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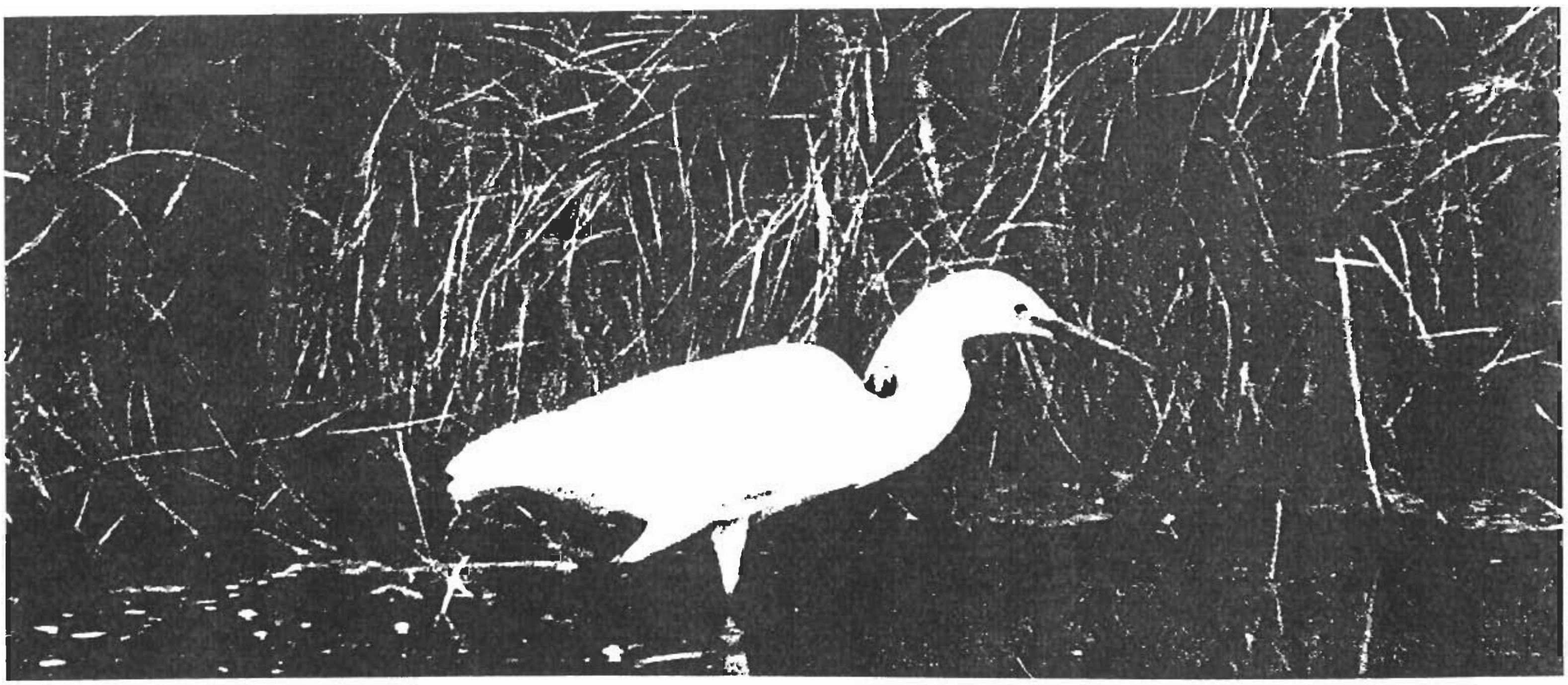
Appendix B: Strategies for Exposure Assessment Research



Report of the Exposure Assessment Subcommittee

Research Strategies Committee

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TABLE OF CONTENTS

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1.0 EXECUTIVE SUMMARY

1.1 Overview

Reducing uncertainty in environmental risk assessments is a major problem facing the U.S. Environmental Protection Agency (EPA). A critical factor in understanding those risks is the amount of available information concerning the number of people exposed to environmental pollutants and at what doses. Although there are efforts underway within EPA to develop such information, a clearly defined research strategy is required to focus the scarce resources available to the Agency.

Strategies for assessing environmental exposures should be based on the need for exposure characterizations in quantitative risk assessment. Such a strategic approach is essential for EPA to effectively carry out its risk assessment functions. At a minimum, the overall strategy should address: interfaces between the three principal methods of exposure assessment (personal monitoring, modeling, and biomarkers); accountability of specific research efforts to overall needs; long-term research commitment; closer ties with other Federal agencies doing similar research; and educational efforts.

In this report, we identify examples of research needed to support a strategic research effort in exposure assessment. These include research on acidic aerosols and gases, biological aerosols, environmental tobacco smoke (ETS), pesticides, volatile organic compounds (VOC), and time-activity patterns and behavior. We also identify the development of biological markers as a promising form of research into determining human exposure.

1.2 Recommendations

The following recommendations represent the most critical issues that we believe the EPA should consider in developing its research strategy for exposure assessment.

