 4) total human exposure field studies; and 5) dosage research investigations. This program document was well organized, informative, and provided the Panel with an excellent means to focus their questions and discussion.

The Review Panel was impressed with the quality of the scientific effort being expended by Agency staff scientists. It was clear to the Panel that certain dedicated professionals have recognized the importance of this issue and have carried out research of high scientific quality to improve our understanding of total human exposure. While the Panel recognizes this laudable effort, it also notes that the level of support for this effort is less than it should be. The criticisms noted in this report should be taken as the Panel's effort to help the Agency improve the total human exposure program.

Based on a review of the Agency's program document and the presentations made at the meeting, the Panel has three major recommendations. These are that the Agency:

- Identify the issue of total human exposure as an emerging scientific issue of critical importance to the Agency's responsibilities;
- Coordinate future research activities related to total human exposure at senior levels of the Agency; and
- Base future data collection activities on carefully developed experimental design and probability sampling protocols.

The Panel has organized its overall findings into three areas. These are: 1) program management; 2) research activities; and 3) areas of research not currently being performed.

The overall objectives, mandate, organizational structure, and level of support of the Total Human Exposure Program were not clearly stated during the presentations. There also appeared to be no strategic planning, coordination or organized direction of this program from senior levels of the Agency. The technical work is generally excellent but the significance, cost effectiveness, and ultimate regulatory impact is so far-reaching that the EPA management should pursue the program with far more emphasis and central leadership than it currently receives.

The Panel recommends that the exposure assessment activities within the Agency have a central management and administration such that activities in the required technical areas (development of instrumentation, field studies, modeling, and health effects) are thoughtfully integrated. This project integration can only be accomplished effectively by coordination among the EPA Research Committees and project officers at the highest levels within the Agency. This focus and concept of a strategy must be formalized into a commitment by senior EPA management to understand total human exposure to pollutants and its relationship to sources, doses, toxicity, and the protection of public health.

The Agency's ability to perform credible quantitative risk assessments is severely constrained by the limitations in current capabilities in exposure assessment. Although much of the progress in exposure assessment technology that has taken place in recent years was supported by the EPA, the level of support from the Office of Research and Development (ORD), as well as from the program offices has been limited in terms of absolute dollars invested.

The Panel recommends that future advances in the Agency's capabilities for total human exposure assessments should be built on its past accomplishments. In particular, the Panel refers to the pioneering and successful major field studies represented by the Total Exposure Assessment Methodology (TEAM) Study and the Denver, CO and Washington, DC carbon monoxide exposure field studies. The results of these studies can help guide the Agency's approach to environmental monitoring, assessment, and regulation of air pollutants. In addition, work needs to be done on other pollutants besides carbon monoxide.

In reviewing specific research programs, the Panel had several observations: 1) Instrumentation - The Panel recognizes the importance of instrument and method development in meeting the needs of exposure assessment; the current EPA work is very good, however, this effort is not sufficiently comprehensive at the existing level to meet the needs of the field studies. Moreover, the reliance on passive and active sorbent devices should be complemented by other sampling schemes such as sensor arrays, fiber optic devices, solid-state transducers, and electrochemical sensors. 2) Field Studies - The EPA staff are to be commended for their scientific contributions to development of the indirect and direct approaches to exposure assessment, and for their early recognition of the critical role of survey sampling methodology in development of valued exposure assessments. In addition, the Panel applauds EPA's efforts in conducting the TEAM Study and recommends that comprehensive exposure studies of this type be continued and expanded to other pollutants and additional locations. 3) Modeling - The Panel endorses the plan to validate the SHAPE (Simulated Human Air Pollution Exposure) model with actual field data, and the effort to validate and modify the National Ambient Air Quality Standard (NAAQS) Exposure Model (NEM) to accept empirical activity data as input. Such validation would enhance the use of those models in future studies. 4) Dosage Research - Although the Panel's review of this program was brief, it was apparent that the work being done in this area was reasonable and productive. However, it was clear that dosage research was not being conducted in connection with exposure research. The Panel views this as a weakness since a coordinated health component is important to the exposure assessment activity.

