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STRATEGIC PLAN FOR THE ANALYSIS OF THE NATIONAL HUMAN EXPOSURE ASSESSMENT SURVEY (NHEXAS) PILOT STUDY DATA

National Exposure Research Laboratory
and
National Center for Environmental Assessment
Office of Research and Development
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EXECUTIVE SUMMARY

The Office of Research and Development (ORD) of the U.S. Environmental Protection Agency (EPA) initiated the National Human Exposure Assessment Survey (NHEXAS) in the early 1990's. It was a population-based pilot study of the exposure of over 500 people in three areas of the U.S. to metals, pesticides, volatile organic compounds, and other toxic chemicals. Measurements were made of the air people breathed, the foods and beverages they consumed, and the soil and dust in/near their home. Chemicals in their blood and urine were measured. The participants also completed questionnaires to help identify possible sources of exposures and to characterize activities that might contribute to exposure. To this date, NHEXAS remains the largest multimedia, multipathway, multichemical study of its kind. Key goals included evaluating the feasibility of conducting such a large study, documenting the population distribution of exposure to the chemicals examined, understanding the factors that contribute to high exposures, and improving the accuracy of exposure models.

Such a study produces a multitude of data that must be thoughtfully analyzed to realize its full potential. EPA's Science Advisory Board (SAB) recommended that EPA develop a strategy to analyze the data to ensure the optimal use of the data (EPA-SAB-IHEC-ADV-99-004, www.epa.gov/sab). Therefore, ORD developed this Strategic Plan. ORD began with a workshop at which about 70 scientific and policy experts from ORD, EPA program offices, EPA regions, other federal agencies, state health agencies, academia, and private institutions offered their suggestions on the most useful analyses of the NHEXAS pilot data. ORD used their thoughtful contributions as the basis to begin development of the Strategic Plan. The draft Plan was reviewed by the SAB (EPA-SAB-IHEC-00-018, www.epa.gov/sab), and made available to all EPA program offices and the public. This document has been revised based upon those recommendations.

The Strategic Plan describes projects in six topic areas: descriptive statistics; predictors of exposure and dose; spatial and temporal variability; aggregate exposure, pathway analysis, and cumulative risk; evaluation/refinement of current exposure models and assessments; and designing exposure studies. Criteria, founded on both the near- and long-term value to EPA, were established for ranking projects within each of these topic areas. The text describes how the criteria were applied to each project. The projects are described in the appendix. This prioritization will be used as a guide

for ORD to implement the analyses. To expand the opportunities for all interested persons to get involved, the NHEXAS information is being prepared for entry into a publically available database, with appropriate metadata, in late 2001.

1. INTRODUCTION

To evaluate the risks posed by chemical pollutants in the environment, the U.S. Environmental Protection Agency (EPA) must be able to estimate the number of people exposed to the pollutants, as well as the magnitude and duration of the exposure. Typically estimates of exposure have been based on "default assumptions" such as emissions or environmental concentration data, rather than actual measures of human exposure to contaminants. Without measurements of human exposure, these default assumptions are of limited value because they do not reflect actual patterns (distributions) of human exposure to chemicals in the environment.

Increasingly, EPA's scientific advisors are concerned about reliance on these default assumptions—particularly when evaluating the risks from exposure to environmental contaminants or when estimating the benefits that may be obtained from managing these risks. Addressing these concerns is a vital link in reducing the scientific uncertainty in health risk assessment and in regulatory decision making.

To respond to these concerns, EPA's Office of Research and Development (ORD) sponsored three related pilot studies known as the National Human Exposure Assessment Survey (NHEXAS). The NHEXAS studies tested protocols for acquiring population distributions of exposure measurements and developed exposure databases for use in exposure models and assessments and, hence, risk assessments. The principal objectives of the NHEXAS pilot studies were to (1) evaluate the feasibility of NHEXAS concepts, methods, and approaches for the conduct of future population-based exposure studies; (2) evaluate the utility of NHEXAS data for improved risk assessment and management decisions; (3) test the hypothesis that the distributions of exposure given by modeling and extant data do not differ from the measurement-based distributions of exposure; (4) define the distribution of multipathway human exposures for a relatively large geographic area; and (5) stimulate exposure research and forge strong working relationships between government and nongovernment scientists.

During 1998, the Science Advisory Board's (SAB's) Integrated Human Exposure Committee (IHEC) conducted a review of the NHEXAS pilot studies. The SAB issued a report of their review early in 1999 (Appendix B). This report—*An SAB Advisory: The National Human Exposure Assessment Survey (NHEXAS) Pilot Studies* (EPA-SAB-IHEC-ADV-99-004, February

1999)—praised the NHEXAS pilot studies and recommended several actions to ensure that as much benefit as possible is derived from this very rich database. One major recommendation was to develop a strategic plan for completing the analysis of the NHEXAS pilot data.

This report represents the strategic plan requested by the SAB. To develop background information for this strategic plan, ORD convened a workshop from July 26 through 28, 1999, to obtain a wide range of expert opinion on which scientific analyses would be helpful to interpret the NHEXAS data. The scientific analyses identified during the workshop are documented in a report entitled *Proceedings of the NHEXAS Data Analysis Workshop* (EPA 600/R-99/077; October 1999). An electronic version of the proceedings document is available on the Internet at www.epa.gov/nerl/nhexas. The proceedings document represents one significant source of information considered by the authors of the ORD strategy for the analyses of the NHEXAS pilot study data. A draft was reviewed by the IHEC in July, 2000. Copies were sent to the EPA Program Offices and made available to the public. The IHEC recommendations served as the basis for revising the Strategy (*An SAB report: the draft strategic plan for the analysis of national human exposure assessment survey (NHEXAS) pilot study data* (EPA-SAB-IHEC-00-018, September 2000, www.epa.gov/sab)).

Two projects discussed during the NHEXAS Data Analysis Workshop are *not* included in this strategy: a project to develop and review a publicly accessible NHEXAS database and a project to document the lessons learned from the field recruitment and sampling portions of the pilot studies. ORD initiated work on these projects during FY99 because they represent essential precursors to the data analysis projects discussed in this plan. For example, many NHEXAS data analyses described in this report cannot proceed until ORD completes a publicly accessible database. These projects are described in more detail in Appendix C.

This report incorporates both strategic objectives and a description of projects arising from those objectives. On one hand, it has more structure than a typical strategy because of the need for a framework for classifying and describing a large number of highly related analyses. On the other hand, it avoids the prescriptive approach of a detailed workplan to permit researchers to engage their creativity and expertise in defining the details. Although this approach represents more narrative than that found in some strategies, it represents a necessary elaboration on the extensive information

presented in the two documents cited above. Therefore, most projects are relatively broad in scope and large in size.

Section 2 of this strategic plan contains an overview of the NHEXAS pilot studies to provide the background on the broad types of data available. Section 3 describes the strategic framework that ORD developed to prioritize and recommend analyses of the NHEXAS pilot study data. Section 4 summarizes the analysis projects and presents the priorities for implementing them. Appendix A lists the participants in the July 1999 NHEXAS Data Analysis Workshop. Appendix B lists the IHEC participants in the July 2000 SAB review. Appendix C describes the ongoing analyses, including the development of the database and the scope of the lessons-learned project, and lists the titles of NHEXAS papers that have been published or are in preparation at this time. Appendix D is a listing of the priorities for all of the projects. Appendix E contains the description of the projects referred to in the main text.

It is clear that many organizations and individuals are interested in the NHEXAS databases, in learning about the major findings of the NHEXAS pilot studies, or in performing their own analyses of the data. ORD plans to respond to this interest by establishing a web site to communicate about the NHEXAS analyses and to ensure ease of access to the NHEXAS data.

2. OVERVIEW OF NHEXAS

2.1 BACKGROUND ON EXPOSURE TO CHEMICAL POLLUTANTS

To assess the risks posed by chemical pollutants in the environment, EPA must be able to estimate the number of people exposed to these chemicals and the intensity of exposure. In the past, most studies have focused on exposure to one chemical at a time by one route of exposure. For instance, a study might look at how much of a particular chemical is found in outdoor air. In many cases, these studies have relied on very indirect measures to estimate exposure to the chemicals. An example would be to sample emissions from a smokestack and then apply air transport models to predict exposure to residents in the surrounding area.

Although such studies are important, studying chemicals and sources in isolation does not reflect actual patterns (distributions) of human exposure to chemicals in the environment. In reality, people can be exposed to chemicals from a variety of sources that contaminate water, food, air, dust, and other media. Exposure to a single chemical may occur from contact with several environmental media (e.g., air, water), via several pathways (e.g., hand-to-mouth transfers, food), and through several routes (i.e., inhalation, oral, dermal). Additional complexities arise when considering an individual's exposure to multiple chemicals at any point in time or over extended periods. The fact that different people also spend varying amounts of time indoors and outdoors or otherwise engage in activities that can have important impacts on chemical exposure adds to this complexity. More accurate assessments of risks, therefore, must take into account exposure to multiple chemicals from various routes and media. By understanding total or aggregate exposure, it also will be possible to identify those pathways and routes responsible for the greatest exposure, thereby providing direction for decisions on the most effective strategies to reduce risks.

2.2 THE PURPOSE OF NHEXAS

NHEXAS, in its fullest sense, is a conceptual design, which, on implementation, will have long-term implications to exposure research and assessment. The ultimate goal is to document status and trends of national distributions of human exposure to potentially high-risk chemicals to improve the accuracy of exposure (and risk) assessments and to evaluate whether exposure (and risk) is deteriorating or improving over time with the application of risk management steps. However, such an extensive program requires much preparation, including making improvements in the state of exposure science. The Phase I pilot projects are the initial phase of this long-term program. Based on the scientific advances from this first phase of NHEXAS, two follow-up phases are envisioned. One encompasses special studies to test particular hypotheses related to issues, such as characterization of a pathway of concern for a specific subpopulation or a chemical of concern at specific geographic scales (community and regional) or an uncertainty related to the effect of temporal variability in an exposure assessment model. The second is the design and implementation of a much broader national survey of population-based exposures, building on the foundation laid by the pilot-phase investigations.

Phase I of NHEXAS (hereafter referred to as just NHEXAS or pilot NHEXAS studies) is perhaps the most ambitious study ever undertaken to evaluate *total* human exposure to multiple chemicals on both community and regional scales. It focuses on the exposure of people during their daily lives to environmental pollutants. To accomplish this, hundreds of volunteer participants were selected randomly from several areas of the country to obtain a population-based probability sample. NHEXAS scientists measured the levels of a suite of chemicals to which participants were exposed in the air they breathe, in the foods and beverages they consume, in the water they drink, and in the soil and dust around their homes. Measurements also were made of chemicals or their metabolites in biological samples (including blood and urine) provided by the participants. Finally, participants completed questionnaires to help identify possible sources of exposure to chemicals and to characterize major activity patterns and conditions of the home environment.

In addition to improving measurement-based estimates of total exposure to chemicals and contaminants, NHEXAS has the following aims.

- Identify subgroups of the general population that are likely to be highly exposed (at least the 75th percentile) to chemicals in their environment.
- Provide a baseline of the normal range of exposure to chemicals in the general population that can be used to compare to the results of other investigations conducted at particular sites of concern or to address specific routes.
- Compare the results of a 1-week "snapshot" of exposure to the results obtained from multiple sampling cycles over a year.
- Evaluate and improve the accuracy of models developed to predict or diagnose exposure of people to chemicals.
- Test and evaluate different techniques and design approaches for performing multimedia, multipathway human exposure studies.

2.3 HISTORY AND PARTICIPATING ORGANIZATIONS

NHEXAS has been implemented with extensive research collaboration that includes scientists from EPA's ORD, from other federal agencies, and from leading academic and research institutions.

Scientists from the Food and Drug Administration (FDA) and from the Centers for Disease Control and Prevention (CDC) participated through interagency agreements with EPA scientists in the analysis of samples. Scientists from the National Institute for Standards and Technology provided quality assurance (QA) support through an interagency agreement with EPA. The NHEXAS projects were funded as cooperative assistance agreements and coordinated by EPA's ORD. These cooperative agreements were awarded after a national research solicitation and peer review by national scientific experts.

(1) The cooperative agreement supporting the Arizona study included the University of Arizona, Battelle Memorial Institute, and the Illinois Institute of Technology.

(2) The cooperative agreement supporting the Region V study (states of Illinois, Indiana, Michigan, Minnesota, Ohio, and Wisconsin) included the Research Triangle Institute and the Environmental Occupational Health Sciences Institute (EOHSI). A related smaller-scale study in Region V focused on children's exposures to pesticides and was conducted with the participation of the Minnesota Department of Health.

(3) The cooperative agreement supporting the Maryland study included Harvard University, Emory University, Johns Hopkins University, the Southwest Research Institute, and Westat, Inc.

2.4 MAJOR DESIGN ELEMENTS

Table 1 summarizes the major design elements of NHEXAS. There were common features across the three consortia. All three consortia used the same basic set of questionnaires. Within chemical classes selected by the consortia, each consortium analyzed for a basic set of chemicals (primary analytes). However, by utilizing three consortia, alternative and innovative variations on the theme of multimedia measurements to estimate total human exposure were possible. For example, each consortium was able to target some specific concerns or opportunities. Two of the consortia focused on measuring potential exposures of each participant once; one consortia studied fewer people but repeated the measurements several times over the year to enable estimates of temporal variability for the exposures and activities of interest.

The participants were selected through a probability sample to permit subsequent statistical inferences about the larger population. The only exception was a special panel on children exposed to pesticides. This was based on oversampling households reporting more frequent applications of insecticides and on a commercial listing of households with listed telephone numbers that were predicted to have age-eligible children.

TABLE 1. SUMMARY OF NHEXAS STUDIES

	Consortium		
	University of Arizona/Battelle Memorial Institute/Illinois Institute of Technology	Research Triangle Institute/Environmental and Occupational Health Sciences Institute	Harvard/Emory/Johns Hopkins/ Southwest Research Institute/Westat
Type of Study	Exposure field study	Exposure field study	Special study: relation of short-term data to longer term exposures
Geographic Region	Arizona	Region V (Illinois, Ohio, Indiana, Michigan, Minnesota, and Wisconsin)	Baltimore and surrounding counties
Design	Representative sample of general population	Representative sample of general population	Representative sample includes suburban, urban, and rural groups
Approximate Number of People	179 (plus others in sampled households)	249, plus 52 for pesticides (no others in sampled households)	53 people sampled six times over 1 year
Analytes	Pb, As, Cd, Cr, Ni, Ba, Mn, Se, V, Cu, and Zn; benzene, chloroform, perchloroethylene, trichloroethylene, methylchloroform, styrene, toluene, xylene, *p*-dichlorobenzene, formaldehyde, 1,3,-butadiene, methylene chloride, carbon tetrachloride, plus 11 additional VOCs; chlorpyrifos, diazinon, malathion, and carbaryl	Pb, As, Cd, Cr; benzene, chloroform, perchloroethylene, trichloroethylene, methylchloroform, styrene, toluene, xylene, and *p*-dichlorobenzene; chlorpyrifos, diazinon, malathion, atrazine, chlordane, dieldrin, heptachlor, 4,4'-DDE, -DDD, and -DDT; B(a)P, anthracene, phenanthrene, pyrene, B(a)A, acenaphthylene, fluoranthene, B(g,h,i)perylene, and indeno(1,2,3-c,d)pyrene Children's study (pesticides and PAHs)	Pb, As, Cd, and Cr; chlorpyrifos, diazinon, malathion, atrazine (water only), chlordane, dieldrin, heptachlor, 4,4'-DDE, -DDD, and -DDT; B(a)P, anthracene, phenanthracene, and chrysene
Samples	Air, water, food, and beverages; soil/dust and surfaces; urine and blood	Air, water, food, and beverages; soil/dust and surfaces; urine and blood	Air, water, food, and beverages; soil/dust and surfaces; dermal; urine and blood
Questionnaire	NHEXAS	NHEXAS	NHEXAS

Chemicals to be analyzed by NHEXAS were chosen because they are known (or strongly suspected) to present major environmental health risks, had been found in two or more environmental media (air, water, soil, or food), and had been identified as being of importance to several EPA program or regional offices or to other federal agencies. Chemicals were selected only if it was feasible to collect and analyze them. The chemicals fall into three categories: (1) volatile organic compounds (VOCs), such as trichloroethylene, benzene, and perchloroethylene; (2) metals, such as lead, arsenic, and cadmium.; and (3) pesticides, such as the herbicide atrazine and the insecticides, chlorpyrifos, diazinon, and malathion. In some media, measurements of selected polycyclic aromatic hydrocarbons (PAHs) were made.

3. STRATEGIC FRAMEWORK

This Section describes the strategic framework that ORD developed to identify, characterize, and prioritize important analyses of the NHEXAS pilot study data. The starting point for developing the strategic framework was the NHEXAS Data Analysis Workshop that ORD convened in July 1999. About 160 scientists and science policy experts were invited to the workshop; Appendix A identifies those who were able to attend. Each participant received a copy of the SAB advisory report and extensive background information on NHEXAS well in advance of the workshop itself. Workshop participants identified and described a number of analysis projects for interpreting the NHEXAS pilot study data. These projects are documented in the *Proceedings of the NHEXAS Data Analysis Workshop* (EPA 600/R-99/077).

After the workshop, each analysis project was reviewed and projects with a substantial amount of overlap or duplication were merged. The large number of very worthwhile analysis projects created a significant challenge for ORD: that of establishing priorities to ensure that the "critical" projects are funded as quickly as possible. Many criteria were considered for sorting these projects and establishing priorities (e.g., relevance to Agency GPRA Goals, relevance to previous SAB recommendations, relevance to regulatory needs or timeframes, degree of scientific uncertainty in a

given component of exposure assessment, feasibility). Ultimately, the strategic framework adopted consists of two logical steps.

A. In the first step, analysis projects were classified according to the type of scientific interpretation contemplated. This classification resulted in six distinct topic areas:
    1. *Descriptive Statistics* These projects describe the basic features of the NHEXAS study results, both for the measurements and the questionnaires, and provide comparisons between demographic groups.
    2. *Predictors of Exposure* These projects address the relationships among various type of measurements (environmental, exposure, and biomarkers), questionnaires, and activity diaries with a view towards whether one type of measurement, possibly in combination with questionnaire/activity information, can be an indicator of another type of measurement.
    3. *Spatial and Temporal Variability* These projects involve analyzing the variability in human exposures to both single and multiple chemicals, as well as the key factors that affect inter- and intra-individual variability in exposures.
    4. *Aggregate Exposure, Pathway Analysis, and Cumulative Risk* These projects focus on assessments enabled by the multi-pathway and multi-chemical nature of the NHEXAS studies.
    5. *Evaluation/Refinement of Exposure Models and Assessments* These projects describe the testing of existing exposure models and developing new or improved exposure and dose models.
    6. *Designing Exposure Studies* These projects involve examination of the feasibility of NHEXAS concepts, methods, and approaches for the conduct of future population-based exposure studies.

B. In the second step, four "ranking" criteria were developed and applied in a hierarchical fashion to establish priorities for the projects *within each of these six topic areas*.