1.2.1 Establishment of an Agency-wide research program to provide a basis for improved capabilities for quantitative exposure assessment. Research needs which should be addressed include:

a) development of sampling and analytical instruments and techniques,

b) exposure models and their validation,

c) selection criteria for human populations and other target species for exposure evaluations,

d) protocols for quality assurance of exposure data, and

f) systems for exposure data management and access to data banks.

1.2.2 Development of methods to optimize and facilitate utilization of indirect indices of exposure, such as environmental monitoring data (e.g., ambient air, drinking water) and effects data (e.g., biomarkers, impacts on ecosystems).

1.2.3 Establishment of methods to derive the uncertainties of exposure estimates based on both direct and indirect indices.

1.2.4 Use of the concept of total exposure, recognizing all exposure pathways. Therefore, research should incorporate three principal methods of exposure assessment - personal monitoring, modeling, and biomarkers.

1.2.5 Utilization and development of resources in the academic community to facilitate technical innovation and more universal application of developments in exposure technology.

1.2.6 Establishment of a data management resource on exposure data and encouragement of contributions and utilization by program offices, other governmental agencies, the academic community, and other interested groups.

1.2.7 An increased commitment to extramural research including targeted requests for proposals to increase efficiency, and greater use of the EPA Centers of Excellence program, providing greater support to those Centers which assist the Agency in achieving the goals laid out in its Research Strategy.

2.0 INTRODUCTION

2.1 Overview and Examples

The development of a strategy for research on exposure assessment requires the definition of goals, a recognition of constraints, and the examination of options for achieving the goals. The choice of options should allow for contingency plans which would permit adjustments in the strategy as conditions change.

A good example of a long term research effort with significant payoff for EPA is the Total Exposure Assessment Methodology (TEAM) study. The success of this study has been dependent upon basic approaches to:

a) analytic methodology capable of measuring relatively minute levels of air pollutants,

b) technical developments leading to personal samplers,

c) fundamental improvements in sampling strategy related to assessing individual and community exposures, and

d) the recognition that EPA's focus should be on an individual's total exposure to environmental health hazards.

Successful TEAM products could have been achieved far earlier by EPA scientists if there was a recognition of the importance of long term funding in this area by other EPA offices and by the Office of Management and Budget (OMB).

The relevance of TEAM study findings includes the ability to measure actual human exposure to volatile organic compounds and to assess the relative importance of indoor vs. outdoor exposures; including the recognition that for most toxic air pollutants the home is the major source of exposure. It has provided techniques permitting EPA and state agencies to be responsive to questions concerning extent of exposures in local communities. Much more support of long-term studies of this nature is necessary.

Another example of successful long term research in the development and effective use of tools for exposure assessment, is the study of lead exposure. This has increased understanding of the multiple routes of entry of a single source. EPA in essence has conducted a natural experiment by lowering airborne lead through markedly decreasing allowable gasoline lead content. This has produced a clearcut decrease in lead inhaled directly from automobile exhaust. The larger part of the reduction in body burden was due to a reduction in lead in automobile exhaust which settles as dust on the ground where it can be eaten by children who lick their fingers, where it can be stirred up by human activities and inhaled, and where it can enter the food chain through deposition on edible foliage and through soil from which it is taken up by growing plants.

Finally, we note the recent completion by EPA staff of the draft of an extensive Strategic Plan for Research on Total Human Exposure to Environmental Pollution. While the document is misnamed in that it is really not focused on the strategic level, it contains a good road map which lays out important options for the approach to short term and long term research needs and can profitably serve as a blueprint for agency actions. We understand that a revised draft of the strategic plan is under preparation.

Although these are good examples of relevant long-term research efforts, there have been many opportunities missed because of the relative paucity of long-term research in the area of exposure, an area which is so central to EPA's mission. The Agency has a need to develop a clearly focused centralized program of long term research aimed at improving exposure assessment. In part because of the relative lack of past efforts, and in part because of the many exciting new advances in basic science pertinent to improved exposure assessment, we are highly confident that a long term research program of this nature will lead to major advances of great value to EPA's regulatory decision making.

2.2 Definition of "Exposure"

The term "exposure" is often used without clear definition. For the purposes of this strategy statement, exposure is defined as the environmental concentration of a substance in immediate contact with an organism. Exposure is not synonymous with "absorbed dose". To convert exposure measurements into absorbed dose could require additional information on bioavailability, uptake, and the efficiency of absorption.

2.3 Goal Statement

The Agency's goal for research in exposure assessment should be to develop a system which will provide the most accurate determinations of exposure possible for any given set of constraints. Central to all aspects of research into exposure is the definition and reduction of uncertainties of the determination arising from the assumptions in the conceptual framework for making the determinations.

2.4 Categories of Exposure Determinations and Their Limitations

Exposure determinations are made up of qualitative and quantitative components, as described in more detail below. The exact methods selected have a significant impact on the list of chemicals which will be included and excluded from analysis. The Agency needs to develop an assessment system which differentiates between the inital reconnaissance stage, where qualitative analyses should receive emphasis, and the definitive stage where quantitative analyses should receive primary attention.

Determinations of exposure may be made by measurements, by reconstruction, or by the use of mathematical models. The uncertainties associated with each of these approaches can differ greatly, and in many instances they have not been appropriately defined.