The Panel has developed a set of issues that the Agency should consider in defining its research agenda for future human exposure assessments. These include:

1) further efforts in understanding human exposure to nitrogen dioxide and size-fractionated particulate matter;

2) exposure studies should be undertaken for other criteria pollutants;

3) a coordinated effort should be undertaken to develop the tools and methods required for these exposure assessment activities;

4) residential and commercial applications of pesticides and termiticides represent an important potential source of inhaled or ingested exposure; and

5) exposure studies and health assessments should be more carefully coordinated.

II. INTRODUCTION

At the request of the Agency's Office of Research and Development, the Science Advisory Board has agreed to conduct a series of one-time reviews on a number of ongoing research programs within the Agency. The reviews will be coordinated under the auspices of the SAB's Subcommittee on Strategic and Long-Term Research Planning (SALTRP). The purpose of these reviews is to conduct a peer review of an ongoing research program by a review panel of recogized experts in order to communicate to the Agency the progress, or lack of progress being made in meeting research needs pertinent to the development of Agency regulations and policy.

Each review will be conducted by a different review panel and will take place at an appropriate laboratory or other location where the panel will receive briefings and prepare its report. Approximately two reviews will take place each calender quarter. Once a review is completed, the chairperson of each review panel will brief the Deputy Administrator on the findings and recommendations of that panel.

The Review Panel on Total Human Exposure was charged with the task of advising the Agency on how well the research program for Total Human Exposure is progressing toward answering the needs of the Agency, including both whether or not the right research is being conducted to address issues defined by the Research Committee process, and whether the research is being conducted properly.

This report presents the results of the first program review in this series: The Review of the Total Human Exposure Program.

III. REPORT OF THE PROGRAM REVIEW ON TOTAL HUMAN EXPOSURE

A. Background and Limitations of This Review

This is the report of the Science Advisory Board's Total Human Exposure Review Panel which met on February 25-26, 1985 in Research Triangle Park, North Carolina. On the first day the Panel received briefings, allowing EPA project managers and scientists to present the highlights of the Total Human Exposure Program. On the second day the Panel prepared the present report.

The Panel found the material presented to be both interesting and useful. This review was a first, both for the Panel members and EPA staff. There were, inevitably, a number of informational areas, mostly of a non-scientific nature, that were not presented and which would have been useful, in fact necessary, for the Panel to make a clear assessment of the overall merits of the program. Some of these areas were:

- The overall objectives of the program were not clearly delineated, and some of the scientific presentations did not discuss the hypothesis being tested.
- There were no cost or effort estimates of the entire program or its specific components. This made reviewer's curious about the emphasis placed on each program component and its cost-effectiveness.
- No attempt was made to elucidate the mandate for the program, its organizational structure within the EPA, or the chain of command of the staff involved.
- In many cases staff did not discuss their future plans for continuation of their projects, or if they did not expect to continue, why not.
- There was no discussion of other EPA projects that, at least to some degree, could be termed Total Human Exposure Assessments, or why there was not more integration with these projects.
- The charge to the Panel with respect to the report was not adequately expressed, either formally or informally.

On a positive note, the Panel was pleased with the content of the scientific presentations, the manner of presentations, and the fact that the scientific format was geared to the Panel's needs. The research summaries delivered to the Panel prior to the meeting were well organized and informative. Clearly the staff involved in the total assessment program is of very high caliber. The Panel was pleased with the flexibility displayed by EPA staff when requested to substantially alter the afternoon's proceedings, at some inconvenience to individual staff.

The criticisms discussed above should not reflect on the EPA staff or the Panel members so much as on the newness of this particular review process. The Panel recommends that, for future reviews, the Panel chairperson be responsible for consulting with Agency staff prior to the meeting in order to set the agenda and format, taking into account the items discussed above. Whenever possible, the formats of the presentations of the individual scientists should follow, within reason, a standard format, including hypothesis, methods, cost, results, technical problems and future plans.