1. ***Timing:*** Identifying projects that should begin in the near-term, in an intermediate timeframe, and in the long-term was influenced by:
    - Critical path issues: For example, the completeness of the analytical results should be evaluated for each type of sample before making comparisons between measurements.
    - Sequencing issues: For example, simpler analyses should be undertaken to understand the distributions of the measurements data before more complex analyses of these data are performed.
    - Note: This refers to the timing for initiation of research, rather than the immediacy of regulatory needs (see Demand bullet that follows). For example, there is an "immediate" need to begin projects with both short-term regulatory and long-term scientific impacts that ultimately improve regulatory foundations.
2. ***Feasibility:*** The feasibility of completing any individual project depends on:
    - Limitations in the NHEXAS designs and data: For example, limitations in the designs of the NHEXAS pilot studies, types of samples and questionnaires collected, quantity and quality of results, and in the ability to combine data sets influence feasibility.
    - Other scientific limitations: For example, limitations in the current state of the science (e.g., the lack of cumulative risk models) and in the availability of data (from outside the NHEXAS database), statistical methods, or models needed to complete the analysis project will affect feasibility.
3. ***Applicability:*** The broad applicability–or relevance--of a project to important objectives described in three other sources.
    - SAB recommendations about NHEXAS: The extent to which any individual project responds to the SAB recommendations in its advisory report (Table 2) influences applicability.
    - EPA strategic goals, as identified by the Government Performance and Results Act (GPRA): The extent to which any individual project is relevant to EPA's GPRA

objectives (Table 3) increases the significance of the exposure assessment, risk assessment, or risk management information that may result from that project.

TABLE 2. KEY SAB/IHEC RECOMMENDATIONS FOR THE ANALYSIS OF NHEXAS PILOT STUDY DATA

Exposure Assessment

•critical evaluation of the potential value of meta-analysis across the three subcomponents of NHEXAS and development of a plan for any meta-analysis

•identification of findings of considerable importance to help the Agency in some current risk management efforts

•once descriptive and summary statistics have been completed, concentration data should be transformed into exposure data

•integrate total exposures from all media and to estimate long-term exposures from short-term measurements

•prototypical analyses of exposure and assessments of intervention strategies should be made for a variety of chemicals measured

•improve the quality and utility of the databases from the three pilot studies

- integrate databases (Region V and Arizona)
- assess the implications of the Maryland study for the Arizona and Region V study
- integrate NHEXAS results with information on criteria pollutants

• assess source-to-dose trends

Exposure Analysis

•complete QA and quality control (QC)

•conduct descriptive analyses

•test study hypotheses which can be addressed

•evaluate questionnaires and activity diaries and the relationships with measurements

•integrate total exposures across all media, and assess the relative contribution of different sources, pathways, routes to exposure and body burden

•identify factors related to high-end exposures and correlate exposure to various chemicals/classes

Lessons Learned

•how to optimize the measurement and analytical approaches

•amount and nature of the new knowledge ... as it relates to the methodologies implemented

•national survey ... uses the experience of the pilot study so that the most appropriate multimedia measurements (including questionnaires) are used

Modeling

•develop physical models that integrate exposures from different media in order to estimate long-term exposures from short term-measurements.

•models for identifying factors related to high-end exposures

•address model validation and refinement

TABLE 3. RELATIONSHIP OF NHEXAS PILOT STUDY DATA TO ADVANCING EPA STRATEGIC GOALS IDENTIFIED IN THE GOVERNMENT PERFORMANCE AND RESULTS ACT (GPRA)

1. Clean Air

   - NHEXAS-collected data on personal, indoor, and ambient concentrations of several air toxics can be used to estimate exposure distributions and to verify models that predict ambient concentrations/exposure from emissions inventory data
   - NHEXAS data can contribute significantly to identifying some of the key pollutants likely to cause urban toxics risks, to making determinations of the adequacy of existing rules in addressing risks, and to estimating whether residual risks remain after technology-based standards are put in place for individual source categories

2. Clean and Safe Water

   - NHEXAS data can show the distribution of exposures to disinfection byproducts (e.g., chloroform), arsenic, and other compounds from drinking water.
   - NHEXAS multipathway data can provide information on the relative source contribution of water to exposure to the chemicals studied.

3. Safe Food

   - NHEXAS data on multipathway exposures of children to pesticides can provide the scientific foundation for reducing uncertainties and reliance on default assumptions used by EPA in determining potential risks to children exposed to pesticides, especially through the dietary pathway
   - NHEXAS data can be used to develop and evaluate aggregate and cumulative exposure model(s) of pesticides for infants and children.
   - NHEXAS measurement-based results and probabilistic models can provide better exposure and risk assessments for the pesticides studied
   - NHEXAS provided direct measurements of dietary exposure that can be used to evaluate uncertainty in the pesticide tolerance approach (i.e., indirect estimates of dietary exposure).

4. Preventing Pollution and Reducing Risk in Communities, Homes, Workplaces and Ecosystems

   - NHEXAS measurement-based information on population distributions of exposures to the selected pesticides and toxic substances can improve exposure assessments of communities.
   - NHEXAS characterization of multiple pathways of exposures can assist the Agency in identifying high-risk pathways to target risk reduction.
   - NHEXAS results will also help to evaluate the contribution of various pathways by examining blood lead in the context of both environmental concentrations and activities.
   - NHEXAS measurements of indoor air quality and total personal exposure can be used to estimate the sources (e.g., indoor, outdoor) of the greatest exposure to chemicals studied.

5. Better Waste Management, Restoration of Contaminated Waste Sites, and Emergency Response

   - NHEXAS data can provide baseline population exposure data to contrast with non-NHEXAS exposure data collected at Superfund or hazardous waste sites.

TABLE 3 (cont'd). RELATIONSHIP OF NHEXAS PILOT STUDY DATA TO ADVANCING EPA STRATEGIC GOALS IDENTIFIED IN THE GOVERNMENT PERFORMANCE AND RESULTS ACT (GPRA)

6. Reduction of Global and Cross-border Environmental Risks

   - NHEXAS data on persistent chemicals (e.g., some pesticides, limited mercury data) can be used to understand exposure to these compounds.

7. Expansion of Americans' Right to Know About Their Environment

   - NHEXAS provided data on the distribution and predictors of exposure to selected chemicals.
   - NHEXAS can help to identify factors (environmental indicators and sources) responsible for the highest exposures (and body burden), enabling people to identify their behaviors that contribute significantly to exposures.
   - NHEXAS data can be used to develop substantially more cost-effective community exposure study designs, enabling others to conduct such studies in their communities.

8. Sound Science

   - NHEXAS data can be used to significantly improve understanding of exposure factors that are fundamental to conducting exposure assessments.
   - NHEXAS information on multipathway exposure to a variety of compounds can be used to develop and verify improved aggregate and cumulative probabilistic exposure models.
   - NHEXAS data could be evaluated to estimate whether some of the compounds measured suggest an emerging risk.
   - NHEXAS measurements of biomarkers of exposure, together with environmental and exposure measurements and activity information, can be used to estimate total absorbed dose and to evaluate pathway contributions.

- NHEXAS objectives: The extent to which any individual project helps to meet overall NHEXAS objectives and those identified for each study (based on the July-Sept., 1995 issue of Journal of Exposure Analysis and Environmental Epidemiology; summarized in Table 4) will further achieving NHEXAS goals.

4. ***Demand:*** Projects for which an urgent demand for the results has been identified by the EPA's Program Offices (e.g., aggregate pesticide exposures for Food Quality Protection Act)

TABLE 4. KEY NHEXAS OBJECTIVES

- Evaluate the feasibility of NHEXAS studies for conducting future studies (e.g., better methods and approaches)
- Document the occurrence, distribution and determinants of exposures (e.g., population distributions of measurements, analysis of questionnaire information on sources and activities relative to exposures)
- Understand the determinants of exposure for potential at-risk populations as a key element in developing effective risk management strategies
- Evaluate and improve the accuracy of models developed to predict or diagnose exposure of people to chemicals.

As mentioned, these criteria were applied in a hierarchical fashion *within each of these six topic areas*. For example, those projects with a scientific focus on Predictors of Exposure and Dose (Table 6 on page 25), were first sorted based on the timing criterion. Next, those projects that are needed in the near-term were sorted as to their feasibility. Subsequently, the highly feasible projects were examined to identify those with broad applicability. Ultimately, those with high demand were identified. The next cycle focused on those the Predictors of Exposure and Dose projects that are needed in an intermediate-term time frame to determine their feasibility, applicability, and demand. No long-term Predictors of Exposure projects were identified. But had they been, the hierarchal process of ranking for feasibility, applicability and demand would have been repeated.

The remaining strategic issue not yet discussed is the relative priority of projects across the six topic areas. Recognizing the limitations of future resources that may be available to support these data analysis projects and the scientific merit of these categories, we conclude that the priorities for supporting analysis projects across the six topic areas are inherently equivalent. Thus, over the next several years, the highest priority projects across the six areas will be funded, in priority order, within each area. Ultimately, judgement will be required for implementation decisions, but this judgement will be guided by the criteria and priorities discussed here.

The prioritization criteria relate to overall EPA needs. Others may have different specific priorities that are valid for them. We expect that when the database is completed and publicized, many scientists and organizations will find additional analyses of interest to them. For example, an

EPA Region or a state public health department may have an immediate need for an exposure assessment of one chemical from only one pilot study. They might then apply their resources for this specific analysis. A graduate student with funding may use the publically available database to test a hypothesis for his/her dissertation, even if it is not ranked high in this strategy. Many such examples could be given. Having this variety of thinking can be very valuable and will add to the breath of what will be learned from NHEXAS. This value will be enhanced if the people performing these analyses contribute to the NHEXAS web site so that others do not unnecessarily duplicate analyses and citations for the resultant publications are readily available to everyone. We do respectfully request that all persons contemplating their own NHEXAS analyses carefully reflect on the priorities described here, understanding that these analyses are likely to have a high impact on environmental health decision making.

Any classification scheme requires compartmentalization of projects that can obscure their interrelationships. Thus, one of the implementation goals of the ORD staff is to ensure the appropriate degree of project integration. For example, some analyses within the area of Predictors of Exposure and Dose provide inputs into model comparisons under Evaluation/Refinement of Current Exposure Models and Assessments. Interdisciplinary integration with data or research outside the NHEXAS realm is also important. For example, some of the exposure assessments based on NHEXAS data will be compared to health effects information to create some risk assessments.

4. TOPIC AREAS AND PROJECTS

This section briefly summarizes the topic areas and the projects within them and explains the basis for the prioritization relative to the criteria of Section 3. Each subsection contains a table of the priorities for each project. Although the projects are listed in rank order, all projects are highly valuable. Appendix D contains a single table that combines the priorities for each topic area. The individual project descriptions are in Appendix E. The project descriptions are intentionally at a level of detail that provides goals and guidance to the investigators, while allowing them the freedom to apply their ideas in developing the details of the analyses based on the specifics of the data available

and their creativity. Therefore, each project has numerous options. Use of an external peer-review process for analysis tasks performed by ORD and external scientists will assist in ensuring the quality of the analysis approach chosen.

The first three project descriptions in each topic area contain estimates of the level-of-effort expected for each project. Such information is subjective and only intended to provide guidance for what resources may be needed. We chose to indicate personnel needs because they form the predominant cost category and costs/person can vary widely across performing organizations. We did not develop such estimates for each project because, at this time, it is not credible to make estimates for projects that will not begin for several years and that are dependent on information not yet available.

One overarching issue is the need to maximize utilization of resources by adhering to priorities and avoiding unnecessary duplication of effort. Because so many analyses are going on concurrently, the possibility of duplication arises. Insofar as the analyses are funded by ORD, internal communication can prevent this problem. However, we are hopeful that many others will be using the publically available database independent of ORD. As mentioned elsewhere, ORD intends to develop and maintain an NHEXAS website that provides summaries of ongoing analyses, with contact information, and citations to completed studies. This will provide important information to these other scientists. Even so, it is critical for everyone working with the data sets to be knowledgeable of the full range of analyses to ensure that the research is not redundant. Thus, we will be developing an easy way to engage all NHEXAS analysts in communication through the website.

4.1 DATA ANALYSIS AREA ONE: DESCRIPTIVE STATISTICS

4.1.1 Overview

This data analysis area contains research projects that describe the basic features of the NHEXAS pilot study results, both for the measurements and for the questionnaires and activity diaries. Residential environmental concentrations were measured for air (indoor and outdoor), tap water, soil, house dust, and surfaces for multiple target chemicals. Corresponding personal

measurements were obtained for air, diet, and dermal exposures; biomarkers of exposures were determined for blood, urine, and hair. However, not all sample types were collected for all chemicals nor for all participants within a study. The NHEXAS studies collected information using questionnaires for demographic and housing characteristics and potential sources of pollutants; and used diaries for personal activities, such as duration of time spent in different locations, source- and contact-related activities, and dietary consumption. Sampling weights have been calculated and can be used to draw inferences to the target populations and subgroups (limited by sample sizes). These include adjustments for nonparticipation in different elements of the study, including those providing only questionnaire information or participating in selected measurements.

As a first step in the analyses of these data sets, information on the summary statistics for the questionnaire and measurement results will be collected. This includes collecting and comparing results of analyses reported by the individual study investigators and conducting additional analyses using a common set of statistical methods, including weighted variance estimates. These studies will provide summaries for different population groups and supply a broad range of information about distributions (for continuous variables) or frequency of responses (for categorical variables). In addition, the completeness of the measurements data is to be evaluated relative to the potential utility of the data in the analysis or modeling of multipathway or multiroute exposures.

4.1.2 Developing Priorities for the Projects

Timing was first used to prioritize studies (Table 5) because of the need to understand the basic structure of the NHEXAS data prior to conducting more complex analyses. These descriptive analyses can be used to provide estimates of various exposure concentrations and exposure factors for exposure assessments. These assessments often rely on point estimates or distributions obtained from limited data sets that may not be appropriate to the populations of interest for that assessment. The NHEXAS results also can provide reference ranges (baseline information) for comparison to other locations, such as Superfund sites. Another use of these results is to determine the potential bias in estimates of national exposure factors and distributions that may result from the use of local or regional sampling. The projects described

TABLE 5. DESCRIPTIVE STATISTICS PROJECTS AND PRIORITIES[a]

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
D-01	An Analysis of Media Concentrations, Exposure, and Biomarkers by Demographics	N	H	H	
D-02	Univariate Statistics for Use in Exposure and Risk Assessment	N	H	M	Y
D-03	Impact of Censoring and Method Sensitivity and Precision on Multimedia Exposure Distributions and Associations	I	H	H	
D-04	Quantify Uncertainties in NHEXAS Data and Assess Contribution to Model Errors	I	M	M	
D-05	Investigate National Representativeness of NHEXAS Sampling Results by Comparing Measurement and Exposure Results Across the Three Regions	I	L	M	

[a]N = near term; I = intermediate term; H = high; M = medium; L = low; Y = yes.

in this section also address specific recommendations by the IHEC for conducting descriptive analyses and examining the shapes of exposure distributions.

Simple breakdowns by demographics (Project D-01) and providing univariate statistics for exposure and risk assessments (Project D-02) were identified to be completed first among the other projects in this topic area. Both of these projects also were identified as being highly feasible, given the availability of the NHEXAS data sets and current statistical methods and software. Several Agency needs include describing differences in exposures for different population subgroups. NHEXAS objectives to document distributions, including those of subgroups, also are met. Thus, Project D-01 was viewed as having slightly broader applicability than Project D-02. The next three projects involve more complex analyses, including multiple media and pathways (Projects D-03 and D-05), or model-based uncertainty analyses (Project D-04). Feasibility of completing these studies, given the limitations of the NHEXAS studies, was used to prioritize them: describing the impact of detection limits in various media (Project D-03) should be highly feasible, quantifying uncertainties (Project D-04) was viewed as being more difficult, and comparing measurement results across the

three studies (Project D-05) was considered less feasible. Specific comments are provided below for each project.

D-01 An Analysis of Media Concentrations, Exposure, and Biomarkers by Demographics — The goal of this project is to provide descriptive analyses of media concentrations, exposure, and biomarkers measurements for population subgroups (age, gender, ethnicity, socioeconomic status [SES], urban/rural, or other important groupings) in each NHEXAS study to identify differences among subgroups and to compare distributions with other studies.

Summary analyses need to precede more complex analyses; these descriptive analyses and simple demographic comparisons should be highly feasible. The project meets several EPA needs, related to subpopulation differences, as well as NHEXAS objectives and SAB/IHEC recommendations.

D-02 Univariate Statistics for Use in Exposure and Risk Assessment – The goal of this project is to develop univariate descriptive statistics (distributional information) for NHEXAS data that can be used broadly in exposure and risk assessment and in the design of human health effects studies.

This project develops summary statistics for those measurements and factors identified (by EPA's National Center for Environmental Assessment [NCEA]) as being commonly used in risk assessment, for which data were collected in one or more of the NHEXAS pilots. The data collected by NHEXAS can be used to better define distributions of these concentrations and exposure factors, such as activities, time spent in specific locations, dietary intake, and product usage. Although there are similarities between this project and Project D-01, this project is intended to support revision of the EPA Exposure Factors Handbook, and the selection of measurements and factors analyzed may be more limited than the previous project. Several program offices have identified access to summary information from the NHEXAS studies for use in exposure and risk assessments as an "urgent" need.

D-03 Impact of Censoring and Method Sensitivity and Precision on Multimedia Exposure Distributions and Associations – The goals of this project are twofold: (1) to examine how method sensitivity and precision and the censoring of data below detection limits affect the estimation of distributions and means for exposure, media concentration, and biomarker measurements and (2) to evaluate associations among such measurements.

The timing for some components of this project (i.e., summary of measurement sensitivity, proportion of samples above detection limits) is near-term, although identification of measurements to represent multiroute exposures for selected chemicals will be more complex. The feasibility is high, given the availability of codes in the database that indicate whether each sample's analytical results were above the detection limits. The applicability was also high, given the need for this information before conducting analyses (or assessments) involving multiple pathways or routes of exposure.

D-04 Quantify Uncertainties in NHEXAS Data and Assess Contribution to Model Errors – The goal of this project is to provide uncertainty estimates within the NHEXAS database that are available to researchers and the public, so that uncertainty is addressed consistently and does not lead to redundant effort by modelers. The results will identify how the data uncertainties may impact modeling uncertainties and will be illustrated with case studies.

The timing for this project is intermediate (or longer) term, based on the need to first determine the completeness of the NHEXAS measurements for multiroute exposures (Project D-03). The first component of the project, to identify variability and potential measurement errors (i.e., survey, sampling, analytical), should be feasible as an extension and publication of the QA results from each study. However, feasibility to quantify the impact of these sources of uncertainty on models may be limited by the need to identify and apply a suitable multimedia human exposure model (or framework).

D-05 Investigate National Representativeness of NHEXAS Sampling Results by Comparing Measurement and Exposure Results Across the Three Regions – The goal of this project is to evaluate the effects of using local or regional studies to provide estimates of national exposure factors and distributions. Very few national studies are available for use in

development of national distributions for exposure factors or related measurements; therefore, local or regional studies are used instead. The three NHEXAS studies provide a method for comparing very similar studies to determine the magnitude of regional differences for various exposure factors.