Measurements taken in the immediate proximity of an exposed organism are subject to the variabilities of local concentrations, as well as errors introduced as part of measurement techniques. When measurements are no longer made in the immediate proximity of the organism, then additional uncertainty accrues. Thus, the concentrations measured at an ambient air monitoring station may have only a remote connection with actual human inhalation exposures, which are mostly due to indoor air. Similarly, concentrations of contaminants at the municipal potable water plant may be poor predictors of actual exposures from ingested liquids. A further complication is that contamination of one medium can lead to exposure through another medium; thus, contamination of potable water by volatile compounds can lead to inhalation exposures.

Exposures may be inferred on the basis of observed retention or effects in humans, using concentrations of substances or their metabolites in body fluids or tissues, or using other biological markers. These approaches directly estimate absorbed dose, rather than exposure. In addition, they are often unable to distinguish between shorter exposures at higher concentrations and longer exposures at lower concentrations.

Exposures may be reconstructed by duplicating chemical releases and measuring the resulting concentrations, or by modeling their transport and fate from source to receptor. Lastly, exposures may be derived from transport and fate models which stipulate source terms, environmental conditions and the location of the receptor organism. Source terms may be based upon measurements or may be assumed.

Both the costs and the uncertainties associated with these various exposure determinations can greatly differ. Important constraints for exposure assessment include: available resources, area and duration of exposure assessment, exposure assessment methods applicable to a specific problem, uncertainties associated with a specific approach, and the precision and accuracy requirements of the user of the exposure assessments. These constraints impose opposing forces on the selection of specific protocols for exposure assessments. For instance, under certain conditions the available resources may allow only the application of a very simple mathematical model, with a resulting uncertainty which would make the exposure assessment valueless for a subsequent risk assessment.

3.0 RATIONALE FOR EXPOSURE ASSESSMENT

Exposure assessments are integral requirements for risk assessment, they are required to identify populations and ecosystems at risk, and they are necessary to determine compliance with certain standards. They are also important components in the development of regulatory strategies. The accuracy and precision of the exposure assessments obviously has a major influence on the reliability of decisions which depend upon such exposure assessments.

During his second tenure as Administrator (1983-1985), Mr. Ruckelshaus promoted the use of uniform, agency-wide risk assessment procedures in the exercise of its regulatory responsibilities. This approach has been highly successful in some areas, but much less so in others. It has frequently been limited by the lack of reliable information on exposure to targets and receptors, i.e., to people, vegetation, fish, etc.

Experience has demonstrated that exposure assessment techniques are at a relatively less advanced state than are techniques for toxicity assessment, and that a sustained research program will be needed to facilitate and encourage their use in the EPA's risk assessment program. A long-term commitment to research in this area will have immediate as well as long-term benefits to EPA. This is based upon our belief that much of the exposure technology that has already been developed has not been utilized by EPA, but could be after review and evaluation. In the longer term, newer techniques and approaches can be developed, validated, and applied.

4.0 APPROACHES TO HUMAN EXPOSURE ASSESSMENT

4.1 Overview

Exposures to a variety of environmental contaminants have been shown to be associated with adverse health and comfort responses in humans. Assessing human exposures to a single environmental contaminant or group of contaminants is necessary in utilizing a risk-based environmental management approach directed toward determining the cause(s) of human health risks and formulating cost effective mitigation efforts to reduce or minimize those risks. Efforts to assess total human exposure to environmental contaminants, and to develop effective measures to reduce those exposures need to be guided by a theoretical framework or methodology.

Central to the design of a human exposure assessment effort is the identification of the health or comfort effect under study, the ascertainment of the individual contaminant or general category of contaminants thought to be associated with that effect, and specification of the contaminant exposure on a time scale corresponding to the effect. The impact of exposure to environmental contaminants should, ideally, be evaluated in terms of the dose of the contaminant or its metabolites received. Dose can be considered as the internal dose (amount of the contaminant deposited or absorbed by the body) or biologically effective dose (amount of the contaminant deposited or absorbed which contributes to the dose at the cells where the effect occurs). The use of dose (particularly the biologically effective dose) in assessing the impact of exposure to environmental contaminant(s) is, however, often not practical since it can seldom be measured directly. Exposure is generally the only direct link available to the effect of interest. In fact, for regulatory and control strategies the relationship between exposure and concentration in air, water, soil, and food is of primary interest.

4.2 Methodologies

Assessment of total human exposures to environmental contaminant(s) must consider concentrations that occur in one or more of the possible media of exposure (air, water, food and soil), or through rates of uptake via routes of exposure such as skin, ingestion, or inhalation. This approach is much broader than the traditional EPA approach which considers exposures from only one route of exposure and typically from only one microenvironment within that media (e.g. air exposures with specific focus on ambient air). Human exposures across all environmental media can be assessed by three complementary methods: personal monitoring, exposure modeling, and biological markers.

4.2.1 Personal Monitoring

Personal monitoring provides a direct measure of total human exposure to environmental contaminant(s) of interest. This approach involves the direct measurement of the pollutant concentrations reaching the individual or population through all media (air, water, food, and soil) integrated over some time period. The emphasis in this approach is to directly measure total exposure at the target to contaminant(s) emitted from multiple sources and traveling along multiple routes of exposure. Personal exposures are monitored over the course of normal activity for appropriate periods of time ranging from several hours to several days. Integration over inappropriate times can obscure toxicologically significant excursions in exposure.