The Panel trusts that the criticisms made above will not detract from its general view of the merits of the program or of the excellent scientific base developed thus far.

B. Overview of Exposure Assessment Needs Within EPA

Based on its review of the Agency's research program on Total Human Exposure, the following represents the Review Panel's overall conclusions and overview of EPA's programmatic needs.

The EPA's ability to perform credible quantitative risk assessments is severely constrained by the limitations in current capabilities in exposure assessment. Recent research has demonstrated that individual exposure to criteria air pollutants is strongly influenced by indoor environments. The contribution of gas cooking stoves to personal exposure to nitrogen dioxide is one dramatic example, but indoor sources and sinks modify exposure to all air pollutants. Recent work by EPA scientists has shown that indoor sources are equally important for volatile organic compounds (VOC). Better understanding of total human exposure to air pollutants is critical to the long-term effectiveness of EPA's regulatory strategy, to the choice of margins of safety to ambient standards, to the identification of high-risk populations, and to future epidemiologic research.

In another setting, a recent study by the National Academy of Sciences on Toxicity Testing Needs found that the toxicity data base was inadequate for toxicity evaluation for 50% of pesticides and 88% of chemicals in commerce. The Academy recommended that priorities for further testing should be guided by the potential for human exposure, for which the data base was even more inadequate than for toxicity. For toxicity testing, there may be inadequate data for most chemicals, but there is at least general agreement on how the tests should be performed. The science of exposure assessment is less well developed, especially for general population exposures.

Much of the progress in exposure assessment technology that has taken place in recent years was supported by EPA. However the level of support from the Agency's Office of Research and Development (ORD) and the program offices has been limited, and in its aggregate the level of effort has been too meager to permit advances in capability commensurate with the needs for increased numbers of ever more sophisticated risk

assessments. While each program office has specific needs in exposure assessment technology, they also share some generic needs with each other and the ORD. Therefore, it is in their best interests to support a research program focused on improvements in exposure assessment technology. Such a program should be carried out by the ORD, in cooperation with appropriate program office personnel, for several reasons. First, the ORD has personnel with much valuable insight and experience on these issues and is familiar with the needs of the program offices. Second, none of the individual program offices is likely to invest in research which is not closely tied to immediate program needs.

Future advances in the EPA's capabilities for total human exposure assessments can, and should, be built on its past accomplishments. Among these are the pioneering and successful major studies represented by the TEAM (Total Exposure Assessment Methodology) Study and the Denver and Washington, D.C. carbon monoxide exposure field studies.

The results of these studies can help guide the Agency's approach to environmental monitoring, assessment, and regulation of air pollutants. The issues these studies raise include:

- What should be the Agency's regulatory stance toward indoor exposure? Even if the Agency were to take the position that it has no regulatory role in indoor environments, it must recognize in its approach to assessment and regulation that indoor exposures are often greater than outdoor exposures.
- The emerging information about the indoor environment raises doubts about the adequacy and, for the same pollutants, even the relevance, of outdoor monitoring for protection of public health.
- To assess the importance of sources and the amount of a dose, exposures must be characterized.
- What advances in measurement technology are needed for future studies?

On a more operational level, other questions arise:

- Are current and planned expenditures for total human exposure assessment consistent with the Agency's information needs for assessment and regulation?
- What level of precision of exposure information is appropriate in different research and regulatory settings?
- How should monitoring resources be allocated between studies of exposure distributions and monitoring activities in support of epidemiologic research?

To address these issues, the Panel recommends that the Agency:

- Identify the issue of total human exposure as an emerging scientific issue of critical importance to the Agency's responsibilities;
- Coordinate future research activities related to total human exposure at senior levels of the Agency; and
- Base future data collection activities on carefully developed experimental design and probability sampling protocols.