The timing for this project follows that of the projects to conduct basic summary analyses within each study. Feasibility is limited by the number of chemicals that were measured in all three studies, by potential differences in the methods or protocols employed (especially for sample collection), and by differences in the target populations for some chemical classes (e.g., a limited number of children in Arizona and Maryland studies, compared with the Minnesota study for pesticides).

4.2 DATA ANALYSIS AREA TWO: PREDICTORS OF EXPOSURE AND DOSE

4.2.1 Overview

This data analysis area includes research projects to analyze the relationships among the various type of measurements (environmental, exposure, and biomarkers), questionnaires, and diaries that were collected in the NHEXAS pilot studies. The comparisons included in this section include measurement and questionnaire data related to

- sources, characteristics, concentrations, activities, exposures, and biomarkers;
- multiple environmental media or exposure pathways;
- indoor and outdoor concentrations and estimated contributions of indoor and outdoor concentrations to integrated inhalation exposures;
- residential environmental media concentrations and existing monitoring data (e.g., fixed sites);
- biomarkers of internal dose and risk factors, including demographics, housing characteristics, questionnaire data, and measures of exposure and correlations among risk factors; and
- biomarkers and questionnaire responses and exposure and environmental media concentrations using multivariate analysis methods.

NHEXAS provides a rich source of information to support analyses of exposure and internal dose based on data collected from questionnaires and measurements of chemicals in residential and other environments. These analyses will be explored within each study and compared among studies.

Several of the projects involve hypotheses-testing, including hypotheses identified for the design of the pilot studies, or structural (model-based) analyses of exposure and dose. Included is an analysis of the relationships between measurements and estimates of dietary exposures. Other projects involve analyses of questionnaires and activity diaries. These analyses will evaluate the information content obtained from the questionnaires and compare that with exposure and environmental measurements to determine the value of the questionnaire items. Regression analyses will be used to identify the predictors of exposure. Factor analysis or principal components analysis will be used to identify the most important questions (or groups of questions) that would be used to analyze chemical exposures. Categorical or exploratory data analyses (e.g., classification and regression trees [CART]) could be used to identify questions useful in identifying those who are highly exposed, both to single chemicals or classes and to multiple chemicals.

4.2.2 Developing Priorities for the Projects

Timing was considered relative to other projects within this area (i.e., which of these projects should be done first), given the increasing complexity of these projects relative to the previous topic area (Table 6). The types, complexity, and scope of proposed analyses were used to identify Projects P-01 and P-02 as near-term. Feasibility of conducting the analyses using the NHEXAS study data and requirements for other models or data then were used to further rank both near- and intermediate-term projects. For projects related to biomarker analyses and interpretation (Projects P-04 through P-06), broad applicability and demand were used to help set the priorities.

TABLE 6. PREDICTORS OF EXPOSURE AND DOSE PROJECTS AND PRIORITIES[a]

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
P-01	Analysis and Comparison of NHEXAS Exposure Data to Residential Pollutant Sources, Concentrations, and Activity Patterns	N	H	H	Y
P-02	Compare Traditional Indirect Method of Estimating Dietary Exposures with Duplicate Diet Data and Compare Methodologies Utilized in NHEXAS	N	M	H	
P-03	Identifying Predictors of Exposure	I	H	M	
P-04	Risk Factors for Biomarkers of Internal Dose: Demographics, Questionnaire Data, Concentrations, and Exposures	I	M	H	Y
P-05	Determinants of Dose Measurements (Biomarkers) from the NHEXAS Studies	I	M	H	
P-06	Exploratory Data Analysis Methods for Evaluating Relationships Among Questionnaires, Exposure, Dose, and Risk Factors	I	M	M	
P-07	Use of NHEXAS Data To Test Assumptions About Activity Pattern Factors and Other Exposure Factors in EPA Risk Assessments	I	L	M	

[a]N = near term; I = intermediate term; H = high; M = medium; L = low; Y = yes.

P-01 Analysis and Comparison of NHEXAS Exposure Data to Residential Pollutant Sources, Concentrations, and Activity Patterns – The goals of this project are to (1) evaluate hypotheses about relationships among residential pollutant sources, characteristics, concentrations, and human activity patterns that contribute to personal exposures, especially for high-end exposures, and (2) to determine the value of questionnaires for understanding various aspects of exposure and the reliability and validity of the instruments used for ascertaining these factors.

This project was identified as near-term, given its ability to help identify the major predictors (or explanatory factors) of exposure. The feasibility should be high, given the range of questions and

associated measurement data and the availability of analysis methods. The project has very broad applicability for identification of factors associated with higher exposures, relating ambient and indoor concentrations to exposures, evaluating the value of questionnaires (and items) for understanding public health and exposures, and classification of exposures in epidemiological studies. Demand for this study was classified as "urgent" given several of the needs identified by IHEC, including descriptive analyses, evaluation of questionnaires, and characterization of high-end exposures.

P-02 Compare Traditional Indirect Method of Estimating Dietary Exposures with Duplicate Diet Data and Compare Methodologies Utilized in NHEXAS – The goals of this project are to (1) compare dietary exposure estimates from a dietary exposure model with direct measurements of dietary exposure; (2) evaluate the reliability and validity of dietary intakes determined in NHEXAS; and (3) evaluate alternative and less costly methods for measuring dietary exposure. This will involve comparison of direct exposure data from NHEXAS duplicate diet measurements with indirect exposure estimates derived from recorded food consumption combined with concentrations of NHEXAS chemicals measured in other diet studies, and of food intake rates from NHEXAS questionnaire surveys with those from the U.S. Department of Agriculture (USDA) and the National Health and Nutrition Examination Survey (NHANES) for comparable years, geographical regions, and population subgroups. This project was identified as near-term, given its potential contribution to the understanding of dietary exposure and methods. Indirect estimates of dietary exposure, based on combining food intake rates with residue data, have been used for regulation of pesticides and for assessing exposures to metals and other chemicals. The NHEXAS data provide a unique opportunity for evaluation of indirect estimates using direct monitoring data (duplicate diet) to enhance the scientific basis for decision making. Feasibility was considered moderate, because the food diaries may require recoding and these data then need to be linked to existing dietary concentration databases. Applicability is broad because this study relates to several EPA needs (e.g., Safe Food) and also tests a basic NHEXAS study hypothesis (e.g., the adequacy of extant data and models to predict exposure). The results also will help to evaluate survey instruments (diet diary and recall

questionnaire), assess the contribution of dietary exposure, and identify less costly alternatives for dietary exposure monitoring.

P-03 Identifying Predictors of Exposure – The goal of this project is to identify primary predictors of exposure, using questionnaires and biological or environmental measures for use in epidemiology studies and other studies where individuals' exposure levels are sorted into categories, such as high, medium, and low.

The timing for this project was identified as being intermediate-term because the proposed multivariate analyses are likely to be more complex than those identified in the previous projects. Feasibility to conduct these analyses should be high, given the availability of statistical methods. The applicability appears to be less broad, in terms of meeting multiple EPA needs, than the previous projects but will help to meet the needs of epidemiologists, risk assessors, and risk managers who need exposure classification methods.

P-04 Risk Factors for Biomarkers of Internal Dose: Demographics, Questionnaire Data, Concentrations, and Exposures – The goal of this project is to develop methods of estimating internal dose that can be used in studies of health outcomes, based on an analysis of the association of biomarkers of internal dose with (1) demographics; (2) questionnaire information on behaviors, activity patterns, health indices, etc.; and (3) measures of personal exposures and media concentrations.

The timing for this project was identified as being intermediate-term, given the broad scope and complexity of the proposed analyses. Feasibility may be limited by the need for other models and information (e.g., absorption and elimination rates, timing and routes of exposures) to interpret biomarker measurements relative to dose and by the timing of the NHEXAS exposure and environmental measurements relative to the time periods represented by the biomarkers (e.g., short-term for blood-VOCs; long-term for blood-lead). Further understanding of the interpretation of biomarker levels is valuable because they may be a better predictor of health outcome than environmental concentrations, which do not account for multiple routes or for uptake/intake and absorption processes. The ability of these markers to account for multiroute exposures gives this

study broad applicability in addressing EPA needs, as well as those identified by IHEC (evaluate questionnaires, activities, concentrations, and biomarkers) and for the NHEXAS studies (distribution and determinants of exposures; provision of baselines for biomarker distributions). Demand has been high for information on distributions of biomarker measurements and their interpretation relative to questionnaire information and environmental concentrations.

P-05 Determinants of Dose Measurements (Biomarkers) from the NHEXAS Studies – The goal of this project is to identify and evaluate environmental and questionnaire determinants of absorbed dose and to better understand the time course and associations between exposure and dose. Questionnaire response data will be considered as a modifier of the exposure/dose association. This association will be evaluated further by taking into account existing pharmacokinetic models and parameters. Methods and approaches for assessing the dermal exposure contribution relative to the biomarker measurements are of particular importance because dermal exposure methods are not well developed.

The time frame for this project was identified as intermediate, given the complexity of the analyses. Feasibility is moderate, given the need to link pharmacokinetic models and parameters with statistical analyses. There is broad applicability for improving the ability to interpret biomarker measurements to a range of EPA goals, IHEC recommendations (integration of exposures and relative contributions and questionnaire analyses), and NHEXAS objectives (occurrence and determinants of exposure and dose). Demand for these analyses appear to be less than for Project P-04.

P-06 Exploratory Data Analysis Methods for Evaluating Relationships Among Questionnaires, Exposure, Dose, and Risk Factors – The goal of this project is to identify the factors that contribute to high exposures, to establish relationships among these factors and exposure magnitudes and distributions, and to understand subpopulation differences. Several analysis methods are now available for analyzing complex data sets to identify patterns, relationships, sociodemographic variables, important factors, and combinations of factors that influence or affect exposure distributions. These data will be analyzed without a priori

decisions about relationships among the variables to generate new hypotheses regarding environmental exposures.

This project involves more complex analytical approaches and a very broad scope that will probably require a longer time frame for completion. Feasibility may be limited by the completeness of the NHEXAS study data and by limitations in applying some analytical techniques to categorical response data (i.e., questionnaires). However, the results could have fairly broad applicability by helping to classify the NHEXAS data into variable groups and focus future exposure assessments in national surveys, epidemiological studies, and risk assessments. Refinements could be made to the questionnaires used in subsequent studies that reduce participant burden and study costs. This project addresses some EPA needs, as well as IHEC recommendations for questionnaire analyses and NHEXAS objectives to understand the determinants of exposures.

P-07 Use of NHEXAS Data To Test Assumptions About Activity Pattern Factors and Other Exposure Factors in EPA Risk Assessments – The goal of this project is to test assumptions and scenarios used in current assessment procedures, to improve current exposure assessment methodologies, and to identify factors where further study is needed. This project will examine the use of activity pattern factors and other exposure factors in risk assessments as they are done in EPA's Air, Water, Hazardous Waste, Pesticides, and Toxics programs. Examples include (1) examining NHEXAS time/activity diaries and follow-up questionnaire data to determine the repetitiveness (frequency) of behavior over a 6- or 7-day period and comparing this with existing time/activity databases; (2) examining the relationship among climate, season, level of exertion, and drinking water intake; (3) preparing exposure scenarios, evaluating scenarios with NHEXAS data, and comparing those results to results obtained using current exposure assessment methods, scenarios, and assumptions; and (4) using NHEXAS data to design scripted sampling protocols for subsequent model testing or trend monitoring.

The timing for this project was identified as intermediate, given the complexity of tasks relative to other analyses. Feasibility was estimated to be low, given the limited resolution (time and locations) of the NHEXAS time/activity diary used for a week-long collection period, as compared to more

detailed recall diaries that have been used for a 1-day period and without the additional requirements involved in a monitoring study. The analysis of activity patterns could be used to test assumptions and scenarios used in current assessment procedures, to improve the current EPA methodologies, and to identify factors where further study is needed. Applicability was considered moderate for addressing EPA needs, as well as IHEC recommendations and NHEXAS objectives.

4.3 DATA ANALYSIS AREA THREE: SPATIAL AND TEMPORAL VARIABILITY

4.3.1 Overview

Environmental media concentrations of chemicals and exposure patterns of individuals vary over both space and time. NHEXAS studies have collected extensive data on environmental concentrations, exposures, questionnaires, time activity, and dietary patterns from participating subjects and households selected from many different communities in EPA Region V, Arizona, and Maryland. Moreover, the Maryland component of the NHEXAS study has gathered exposure, activity, and dietary survey data on a large cohort of subjects over multiple months and seasons and over seven consecutive days in each cycle. Thus, the NHEXAS database (particularly the Baltimore Study) offers a unique opportunity to examine the spatial and temporal variability in human exposures to both single and multiple chemicals and to identify key factors that effect inter- and intraindividual variability in exposures.

The analysis of temporal variability in exposures and concentrations will include analysis of both single and multiple chemical concentrations measured in each of the environmental media by the three NHEXAS studies. Both within- and between-study variability will be examined. Temporal variability in human behaviors and dietary patterns will be analyzed and interpreted in relation to observed changes in the exposure patterns over time. Specifically, NHEXAS Maryland dietary and activity pattern data will be used to develop predictive relationships between single-day and longer term observations. This analysis will determine the reliability of using short-term measures of exposure in the assessment of long-term or chronic exposures of individuals and populations.

NHEXAS data from all three studies also will be used to investigate the spatial variability in concentrations exposures, doses, and activity patterns. Geographical factors (i.e., differences because of various spatial aggregations, states versus counties, rural versus urban) and climatic factors influencing these measurements will be evaluated. The spatial and temporal analysis of the NHEXAS data will be used to characterize the variance components of NHEXAS data, including the inter- and intrapersonal, temporal (e.g., integration time, seasonal, weekly), activity-related, and spatial variabilities by sample size for each of the pollutants by pathway, medium, and integrated total exposure. Results will be used to optimize future NHEXAS-like study designs. Finally, the results from these analysis and the NHEXAS database will be used to develop and evaluate models for quantifying within- and between-subject variability in pesticide exposures and biomarker concentrations.

4.3.2 Developing Priorities for the Projects

Seven projects were identified in this topic area. The ranking scheme and criteria described earlier—timing, feasibility, and broad applicability—were used to rank the projects in this area. Table 7 provides the rankings, and the following sections discuss the rationale for the rankings. Once again, relative timing was considered as the first criterion to establish rankings for the projects in this research area. Many of these investigations can be started in the near term, when the NHEXAS data sets are available (Projects ST-01 through ST-04). The methodologies and expertise are available to start these projects immediately. However, Project ST-01 was the highest ranked project because it scored best in all categories (timing, feasibility, and broad applicability). Second-ranked Project ST-02 also received the highest rankings in terms of timing and feasibility. However, it does not have the broad applicability that Project ST-01 has because it focuses solely on the temporal aspects of dietary and activity behavior. The other two projects, which were ranked highest for the timing criteria (Projects ST-03 and ST-04), both received a medium feasibility criteria ranking because comparisons of personal exposures with point sources cannot be accomplished without the cooperation of the principal investigators of the various NHEXAS consortia who need to maintain the anomymity of the location of the subjects.

Projects ST-05 and ST-06 were ranked as intermediate projects in terms of timing because of the complexity and scope of the analysis required for their successful completion. Also, this sequence of rankings is consistent with the philosophy of completing simpler building blocks before more complex tasks are undertaken.

The project that ranked last in terms of timing was ST-07. This project requires the development and refinement of pharmacokinetic models.

TABLE 7. SPATIAL AND TEMPORAL VARIABILITY[a]

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
ST-01	Temporal Variability in Exposure Concentrations and Aggregate Exposure Using NHEXAS Data	N	H	H	
ST-02	Use NHEXAS Dietary and Activity Pattern Data To Develop Predictive Relationships Between Single Day Observations and Long-Term Patterns of Behaviors	N	H	M	
ST-03	Characterization of the Variance Components of NHEXAS Data to Optimize Future Designs	N	M[b]	H	
ST-04	Spatial Variability	N	M[b]	H	
ST-05	Investigate Stability of Individuals in Population Exposure Ranks Over Time	I	H	M	
ST-06	Spatial and Temporal Variability in Multichemical Exposure	I	M[b]	H	
ST-07	Development and Evaluation of Models for Interpreting and Quantifying Inter- and Intraindividual Variability in Pesticide Exposure/Dose Using NHEXAS Data.	L	M	H	

[a]N = near term; I = intermediate term; H = high; M = medium; L = low; Y = yes.

[b]Spatial variability can be determined on national, regional, and community bases when the NHEXAS data sets are available. However, the exact location of NHEXAS participants will not be included in the NHEXAS data sets to protect the confidentially of the individual participants of the study. Thus, comparisons of personal exposures with point sources cannot be accomplished without the cooperation of the principal investigators of the various NHEXAS consortia. Therefore, the criterion of feasibility was ranked medium for these projects, as compared to other projects without such concerns.

ST-01 Temporal Variability in Exposure Concentrations and Aggregate Exposure Using NHEXAS Data — The goal of this project is to determine optimum strategies and designs for future exposure investigations. Questions to be addressed include when is it possible to estimate exposure from a single set of cross-sectional measurements, and what is the optimum number of such measurements that must be made for each pollutant medium class and for total exposure? Of interest is an understanding of the temporal span of the toxicological effect (i.e., What is the exposure duration of interest? Does variability occur over such a duration?).

This project has important implications for risk assessment because it will help account for uncertainty because of intraindividual variability over time and the factors that influence that variability. Most personal exposure measurement data are collected over a relatively short period of time (e.g., a day or week). However, exposure scientists often are interested in chronic individual exposure distributions (e.g., a season, a year, or even 70 years) for risk assessments and for the mitigation of unwanted exposures. In the past, exposure scientists often were forced to use population exposure distribution data (a large number of individual snapshots sampled once at various times) to attempt to predict individual distributions. This project has implications for epidemiology because it will help reduce uncertainty because of misclassification resulting from bias introduced by failing to account for temporal variability in exposure indicators for a given individual. In addition, it will help determine optimum strategies and designs for future national exposure studies.

ST-02 Use NHEXAS Dietary and Activity Pattern Data To Develop Predictive Relationships Between Single-Day Observations and Long-Term Patterns of Behaviors — The goal of the project is to describe the relationship between short- and long-term measurements of exposure-related behaviors that can be used in models of long-term exposures. This will be accomplished through the use of statistical techniques to determine the relationships between measurements of exposure-related behaviors (e.g., dietary and activity patterns) on a single day and in subsequent longitudinal measurements. Therefore, the short-term relationships will be used to develop predictive models of longer term behaviors. Such data are critical to the accurate estimation of dose rates over periods longer than a single day.

This project was ranked second because of timing and feasibility considerations (it received the highest scores possible in these categories). The ability to predict long-term behaviors from short-term observations is extremely important to understand exposure patterns over time. However, this project does not have the broad applicability of that of Project ST-01.