4.2.2 Modeling

This approach conceptually combines monitoring of contaminants in the media they occur, activity time budgets or food or water consumption patterns and questionnaries to estimate (model) the average exposure of an individual or population as the sum of the levels of contaminant(s) in each media weighted by time in an environment or quantity of food or water consumed. When personal monitoring or media concentrations are not available or possible, it may be necessary to model personal exposure from statistical and/or physical models based on sources, transport and transformation of constituents. However, models are based on mathematical representations of physical and chemical processes. The more complex the system, the greater the uncertainty of the results of the predicted exposures.

Questionnaires provide information on the media in which the exposure takes place (e.g. physical properties of indoor environment - sources, source use, ventilation, etc.) as an input to the predictive model. The development of a predictive exposure model attempts to measure and understand the basic relationships between causative variables and resulting exposures. Such models, once validated, can then be used to estimate population exposures of a wide range of potential mitigation efforts to reduce or minimize exposures. It is the modeling which provides the essential link between the exposures, the microenvironments or media in which the exposures take place, and the factors which determine the contaminant levels in the media and micro-environments.

Environmental contaminant levels are the result of a complex interaction of several interrelated variables in each medium (e.g. air pollutant concentrations are a function of sources, source use, meteorology, chemical reaction processes in air, etc.). It is essential that exposure models incorporate data on the factor controlling the exposures, so that cost efficient and effective mitigation (risk reduction) can be instituted.

4.2.3 Biomarkers

The term "biomarker" includes a large array of measurable molecular constituents in humans. Such markers include residues of chemicals and their metabolites in body tissues and fluids, products of molecular changes such as DNA adducts and chromosome aberrations, changes in levels of endogenously produced molecules, and genetically determined biochemical susceptibilities that vary among individuals. Such markers can be used as indices of exposure, current disease state or susceptibility to disease.

Biomarkers of exposure can theoretically integrate total intake to the body from multiple sources of exposure to environmental contaminants. If they are stable over time they can be used to indicate levels of steady-state exposure. They can be useful tools in elucidating mechansims of disease, or for extrapolations between internal doses, routes of exposure, species or tissues. They do not, however, necessarily provide the direct link between environmental exposure and disease. Biomarkers may be measures of the contaminant or its metabolites that are directly related to the specific contaminant associated with the effect outcome (e.g. lead) or may only be a surrogate for exposure to a complex source of environmental contaminants (e.g. cotinine). The sole use of biomarkers to assess exposure to environmental contaminants, like the sole use of personal monitoring, can provide only limited guidance in the selection of effective mitigation measures to reduce exposures since biomarkers do not provide information on the factors controlling exposure to the contaminant(s) in the physical environment.

It is important that the Agency develop a system that can effectively respond to information needs for risk based decision making. One part of such a general system would be a sub-system concerned with exposure determinations. Research problems in exposure determinations are strongly linked to scientific problems in transport and fate, and research on effects and risk assessments. Important linkages also extend to areas such as pollution control research. These linkages result in an interdependence, so that decisions made in one area can have strong effects on other areas.

Dealing with these complex relationships, as well as the constraints mentioned previously, requires a systems approach in which exposure assessment is one aspect of the entire environmental assessment and management structure. Within the area of exposure assessment, it is important to develop an optimization among resources, uncertainties, and utilities.

4.3 Intermedia Concerns

An obvious and well-documented problem in EPA's approach to environmental pollutants is the strong tendency toward looking at a pollutant in one medium only. Sometimes this has led to regulatory approaches which control a pollutant in one medium by releasing it into another.

The physicochemical characteristics of the overwhelming majority of common pollutants permit them to distribute in all media - air, water, soil and food. Work done at an EPA research center readily allows the prediction that leaky underground storage tanks leading to groundwater pollution may result in greater human exposure by inhalation due to offgassing from water than by contamination of drinking water. Any attempt to ascertain the potential impact of an environmental chemical should include assessment of the extent of exposure in all relevant media. This supports development of a centralized integrated approach to exposure which can consider long term needs in exposure assessment.

5.0 ELEMENTS OF EXPOSURE

5.1 Overview

The studies of human exposure provide information that can fill a basic need in risk assessment and risk management. These studies can identify:

a) relative importance of different exposure pathways.

b) quantify sources and or activities that contribute to exposures

c) identify populations at differential risk

This information is essential to the design of public health and cost effective strategies. For instance, the risk may be unequally distributed across the population due to the influence of specific sources or activity patterns. A mitigation strategy aimed at a nation-wide reduction of emissions may be ineffective for the highest risk groups.

5.2 Components

In order that exposure studies be useful to future decisions, some basic components must be adequately addressed. These components will determine not only the general ability of results but the specificity of possible subsequent actions. Included in these elements are:

a) Selection of representative sample,

b) Defining sample size,

c) Sampling, monitoring methods, and averaging times, and

d) Defining time-activity patterns.