C. Review of Current EPA Programs

1. Program Management

The presentations to the Review Panel by EPA management and staff scientists reflected the view that total exposure assessment is required in order to perform credible risk assessments and, ultimately, to perform the regulatory functions of EPA. The Review Panel agrees with this concept. Moreover, the individual presentations made it clear that several dedicated professionals within the Agency have recognized the importance of this issue and have carried out research of high scientific quality to improve our understanding of total human exposure. Important findings have been reported that can affect both exposure assessment and the EPA's regulatory policies of the future. It was also clear, however, that there is no strategic planning, coordination, or organized direction of this total human exposure assessment activity from senior levels of the Agency. The technical work is generally excellent but the significance, cost-effectiveness, and ultimate regulatory impact is so far-reaching that, in the Panel's opinion, EPA management should pursue the program with far more emphasis and central leadership than it currently receives.

The Panel recommends that the exposure assessment activities within EPA have a central management and administration such that activities in the required technical areas (development of instrumentation, field studies, modeling, and health effects) are thoughtfully integrated. Further, the exposure assessment activities should be linked to the overall risk assessment model presented, i.e., to sources and to the dose/toxicity assessment activities.

This project integration can only be accomplished effectively by coordination among the EPA Research Committees and project officers at the highest levels within the Agency. This focus and concept of a strategy must be formalized into a committment by senior EPA management to understand total human exposure to pollutants and its relationship to sources, doses, toxicity, and the protection of the public health.

2. Research Activities

Of the many components that relate to an overall risk assessment for any particular chemical, many, but certainly not all, were presented to the Review Panel. The overall focus of the research activities presented was on exposure assessment, but there was also some discussion of dosage assessment. Dosage assessment activities, however, do not appear to be coordinated with any of the exposure assessment activities.

Agency scientists have made significant progress in developing the conceptual approach and methodology for determination of total human exposure to pollutants. Basically, two procedures have been suggested and actually implemented on a limited scale. The first is the concept of personal exposure monitoring (PEM). This requires that a small measuring device actually be worn by subjects as they go about their normal activities. The second concept is that of microenvironmental monitoring (MEM), which requires the measurement of a pollutant's concentration in a variety of locations inhabited by people during a normal day's activity and a reconstruction of a complete exposure history by combining these measurements with an activity log. The two methods should yield comparable results if each is performed properly. As yet, comparable results have not been achieved. For example, exposure estimates differ by about forty percent for the Washington, D.C., carbon monoxide study.

The EPA has a substantial program in the development of measurement methods for assessing total human exposure, although most of this activity is clearly funded by the base research and development program. Most of the research presented to the Panel was concerned with the measurement of volatile and semi-volatile hydrocarbons, either by means of a personal exposure monitor or by means of a larger sampler suitable for micro-environmental monitoring. Although there is a major expenditure in developing a sensor for nitrogen dioxide and some effort in developing a sampler to measure volatile organic compounds that are associated with particles of diameter less than 10 μm, there is very little activity in developing instrumentation for the measurement of other pollutants.

Several field studies have been conducted in the past by the EPA. Two of these were related to exposures to carbon monoxide and have been essentially completed and reported. Another study, the Total Exposure Assessment Methodology (TEAM) study was presented in detail. This study is examining exposure to airborne volatile organic pollutants in several locations over time periods long enough to establish temporal patterns. The results, as they define sources of exposure to organic chemicals, are most provocative and indicate that "traditional" sources of exposure may be minor compared to other more "personal" sources. This study, more than any other, provides compelling evidence of the necessity of evaluating total human exposure and of not basing exposure estimates on pollutant concentrations measured only by fixed station monitors.

Finally, some material on dosage evaluation was presented to the Panel. Most of the time was devoted to a study in China that seeks to explain the very high incidence of lung cancer in a small region. Other material of a diffuse and general nature was presented, but it was fairly clear that there is no dosage-research study that is connected with the exposure-research study. The Review Panel views this as a weakness since a coordinated health component is important to this exposure assessment activity. The present health-component would need significant redirection in order to complement the exposure studies reviewed here.