ST-03 Characterization of the Variance Components of NHEXAS Data To Optimize Future Designs — The goal of this project is to characterize the variance components of NHEXAS data, including the inter- and intrapersonal, temporal (e.g., integration time, seasonal, weekly), activity-related, and spatial variabilities by sample size for each of the pollutants by pathway or medium and by integrated total exposure. Results will be used to optimize future NHEXAS design. Exposure data from each of the three NHEXAS studies will be analyzed to determine the inter- and intrapersonal, temporal, and spatial variabilities in exposure distributions. Analysis will be performed by pollutant, both pathway-specific and as integrated total exposure, as well as by subpopulation. Variabilities will be assessed using standard statistical approaches, including the coefficient of variation and one-way analysis of variance (ANOVA) and mixed model approaches. Graphical techniques will be used to evaluate and determine appropriate pollutant- and media-specific sampling strategies. As possible, pollutants will be grouped based on identified appropriate sampling strategies. This project should be limited to representatives of the various chemical classes (e.g., metals, pesticides, VOCs).

This project was rated highly in terms of timing and broad applicability. The proposed project directly addresses SAB concerns and, as a result, will improve substantially the ability to optimize the design of future NHEXAS and other exposure studies. It will incorporate findings from each of the three NHEXAS consortia and will allow the sampling plan of each consortium to be examined in a systematic and quantitative manner. However, the spatial variability aspects of this project give it a medium feasibility rank because comparisons of personal exposures with point sources cannot be accomplished without the cooperation of the principal investigators of the various NHEXAS consortia (see Table 7 note).

ST-04 *Spatial Variability* — The goals of this research are to identify spatial and geographic factors contributing to high exposures for consideration in exposure assessment, to determine representativeness of local and regional data for use in assessments of other regions, and to identify geographically defined point and area sources. These analyses will help assessors understand the geographic variability of pollutant concentrations and exposures and the impacts of such things as population density, climate, elevation, and local cultural factors. It also will examine the impact of identifiable, geographically located sources on exposure levels. Information on spatial variability also will contribute to the more efficient design of future studies.

This project was highly rated in terms of timing and broad applicability. However, the spatial variability aspects of this project give it a medium feasibility rank because comparisons of personal exposures with point sources cannot be accomplished without the cooperation of the principal investigators of the various NHEXAS consortia (see footnote for Table 7).

ST-05 *Investigate Stability of Individuals in Population Exposure Ranks Over Time* — This project will investigate the effect of using cross-sectional studies on estimates of exposure factor distributions. Cross-sectional studies are cost efficient because they collect minimal observations per individual, but they provide no indication of temporal variability. Measures of intraindividual temporal variability do not necessarily tell the complete story, as individuals may vary in concert because of factors such as seasonal changes. It is also useful to examine the stability of individual's position or rank in the population exposure distribution to determine how this stability influences the predictive ability of various exposure distribution parameters. This will be accomplished by identifying feasible and relevant variables from NHEXAS for study, developing and evaluating methods for examining temporal variability (and stability) of individuals, and through the use of mixed models to develop repeated measure, temporal correlation estimates.

Timing of this project was rated intermediate, resulting from the complexity of the task because of the suggested approach (i.e., identification of relevant variables and the need to develop methods to

examine temporal variability and stability and models to provide repeated measure, temporal correlation estimates).

ST-06 *Spatial and Temporal Variability in Multichemical Exposure* — The goal of this project is to characterize the magnitude and variability of exposure to multiple chemicals measured in all environmental media by the three consortia. This study will provide some of the first information on multichemical and multipathway exposures required for cumulative risk assessments. The suggested approach is to examine multiple chemical exposure, first for each route of entry and second for aggregate exposure.

The need to assess risks of cumulative chemical exposures is well recognized within the scientific and regulatory communities. Little information is available for such assessments. Analysis of the temporal and spatial aspects of the NHEXAS data is important to reduce uncertainty in the exposure estimates for these assessments. However, methods and data to support cumulative chemical exposure generally are lacking at this time. In addition, the spatial variability aspects of this project give it a medium feasibility rank because comparisons of personal exposures with point sources cannot be accomplished without the cooperation of the principal investigators of the various NHEXAS consortia (see footnote for Table 7).

ST-07 *Development and Evaluation of Models for Interpreting and Quantifying Inter- and Intraindividual Variability in Pesticide Exposure/Dose Using NHEXAS Data* — The goal of this project is to develop, test and evaluate, and make available to EPA and the scientific community at large, a mechanism-based computational tool for characterizing and quantifying inter- and intraindividual variability (i.e., cross-sectional and longitudinal variability) in pesticide exposures/doses of human populations. This project will analyze cross-sectional and longitudinal biomarker and exposure data for pesticides considered in NHEXAS (such as chlorpyrifos and atrazine) to develop and test population-based pharmacokinetic (i.e., pharmacostatistical) models that explicitly discern and quantify intra- and interindividual variability in human doses.

Quantitative characterization of inter- and intraindividual dose (and corresponding exposure) to common pesticides will reduce the uncertainty in risk assessments. The mechanistic approach to be developed and evaluated should be applicable to a wide range of exposure situations and U.S. population segments. However, this was deemed a long-term project because the development and refinement of pharmacokinetic models is required.

4.4 DATA ANALYSIS AREA FOUR: AGGREGATE EXPOSURE, PATHWAY ANALYSIS, AND CUMULATIVE RISK

4.4.1 Overview

This data analysis area addresses exposure via multiple pathways and risks from exposure to more than one environmental agent. EPA risk assessments are evolving from a focus on single environmental agents and, often, a single medium to assessments of total risk from exposure to multiple chemicals via multiple pathways. NHEXAS was designed as a multipathway, multichemical exposure study, which will provide the data to test many hypotheses related to aggregate exposure and cumulative risk. Aggregate exposure is defined for purposes of this strategy as total exposure to a single environmental agent. The term "cumulative risk" is used in different ways by different programs in EPA. It may be used to mean risk from exposure to a set of environmental agents that have the same health endpoints or modes of action, the risk from exposure to all such agents in the environment regardless of endpoint or mode of action, or in the broadest sense, the risk from all environmental stressors and their interaction with genetic factors. NHEXAS provides a rich database of multiple measurements of environmental and biological concentrations of chemicals and personal data on individual activity patterns that will help in the study of many of these issues.

4.4.2 Developing Priorities for the Projects

Four projects were identified in this topic area (Table 8). The ranking scheme and criteria described earlier—timing, feasibility, broad applicability, and demand for results—were used to rank the projects. The two near-term projects (Projects AE-01 and AE-02) are those for which techniques are available to analyze the NHEXAS data and to achieve the desired results. These two projects then were sorted by feasibility. Project AE-02 was rated lower for feasibility because it requires comparison of data from separate NHEXAS studies, which may not always be directly comparable. The multipathway exposure model (Project AE-03) is rated intermediate for timing. Development of probabilistic multipathway models is complex and requires the preliminary assessments of Project AE-01, as well as completion of exposure analysis projects, to complete the model. The cumulative risk project (Project AE-04) is considered long-term. Cumulative risk assessments are highly complex. Some parts of the

TABLE 8. AGGREGATE EXPOSURE, PATHWAY ANALYSIS, AND CUMULATIVE RISK[a]

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
AE-01	Aggregate Exposure	N	H	H	Y
AE-02	Comparison of Children's and Adults' Exposures to Pesticides and Other Chemicals in the Region V, Arizona, and Maryland Studies	N	M	H	Y
AE-03	Construction of an Empirical Multimedia/Multipathway Exposure Distribution Model Including Temporal Variability Based on NHEXAS Data	I	M	M	
AE-04	Cumulative Risk from Exposure to NHEXAS Chemicals	L	M	H	

[a]N = near term; I = intermediate term; H = high; M = medium; L = low; Y = yes.

project, such as examination of correlations among exposures to different chemicals can be examined in the short term, but the overall project will take considerable time to accomplish.

AE-01 *Aggregate Exposure* — The goal of this project is to estimate multiroute, multipathway exposures and risks from exposure to single NHEXAS target chemicals. Environmental and personal concentration data and questionnaire data, supplemented by data from other sources and professional judgment will be used to estimate total exposure for each individual respondent. Existing models will be used to combine data to estimate aggregate exposure as a total absorbed dose. Total absorbed doses will be compared to biomarker data. Absorbed doses for each individual will be disaggregated by pathway, allowing identification of the contributions of each pathway to absorbed dose. Contributions of exposure factors (e.g., activity patterns, dietary intakes, season, climate) to high-end exposure will be investigated by comparing factors to total absorbed dose or biomarkers. Risks of adverse health outcomes will be estimated using standard EPA methods and risk factors from EPA's Integrated Risk Information System (IRIS).

This project is near term and can be started as soon as the NHEXAS database is available. Aggregate exposure assessments have been conducted for many years in ORD and in multimedia EPA programs, such as the Hazardous Waste Program, the Toxics Program, and, more recently, the Pesticides Program. The expertise and methodology are available to start this project immediately. Feasibility is high, given that the NHEXAS studies were designed specifically to assess total exposure. There will be data gaps for some parts of the exposure model, but missing information can be obtained from other sources and supplemented by professional judgment where necessary. The project has broad applicability. It will provide information on important pathways of exposure for particular target chemicals, identify pathways or exposure factors that have not been considered in assessments, and may show that some pathways are not as important as they were believed to be. Parts of this project could be characterized as "urgent" in the sense that the results will be useful to ongoing EPA programs, such as the Pesticides and Air programs.

AE-02 Comparison of Children's and Adults' Exposures to Pesticides and Other Chemicals in the Region V, Arizona, and Maryland Studies — The goal of this project is to conduct aggregate exposure and cumulative risk assessments that compare children's and adults' exposures to NHEXAS target chemicals. The Minneapolis-St. Paul, MN, study of children aged 3 to 12 will provide the data on children. The Region V and the Arizona studies will provide the data on adults and a small number of children. Systematic procedures for comparing the data across studies will be developed. Many different endpoints for children and adults can be compared: biomarkers, personal exposure measurements (e.g., dietary intakes of chemicals per unit body weight), activities, and absorbed doses by single or multiple pathways. Health risks also will be assessed and compared using appropriate toxicity values.

This project is rated a near-term project for the same reasons given for Project AE-01. Feasibility is rated medium for two reasons. First, children's exposures in the Minnesota study may have to be compared to adults' exposures in Region V and Arizona. The Arizona study used different sampling protocols in some cases, and, therefore, comparisons may not always be possible. Second, in most cases, toxicity measures for childhood exposures and endpoints may not be available because of lack

of data. Thus, it may not be possible to make a real comparison of age-related risk but, rather, only a comparison of exposure. The project is rated high for broad applicability because all EPA programs are interested in the conditions under which children are at greater risk than adults from exposure to environmental contaminants. Two recent statues, FQPA and the Safe Drinking Water Act Amendments of 1996, specifically require EPA to consider risk to children in regulatory actions. This study will provide comparisons of exposures and help identify the exposure pathways and factors that contribute to the greatest differences between children and adults. For programs such as the Office of Pesticide Programs (OPP) residential exposure programs, this comparison of children and adults could be considered urgent.

AE-03 Multi-Pathway Exposure Modeling — The goal of this project is to develop multipathway models for NHEXAS target chemicals. Current multipathway exposure models are based on studies that usually were limited to a single medium and generally lacking in longitudinal data. Existing models will be enhanced to allow use of empirical multivariate distributions derived from NHEXAS data. Temporal variability will be incorporated into the models using the Maryland data.

This project is ranked as intermediate because some preliminary exposure analysis will have to be conducted prior to development of a comprehensive model. Feasibility is rated medium. The development of the model will require the integration of the Maryland longitudinal study with the cross-sectional studies in Arizona and Region V. Problems of different sampling protocols will arise. It will be somewhat difficult to integrate children's scenarios into the model. Although of some interest to the various programs, a multipathway exposure model is more immediately useful as a research project that integrates results of many of the other projects described in this strategy. The project will extend empirical models to include temporal variability, allowing for the estimate of exposure distributions over a 1-year period. The likelihood of developing a complex multipathway aggregate exposure model that could be used for a wide number of chemicals may be somewhat limited because each chemical has a different set of exposure scenarios, and incorporation of all possible scenarios would be very labor intensive. In addition, it is difficult to update the model as new data becomes available. Thus, EPA programs use general models for screening purposes, but

usually develop their own models for more intensive assessments. This project is ranked below the others as having somewhat less applicability across EPA.

AE-04 *Cumulative Risk from Exposure to NHEXAS Chemicals* — The goal of this project is to examine cumulative risks of exposure to more than one NHEXAS target chemical. Multivariate statistical methods will be used to determine whether concentrations in personal air, dust, diet, and biological samples co-vary across subjects for different chemicals. Groups of NHEXAS chemicals will be identified that are appropriate for cumulative risk assessment, based on factors such as common toxicity endpoints and like modes of action. If data are available, synergistic and antagonistic interactions will be taken into account. Otherwise, additivity will be assumed. EPA guidance on assessment of mixtures will be followed. This project calls for innovative approaches to using the NHEXAS data in assessing the impact of exposures to multiple chemicals.

Methods and data to support dose-response assessment for mixtures of chemicals generally are lacking. There are a few cases where assessments have been done for chemicals with common modes of action (e.g., dioxin-like compounds, organophosphate pesticides). In general, however, most such assessments tend to focus more on aggregate exposure than on the risk component of the assessment. There are few methods for assessing cumulative risk for chemicals with different endpoints. Therefore, this project is ranked as a long-term project. The feasibility is rated medium. The NHEXAS database will support the aggregate exposure analysis required for cumulative risk assessment. The dose-response data are probably available now for many chemicals. If additivity is assumed, a cumulative risk analysis of some sort might be feasible. However, success likely will increase if the project is delayed until some additional guidance and methods have been developed. Cumulative risk assessments are rated high for broad applicability to all program offices. These analyses will provide insights into whether high exposure to one chemical in a class correlates with high exposure to others and will allow comparison of chemicals across classes. The analysis will contribute to development of guidelines for cumulative risk assessment. This area is ranked below the aggregate exposure project because that project is likely to provide analyses that can be used immediately in EPA assessments.

4.5 DATA ANALYSIS AREA FIVE: EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS

4.5.1 Overview

NHEXAS studies have generated a rich database on some source emission characteristics, environmental media concentrations, time-activity and dietary patterns, and individual measures of exposure and dose. Thus, the NHEXAS database offers a unique opportunity to test existing exposure models and to develop new or improved exposure and dose modeling methods. This topic area includes a number of proposals on evaluating and developing human exposure and dose models by utilizing the NHEXAS database.

One of the main objectives of the NHEXAS pilot studies was to compare NHEXAS exposure measurements with exposure projections derived from exposure models and data that were available prior to conducting the NHEXAS studies. Comparison of pre-NHEXAS study model results with data and findings from the NHEXAS study will allow both the evaluation of the current exposure and dose models and the implementation of research to refine these models in areas where significant discrepancies are observed. This analysis will involve evaluating the results from the multimedia multipathway population exposure models for benzene, lead, and chlorpyrifos that were developed using only the information available prior to the NHEXAS study measurements. Following these evaluations, the pre-NHEXAS models will be updated using the information collected during the NHEXAS studies. NHEXAS data also will be used to evaluate other existing or emerging air quality and multimedia models, such as the Hazardous Air Pollutant Exposure Model (HAPEM4) used in the recent National Air Toxics Assessment (NATA) study, the Multimedia Pollutant Assessment System (MEPAS), Hazardous Waste Identification Rule, Stochastic Human Exposure and Dose Simulation, Modeling Environment for Total Risk Studies, CalTOX, Total Risk Integration Methodology (TRIM), and LifeLine™, etc. In addition, NHEXAS data will be used to evaluate the limitations of the current screening methods or models used to make regulatory decisions for Superfund sites, pesticide regulations, and emissions to air or water.

Development of new or refinement of existing multimedia multipathway models also requires detailed information on various model parameters, such as ingestion rates, source strengths, air exchange rates, etc. In addition to generating average estimates for these parameter values, more

complete characterization of ranges and uncertainties associated with these model parameters are beneficial to most of the current probabilistic exposure models. Following the model evaluation project, the plan is to develop model input parameter distributions using the NHEXAS monitoring, questionnaires, time-activity, and survey data. Specific emphasis will be placed on key exposure parameters that are likely to contribute to high-end exposures. Related analysis projects will examine the nature and magnitude of uncertainties in the NHEXAS data, and how they may contribute to modeling errors. Finally, NHEXAS data on biomarker concentrations will be analyzed to develop new methods for reconstructing individual exposure profiles using questionnaires and time-activity data. Several assumptions regarding the route and timing of dose will be studied in estimating exposure profiles. Children, as well as the general population, will be considered during all of these investigations.

4.5.2 Developing Priorities for the Projects

TABLE 9. EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS[a]

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
M-01	Compare Pre-NHEXAS Model Results with NHEXAS Measurements	N	H	H	Y
M-02	Comparison of NHEXAS Findings with NATA Estimates for Ambient Air Levels and Exposures for Selected VOCs and Metals	N	H/M	H	Y
M-03	Develop Model Parameters from Qualitative and Quantitative NHEXAS Monitoring Data, Questionnaires, Time/Activity, and Survey Data	N	M	H	
M-04	Evaluate Implications of NHEXAS Results for Existing Chronic Exposure Assessment Methodologies	I	H/M	H	Y
M-05	Evaluation of Existing Multimedia Models Using the NHEXAS Data Set	I	M	H	
M-06	Quantify Uncertainties in NHEXAS Data and Assess Contribution to Model Errors	I	M	M	
M-07	Reconstruct Exposure and Dose Profiles from Biomarker Data Utilizing Questionnaire and Environmental	I	M	M	

[a]N = near term; I = intermediate term; H = high; M = medium; Y = yes.

Seven projects were identified in this topic area (Table 9). The ranking scheme and criteria described earlier (timing, feasibility, broad applicability, and demand for results) were used to rank the projects. Timing was considered relative to other projects within this area (i.e., which of these projects should be done first), given the increasing complexity of these projects relative to the other topic areas. This assumes that some of the simpler modeling-related analyses would be conducted in conjunction with other descriptive statistics and mutivariate analysis projects, and that these results would be available to the modelers. The types, complexity, and scope of proposed analyses were used to identify three projects (Projects M-01, M-02, and M-03) as near-term. Feasibility of conducting the analyses using the NHEXAS study data and requirements for other models or data then were used to further rank both near- and intermediate-term projects (e.g., Project M-02 versus Project M-03, and Project M-04 versus Project M-05). After feasibility, broad applicability and level of demand (or urgency of this information to EPA) were used as criteria to rank near-term projects within the same category of timing or feasibility (e.g., Project M-02 versus Project M-03). Likewise, for the three intermediate-term projects related to evaluation of existing multimedia models or uncertainty or biomarker analyses (Project M-05 versus Project M-06 and Project M-07), broad applicability was used to help set the priorities. Table 9 provides the rankings, and the following section describes the rationale for these rankings.

M-01 *Compare Pre-NHEXAS Model Results with NHEXAS Measurements* — The goal of this project is to compare pre-NHEXAS model results for benzene, lead, and chlorpyrifos with NHEXAS measurements. If models and data compare well, this provides an evaluated model for use in predicting human exposures to these pollutants. These models and methods then can be applied to populations outside of the NHEXAS study region. Differences between measured and modeled results can be used to improve model predictions and to provide information on limitations in the use of disparate studies. Overall, this comparison will provide confidence in using models to estimate multimedia exposures and will allow updating

pre-NHEXAS models with information obtained from the NHEXAS program measurement data.