Obviously these items are interrelated. The percent of people conforming to the specifications of the sampling protocol is in part dependent on the details and complexity of the studies.

5.2.1 Selection of Representative Sample

There are well established methodologies for survey research. The Agency has used proven survey techniques in the VOC and carbon monoxide (CO) exposure studies. However, the participation rate in exposure monitoring studies has been only approximately 50%. The issues of selection bias must be addressed in future studies. Experience indicates that both upper and lower economic groups are less likely to participate. Studies do not have to be designed to represent the entire U.S. or urban population, but should include a suitable representation from a broad representative cross section of the population.

Depending on the contaminant and distribution of sources, target groups may be selected. Nevertheless, even these exposure studies should use established survey research methodologies. At this time, the difficulty with sample selection is the lack of knowledge about the distribution and use of contaminant sources. Without some prior knowledge, investigators must speculate on how to over-sample low frequency categories. Therefore, a variety of survey studies will be necessary.

5.2.2 Defining Sample Sizes

Determination of the number of participants in an exposure study is a critical component. Representativeness and cost are obvious tradeoffs.

Microenvironmental models are useful in determining sample size by calculating the uncertainty in representing exposures in the mean as well as percentiles. Microenvironmental exposure and dose models must be developed and tested. In some cases, targeted studies might be needed to develop the input conditions. Statistical methodologies should be improved in the current microenvironmental models. For some contaminants, the concentrations co-vary with activities and for source use. Air pollution dose will vary with activity level and anatomical structure of the respiratory tract among other factors. These relationships must be better understood to advance microenvironmental models.

5.2.3 Sampling, Monitoring Methods, and Averaging Times

Conducting human exposure studies will require the development of new equipment and methods. Currently, information or actual human exposures is limited, in part, because appropriate equipment and methods do not exist for many contaminants. The exposure times of interest can vary from a single breath to multi-year averages. It is not practical to develop instruments and methods to cover all averaging times and still have them inexpensive, light-weight and durable for personal monitoring studies. However, EPA's engineers and chemists should interact more closely with health scientists to define instrument needs with the appropriate time resolution. This does not imply that exposures studies could not continue. A combination of personal measurements with portable equipment and fixed location microenvironmental measurements can provide needed exposure data.

5.2.4 Time-Activity Patterns

Our population is very mobile. More is known about the movements of working adults than of other groups. The time-activity patterns of youth, retired individuals or people in general during different seasons, climates, and weather conditions are not well described. The interactions or co-location of people and pollution sources also are not adequately known. These are more than subtleties. Knowing the indoor/outdoor concentration of pollutants such as ozone and acid particles, and knowing the outdoor time patterns of people with their activity levels allows the calculation of exposure and possible dose on time scales consistent with clinical studies. For some physiological responses, exposures with time frames of minutes to hours are more relevant than either our current standards or long-term averages.

In general, human exposure studies need more carefully defined averaging times. Studies of indoor, outdoor, and personal exposures can be misleading if careful attention to averaging times are not considered. It may be true that indoor concentrations are highly correlated to personal exposures when considering 24-hour or longer integrations. However, short-term concentrations may be more relevant to a particular physiologic effect.

Formaldehyde in homes illustrate a similar point. A combination of increased emissions (because of thermal heating) and decreased ventilation may result in transient sensory irritation and odor. Averaging formaldehyde over 24-hour or a week with the current survey instruments may indicate low average concentrations, which may suggest that problem concentrations do not exist. Time variation in indoor radon concentrations presents a similar monitoring problem. Short-term charcoal grab samples may misclassify a home where the longer term integration would be more appropriate.

6.0 EXAMPLES OF EXPOSURE ASSESSMENT RESEARCH NEEDS

6.1 Exposure Assessment - General

a) Develop better understanding of time use patterns in our society, how people spend time indoors and outdoors, and activity levels associated with microenvironments.

b) Develop better understanding of ingestion of food, water, and soils by segments of society.

c) Population exposure studies, e.g., for criteria pollutants, drinking water, pesticides, to determine relationships among control strategies and public health benefits, and to develop new exposure reduction strategies.

d) Where sources are indoors - understand patterns of use, repair, maintenance and how these factors affect exposures.

6.2 Acidic Aerosols and Gases

The primary means of exposure to acid aerosols and gases is through inhalation of their concentrations in the ambient air. Although research has been conducted in this area, information on the following is not well known:

a) Distributions of Hydrogen ion (H+) concentrations across the United States in aerosols and vapors.

b) Deposition velocities.

c) Importance of facial and nasal deposition to sensory irritation.

6.3 Exposures to Biological Aerosols

Evidence indicates that inhalation of aeroallergens, and aeropathogens may be important contributors to respiratory symptoms and illnesses. Investigations might lead to:

a) Quantifying relationships among questionnaires and actual indoor concentrations of spores and other antigenic materials.

b) Knowledge about the variations in species and concentrations within homes, offices, etc. and between structures.

6.4 Environmental Tobacco Smoke (ETS)

Evidence indicates that exposures to ETS may lead to increased respiratory symptoms in children, decreased lung performance and perhaps lung cancer in adults. Nevertheless, there are still many unresolved exposure issues.

a) Distribution of population ETS exposures is not known. It would be worth while identifying high exposure group in addition to characterizing factors influencing exposures.

b) Relationship between ETS environmental concentrations and the deposited dose is important. The lung retention in children as a function of age and activity would be important.