3. Additional Issues Not Currently Being Addressed

As discussed above, the current "Total Human Exposure to Air Pollutants" program within the EPA has been limited in scope. Human exposures have been examined for only a few pollutants. These projects were primarily directed toward deriving a frequency distribution of exposures in a representative population. The relevancy to other useful applications of exposure assessments was not explicitly considered, although further data analysis will greatly enhance their usefulness. Further, the biological and health related endpoints of the EPA's exposure assessment work are not well characterized, are limited primarily to mutagenicity, and are not an integral part of the field and laboratory studies.

This section sets forth a set of issues that the Agency should consider in defining its research agenda for future human exposure assessments. This research should help to quantify population exposure, identify the portion of the population at greatest risk, and identify determinants of exposure (including specific sources, locations, and activity patterns). When linked to health studies, human exposure studies can assist in the quantification of potency factors for a variety of hazardous substances and air contaminants.

a. Nitrogen Dioxide (NO_2) - Studies have demonstrated the importance of unvented combustion sources (mostly in homes) to integrated and peak NO_2 indoor concentrations. Limited personal monitoring has identified the importance of these indoor sources as contributors to total human exposure, but these studies did not utilize probability sampling in selecting participants or monitoring plans. Health endpoints were not examined concurrently with exposures. Actual peak exposures are not well-documented and will not be until instrumentation is improved. The EPA has a direct interest in understanding human exposures to NO_2 in order to provide improved estimates of health effects and to properly restructure air quality standards.

b. Particles - Human exposures to particulate matter is a vexing problem. Indoor concentrations are an important contributor to the integrated exposures to respirable size particles.

However, the size distribution, chemical composition, and, quite likely, general toxicity of indoor particulate matter will differ from that of outdoor particles. The Agency needs to understand human exposures to size-fractionated particulate matter from the perspective of source contributions and by fractional components. Fractional components will have different toxicological effects. The relevant issues include:

1) Characterizing acute integrated exposures to acid aerosols: The covariance of outdoor activities and acid events should be examined. The penetration of acid aerosols into indoor environments, the neutralization of acid aerosols indoors and the generation of acid gases and particles indoors could be additional area of inquiry. Panel members disagreed about the importance and cost-effectiveness of research on these issues.

2) Characterizing human exposure to vehicle exhaust: Receptor modeling of urban aerosols has identified vehicle exhaust as a ubiquitous contributor to ambient particulate matter. Limited in-vehicle studies have demonstrated several-fold higher concentrations than measured at fixed sites. Although in-transit time may be only 5 to 10% of an individual's daily activities, this may represent an important exposure opportunity for specific compounds and metals.

3) Characterizing human exposure to fossil and biomass fuel related primary emissions: It will be important to quantify the amount and location of human exposure to combustion derived particulate matter. The emphasis should be on condensible organic fractions and a few metals (e.g. arsenic, vanadium, selenium).

4) Characterizing human exposures to cigarette smoke: Passive smoke exposure occurs predominantly indoors. Respiratory health effects, including cancer, are either documented or suspected to be associated with exposure to passive smoke. Discerning possible health effects associated with other components of respirable particulate matter will require careful separation of the possible passive tobacco smoke effects. Therefore, an exposure assessment program should utilize appropriate markers for tobacco smoke in characterizing exposures to segments of our population. This might be an area where microenvironment sampling is an appropriate approach.

5) Characterizing asbestos fiber exposures: While friable asbestos insulation material has been noted in schools, offices and homes, an understanding of actual airborne concentrations of asbestos fibers is missing. To undertake appropriate risk assessment and to determine remedial actions, better information on either environmental

concentrations of, or personal exposures to asbestos fibers is needed. These studies should be longitudinal because of the episodic nature of fiber release. They should include residential locations.

c. Exposure studies should be undertaken for other criteria pollutants - The emerging evidence on the importance of indoor environments and personal activities to air pollution exposure suggests that current approaches to air pollutant regulation based on outdoor measurements may become less defensible in the near future. The importance of total human exposure assessment should be reviewed for each criteria pollutant to identify those for which integrated exposure assessment is most urgently needed.