This project ranked first because of its importance in testing one of the important NHEXAS study hypothesis regarding testing pre-NHEXAS study models against the data obtained from the NHEXAS program. This analysis project also responds to several IHEC suggestions pertaining to exposure model validation and refinement and integrating exposures from different media. It also provides a tool for identifying factors related to high-end exposures among sensitive and general population groups. This project can be started in the near term as soon as the NHEXAS database becomes available because the pre-NHEXAS study models for benzene, lead, and chlorpyrifos have been completed. For these three chemicals, the project has high feasibility because they have sufficient number of detects in the various media sampled during the NHEXAS study. This project will have broad applicability. It will provide information for specific program offices on important pathways of exposure for a particularly important pesticide, a metal, and a VOC. The pre-NHEXAS study models will provide EPA with new probabilistic aggregate exposure assessment models and help to advance the population exposure and dose assessment methodology. In addition, this analysis project may reveal important pathways or exposure factors that have not been considered in previous assessments; and also may show that some pathways are not as important as they were believed to be. This project is characterized as urgent because ORD and various program offices (e.g., OPP, Office of Air Planning and Standards [OAQPS]) are currently involved in the analysis and modeling of exposures to chlorpyrifos, lead, and air toxics. The models also will characterize exposures of children and other sensitive or highly exposed populations. This is particularly important for EPA under the FQPA for assessing acute and chronic exposures to children.

M-02 Comparison of NHEXAS Findings with Cumulative Exposure Project Estimates for Ambient Air Levels and Exposures for Selected VOCs and Metals — The goal of this project is to (1) compare patterns and trends in monitored neighborhood ambient air levels of VOCs and metals as well as available biomonitoring data to the annual average estimates of

the same compounds derived through NATA and (2) evaluate the relevance of the NATA model predictions to the types of exposure situations characterized in NHEXAS.

This is a near-term project with a high-to-moderate degree of feasibility and high applicability and relevance to EPA's air toxics program. It deals only with the air media and the inhalation route. The analysis will be feasible only for a subset of VOCs and metals that have been detected in the NHEXAS air samples. The monitoring duration and frequency and the location of samples collected in the NHEXAS study also may restrict a more complete evaluation of NATA model results. Spatial and temporal aggregations of the NHEXAS data most likely will be required.

M-03 Develop Model Parameters from Qualitative and Quantitative NHEXAS Monitoring Data, Questionnaires, Time/Activity, and Survey Data — The goal of this project is to develop exposure model parameter (e.g., ingestion rates, emission rates) values, ranges, and distributions, making use of both quantitative and qualitative data generated in NHEXAS. Exposure parameters will be developed in accordance with the current state-of-the-art exposure assessment and corresponding model input requirements. Specific emphasis will be placed on key exposure parameters common in multimedia exposure assessments and those that are likely to contribute to high-end exposures.

This project is ranked third because it has a moderate level of feasibility of achieving all of its goals. Ideally, some aspects of this project may need to be deferred until certain basic descriptive statistics or exploratory analyses of the data are completed. However, analysis of exposure factors and survey data on known model input parameters can be initiated in the near term. This project has high significance. Multimedia models currently developed by EPA and other groups require exposure factor information in the form of distributions. This project will improve existing exposure parameter distributions used in models and also evaluate the utility of questionnaires for quantitative exposure analysis.

M-04 Evaluate Implications of NHEXAS Results for Existing Chronic Exposure Assessment Methodologies — The goal of this project is to take the dose estimates from personal monitoring or biomarker measurements and compare them to those predicted from EPA

screening methodologies (also referred to as Tier 1 or Initial Tier assessments). Examples of these methods include recommended exposure models under the Superfund program and the residential standard operating procedures (SOPs) developed by EPA's OPP. Screening models (sets of algorithms) are used widely to make preliminary decisions for Superfund sites, pesticide regulations, and the evaluation of emissions to air and water. However, high quality and reliable multimedia monitoring data to validate these models are virtually nonexistent in the literature, and, as such, the opportunity to test screening models, even on a qualitative scale, is rarely available. NHEXAS data will allow for testing and evaluating these screening level models and methods currently used by EPA.

This project is ranked lower than the ones above mainly because of timing considerations. Projects M-01, M-03, and others, such as Projects D-01 and D-02, are expected to precede this fourth ranked modeling project. Projects D-01 and D-02 , for example, will develop the basic statistical summaries on personal exposure monitoring and biomarker data that will be used as inputs for this modeling project. Likewise, Projects M-01 and M-02 will be generating the necessary exposure factor, dietary survey, time-activity, and environmental concentration information needed to initiate this project. This project is quite feasible, depending on the pollutant type and the media selected. Measurements that are below the limits of detection for certain chemicals may limit the utility of this project. However, this project has broad applicability and high demand within EPA. Both chronic and acute exposure and risk assessments conducted by the program offices (e.g., Office of Solid Waste and Emergency Response, OPP) will benefit from the results of this project.

M-05 Evaluation of Existing Multimedia Models Using the NHEXAS Data Set — The goal of this project is to evaluate the existing multimedia human exposure and dose models using the NHEXAS data set. High-quality and reliable multimedia monitoring data are virtually nonexistent in the literature, and, as such, the opportunity to test existing models, even on a qualitative scale, is rarely available. Several multimedia models have been developed, or are under development, that predict media concentrations in residential environments based on inputs such as source characterization, fate, and transport. Examples of models that are proposed to be evaluated include TRIM, MEPAS, Cumulative and Aggregate Risk

Evaluation System (CARES), LifeLine™, and Consumer Exposure (CONSEXPO), as well as other linked and nested compartmental models.

Timing of this project is ranked intermediate because of complexity and diversity of the task. Moreover, some of the models mentioned above are still in developmental stages and may not be available for complete evaluation for another 2 to 4 years (e.g., CARES, TRIM). Relevant variables, exposure factors, and other model inputs have to be developed first also. Feasibility of this project also depends on the type of model selected and the feasibility of inputs or information that can be obtained from the NHEXAS study. The project has broad applicability within EPA because ORD and program offices are currently engaged in developing or refining a number of different exposure and dose models for pesticides, metals, particulate matter, air toxics, PAHs, etc.

M-06 Quantify Uncertainties in NHEXAS Data and Assess Contribution to Model Errors — The goal of this project is to address an important component of most population exposure models dealing with proper characterization of parameter and model input uncertainties. This analysis will provide a comprehensive set of uncertainty estimates based on the NHEXAS database, so that uncertainty is addressed consistently and does not lead to redundant effort by modelers. The project also will examine how the data uncertainties may impact modeling uncertainties and illustrate with case studies. Inclusion of uncertainty estimates and descriptions in exposure assessments and models will improve the risk assessment process and will inform the scientists, the public, and the regulatory community of possible limitations in the use of the data.

Timing of this project was rated intermediate, again because of the complexity of this task and the suggested approach (i.e., identification of relevant factors, data sets, correlations among variables, and spatial and temporal dependencies among the various parameters and values). The project has a medium level of feasibility and moderate applicability because proper characterization of uncertainties will be limited by the NHEXAS study design. Namely, the types and numbers of measurable or quantifiable variables available for analysis will vary by NHEXAS region and pollutant type.

M-07 Reconstruct Exposure and Dose Profiles from Biomarker Data Utilizing Questionnaire and Environmental Measurements — The goal of this project is to develop and evaluate a methodology that provides realistic estimates of the dose and exposure associated with a biomarker measurements as a function of the types of exposure that occurred. The relationships among environmental measurements, time/activity data, and biomarker levels will be investigated, with the goal of classifying exposure scenarios into steady-state cases (e.g., from long-term average exposures) and intermittent events. There are several assumptions regarding the route and timing of dose that need to be addressed in making these estimates, and the questionnaires and time/activity data will be used to make these determinations. The analysis will attempt to focus on the exposures of children, in addition to the general population.

This project needs to be scheduled after the earlier or near-term projects because it requires inputs and information from chemical-specific exposure and dose assessments. Biomarker data will be restricted to a few analytes only (e.g., 3,5,6-trichloropridinol[TCPy] and arsenic in urine, VOCs and metals in blood). Development or application of these models also requires information on absorption, metabolism, and elimination of these chemicals, and data regarding the timing and routes of exposures. Consequently, the applicability of this project will be restricted to few chemicals. NHEXAS study design also introduces some difficulties in reconstructing exposure profiles. Temporal or repeated personal or microenvironmental measurements are not widely collected. Questionnaire and time-activity diaries also have limitations in providing high-level time-resolved information on source use (e.g., pesticide applications), activities, and concentrations. Estimation of individual dose and biomarker concentrations could be limited if sufficient temporal or spatial information on concentrations or exposure factors are not available or need to be estimated.

4.6 DATA ANALYSIS AREA SIX: DESIGNING EXPOSURE STUDIES

4.6.1 Overview

A major objective of the NHEXAS studies was to evaluate the feasibility of NHEXAS concepts, methods, and approaches for the design and conduct of future population-based exposure

studies. To this end, ORD encouraged creative thought in both design and implementation of the NHEXAS pilot studies. Although each study had the same basic goal of measuring multimedia, multipathway exposures for defined populations, each employed different approaches to many of the design, sampling, and evaluation procedures. Components, such as the hypotheses tested, selection criteria of participants, incentives for participation, and sampling designs, differed among studies. In some cases, state-of-the-art field measurement approaches were employed, whereas, in others, new and novel approaches were tested. Coupled with other aspects of the studies that were common, such as the NHEXAS questionnaire, food, water, and biological analyses, and comparative quality assurance, the contrasting approaches provide a lucrative database for evaluation and comparisons among the studies. The lessons learned from these evaluations and comparisons of the NHEXAS studies will advance the state-of-the-science for future residential-based, multimedia, multipathway exposure studies and will serve as an important first step in the design of future large- or national-scale exposure studies based on the NHEXAS concept.

Future large-scale exposure studies must be done smarter and more efficiently. Fundamental in attaining this goal is the use of cost-effective approaches that will provide sufficiently accurate measures of exposure and the data needed for improving exposure models. The cost-benefit of the various approaches used within the three studies can be evaluated to determine which procedures worked well and where improvements are required. For example, an evaluation of the effectiveness of the questionnaires and simplified or indirect sampling schemes may identify screening tools that can classify more highly exposed individuals at reduced costs. Evaluations among the NHEXAS studies of study design components, such as communication strategies and quality assurance and data management procedures, will determine the optimum set of criteria and recommendations for standardization in future studies.

4.6.2 Developing Priorities for the Projects

This data analysis area (Table 10) has the single goal of using the NHEXAS experience to improve the design of future exposure studies, a specific recommendation of IHEC. With multiple large and small-scale exposure studies currently in their early planning phase, each of the projects identified is critical and urgently needed to meet the goal of this data analysis area, dictating that all

projects need to be conducted in the near term. Therefore, the "Timing" criteria alone can not distinguish projects for the purpose of sorting them; all projects are designated as near term. However, as the success of the design of an exposure study depends on a certain sequence of events, so does the timing of certain projects within this data analysis area. Projects DES-01 and DES-02 are fundamental in planning the design of future large-scale exposure studies, and clearly need to be started first, irrespective of other ranking criteria.

TABLE 10. DESIGNING EXPOSURE STUDIES[a]

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
DES-01	Survey and Statistical Aspects of the Design of an Exposure Field Study: Lessons Learned from the NHEXAS Pilot Studies	N	H	H	Y
DES-02	Evaluating Modeling Considerations for the Design of Future Exposure Field Studies	N	M	H	Y
DES-03	Scaling Up: Evaluation of the NHEXAS Pilot Fixed Costs, Coordination and Communication Strategies, and Degree of Standardization	N	H	H	
DES-04	Influence of Incentives, Response Rates, and Nonresponse Bias on Survey Design	N	H	M	
DES-05	Cost-Effectiveness of Exposure Measures and Comparisons to Indirect Methods	N	M	H	Y
DES-06	Optimizing NHEXAS Pilot Information and Methods to Move to a National-Scale Exposure Field Study	N	M	H	
DES-07	Cross-Studies Evaluation and Recommendations for Standardization of Data Management Procedures in Large-Scale Exposure Field Studies	N	M	M	
DES-08	Evaluation of NHEXAS Results To Derive an Optimal Set of QA/QC Activities for Human Exposure Field Studies	N	M	M	

[a]N = near term; I = intermediate term; H = high; M = medium; L = low; Y = yes.

Both of these projects are urgently needed because they provide critical information to begin the design process of a population-based exposure field study. A few of the projects (e.g., Project DES-03) will compare various procedures used in the NHEXAS studies and depend on feedback of lessons learned from those involved in conducting the studies. These projects need to be initiated while there is still historical knowledge and availability of personnel. One such project, which will

document important lessons learned from those conducting field monitoring and laboratory analyses, has been initiated (Appendix C).

Fortunately, all design-related comparisons among the three NHEXAS studies are not dependent on the availability of a complete NHEXAS database and are more feasible in the near term (Projects DES-3 and DES-4). Still other critical projects require results-oriented comparisons and are dependent on availability of both media concentrations and identifying information, as well as on preliminary analysis of the NHEXAS database descriptive statistics. These projects are judged somewhat less feasible in the near term because of fundamental differences in the NHEXAS study designs, but it is equally important that these projects be initiated as soon as practical to provide critical components for future design processes.

The required sequence for conducting the projects in the Designing Exposure Studies data analysis area, along with other applicable prioritizing criteria for each project, is summarized in Table 10. Specific comments and rationale for near-term sequencing are provided below for each project.

DES-01 Survey and Statistical Aspects of the Design of an Exposure Field Study: Lessons Learned from the NHEXAS Pilot Studies — The goal of this project is to provide directly relevant and specific guidance for the sample and survey design aspects of future large-scale, multichemical, multimedia exposure field studies. A review, revision, and updating of the discussions, analyses, and conclusions that provided the foundation for the NHEXAS design, as presented in the Callahan et al. paper (JEAEE, 1995), will be conducted in light of the NHEXAS studies experience. The hypothetical calculations would be replaced with calculations based on actual NHEXAS studies data. In addition, the analytical and statistical hypotheses that were generated in the design of the NHEXAS pilot studies will be reviewed to determine which hypotheses were testable and which were not.

This is the first of two projects identified that provides foundational information and should be conducted before future exposure study design processes are initiated. Fundamental in the design process is the selection of the appropriate survey and sample designs (sampling units, households, screening strategies, household members, etc.) that will support the hypotheses to be tested. The

NHEXAS studies provide the information needed so that hypothetical interclass correlations, design effects, and variances now can be replaced with actual data for different pollutants and classes of pollutants. The project is highly feasible and should commence with the availability of the NHEXAS database. It has broad applicability for exposure studies in general and is urgently needed for the design of currently planned ORD national-scale exposure studies.

DES-02 Evaluating Modeling Considerations for the Design of Future Exposure Field Studies — The goal of this project is to establish a procedure wherein modeling considerations are accommodated in the early stages of the design of future exposure field studies. In conducting field studies, usually a study is designed, monitoring data and other related data are gathered, and then statistical analyses are performed to interpret the data. However, from a model development, model application, or model evaluation perspective, the data gathered may be insufficient, particularly for inferential purposes, if information on important exposure model variables have not been obtained during the study. To achieve the goal of this project, the model parameters for incorporation into the study design must be understood at the earliest stages of study planning. Sample parameters include those related to time/activity patterns, contact rates, and dermal and dietary exposure (e.g., surface coverings in residences, contact times with these surfaces).

This is the second project identified that is sequentially required in the near term , and that provides critical input to begin the design process of an exposure study. Exposure measurement studies alone cannot provide all the information required in the risk assessment/risk management paradigm used by EPA. Models are required to interpret measurement results and select actions to protect the public. It is critical that exposure studies provide the correct information for exposure modeling, and that this information is considered from the very inception of the design process. This project is equally applicable and as urgently needed as the higher ranked project, but it is judged somewhat less feasible because of the pilot nature of NHEXAS studies and the need for more complete evaluation of the most effective procedures and methodologies employed in each of the studies.

DES-03 *Scaling Up: Evaluation of the NHEXAS Pilot Fixed Costs, Coordination and Communication Strategies, and Degree of Standardization* — The goal of this project is to compare and contrast the implementation and communication strategies of the three consortia to determine which worked well and which components need improvement and standardization for the most cost-efficient exposure field study possible. This project evaluates the NHEXAS pilot start-up expenditures and cost implications for various scales of coverage, the effectiveness of coordination approaches that were used and their application to a full scale survey, and communication approaches as results were shared with respondents and with local, state, and federal officials and organizations. A key component of the analysis will be the evaluation of approaches that were standardized explicitly and a determination of whether or not the degree of standardization was adequate.

This is a highly feasible project that must be initiated immediately before opportunities for feedback from the consortia and cooperating agencies involved in conducting the NHEXAS field studies are lost. Experiences gained from coordinating and implementing the pilot studies provide valuable information for the design of future studies. Cost of implementation and standardization of various components can be compared among studies to provide a relative basis for scale-up. Communications strategies are an important aspect of the success of an exposure field study, and the three studies provide the opportunity to optimize approaches. All information is currently available and not dependent on the combined NHEXAS database, making this project highly feasible for immediate initiation. Applicability is high because the over-arching goal of all future field studies is cost-effectiveness.

DES-04 *Influence of Incentives, Response Rates, and Nonresponse Bias on Survey Design* — The goal of this project is to analyze NHEXAS recruitment procedures and incentives and their effects on response rates for various subpopulations. Analysis will be conducted of potential bias resulting from NHEXAS nonresponse based on information obtained from the descriptive questionnaire, and information and observations recorded by interviewers

on noncontacts or nonrespondents for each study and for various subpopulations, important elements in the design of future exposure studies.

This project will investigate other critical elements for the design of a successful field study. This project is highly feasible and is also not dependent on the availability of the combined NHEXAS database. It can be initiated immediately. Applicability is ranked as medium because the NHEXAS pilot studies cannot provide information on the procedures and approaches not specifically incorporated in them.

DES-05 Cost-Effectiveness of Exposure Measures and Comparisons to Indirect Methods — The goal of this project is to evaluate the cost-effectiveness of exposure measures for pollutants and pathways using decision analysis, value of information, and cost-benefit analysis techniques. Data from NHEXAS pilot studies questionnaires, environmental sampling, personal sampling, and biomarkers will be analyzed to assess the reproducibility, accuracy, limits of detection, ranges, interferences, uncertainty, and costs, for the purpose of evaluating direct measures relative to indirect methods that use existing data and models. From the analysis, methods that were unsuccessful and other methods (i.e., questionnaires, simplified or indirect sampling schemes) that could serve as screening tools in large-scale exposure studies to classify more highly exposed individuals and reduce costs will be identified.

As with each project in this analysis area, this project is desirable in the near term to provide important information for a specific component of the exposure study design process. This project is broadly applicable to all exposure field studies to meet the goal of better information at reduced cost. For this reason, it is very much in demand for exposure studies that are entering the planning phase in the near future, including a potential national-scale NHEXAS and a longitudinal birth cohort study. This project is ranked moderately feasible because the NHEXAS studies provide only limited instances where comparisons are possible between direct measures and indirect methods.