6.5 Pesticides

Pesticides are widely used in commercial buildings and residences. Yet, the exposure to people in these settings by inhalation, contact or ingestion is not well characterized.

6.6 <u>Volatile Organic Compounds (VOC)</u>

Investigations of VOC's, particularly EPA's TEAM studies, have revealed that for many compounds, exposure is dominated by the indoor air contribution.

a) Repeat measures are needed to determine within-structure variation.

b) The influence of source use on personal exposure needs to be determined for many VOC's.

c) Transportation among other microenvironments needs to be studied.

d) Compounds studied must be expanded to include irritants, immuno-toxic and neurotoxic materials.

6.7 <u>Time-Activity Patterns and Behavior Factors</u>

Extrapolating from a relatively few time-activity studies the average employed person spends their time in the following manner: 28% at work, 63% at home, 6% in transit, 1% in other indoor locations and only 2% outdoors. For women not working out of the home, the total indoor time is 94.1% with 4.2% in transit and only 1.7% outdoors. Obviously on any given day, individuals will deviate substantially from these average numbers. However, there are substantial gaps in understanding the time-activity patterns in our society.

Knowing these patterns and the potential exposures to sources and/or harmful substances would benefit environmental management and policy decision. Time-activity surveys should be designed to resolve behavioral patterns relevant to discerning human exposures to environmental contaminants.

Factors that should be considered include:

a) Cross-section of population by age, sex, income, job classification

b) Ethnic differences

c) Regional differences by season

d) Temporal differences by weather conditions

e) Level of activity (metabolism, minute ventilation)

f) Physical condition

g) Intra-regional differences by degree of urbanization

7.0 BIOMARKERS OF EXPOSURE

Biological markers of exposure and/or effects are one of the most promising avenues of research. A National Academy of Sciences (NAS) Committee is in the process of evaluating the use of biological markers in environmental health research. They have defined biological markers as indicators of variation in cellular or biochemical components or processes, structure, or function that are measurable in biological systems or samples.

Markers can be divided into those reflecting exposure, effect, or susceptibility. There is a continuum between exposure and effect extending to overt human disease. The goals of research into biological markers are the prevention and early detection of human disease. Markers of exposure are particularly valuable in reflecting the earliest steps in the process by which environmental agents lead to adverse effects. Perhaps the ideal marker is one which accurately indicates both exposure and effect. A reasonable example is the formation of carboxyhemoglobin (COHb), which provides an integrated measure of exposure to carbon monoxide and is also the mechanism which is responsible for the toxic effect of this gas. A marker of this nature appears to be particularly suitable for what is now being called biochemial epidemiology or molecular epidemiology. In the past, occupational and environmental epidemiological studies have generally used surrogates for exposure, e.g. job description, geographical proximity to superfund site. Marked improvement in the precision and effectiveness of epidemiological studies can be obtained through the use of molecular markers of exposure in conjunction with outcome variables, if there is a well defined association between actual exposure and the biological marker.

The availability and development of biological markers stems in part from rapid advances in our understanding of biological processes, particularly in the exciting field of molecular biology. Such techniques as the use of monoclonal antibodies, recombinant DNA technology or Potassium-32 post-labelling to detect DNA or protein adducts open whole new approaches to biological markers for exposure and effect. These new developments appear to promise the ability to determine the extent of exposure of individuals to relatively low levels of environmental chemicals. For example, it would not be surprising to find through the use of sensitive biomarkers of exposure that the bulk of a population living in the vicinity of a hazardous waste site has no more evidence of exposure to chemicals at that site than does a control population; yet a few individuals, through their activities at the site, or an unexpected exposure route, will be found to have markedly elevated exposure. Of particular importance will be studies to validate any markers used in human studies. Furthermore, ethical issues raised by the use of biological markers of exposure must be carefully addressed.

The importance to EPA of improvements in biomarkers of exposure is evident. EPA has invested heavily in the process of risk assessment as a tool for environmental decisionmaking and for priority setting within the Agency. While there is much focus on uncertainties on the hazard side of the risk assessment equation, the uncertainties concerning exposure can often be greater.

The failure to appropriately perform exposure assessment at EPA has perhaps nowhere been more evident than in the Tacoma smelter situation. In the summer of 1983, EPA was faced with a specific decision concerning instituting control technology on a smelter which produced a substantial burden of arsenic to the local community. The smelter was a major employer with much of the local economy dependent upon its operation. Owners of the smelter claimed that they would close it down if they were forced to spend substantial sums for air pollution control. William Ruckelshaus, who had only recently returned to head EPA, decided in essence to make this situation into a test case for the policy of carefully communicating risks to the community so that the community could discuss these risks intelligently and participate appropriately in the decision process. Risks as high as one in 100 were computed for the immediate vicinity of the smelter with lower risks for surrounding communities depending upon their distance and the wind patterns.