d. A coordinated effort should be undertaken to develop the tools and methods required for these exposure measurement activities.

e. Residential and commercial applications of pesticides and termiticides represent an important potential source of inhaled or ingested exposure - The Agency should undertake a carefully designed study (i.e., such as TEAM) of human exposures to halogenated compounds and to quantify the sources and routes of exposure.

f. Exposure studies and health assessments should be more carefully coordinated - These two components do not necessarily have to be integrated into every study. However, the relevance of the health related research to actual human exposures should be explicit. For example, the mutagenicity work currently associated with the indoor air pollution research program, and identified as a component of the total human exposure program, could be better integrated into measurement and risk assessment activities. Because of the cost and time involved in conducting multi-dose bioassys with pollution mixtures, carefully designed sampling schemes should be employed. Environmental conditions and sample composition must be well characterized. The products of bioassays will be more useful if consistent with observational data (clinical and/or epidemiological). For example, bioassay analysis on suspended particulate matter containing tobacco smoke obtained in homes and offices might help to elucidate the relative hazards of different environments. A significant effort has been made (>$20 million) by the Department of Energy in recent years to provide a battery of chemical fractionation and bioassay techniques that can be used in complex mixtures. This useful published literature should be considered by the Agency in its health effects component.

D. Reviews of Specific EPA Programs

1. Instrumentation

The program described instruments developed primarily for measurements of chemical exposure to selected air pollutants. This work has been successful and useful to field activities. The prime focus has been the development of passive and active sorbent collection devices that are returned to the laboratory for analysis. Plans were suggested to further develop such approaches. This does not seem a proper focus for continued effort. The types of measurement needs for field exposure assessment are broad. Requirements for real-time data, temporal and spatial resolution, large dynamic range, and multidimensional measurements can never be totally met by more or even better sorbent collection schemes. Such schemes have limitations and, therefore, must be complemented by others.

The Panel recognizes the importance of instrumentation in meeting the needs of exposure assessment; however, the current effort is not sufficiently comprehensive at the existing level to meet these needs. A recent workshop at Harvard University sponsored by the EPA and the Gas Research Institute defined the need for field instrumentation to perform exposure measurement. The latest technology in chemical monitoring (sensors and detectors) should be used by EPA researchers to provide new concepts and approaches for chemical pollutant measurement. Such modern technologies as integrated sensing systems (sensor arrays), fiber optic devices, solid-state transducers, and electrochemical sensors can be applied to field sensing problems and should be a part of the EPA's future instrumentation research program.

The development of instrumentation (and all field techniques) is related to the prioritizing of compounds, situations, and parameters required in exposure measurement studies. Then, appropriate strategies (near-term and long-range) should be proposed by instrument developers to satisfy these most important needs using the best available technology. The present schemes for sorbent measurement have important field uses and should be supported but should not be the main focus of future efforts.

2. Field Studies

The EPA's measurement activities related to total human exposure to environmental pollutants fall with the following areas:

- Statistical protocols and experimental design
- Microenvironmental field studies
- Total human exposure field studies

- Dosage research investigations

The first three topics are discussed in this section; dosage research will be discussed in Section D.4 of this report.

a. Statistical Protocols and Experimental Design - The EPA staff are to be commended for their scientific contributions to development of the indirect and direct approaches to exposure assessment, and for their early recognition of the critical role of survey sampling methodology in development of valued exposure assessments. This work has raised a number of outstanding critical statistical issues associated with exposure assessment, such as:

1) optimal designs for direct and indirect exposure assessment studies;

2) statistical validity of indirect exposure assessment;

3) evaluation of benefits (in reducing uncertainty) versus costs of various levels of effort of exposure measurement, with regard to both epidemiological studies and risk assessment.