DES-06 Optimizing NHEXAS Pilot Information and Methods To Move to a National-Scale Exposure Field Study — The goal of this project is to provide a defensible scientific basis

to design and implement national-scale exposure field studies. The information obtained in the pilot studies and other source and effects information will be utilized to prioritize the selection of pollutants and pathways leading to exposure. Included would be an evaluation of the ability of each consortium to achieve the objectives or hypotheses originally proposed for each type of investigation. A thorough evaluation of single- and multimedia pollutant issues and regulatory initiatives for the purpose of designing a large-scale exposure study will be performed.

This project will capture and integrate the knowledge gleaned from the analysis, interpretation, and evaluation of the experiences in undertaking the NHEXAS pilot studies for assisting in designing and planning the next generation of large-scale exposure field studies. The products of this project will provide input for developing hypotheses based on priority pollutants and pathways. This project specifically addresses large-scale studies, although the concepts and determinants are equally applicable to any exposure field study. The project is feasible using data from both the NHEXAS studies and other sources, but depends heavily on the results of other elements of the strategic analysis plan.

DES-07 *Cross-Study Evaluation and Recommendations for Standardization of Data Management Procedures in Large- Scale Exposure Field Studies* — The goal of this project is to analyze the data collection and automated survey management procedures developed for each NHEXAS pilot study from sampling, through sample analysis and to inclusion in the final database. The data QA/QC procedures and QC data will be evaluated, and the resulting database structures will be examined. The strengths and weaknesses of the three approaches will be noted with respect to ongoing EPA data management initiatives. NHEXAS pilot QC data will be analyzed, and recommendations for future studies will be developed. These recommendations will include areas that would benefit from standardization; for example, data transfer from analytical laboratories, database elements, QA/QC codes, information shells, etc.

This, and the last project (Project DES-08) in this data analysis area, address two design components that have received inadequate consideration during the design processes of previous exposure

studies. Consequently, insufficient planning and budgeting of resources have resulted in abbreviated QA programs and databases. This project is feasible in the near term using the results and comparisons of the approaches used in the NHEXAS studies. This project, completed in a timely manner, will provide valuable information to more effectively complete the design and budgeting processes to create quality databases for planned and future large-scale exposure studies.

DES-08 Evaluation of NHEXAS Results To Derive an Optimal Set of QA/QC Activities for Human Exposure Field Studies — The goal of this project is to identify and evaluate the QA/QC programs implemented across laboratories and consortia in the NHEXAS studies. This will include an analysis of the across-studies QC program conducted by NIST and the EPA comparability study data. The project will develop an annotated inventory of recommended QA/QC activities needed to successfully conduct large-scale human exposure measurement studies. This will include all phases of the study, from planning to final database development.

A near term analysis of NHEXAS data applicable to this critical component of study design will provide guidance for use in a large-scale study design to assure that the study produces data of appropriate quality, while keeping cost to a minimum. The successes and benefits of various study activities can be evaluated. Feasibility is judged as moderate because the QA/QC programs within and among the NHEXAS studies were not uniformly applied, nor did they necessarily cover all aspects of the studies from data objectives through sample collection, analysis, and reporting. The resulting recommendations would have some applicability to any exposure field studies.

APPENDIX A

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APPENDIX B

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National Human Exposure Assessment Survey Advisory Panel
July 10-11, 2000

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APPENDIX C

NHEXAS Projects and Analyses—Completed and In Progress

Development of NHEXAS Databases

The NERL plans to make the databases from the NHEXAS pilot studies available to the scientific community both within and outside of EPA. The NHEXAS pilot study results, metadata, and documents will be available on the Internet by the fall of 2001. The actual data will be stored and maintained in ORACLE databases on an EPA server. Metadata for the data and documents, available through EPA's Environmental Information Management System (EIMS), will be linked to the actual data sets and documents. This will allow users browse the data and document files and to select the sample types, analyte classes, or questionnaires that they want to download to their own system. The database design and contents were peer reviewed in the summer of 2000.

Database Organization. There will be three types of data sets for each study: questionnaires, analytical results, and QA/QC results data. Each set will include household and individual identifiers (without personal information to identify the specific person), as well as information for applying survey weights. In addition, data dictionary and code files will be included to document the contents of the results data. Their description follows.

(1) Questionnaire Data Sets. The data from each questionnaire will be provided as a separate data set. Questionnaire data evaluate the demographics, housing characteristics, lifestyle, activity patterns, and health of the participants. Data from all questions in a questionnaire will be included in the data set, except for sensitive data. Examples of sensitive information include: name, address, date of birth, and phone number. The following questionnaire data will be available, depending on what was collected in a particular NHEXAS study:

- Baseline
- Descriptive
- Follow up
- Food Diary or Dietary Checklist
- Food Diary Follow up
- Technician Walk-Through
- Time Diary and Activity

The codes for the questionnaire responses will be defined in code files, which are identified in the data dictionary corresponding to each file.

(2) Analytical Results Data Sets. This large complex set of data from three studies covers many types of samples. Analytical data are derived from samples of yard soil, house dust, personal, indoor, and outdoor air, drinking water, food and beverages, dermal wipes, blood, and urine. The analytical result data will be available to the user in subsets which are defined by the sample type and the analyte class. Sample types will be defined for each study based on the sampling medium, location, and collection methods used. Each row of these data sets will provide the results for the analytes of one sample obtained from a given analytical or determinative method. The row will include identifying and sample information (e.g., dates, units), statistical/survey information (i.e., sample weight and strata), and codes to identify the adequacy of the sample results relative to detection (or quantitation) limits or quality control checks.

(3) QA Data Sets. One data set will be provided for each type of QA/QC sample, that is, one for spikes (field and laboratory), one for replicates (field, laboratory and analysis), one for blanks (field, analytical and reagent), etc. Each row in these data sets will contain the analytical result information for all analytes in the analyte class for one sample.

(4) Data Dictionary Files. Each entry in a data dictionary will include information about a variable (column) in the corresponding data set. This includes descriptive labels to define the variable, ranges of acceptable values, units of measurement, missing values, and codes used for categorical variables.

(5) Code Files. A code set will be available for each column in a data set that contains values representing discrete or categorical responses. This includes code values assigned to missing or non-response data. Each code set will provide the link between a unique set of coded values and their descriptions, and will be identified in the data dictionary by a unique code set name.

Database Review. Each of the investigators are required to assess the completeness and accuracy of the data sets provided to the EPA. However, to help ensure that the publicly available NHEXAS databases are complete and accurate versions of the study results, additional reviews of the databases will be conducted. These reviews include assessments of the analytical results and questionnaire data sets, the corresponding data dictionaries and code files, and the document files (QSIPs and protocols) to check the:
- validity and completeness of codes used in the database and the definitions provided in the data dictionary and code files;
- correspondence of the formats, types, and ranges of values in the database to those specified in the data dictionary;
- labels for variables (including units of measurement where necessary);
- completeness of document files for the study design, QA plans, and protocols; and
- consistency of summary statistics with those provided (or published) by the investigators.

Database Summaries. Summary tables of the NHEXAS databases will be developed to document the completeness of the data sets for multimedia and multipathway exposure estimation. This includes identifying the number of samples having valid and measurable results, and providing univariate descriptive statistics (mean, median, percentiles) for the analytical results data by sample type and chemical.

Lessons Learned in the Actual Conduct of the NHEXAS Pilot Studies

Most information from the NHEXAS pilot studies will be derived from analyses of the data. However, the field study professionals have specialized first-hand knowledge of what worked well and what didn't work well in actually performing a study of this complexity and magnitude. Therefore, a project was developed to define the strategies, procedures, and approaches that are likely to work well for future field studies. ORD will conduct interviews with the NHEXAS pilot consortia members, summarize the findings, and then conduct a 1-day workshop to prioritize findings

and develop key recommendations. Information collected will address procedures and practices, including but not limited to the effectiveness of administering questionnaires, sampling methods, sample handling and tracking, laboratory procedures, participant training and burden (time and level of understanding), field staff burden, and database development. The planned products from these activities will be a journal article summarizing the findings and report that provides guidance recommendations on approaches for human exposure field studies. The products will be available in early 2001.

Published Journal Articles

Region V NHEXAS Pilot Study

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MacIntosh, D.L., Kabiru, C., Scanlon, C.A., and Ryan, P.B. (2000) "Longitudinal investigation of exposure to arsenic, cadmium, chromium, and lead via beverage consumption" J. *Expo. Anal. Environ. Epidem.* 10(2): 196-205.

Ryan, P.B., Huet, N., MacIntosh, D.L. (2000) "Longitudinal investigation of exposure to arsenic, cadmium, and lead in drinking water." *Environ. Health Persp.* (in press)

Arizona NHEXAS Pilot Study:

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O'Rourke, M.K., Fernandez, L.M., Bittel, C.N., Sherrill J.L., Blackwell, T.S., and Robbins, D.R. (1999) "Mass Data Massage: An Automated Data Processing System Used for NHEXAS Arizona" *Journal of Exposure Analysis and Environmental Epidemiology* 9(5): 471-484.

O'Rourke, M.K., Rogan, S.P., Jin, S., and Robertson, G.L. (1999) "Spatial Distributions of Arsenic Exposure and Mining Communities from NHEXAS Arizona" *Journal of Exposure Analysis and Environmental Epidemiology* 9(5): 446-455.

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O'Rourke, M.K., Van de Water, P.K., Jin, S., Rogan, S.P., Weiss, A.D., Gordon, S.M., Moschandreas, D.M., and Lebowitz, M.D. (1999) "Evaluations of Primary Metals from NHEXAS Arizona: Distributions and Preliminary Exposures" *Journal of Exposure Analysis and Environmental Epidemiology* 9(5): 435-445.

Lebowitz, M.D., O'Rourke, M.K., Rogan. S., Reses, J., Van De Water, Pl, Blackwell, A., Moschandreas, D.J., Gordon, S., and Robertson, G. (2000) "Indoor And Outdoor PM_{10} And Associated Metals and Pesticides in Arizona" *Inhalation Toxicol.* 12 (suppl 1): 139-144.

Manuscripts in Preparation Under Current ORD Sponsorship

Region V NHEXAS Pilot Study

- "Analysis of Dietary and Other Exposure Pathways for Metals, with Comparisons Between Media Concentrations and Routes of Exposure"
- "Assessment of Data Quality for the EPA Region V NHEXAS Study"
- "Assessment of Data Quality for the Minnesota Children's Pesticide Exposure Study"
- "Contribution of activity patterns to personal exposures of NHEXAS participants"
- "Relationship of residential sources and residential conditions to household contaminant levels"
- "Relationship between pesticide levels in and around the home and hand rinse measurements from children"
- "Relationship between activity pattern data and hand rinse measurements of pesticides in children"

Baltimore NHEXAS Pilot Study

- "Longitudinal investigation of dietary exposure to selected pesticides"

Arizona NHEXAS Pilot Study

- "Occurrence And Distribution of Residential Exposure to Chlorpyrifos and Diazinon"

•"On Prediction of Multi-route and Multimedia Residential Exposure to Chlorpyrifos and Diazinon"
•"Exposure to Pesticides by Medium and Route: The 90th Percentile and Related Uncertainties"

APPENDIX D

Project Priority Listings

PROJECT PRIORITY LISTINGS[a]

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
	Descriptive Statistics				
D-01	An Analysis of Media Concentrations, Exposure, and Biomarkers by Demographics	N	H	H	
D-02	Univariate Statistics for Use in Exposure and Risk Assessment	N	H	M	Y
D-03	Impact of Censoring and Method Sensitivity and Precision on Multimedia Exposure Distributions and Associations	I	H	H	
D-04	Quantify Uncertainties in NHEXAS Data and Assess Contribution to Model Errors	I	M	M	
D-05	Investigate National Representativeness of NHEXAS Sampling Results by Comparing Measurement and Exposure Results Across the Three Regions	I	L	M	
	Predictors of Exposure and Dose				
P-01	Analysis and Comparison of NHEXAS Exposure Data to Residential Pollutant Sources, Concentrations, and Activity Patterns	N	H	H	Y
P-02	Compare Traditional Indirect Method of Estimating Dietary Exposures with Duplicate Diet Data and Compare Methodologies Utilized in NHEXAS	N	M	H	
P-03	Identifying Predictors of Exposure	I	H	M	
P-04	Risk Factors for Biomarkers of Internal Dose: Demographics, Questionnaire Data, Concentrations, and Exposures	I	M	H	Y
P-05	Determinants of Dose Measurements (Biomarkers) from the NHEXAS Studies	I	M	H	
P-06	Exploratory Data Analysis Methods for Evaluating Relationships Among Questionnaires, Exposure, Dose, and Risk Factors	I	M	M	
P-07	Use of NHEXAS Data To Test Assumptions About Activity Pattern Factors and Other Exposure Factors in EPA Risk Assessments	I	L	M	
	Spatial and Temporal Variability				
ST-01	Temporal Variability in Exposure Concentrations and Aggregate Exposure Using NHEXAS Data	N	H	H	

PROJECT PRIORITY LISTINGS[a] (cont'd)

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
	Spatial and Temporal Variability (cont'd)				
ST-02	Use NHEXAS Dietary and Activity Pattern Data To Develop Predictive Relationships Between Single Day Observations and Long-Term Patterns of Behaviors	N	H	M	
ST-03	Characterization of the Variance Components of NHEXAS Data to Optimize Future Designs	N	M[b]	H	
ST-04	Spatial Variability	N	M[b]	H	
ST-05	Investigate Stability of Individuals in Population Exposure Ranks Over Time	I	H	M	
ST-06	Spatial and Temporal Variability in Multichemical Exposure	I	M[b]	H	
ST-07	Development and Evaluation of Models for Interpreting and Quantifying Inter- and Intraindividual Variability in Pesticide Exposure/Dose Using NHEXAS Data.	L	M	H	
	Aggregate Exposure, Pathway Analysis, and Cumulative Risk				
AE-01	Aggregate Exposure	N	H	H	Y
AE-02	Comparison of Children's and Adults' Exposures to Pesticides and Other Chemicals in the Region V, Arizona, and Maryland Studies	N	M	H	Y
AE-03	Construction of an Empirical Multimedia/Multipathway Exposure Distribution Model Including Temporal Variability Based on NHEXAS Data	I	M	M	
AE-04	Cumulative Risk from Exposure to NHEXAS Chemicals	L	M	H	
	Evaluation/Refinement of Current Exposure Models and Assessments				
M-01	Compare Pre-NHEXAS Model Results with NHEXAS Measurements	N	H	H	Y
M-02	Comparison of NHEXAS Findings with NATA Estimates for Ambient Air Levels and Exposures for Selected VOCs and Metals	N	H/M	H	Y
M-03	Develop Model Parameters from Qualitative and Quantitative NHEXAS Monitoring Data, Questionnaires, Time/Activity, and Survey Data	N	M	H	

PROJECT PRIORITY LISTINGS[a] (cont'd)

Project ID	Project Title	Timing	Feasibility	Broad Applicability	Demand (Urgency)
Evaluation/Refinement of Current Exposure Models and Assessments (cont'd)					
M-04	Evaluate Implications of NHEXAS Results for Existing Chronic Exposure Assessment Methodologies	I	H/M	H	Y
M-05	Evaluation of Existing Multimedia Models Using the NHEXAS Data Set	I	M	H	
M-06	Quantify Uncertainties in NHEXAS Data and Assess Contribution to Model Errors	I	M	M	
M-07	Reconstruct Exposure and Dose Profiles from Biomarker Data Utilizing Questionnaire and Environmental Measurements	I	M	M	
Designing Exposure Studies					
DES-01	Survey and Statistical Aspects of the Design of an Exposure Field Study: Lessons Learned from the NHEXAS Pilot Studies	N	H	H	Y
DES-02	Evaluating Modeling Considerations for the Design of Future Exposure Field Studies	N	M	H	Y
DES-03	Scaling Up: Evaluation of the NHEXAS Pilot Fixed Costs, Coordination and Communication Strategies, and Degree of Standardization	N	H	H	
DES-04	Influence of Incentives, Response Rates, and Nonresponse Bias on Survey Design	N	H	M	
DES-05	Cost-Effectiveness of Exposure Measures and Comparisons to Indirect Methods	N	M	H	Y
DES-06	Optimizing NHEXAS Pilot Information and Methods to Move to a National-Scale Exposure Field Study	N	M	H	
DES-07	Cross-Studies Evaluation and Recommendations for Standardization of Data Management Procedures in Large-Scale Exposure Field Studies	N	M	M	
DES-08	Evaluation of NHEXAS Results To Derive an Optimal Set of QA/QC Activities for Human Exposure Field Studies	N	M	M	

[a]N = near term; I = intermediate term; H = high; M = medium; L = low; Y = yes.

[b]Spatial variability can be determined on national, regional, and community bases when the NHEXAS data sets are available. However, the exact location of NHEXAS participants will not be included in the NHEXAS data sets to protect the confidentially of the individual participants of the study. Thus, comparisons of personal exposures with point sources cannot be accomplished without the cooperation of the principal investigators of the various NHEXAS consortia. Therefore, the criterion of feasibility was ranked medium for these projects, as compared to other projects without such concerns.

APPENDIX E

Project Descriptions

DESCRIPTIVE STATISTICS PROJECT

Project Name:	**D-01. An Analysis of Media Concentrations, Exposure, and Biomarkers by Demographics**
Short Project Description:	Descriptive analysis of media concentrations, exposure, and biomarker measurements for population subgroups (age, gender, ethnicity, SES, urban/rural, or other important groupings) for each NHEXAS study.
Goal/Objective:	To provide a descriptive analysis of media concentrations and biomarker measurements by population characteristics in order to identify susceptibility factors and differences among groups and to compare distributions with other studies.
Significance of Project:	(1) Will serve as basis for planning and interpretation of NHEXAS data and to identify subpopulations for further study. (2) Provides baseline information for comparison to other locations such as Superfund sites and to assess trends. (3) Useful to EPA and others doing analysis of NHEXAS data and for planning further studies
Suggested Approach:	Statistical comparison of weighted distributions (frequency, means, etc.) by population subgroups (from questionnaire data) for media concentrations, biomarkers, and exposure to assess differences and similarities between or among subgroups.
Data or Input Needs:	Questionnaires and time/activity data from each of the studies. Biomarker and environmental measurements data from each study. Detection limits for environmental chemicals from each study. Population weights and stratification variables.
Feasibility (of analyses with current NHEXAS databases):	Data currently exists, questionnaires are the same across groups, comparability of analytic results will be assessed using information about detection levels. There is concern over the level of stratification (limited cell sizes) that can be achieved because of measurements below detection and incomplete sampling of some media (e.g., subsampling of homes for outdoor air measurements).

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.1	0.1	1.0	1	1

Research Outputs

(1) Identify those chemicals for which there is adequate data for analysis; determine strata to be used in analysis

(2) Final output: Manuscript, tables, and graphs of distributions by strata and completed statistical analysis and interpretation

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project EA-2.