Unfortunately, the exposures were estimated by a model in which arsenic emissions were based upon the performance of a similar smelter in another state. A wind rose was placed around this point source, with the public assumed to be standing at their front door breathing this arsenic level for 70 years. Not only were ambient measurements not made, no advantage was taken of the fact that urinary arsenic levels are an excellent indicator of arsenic exposure and body burden. In fact, urinary arsenic, which already had been obtained by local authorities, clearly demonstrated that EPA's exposure assessment had overestimated the local exposure by a factor of about 15. In other words, when Administrator Ruckelshaus told local people that their risk was one in 100, an appropriate exposure assessment based upon a biological marker would have led him to clearly state this upperbound risk as being one in 1500.

It should be emphasized that the exposure assessment in the Tacoma case was performed by the Program Office, without any input from the Office of Research and Development (ORD). It reflects an Agency-wide problem in that much exposure assessment is actually performed within the various program offices, using disparate approaches and unvalidated and unpublished models. The SAB has frequently been critical of such efforts, including the exposure assessment which forms a central portion of the Integrated Environmental Management Program (IEMP) of the Office of Policy, Planning and Evaluation.

There are numerous long range research opportunities for EPA in the biomarkers area. It is important that as research proceeds rapidly in assessing biomarkers of effect, e.g. the value of DNA adducts in predicting cancer, that concomitantly research is performed to link adducts of interest to exposure. Such biomarkers would be of particular value in determining the slope of the lower end of the dose response curve for the effect of chemicals, such as carcinogens, for which epidemiology or standard laboratory animal safety assessment studies are inherently inadequate.

Obtaining improved biomarkers of exposure is dependent primarily upon long-term relatively basic research providing the mechanistic understanding of the process by which exogenous agents produce adverse effects.

8.0 STRATEGIES

8.1 Assessing Environmental Exposure

Strategies for assessing environmental exposures to environmental contaminants should be based, in part, upon the need for exposure characterizatons in quantitative risk assessment. For an agency with as broad a range of mandates, responsibilities, and capabiities as EPA, a strategic approach to exposure assessment is essential for the effective execution of its risk assessment functions. Adoption of such an approach will have the further advantage of improving and unifying program office applications of such assessments. The overall strategy will need to address the following major issues: interfaces, accountability, long-term commitment, other Federally funded research, and education.

8.1.1. Interfaces

Efforts to assess exposures to environmental contaminant(s) need to recognize the role of the three principal methods of exposure assessment (personal monitoring, modeling and biomarkers) and incorporate into their study design, where feasible and practical, several of the methods in order to more accurately assess exposure and estimate dose. Such studies need to determine the factors in the physical environment responsible for the environmental concentrations, the multimedia routes of exposure (air, water, etc.) and the number of microenvironments in which exposures take place so that efficient and effective mitigation measures to reduce exposure can be identified and evaluated. Exposure studies should explore the use of nested designs for exposure assessment which utilizes all three methods to a varying degree. Such efforts will require a fundamental change in the EPA's current compartmentalized approach to exposure assessment.

8.1.2. Accountability

Research efforts to develop:

a) new or improved monitoring methods;

b) physical/chemical models for exposure assessment, and

c) biomarkers, should be evaluated within the context of their usefulness in an overall exposure assessment.

Existing information on environmental contaminant exposures should be integrated into the process of setting research priorities for all environmental contaminants. Funding decisions should be tied to such a review and evaluation.

8.1.3. Long-term Commitment

Long term research on instrumentation for characterizing the particle size distribution and the variation of chemical composition with particle size at the University of Minnesota's Particle Technology Laboratory, largely with extramural support from EPA, led to a marked improvement in our understanding of particulate matter source contributions, long-range transport and transformation, human exposure, and the factors influencing atmospheric visibility. The contribution of the atmospheric concentration data base, made possible by the development of this new instrumentation, was a key factor enabling the EPA to develop a new and better index of particulate air pollution which has been incorporated in the 1987 PM_{10} National Ambient Air Quality Standards (NAAQS).

Research in biocentration provides another example of valuable returns from a long-term committment. The U.S. EPA developed many of the basic concepts for the prediction of the bioconcentration of important classes of organic compounds by fish. This work contributed significantly to exposure assessments for consumers of fish.

8.1.4. Other Federally Supported Research

Research pertinent to exposure assessment is being performed at or under the auspices of a number of different Federal agencies, ranging from the U.S. Geological Survey to the National Institutes of Health. It is imperative that EPA establish closer communication with these agencies, so that each can assist the others in incorporating state-of-the-art knowledge in exposure assessment. EPA's scientists need to attend national meetings and keep in close contact with scientists who are performing the basic research pertinent to long term improvements in exposure assessment.

8.1.5. Educational Training

A Research Strategy should consider the establishment of a policy to address the gaps and lack of synthesis in present approaches to various environmental issues. This proposal is directed to the establishment of educational programs and/or re-organization of existing research centers focussed on environmental assessment; both within the Agency and in academia, to integrate the knowledge of specific disciplines.

Given the multiple-faceted nature of problems in all phases of the environment (air, water and land) and the multiple effects on both humans and the ecology, and the relatively specialized character of academic programs in health, science and engineering, we recommend that EPA sponsor an academic Center of Excellence (Research Centers Program) to serve as a focus for both research and academic training in exposure assessment. This would provide an ideal setting for multidisciplinary input from various departments and schools within one or more Universities.