Methodologic research to clarify these issues should be encouraged, so as to determine the incremental value of intensified measurement programs in exposure assessment, and to guide the design of future studies.

b. Microenvironmental Field Studies - These studies characterize the pollutant concentrations to which people are exposed when they are in specific microenvironments. Most of the work conducted so far is related to carbon monoxide exposures. Clearly, additional studies of the concentration distributions of other pollutants in appropriate microenvironments are needed at this stage. Even within a single microenvironment (e.g., a parking garage), pollutant concentrations are highly variable in space and time, and great care must be taken to obtain suitable measurements so that these concentration distributions can be accurately characterized.

We agree that in future personal monitoring studies, the following should be applied:

1) use of closed format questionnaires;

2) use of automated instrument output; and

3) locating activities to specific census tracts.

These are crucial lessons learned from the Denver and Washington carbon monoxide studies and will improve the validity of future studies.

The objectives and expected benefits of the Exposure Methods Test Site (EMTS) project are not clear to the Panel. Although there are advantages to having a single locale where micro-environmental field studies can be conducted, it would be dangerous to assume that the data obtained at such a locale would be representative of exposures in other cities in other parts of the country. This is because of the many demographic, geographic, and climatological differences between various locations. Hence, the Panel recommends that the degree to which the data from an EMTS is expected to be generic and extrapolatable be established before the project is implemented.

c. Total Human Exposure Field Studies - The Panel applauds the EPA's efforts in conducting the TEAM study, and recommends that comprehensive exposure studies of this type be continued and expanded to include other pollutants and additional locations. New developments in pollutant monitoring technology and biological monitoring should be incorporated as they become available.

Some of the findings of the studies conducted to date suggest that greater attention should be given to incorporating source-receptor considerations into the survey design. In some instances, it appears that much of the variability that shows up in the exposure data could be explained by meteorological factors, such as some receptors being downwind of the source(s), while others are not. A more careful experimental design that includes consideration of these factors, including measurement of appropriate meteorological parameters, will likely lead to more meaningful data in future studies.

The following are some technical comments on TEAM:

1) The intraperson temporal variation in VOC exposure is crucial in risk assessment and should be given a high priority in future studies.

2) Given the substantial measurement error, the estimated exposure distributions can be substantially more heterogeneous than the true exposure distributions. For example, the variance of the estimated exposures is the sum of the variance of the true exposures and the variance of the measurement errors, assuming that: a) measurement errors are homoscedastic, and b) there is no correlation between measurement error and true exposure. Empirical Bayes methods are available for such adjustments.

3) We share the concern about the high refusal rate in the sample enrollment. We would like to see more rigorous efforts in the future to assess the impact of the refusal on the generalizability of the sample. For example, a subsample of the accessible part of the refusals can be offered an incentive to participate, or be offered a less intensive protocol for their participation; the data from

the would-be refusals can then be compared with the "regular" participants to assess the possible magnitudes of selection bias.

3. Modeling

As an alternative to direct personal monitoring of human exposure, the indirect modeling approach offers certain attractive features and has the potential to be cost effective. The essence of the indirect approach is to assess human exposure as it is related to human activities, and to combine pollution measurements with activity data (which could be collected separately) to estimate exposure. Simulation models such as SHAPE and NEM are variants of this approach in which either part or all of the input data are simulated or imputed.

Compared to the direct personal monitoring approach, the indirect approach has the following advantages:

a. Existing pollution and activity data can be reused in comparable future studies, thereby reducing the cost of future studies;

b. The human subjects need not be burdened with the inconvenience of carrying personal monitors during their activities;

c. In the absence of feasible personal monitors, it might still be possible to estimate exposure using the indirect approach as a stop-gap measure; and

d. In conjunction with source-transport models, the indirect approach can be used to impute the would-be exposures under alternative regulatory strategies.

The presentation at the review meeting was focused on one aspect of the indirect approach, namely, the use of microenvironmental monitoring to collect pollution data. The indirect approach can also be implemented with pollution data from a personal monitoring study. For example, pollution data from an earlier personal monitoring study can be combined with the activity data from a comparable sample in a new study. Another example is enhanced personal monitoring, in which extra activity data are collected to make more efficient use of the pollution data. We recommend the collection of activity data in future studies whenever feasible.