DESCRIPTIVE STATISTICS PROJECT

Project Name:	**D-02. Univariate Statistics for Use in Exposure and Risk Assessment**
Short Project Description:	Develop univariate descriptive statistics (distributional information) for NHEXAS data that can be used broadly in exposure and risk assessment.
Goal/Objective:	To provide risk assessors and other users with information for use in exposure and risk assessment and in the design of human health effects studies and to compare NHEXAS results to other existing relevant study results.
Significance of Project:	Exposure and risk assessors use estimates of various exposure concentrations and "exposure factors" in their calculations of exposure and risk. These are quite often point estimates or distributions from very limited data sets. The data collected by NHEXAS can be used to better define distributions of these concentrations and exposure factors (e.g., activities, time spent in specific locations, dietary intake, product use). This will reduce the uncertainty associated with these assessments. Major users of this information will be risk assessors in EPA, other federal agencies, industry, academia, and state and local governments, as well as epidemiologists and other health effects researchers who need to classify members of a cohort based on exposure.
Suggested Approach:	Work with EPA/NCEA to identify factors and point estimates that commonly are used in risk assessment and for which data were collected in one or more of the NHEXAS pilots. Develop summary statistics (including distributional information) for these data. These analyses should include distributions for the total population and for selected subgroups where the data will allow. These should be suitable for inclusion in EPA guidance, such as the Exposure Factors Handbook. These analyses should identify the appropriate caveats, limitations, and uncertainties associated with the data and resulting statistics. The results should also compare the statistics with similar information from other studies (e.g., NHANES, TEAM).
Data or Input Needs:	The activity and concentration data collected by all NHEXAS pilot studies. Summary descriptive statistics. Meta-data to understand caveats. Other data sets (e.g., NHANES, TEAM, Exposure Factors Handbook).
Feasibility (of analyses with current NHEXAS databases):	This is highly feasible with NHEXAS data. Each consortium will be developing summary statistics for its data. It should be feasible to identify factors for inclusion in EPA guidance.

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.5	0.5	1.0	1	1

Research Outputs

(1) Provide statistics to EPA, including descriptions of the data and its limitations for use in risk assessment

(2) Final Output: Revision of EPA Exposure Factors Handbook

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project A-2.

DESCRIPTIVE STATISTICS PROJECT

Project Name:	**D-03. Impact of Censoring and Method Sensitivity and Precision on Multimedia Exposure Distributions and Associations**
Short Project Description:	This study will examine how method sensitivity and precision, and the censoring of data below detection limits, affect the estimation of distributions and means for exposure, media concentration, and biomarker measurements; and the evaluation of associations among such measurements. To the extent possible, intakes will be used in order to make the assessment on a total exposure basis.
Goal/Objective:	To investigate the degree to which the NHEXAS goal of measuring total exposure may be limited by the method precision, sensitivity, and censoring of data below DLs.
Significance of Project:	A major goal of NHEXAS was to estimate exposure through multiple routes, especially for those most highly exposed. This goal may be limited by the proportion of measurements that are below DLs for some target analytes and media and because method sensitivities differed across both media and studies. This project will be valuable in determining methods and approaches for conducting future NHEXAS or other multimedia human exposure studies.
Suggested Approach:	(1) Determine the percent of measurements above DLs, and the availability of health thresholds and QC data in order to focus the study on the most relevant media and chemicals. (2) Use uncensored results where available and impose censoring on them (i.e., set values <DL to missing or to some predefined value); compare distributions for the uncensored and censored cases. (3) Use QC (duplicates) data to estimate measurement error variability; generate simulated data that one would expect using another method with more or less precision; summarize/compare the distributions. (4) To the extent possible, evaluate the impacts of steps 2 and 3 both in terms of intakes and of total exposure. (5) Investigate ways of assigning values to measurements that are below DLs.
Data or Input Needs:	Physical measurements from all three studies. (Summaries of distributions and DLs may be used to conduct simulations for intake estimates and for evaluating uncertainties associated with measurements <DLs.) QC data.
Feasibility (of analyses with current NHEXAS databases):	Will be practical and relevant only for some types of measurements (i.e., those with more complete collection of exposures or environmental media for multiple pathways). The selection of measurement and analysis methods for NHEXAS were based on quantifying exposures at the "high-end" of the distribution, which may limit the availability of measurements above detection limits for all media.

DESCRIPTIVE STATISTICS PROJECT D-03

(cont'd)

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.2	0	0.7	3 (Reg V, MD, AZ)	0.5

Research Outputs

(1) Evaluate scope/relevance of project with respect health thresholds, availability of data, degree of nondetects, etc.

(2) Perform analyses and simulations and prepare draft manuscript

(3) Final output: Complete final manuscript

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project EA-7.

DESCRIPTIVE STATISTICS PROJECT

Project Name:	**D-04. Quantify Uncertainties in NHEXAS Data and Assess Contribution to Model Errors**
Short Project Description:	Provide uncertainty estimates within the NHEXAS database that are available to researchers and the public, so that uncertainty is addressed consistently and does not lead to redundant effort by modelers. Identify how the data uncertainties may impact modeling uncertainties and illustrate with case studies.
Goal/Objective:	• Provide consistent, understandable uncertainty estimates of the NHEXAS data within the NHEXAS database • Provide guidance/advice on applicability and use of various types of data in models to minimize inappropriate model construction.
Significance of Project:	The NHEXAS database will be used by many researchers and the public. Inclusion of uncertainty estimates/descriptions will avoid duplication of effort in calculating these values, will mean that the data uncertainties are treated consistently, and will alert the public and regulatory community of possible limitations in the use of the data.
Suggested Approach:	<u>Analytical Measurements</u> (1) Ensure that NHEXAS data are QA'd and flagged appropriately. (2) Ensure that NHEXAS data include Limit of Detection information. (3) Calculate standard errors for each analytical methodology (including sampling and analysis). (4) Tag uncertainty data to all NHEXAS data entries and provide a methodology for error estimation with the public database. <u>Survey and Time/Activity Information</u> (1) Provide qualitative assessments of data and their applicability for modeling by including meta data from field staff on reliability of individual household; include expert panel judgment of uncertainties of the methodology in general, including effects of sample size, inaccuracies of recall diaries, observer effects, time resolution effects, etc.; and compare survey results from NHEXAS with other data sources. (2) Include qualitative assessments in database. <u>Assessment of Model Uncertainties</u> Convene workshop of modelers to evaluate impacts of uncertainties for variety of analytes, with differing critical routes of exposure. Provide qualitative descriptions of uncertainties and caveats for inclusion in the database. Provide case studies to illustrate how errors impact modeling uncertainties.
Data or Input Needs:	Paced by the availability of the database, the NHEXAS data need to be quality assured to flag/remove inappropriate data. Duplicate sample data, split sample data, blanks, and other QA/QC information on the analytical measurements need to be included in the database. A description of the sampling and analytical methods also must be included.
Feasibility (of analyses with current NHEXAS databases):	The first part of the effort is quite doable, and should build on normal QA/QC procedures. This work is to insure that the synopsized uncertainty data also are made readily available for researchers and the public. The impact on modeling errors is much more likely to be case dependent, varying with each analyte and model used.

DESCRIPTIVE STATISTICS PROJECT D-04

(cont'd)

Research Outputs

(1) Review NHEXAS databases now under development for data to be included and make sure that QA/QC data and metadata on QC are in database for both analytical and survey data

(2) NHEXAS database becomes available

(3) Calculate synopsis information from data sets now scheduled to be delivered in FY01

(4) Convene workshop or expert panel to provide qualitative description of uncertainties associated with survey information

(5) Convene workshop or expert panel to evaluate impact of uncertainties of modeling–prepare case studies for specific analytes/major routes of exposure

(6) Final output: Incorporate uncertainty estimates and case studies into public database

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-4.

DESCRIPTIVE STATISTICS PROJECT

Project Name:	**D-05. Investigate National Representativeness of NHEXAS Sampling Results by Comparing Measurement and Exposure Results Across the Three Regions**
Short Project Description:	Very few national studies are available for use in development of national exposure distributions; therefore, local or regional studies are used instead. The question then is raised about the effect of using this restricted information on national exposure estimates. The three NHEXAS studies provide a method for comparing very similar studies to determine the magnitude of regional differences for various exposure factors.
Goal/Objective:	To determine bias in estimates of national exposure factors and distributions by use of local or regional sampling represented by NHEXAS pilot studies.
Significance of Project:	The information provided by this project also will advance knowledge of uncertainty in model parameters used in a variety of exposure models. The information also will help to ascertain the geographic scale at which variables may be collected in future studies.
Suggested Approach:	Examination of sample population distributions for various measurements collected in all three studies. Examination should be based on current methodologies as much as possible to facilitate quick turnaround. Appropriate analysis methods used to determine "similarity" among studies and quantification of uncertainty should be based on methods that provide simple, robust measures as feasible.
Data or Input Needs:	NHEXAS data from all three studies.
Feasibility (of analyses with current NHEXAS databases):	Study should be feasible. Possible difficulties may arise for some variables where collection methods differ among studies.

Research Outputs

(1) Develop/assess framework for comparing study measurements

(2) Implement automation of comparisons

(3) Run analyses for selected variables

(4) Final output: Report on regional differences among studies, suggested values for use in national exposure models, and values of uncertainty.

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-12.

PREDICTORS OF EXPOSURE AND DOSE PROJECT

Project Name:	**P-01. Analysis and Comparison of NHEXAS Exposure Data to Residential Pollutant Sources, Concentrations, and Activity Patterns**
Short Project Description:	Analysis of questionnaire, time/activity, environmental, and exposure data collected in the NHEXAS studies to determine the associations among measured exposures and pollutant sources, housing characteristics, residential concentrations (e.g., indoor/outdoor air), and human activities (e.g., the relationship between the use of cleaning supplies and VOC exposures; the characterization of residential dust and soil measurements; and the relationship to personal exposure monitoring).
Goal/Objective:	To evaluate and identify hypotheses about those residential pollutant sources, housing characteristics, residential concentrations (indoor and outdoor), and activity patterns that contribute to human exposures, especially for high-end exposures. To determine the value of questionnaires for understanding various aspects of exposure, and the reliability and validity of the instruments used for ascertaining these factors.
Significance of Project:	To provide policymakers with information to develop guidance for reducing exposures by both modifying pollutant sources and housing characteristics and educating the public about how their activities contribute to exposure. Information on the relationship between indoor/outdoor concentrations and personal exposures will be used to test assumptions about exposure levels based on fixed monitors. In addition, the relative value of questionnaires and diaries for understanding public health and exposure, as well as the item-by-item value of asking each question, will be determined with the overall goal of minimizing participant burden and costs. Identification of associations with questionnaire information also is useful for classification of exposures in epidemiological studies.
Suggested Approach:	(1) For each of the NHEXAS pilots, perform pollutant-by-pollutant analyses of the associations among residential pollutant sources, concentrations, and exposures; housing characteristics, concentrations, and exposures; concentration measurements in different media; and human activities, concentrations, and exposures. For air concentrations, develop distributions of indoor/outdoor concentration ratios. Subdivide analyses via spatial/source considerations (e.g., urban/rural, smoker/nonsmoker) that are key drivers of pairwise relationships. (2) Compare selected questionnaire items (e.g., sources, activities) with exposure and environmental measurements to determine their relative value. (3) Compare the results among the three studies. (4) Conduct multivariate analysis to determine the combined impact of residential pollutant sources, housing characteristics, and activity patterns on exposures.
Data or Input Needs:	For all three studies, measured concentrations in all media, activity information (diaries and questionnaires), housing characteristics, and occupational data. Information also needed on sample dates, geographic locations, and sampling protocols.
Feasibility (of analyses with current NHEXAS databases):	Need to review availability of samples for some media, proportion of analyses above detection limits, and substitution of measurements obtained from nearby households during the same periods of time (e.g., for outdoor air and soil measurements in Region V study).

PREDICTORS OF EXPOSURE AND DOSE PROJECT P-01

(cont'd)

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Year
0.2	0.3	1.0	3 (metals, VOCs, pest.)	1

Research Outputs

(1) Complete multivariate analysis of individual NHEXAS pilots

(2) Complete questionnaire/measurement analyses

(3) Compare analysis among studies to help combined study analysis

(4) Final output: Complete combined study multivariate analysis and final report

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Projects EA-1, A-9, and LL-11.

PREDICTORS OF EXPOSURE AND DOSE PROJECT

Project Name:	**P-02. Compare Traditional Indirect Method of Estimating Dietary Exposures with Duplicate Diet Data and Compare Methodologies Utilized in NHEXAS**
Short Project Description:	Comparison of direct exposure data from NHEXAS duplicate diet measurements with indirect exposure estimates derived from recorded food consumption combined with concentrations of NHEXAS chemicals measured in other studies, such as the Total Diet Study (TDS). Also compare food intake rates from NHEXAS questionnaire surveys with those from USDA and NHANES food intake surveys of comparable years, geographical regions, and population subgroups. Describe, compare, and evaluate the validity, reproducibility, and cost effectiveness of the duplicate diet collection methods.
Goal/Objective:	To compare dietary exposure estimates from a dietary exposure model (i.e., sum of the concentration × quantity consumed for all foods eaten) with direct measurements of dietary exposure (i.e., from duplicate diet samples); to evaluate the reliability and validity of dietary intakes determined in NHEXAS; and to evaluate alternative and less costly methods for measuring dietary exposure.
Significance of Project:	Although the indirect dietary model approach to dietary exposure assessment is widely used (e.g., for pesticide regulations), validation of such estimates with real monitoring data have not been done. NHEXAS data provide an opportunity for such validation to enhance the scientific basis for decision making. Comparison of dietary measurement and estimation approaches also may help to identify less costly alternatives for dietary exposure monitoring and to provide estimates of long-term exposures from short-term measurements (or estimates). This project also addresses several issues related to analyses of exposures including testing of hypotheses (adequacy of extant data and models to predict exposure), evaluation of survey instruments, and prediction of dietary exposure as a component of total exposure.
Suggested Approach:	(1) Code food intake data from NHEXAS food diary or food checklist into formats that are consistent with USDA food codes. (2) Compare NHEXAS food intake rates with those from USDA and NHANES for comparable time frames, regions, and population subgroups, including evaluation of weighting for nonresponse (where data allow such evaluation). (3) Calculate dietary exposures using individual consumption data (from diary or checklist) and extant food contaminant data (from FDA TDS, USDA Pesticide Data Program data, NHEXAS Maryland minimarket basket survey, and other existing residue data). (4) Estimate exposure using NHEXAS duplicate diet measurements and compare these results with results obtained from indirect method across population subgroups. (5) Comparative analysis of dietary data from checklist, duplicate diet collection, and mini-market basket approach in terms of validity, reliability, and cost effectiveness. (6) Analyses of calculated dietary exposures in relation to various demographic variables.
Data or Input Needs:	NHEXAS food diary and checklist data and duplicate diet data from each study, coding of food consumption to USDA or EPA/Dietary Exposure Potential Model (DEPM) codes, duplicate diet measurements from each consortia, and existing food contaminant data for those target chemicals measured in diet samples (USDA and FDA data, from DEPM).

PREDICTORS OF EXPOSURE AND DOSE PROJECT P-02

(cont'd)

Feasibility (of analyses with current NHEXAS databases):	The duplicate diet studies and diet questionnaires were administered to a sufficiently large number of individuals in the Region V and Arizona studies to support these analysis. In addition, the Maryland data obtained food intake longitudinally to allow an in-depth comparison of short- and long-term average intake. May be limited to quality/resolution of dietary consumption and duplicate diet measurement data. Not all food diaries have been coded, and it may not be possible to code to all the USDA codes. The food checklist is limited to 100 to 200 food items. The discrepancy between number of items could make cross-coding difficult.

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Year
0.1	0.5	0.5	2 (metals, pest.)	1

Research Outputs

(1) Determine the compatibility of the data sets

(2) Harmonize food codes among NHEXAS, USDA, and NHANES

(3) Compare food intake rates among the various surveys

(4) Estimate exposure based on food consumption and concentration data

(5) Compare exposure from NHEXAS duplicate diet studies with those obtained from indirect method

(6) Final output: Report consistency or inconsistency between the two approaches and identify approaches (if any) to improve the indirect method of estimating dietary exposure

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Projects EA-04, A-10, and A-11.

PREDICTORS OF EXPOSURE AND DOSE PROJECT

Project Name:	**P-03. Identifying Predictors of Exposure**
Short Project Description:	To identify primary predictors of exposure, using questionnaires and biological or environmental measures for use in epidemiology studies and other studies where individuals' exposure levels are sorted into categories such as high, medium, and low.
Goal/Objective:	Classification of individuals (and populations) into exposure categories for use in epidemiologic studies and risk assessment. Two products: (1)identify primary predictors of exposure for epidemiologic exposure assessment and (2) identify potentially highly exposed populations for future health effect studies or risk management.
Significance of Project:	Epidemiologists, risk assessors, and risk managers need the ability to classify people into exposure categories. EPA, ATSDR, CDC, NIEHS, and the National Institutes of Health all could use this information.
Suggested Approach:	Using the available NHEXAS data, including questionnaire, biological marker, and environmental data, prioritize chemicals based on the population prevalence or toxicological importance. For the chemicals (or chemical class), construct regression models to identify the predictors of exposure. These analyses should identify which questions predict measured exposure, both biological and environmental. Factor analysis or principal components analysis should be used to identify the most important questions that predict chemical exposure. NHEXAS data should be analyzed to determine how well the environmental data predict exposure and how well questionnaire and environmental measures predict exposure. Predictive models should be developed that can be used in subsequent studies. Key issues would be accurate separation of the population into low, medium, and high categories and development of models to identify highly exposed individuals. Ultimately, efforts should be made to attempt, on an overall basis, to identify which questions identify individuals who are highly exposed to many chemicals and those that are specific for one chemical or one chemical class. Risk managers and study designers will be able to use the results of this analysis to identify sample collection strategies by incorporating predictive ability of the data from each source (questionnaire, biological, and environmental) and the cost to collect and analyze data collected via these methods.
Data or Input Needs:	NHEXAS data from all study sites (or each individually): questionnaires, biological samples, and environmental and personal exposure samples. No additional data needed unless external validation of questionnaire responses is done.
Feasibility (of analyses with current NHEXAS databases):	All data are currently available. Much of the questionnaire data is nominal or ordinal and may not be well suited for the usual regression approaches.

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.2	0.5	1.0	3 (metals, VOC, pest.)	1

Research Outputs

(1) Preliminary analyses by chemical/chemical category

(2) Final output: Identification of potentially highly exposed individuals and the tools to identify them

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project A-5.

PREDICTORS OF EXPOSURE AND DOSE PROJECT

Project Name:	**P-04. Risk Factors for Biomarkers of Internal Dose: Demographics, Questionnaire Data, Concentrations, and Exposures**
Short Project Description:	Analyses to determine the association of biomarkers of internal dose with (1) demographics; (2) questionnaire information on behaviors, activity patterns, health indices, etc.; and (3) measures of personal exposures and media concentrations.
Goal/Objective:	To develop simple methods of estimating internal dose that can be used in studies of health outcomes.
Significance of Project:	Analytic or epidemiologic studies of health endpoints need effective methods for estimating internal dose, but direct measurement is often impractical. For example, studies of chronic health effects may require estimates of long-term average or historical exposures. NHEXAS provides a rich source of information that allows inferences about internal dose based on data collected from questionnaires, measures of chemicals in external media, and other sources.
Suggested Approach:	For appropriate chemicals and classes of chemicals: (1) Bivariate analyses of the association of biomarkers of internal dose and risk factors, including demographics, housing characteristics, questionnaire data, and measures of exposure. (2) Examine correlations among risk factors. (3) Multivariate modeling of the association of biomarkers with risk factors.
Data or Input Needs:	Biomarker concentrations, demographics, questionnaire data, and environmental media concentrations and exposure measurements.
Feasibility (of analyses with current NHEXAS databases):	These analyses will be feasible only for chemicals where biomarkers of internal dose exist at detectable levels for a sufficiently large sample. For a given risk factor, there also must be sufficient variability. Also requires knowledge of biomarker characteristics (e.g., half-life) to relate measurements to time of exposures.