8.2 Exposure Assessment Planning

Strategic planning for exposure assessment will occur only when agency staff with appropriate skills are provided with clearly stated responsibilities and budgets commensurate with the agency's needs. Considering the breadth and diversity of these needs, and the relatively primitive state of the art, the program should be located within the Office of Research and Development and should include the following major components: research, coordination and technical support, development of an Agency-wide program, and an outreach program.

8.2.1. Research in Exposure Assessment

A laboratory based program is needed to investigate and develop:

a) equipment and techniques for sampling and analysis of environmental toxicants,

b) models for environmental transport and transformation of chemicals, and procedures for periodic model validation,

c) selection criteria for human populations and other target species in the environment whose exposures may need to be defined,

d) models for determining total exposure of populations to environmental concentrations,

e) protocols for quality assurance of data from environmental measurements and models, and

f) systems for data management and its accessability to agency staff.

8.2.2. Coordination and Technical Support

A headquarters based program is needed to develop exposure assessment skills in ORD, program office, and regional personnel and to provide technical support for the performance of quantitative exposure assessments.

8.2.3. Development of Agency-wide Program

A headquarters based program is needed which would:

a) identify agency needs in exposure assessment not being addressed, and recommend action programs to the Administrator,

b) identify use of exposure assessment techniques in agency offices, and evaluate them for consistency and reliability, and

c) set up, maintain, and promote the utilization of agency-wide data base on exposure.

8.2.4. Outreach

A headquarters based program is needed to exchange information on exposure assessment techniques with other federal agencies and state and local agencies and groups with interests in exposure assessment. This could include, but should not be limited to sponsorship of symposia and workshops, publication and distribution of a newsletter, and preparation of published Guidelines.

9.0 MONITORING AND RISK ASSESSMENT

9.1 Importance

When exposure assessments for risk assessments are needed, they can sometimes be based on available data such as concentrations in ambient air, drinking water, food, etc. Unfortunately, data on concentrations in environmental media relevant to the specific population or target of interest are seldom available, even for chemicals with established concentration or tolerance limits. In such cases, reliance is placed on less direct and reliable indices of exposure, such as estimates of locations of employment or residence, combined with estimates of inhaled and ingested amounts and patterns of activity. Indirect human exposure data based on tissue burdens of samples collected at autopsy have been of great value to exposure estimation for pesticides, PCBs, and other lipid soluble chemicals. However, the recent decision to terminate the adipose tissue surveillance network will greatly diminish the ability of the Agency to detect trends in population exposure to a variety of toxic chemicals, such as pesticides, dioxins from increasing incineration, and/or new toxic chemicals entering the environment, or to determine the efficacy of the implementation of controls.

9.2 Tools

The tools of exposure assessment are quite varied. They include personal and portable monitors and samplers, highly sensitive analytical procedures for trace concentrations in air, water, food, excreta, blood, tissue specimens, etc., time-activity and dietary diaries, data on dietary habits, and models to relate such information to total or integrated exposure.

9.3 What Can Be Done Now

For some airborne chemicals there are relatively inexpensive and reliable passive monitors which can be used to determine cumulative exposure (nitrogen dioxide, formaldehyde, radon). Continuous measurements of exposure can be made with larger, more complex, and more expensive personal monitors, such as for carbon monoxide. Battery powered personal samplers can collect integrated samples for a broad range of gases, vapors, and aerosols. Personal and other portable samplers can collect air samples in selected micro-environments representative of human occupancy. Market-based survey techniques can be used to collect samples on a statistically reliable basis to determine ingestion exposures to a variety of chemicals. What can be done now is generally limited by the costs of carrying out the studies.

Exposure to ecologic systems and other receptors for welfare effects can often be measured by conventional techniques for sampling air, precipitation, surface waters, and sediments, and these samples can be analyzed by conventional techniques for trace analyses. Indirect indices of exposure include pathogenic changes in receptors such as leaves which are characteristic for known exposures.

Exposures producing both health and welfare effects which are not readily measured involve short-lived reactive chemicals such as sulfuric acid, nitric acid, hydroxy radicals, and photosensitive organics which may be difficult to collect on sampling substrates, or which react, evaporate, or sublimate between sampling and analysis.

Indirect measures of exposure, especially analyses of blood (e.g. carboxyhemoglobin, lead) can be excellent indicators of human personal exposure. Biomarkers utilizing new knowledge in molecular biology are beginning to be useful in indicating exposure to mutagens and may become very useful and sensitive indices of exposure.

9.4 Research Needs

Research is needed on sampling and monitoring techniques for chemically unstable and reactive materials, and for materials lost by volatilization between sample collection and analyses. Research is also needed on time-activity patterns, dietary patterns, and behavioral factors which can strongly modify exposures within human microenvironments. Finally, research is needed on exposure models which can utilize a variety of available data on concentrations within environmental media, time-activity and dietary patterns and yield total exposures to individuals and populations. Further research is also needed to validate such models and to determine their residual uncertainties in quantitative terms.