The indirect approach remains to be validated empirically with comparable personal monitoring data. We endorse the plan to validate the SHAPE model with actual field data and the mentioned effort by the Agency's Office of Air Quality Planning and Standards (OAQPS) to validate and modify the NEM model to accept empirical activity data as input. Such validation would enhance the use of those models in future studies.

However, it is neither clear which microenvironments and chemicals are of greatest importance nor how to define each microenvironment. Further, identification of the microenvironmental scenarios which will be most effective at modeling exposure must be considered. Subsequent to this prioritization and analysis of microenvironments, cost effective research in this field can be planned.

Although the simulation modeling approach to estimating total human exposures is not without difficulties and weaknesses, it is less costly and potentially more generalizable than direct measurements. The most serious problem with the modeling approach is that, before any model can be used with any confidence, its validity must be carefully and completely evaluated. This requires large quantities of experimental data from specially designed field studies. Failure to obtain a probability sample for microenvironment monitoring is a shortcoming of the Washington microenvironment study, and needs to be addressed in future studies.

Logically, the direct (measurement) and indirect (modeling) approaches should be considered complementary, in that the former provides essential information for the development, validation, and refinement of the latter. Hence, the Panel recommends that the planning for human exposure field studies be carefully designed specifically to provide for the needs of exposure models.

4. Dosage Research

The Panel's review of the dosage research program was relatively brief and occurred at the end of a long day. Hence it was, of necessity, somewhat superficial. Nevertheless, we found that the choice of assays to be included in this program review by the EPA staff was reasonable and that productive work was being done. The people involved appeared to have a good grasp of the scientific issues and potential of their methodology, and to be capable of undertaking additional productive work in this important area. The following are some specific comments:

a. The results of the analyses of volatile organic chemicals (VOC's) in exhaled air in the TEAM study provide an excellent example of the utility of such measurements in field studies. They showed that most of the VOC's were traceable to indoor rather than outdoor sources of air pollution, and identified many previously unsuspected causes of human pollutant exposures.

b. The results of the measurements of alveolar carbon monoxide in Denver and Washington were very useful in demonstrating that ambient carbon monoxide concentrations had very little effect on actual variation in individual overall exposures to carbon monoxide.

c. Current research on the use of short-term mutagenesis bioassays offer promise of developing reliable and efficient assays for source-specific pollutant mixtures from common indoor pollution sources such as cigarette smoke, woodstoves and kerosene heaters. Research of this kind may prove to be useful to the EPA for many other applications involving exposure to organic vapors such as waste recovery and disposal sites.

d. Evidence for human exposure to pollutants can often be made from analyses of biological materials such as exhaled air, urine, blood, hair, etc. Such analyses are particularly valuable when there are multiple routes of exposure, and/or highly variable levels of exposure. Biological samples can show evidence for cumulative exposures, and can indicate whether adverse effects are occurring or are likely to occur.

APPENDICES

REVIEW PANEL ON TOTAL HUMAN EXPOSURE

CHARGE

The purpose of the total human exposure research program is to determine the frequency distributions of exposures of the populations to selected chemicals. The issues center around five major topic areas:

1) Development of measurement methods,

2) Statistical protocols, data base development, and exposure models,

3) Microenvironmental field studies,

4) Total human exposure field studies,

5) Dosage research investigations.

The Review Panel on Total Human Exposure shall advise the Agency on how well the research program for Total Human Exposure is progressing toward answering the needs of the Agency, including both whether or not the right research is being conducted to address the issues defined by the Research Committee process, and whether the research is being conducted properly. The Panel's findings and recommendations will be presented both in a report and in a briefing to be presented to the Deputy Administrator.

U.S. Environmental Protection Agency
Science Advisory Board
Total Human Exposure Review Panel

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