Research Outputs

(1) Conduct bivariate analyses

(2) Examine interrelationships of covariates

(3) Final output: Results of multivariate modeling

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project EA-3.

PREDICTORS OF EXPOSURE AND DOSE PROJECT

Project Name:	**P-05. Determinants of Dose Measurements (Biomarkers) from the NHEXAS Studies**
Short Project Description:	Absorbed dose may be estimated by questionnaire and measurement data including air, water, diet, and contaminated surfaces. Predictive associations between measurements of exposure and dose will be evaluated. Questionnaire response data will be considered as a modifier of the exposure/dose association. This association will be evaluated further by taking into account existing pharmacokinetic models and parameters. Methods and approaches for assessing the dermal exposure contribution relative to the biomarker measurements are of particular importance because dermal exposure methods are not well developed. Measured biomarkers will be related to potential exposure using algorithms used to estimate aggregate human exposure.
Goal/Objective:	To identify and evaluate environmental and questionnaire determinants of dose and to better understand the time course associations between exposure and dose. The dermal contribution to exposure will be analyzed.
Rationale for Project:	Study results will aid in the interpretation of exposure biomarker measurements and will help in the efficient design of future exposure and epidemiologic studies. Further understanding in the interpretation of biomarker levels is valuable because they are believed to provide a better predictor of health outcome than environmental concentration measurements that do not account for contact, uptake/intake, and absorption processes.
Suggested Approach:	Biomarker measurements represent the absorption and clearance of chemical contaminants measured in the NHEXAS program. The predictive relationship among these measurements will be evaluated with questionnaire responses, and with exposure and environmental media concentrations using multivariate analysis methods. Pharmacokinetic models will be applied in order to explain the relationship between exposure and dose (biomarker) measurements. Contributions of contaminated media can be estimated using exposure algorithms routinely used in exposure assessment.
Data or Input Needs:	Chemical measurements in biological, exposure, and environmental media, questionnaire data, exposure factors, and pharmacokinetic parameters.
Feasibility (of analyses with current NHEXAS databases):	Sufficient detectable results are needed in media of exposure relevance for biomarker analytes. Need to consider timing of biomarker collection relative to exposure and environmental measurements (e.g., Maryland study samples collected at beginning of sampling), and the availability and suitability of available pharmacokinetic parameters for the subpopulations (e.g., children).

Research Outputs

(1) Multivariate statistical analyses; evaluation of short-term clearance models

(2) Final output: Journal article identifying predictors of dose

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project EA-10.

PREDICTORS OF EXPOSURE AND DOSE PROJECT

Project Name:	**P-06. Exploratory Data Analysis Methods for Evaluating Relationships Among Questionnaires, Exposure, Dose, and Risk Factors**
Short Project Description:	The NHEXAS databases include a wide spectrum of measurements: questionnaire responses, exposure measurements, and dose/biomarker measurements. Several analysis methods are now available for analyzing complex data sets to identify patterns, relationships, sociodemographic variables, important factors, and combinations of factors that influence or affect exposure distributions. These data will be analyzed without a priori decisions about relationships among the variables to generate new hypotheses regarding environmental exposures.
Goal/Objective:	Identifying and evaluating (1) associations among the NHEXAS variables, and (2) appropriate analysis tools for investigating large and complex data sets. Specifically, there is a need to identify the factors that contribute to high exposures, to establish relationships among these factors and exposure magnitudes/distributions, and to understand subpopulation differences.
Significance of Project:	Classification of NHEXAS data into variable groups will help focus future exposure assessments in national surveys, epidemiological studies, and risk assessments. (It also provides a comparison between the questions and the rationale for their use.) It is important to understand the data prior to using it for model evaluation or identification of significant exposure pathways/processes. Methods or approaches for investigating complex data sets should be compared to determine the most appropriate approach to identify important contributing factors in the NHEXAS data.
Suggested Approach:	(1) The strengths and limitations of the data will be evaluated initially using univariate analyses of individual variables. (2) Multivariate classification techniques will be selected and run (e.g., principal components, CART, neural networks, or factor analysis) to identify groupings of variables. Where possible, analyses are to be conducted by pertinent subpopulations because the variables may group differently by subpopulation. (3) Variable groupings will be evaluated in order to generate hypotheses, to guide in the design of other studies, and to identify important questions and/or measurements for future exposure assessments and risk assessments. (4) Identify strengths and limitations for each method in relation to the NHEXAS data. Recommend appropriate methods for analyzing NHEXAS data with special attention paid to the upper tails of the distributions.
Data or Input Needs:	The fully compiled database of complete measurement data including all chemical measurements, questionnaires, dietary and activity diaries, and demographic variables.
Feasibility (of analyses with current NHEXAS databases):	Feasibility of the project will be limited by the number of observations within strata. The large number of qualitative and quantitative data types included in the NHEXAS data sets (ordinal, continuous and binary) require special consideration when identifying appropriate methods or approaches used to analysis data. Attention should be given to the upper tails of the exposure distributions.

Research Outputs

(1) Univariate analyses

(2) Final outputs:
- Journal article on comparative analyses
- Journal article on ability of exposure measurement to predict exposure factors

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-11.

PREDICTORS OF EXPOSURE AND DOSE PROJECT

Project Name:	**P-07. Use of NHEXAS Data To Test Assumptions about Activity Pattern Factors and Other Exposure Factors in EPA Risk Assessments**
Short Project Description:	This project encompasses a series of individual projects that will examine the use of activity pattern factors and other exposure factors in EPA risk assessments as they are done in the Air, Water, Hazardous Waste, Pesticides, and Toxics Programs. Examples of tasks under this project area were raised at the workshop and include the following: (1) examine NHEXAS time/activity diaries and follow-up questionnaire data to determine the repetitiveness (frequency) of behavior over a 6- or 7-day period and compare to existing time/activity databases used to evaluate factors in EPA assessments, (2) examine the relationship among climate, season, level of exertion, and drinking water intake, (3) prepare exposure scenarios, evaluate scenarios with NHEXAS data, and compare those results to results obtained using current exposure assessment methods, scenarios, and assumptions as they are used in EPA programs, and (4) use NHEXAS data to design scripted sampling protocols for subsequent model testing or trend monitoring.
Goal/Objective:	Current regulatory exposure models in the Air, Water, Hazardous Waste, Pesticides and Toxics Programs often use default values that are based on limited and perhaps unrepresentative data. Often, assumptions are used to fill data gaps. NHEXAS data will be used to test assumptions and scenarios used in current assessment procedures, to improve the current EPA methodologies, and to identify factors where further study is needed.
Significance of Project:	The results of this project area will be useful to any program office that does assessments that rely on factors on which data were collected in the NHEXAS study. These include all EPA programs—Air, Water, Hazardous Waste, Pesticides, and Toxics.
Suggested Approach:	These are examples provided by members of the Assessment Breakout Group: compare 6-day sequences of individual time/activity patterns to 6-day sequences of daily patterns stochastically chosen from multiple individuals to determine impacts and frequency of repeated activities. Assess relationships of individual time/activity patterns to food and water ingestion across subject classes (e.g., age, gender, race) and local climate conditions. Compile individual time/activity and exposure data for subjects with complete data sets as input for exposure model testing and validation. Compile behavioral scenarios characteristic of more highly exposed subjects for use in developing scripted sampling protocols in subsequent exposure model testing and analysis.
Data or Input Needs:	Individual time/activity data and exposure measurements from NHEXAS and other appropriate comparative databases (e.g., time/activity, local meteorological data.)
Feasibility (of analyses with current NHEXAS databases):	Feasible. NHEXAS data set contains data on activity patterns, exposure factors, varying climates, and the like that can be used to test and refine current EPA assessment methods.

Research Outputs

(1) Conduct analysis

(2) Final output: Journal article comparing frequency and duration of various activities over 1- and 7-day periods in NHEXAS with data collected in other activity pattern surveys

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project A-6b.

SPATIAL AND TEMPORAL VARIABILITY PROJECT

Project Name:	**ST-01. Temporal Variability in Exposure Concentrations and Aggregate Exposure Using NHEXAS Data**
Short Project Description:	Analysis of NHEXAS databases to determine the temporal components of variability in various measures of exposure. The analysis will include both single-medium, single-pollutant class analyses, as well as total or aggregate exposure estimates over all media.
Goal/Objective:	To determine optimum strategies and designs for future NHEXAS national investigations. Questions to be addressed include when is it possible to estimate exposure from a single set of cross-sectional measurements, and what is the optimum number of such measurements that must be made for each pollutant medium class and for total exposure? Of interest is an understanding of the temporal span of the toxicological effect (i.e., what is the exposure duration of interest and does variability occur over such time spans?).
Significance of Project:	A future national investigation of exposures must be designed to assess exposures to members of the population that are accurate and reflect patterns and variability present in true exposures. Improved understanding of temporal variability across days, weeks, and seasons is necessary to ensure good estimates. This project has important implications for risk assessment because it will help account for uncertainty because of statistical "compression" of chronic exposure distributions compared to single-measure exposure distributions because of intraindividual correlations of exposure over time. It also has implications for epidemiology because it will help reduce uncertainty because of misclassification resulting from bias introduced by failing to account for temporal variability in exposure indicators.
Suggested Approach:	(1) Descriptive analysis of exposure concentration distributions by time period. (2) Use statistical techniques to assess population variability and test whether the population means vary over the duration of the studies. (3) Assess intraindividual temporal variability. (4) Evaluate aggregate exposure by summing potential or absorbed doses, as appropriate (with appropriate weighting for time, etc.), over individual pathways. (5) Evaluate temporal variability in total exposure. (6) Assessment of intraindividual variability versus temporal variability in total exposure. (7) Assess statistical strategies for determining optimum sample number for temporal variability. (8) Implement chosen strategy to determine optimum number of exposure measures to determine exposures of fixed length.
Data or Input Needs:	Repeated measurement exposure data for all studies, particularly the NHEXAS-Maryland investigation, identified with specific individual identifiers and temporal spacing. Certain questionnaire data to identify changes in exposure patterns attributable to other-than-usual exposure variability (e.g., a change in job status or introduction of a new source into the home).
Feasibility (of analyses with current NHEXAS databases):	Data exist in the NHEXAS-Maryland study and, to a limited degree, in the other studies, that would allow this to be completed. Repeated measurement data are available for most media in the Region V study. Sample sizes of 2 to 6 repeated measurements are available.

SPATIAL AND TEMPORAL VARIABILITY PROJECT ST-01

(cont'd)

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
.1	.3	2	3	1.5

Research Outputs

(1) Perform univariate temporal analyses of selected pollutant-class/-medium combinations

(2) Construct aggregate exposure estimates

(3) Evaluate temporal variability in exposure estimates for target chemicals

(4) Construct optimum sampling strategy for target chemicals

(5) Final outputs: Manuscripts on univariate temporal variability and manuscripts on aggregate exposure variability and optimum sampling strategy

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project A-4.

SPATIAL AND TEMPORAL VARIABILITY PROJECT

Project Name:	**ST-02. Use NHEXAS Dietary and Activity Pattern Data To Develop Predictive Relationships Between Single-Day Observations and Long-Term Patterns of Behaviors**
Short Project Description:	To use statistical techniques to determine the relationships between measurements of exposure-related behaviors (e.g., dietary and activity patterns) on a single day and subsequent longitudinal measurements. Use the short-term relationships to develop predictive models of longer term behaviors. The NHEXAS data set provides a unique source of information for this study.
Goal/Objective:	To develop models of the relationship between short- and long-term measurements of exposure-related behaviors that can be used in models of long-term exposures.
Significance of Project:	Collection of longitudinal data on exposure-related activities are resource intensive and subject to a number of technical difficulties. However, such data are critical to the accurate estimation of dose rates over periods longer than a single day.
Suggested Approach:	Longitudinal data on exposure-related behaviors will be extracted from the data set. Statistical techniques such as, but not limited to, random walk, Markov chains, correlation, and pattern recognition will be investigated as potential tools to identify relationships between short- and long-term patterns of behaviors. It is anticipated that the relationships will vary greatly across behaviors. No one method is likely to predict the relationship between short- and long-term behavior. Attention should be given to developing methods of estimating the upper bound of long-term behaviors as a function of short-term data. Patterns in time/activity data from the Maryland NHEXAS study should be compared/contrasted with data collected in the Region V and Arizona NHEXAS studies. Certain endpoints such as dietary records should be compared to the results of other longitudinal dietary studies to determine consistency across different populations.
Data or Input Needs:	The NHEXAS data set and other studies of long-term dietary patterns.
Feasibility (of analyses with current NHEXAS databases):	The data for this task are available. No limitations are anticipated.

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
.1	.2	.4	1	1

Research Outputs

(1) Extract NHEXAS data for data set

(2) Obtain other dietary surveys

(3) Reconcile differences in dietary survey methods

(4) Perform statistical analyses

(5) Final output: Journal article on relationship of single measurements of dietary exposure to long-term dietary exposure

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-10.

SPATIAL AND TEMPORAL VARIABILITY PROJECT

Project Name:	**ST-03. Characterization of the Variance Components of NHEXAS Data to Optimize Future Designs**
Short Project Description:	Characterize the variance components of NHEXAS data, including the inter- and intrapersonal, temporal (e.g., integration time, seasonal, weekly), activity-related, and spatial variabilities by sample size for each of the pollutants by pathway/medium and by integrated total exposure. Also, determine the reliability of a short-term measure of exposure for assessment of long-term exposure for populations and individuals. Results will be used to optimize future NHEXAS design.
Goal/Objective:	The primary goal of the proposed project is to use the NHEXAS data to determine the appropriate sampling strategies for the different pollutants and pathways. To achieve this goal, the proposed project will characterize the variance components of the NHEXAS exposure data to • estimate the optimum sample size and number of repeated measures (SAB comments II.A.2 and 4); • determine how exposure distributions vary across time and space and identify factors that influence this variation (II.A.2); • examine the variability of exposure distributions based on short-term measurements compared to those based on long-term measurements or averages; • assess whether the variance components differ by subpopulation, including susceptible and highly exposed subpopulations (II.A.4); and • investigate how the exposure characteristics of the various subpopulations are influenced by activity patterns, geographic area, and SES (II.A.4).
Significance of Project:	The proposed project directly addresses SAB concerns and, as a result, will improve substantially the ability to optimize the design of future NHEXAS and other exposure studies. It will incorporate findings from each of the three NHEXAS consortia and will allow the sampling plan of each consortium to be examined in a systematic and quantitative manner.
Suggested Approach:	Exposure data from each of the three NHEXAS studies will be analyzed to determine the inter- and intrapersonal, temporal, and spatial variabilities in exposure distributions. Analysis will be performed by pollutant, both pathway-specific and as integrated total exposure, as well as by subpopulation. Variabilities will be assessed using standard statistical approaches, including the coefficient of variation and ANOVA and mixed model approaches. Graphical techniques will be used to evaluate and determine appropriate pollutant- and media-specific sampling strategies. As possible, pollutants will be grouped based on identified appropriate sampling strategies. This project should be limited to representatives of the various chemical classes (e.g. metals, pesticides and VOCs).
Data or Input Needs:	From each pilot study (and primarily the Maryland NHEXAS study for temporal data), the following data will be needed: • environmental concentration and exposure data (including metabolites), • questionnaire data, and • time/activity data.
Feasibility (of analyses with current NHEXAS databases):	High, all the necessary data exists.

SPATIAL AND TEMPORAL VARIABILITY PROJECT ST-03

(cont'd)

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
.3	.9	3	3	2

Research Outputs

(1) Analyses of the data

(2) Final outputs:
- •Reporting of the optimized sampling strategies by pollutant and pathway
- •Publishing in peer reviewed journals

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Projects EA-6 and LL-12.

SPATIAL AND TEMPORAL VARIABILITY PROJECT

Project Name:	**ST-04. Spatial Variability**
Short Project Description:	NHEXAS data will be used to investigate spatial variability in concentrations, doses, and activity patterns. Possible areas of investigation include different states and counties, rural versus urban areas, locations near sources, and different climates and elevations.
Goal/Objective:	The goals of this research are to identify spatial and geographic factors contributing to high exposures for consideration in exposure assessment, to determine representativeness of local/regional data for use in assessments of other regions, and to identify geographically defined point and area sources.
Significance of Project:	These analyses will help assessors understand the geographic variability of pollutant concentrations and exposures and the impacts of such things as population density, climate, elevation, and local cultural factors. It also will examine the impact of identifiable, geographically located sources on exposure levels. Information on spatial variability also will contribute to more efficient design of future studies.
Suggested Approach:	(1) The following is an approach for comparing different geographical areas: select variables for comparison (e.g., a particular chemical/media combination), consider differences in sampling methodology that could account for differences among NHEXAS studies, account for confounding factors, and make statistical comparisons of distribution parameters. (2) The following is an approach for analysis of sources: identify potential sources of NHEXAS chemicals based on other data, such as data in the literature and the EPA Toxic Release Inventory Data; and perform analysis of correlation of exposure concentrations and locations of sources using geostatistical methods.
Data or Input Needs:	(1) Sufficient number of people in each geographic group to make meaningful comparison. Data set needs to have sufficient percentage of detectable levels of NHEXAS target chemicals. Sampling protocols and equipment for each location need to be similar enough so that differences are not attributable to the methods used. (2) Independent database to provide latitude and longitude and perhaps some estimate of emissions for target sources. Latitude-longitude and concentration/exposure data for NHEXAS participants.
Feasibility (of analyses with current NHEXAS databases):	(1) This study could be done for a few categories (e.g., state-by-state) in Region V. There may be a problem comparing environmental samples among studies because of different sampling methodologies. Parameters selected for comparison need to have similar sampling protocols (e.g., blood, urine, drinking water, etc.). (2) Data on latitude and longitude of sources is critical as is data on latitude and longitude of participants (may be available only for Arizona). There also would need to be some method to protect the confidentially of respondents that could be compromised by revealing the latitude-longitude of their residences.

Research Outputs

(1) Final outputs: Comparison of measurements, activity pattern duration/frequency, or total exposures in different geographical areas. Description of similarities and differences between sampling and analytical methods of NHEXAS consortia and potential impact on comparisons of results

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project A-12.

SPATIAL AND TEMPORAL VARIABILITY PROJECT

Project Name:	**ST-05. Investigate Stability of Individuals in Population Exposure Ranks Over Time**
Short Project Description:	Temporal variability in measurements of individuals may have a significant effect on estimates of exposure factors and distributions. This project will investigate the effect of using cross-sectional studies on estimates of exposure factor distributions. Cross-sectional studies are cost efficient because they collect minimal observations per individual, but provide no indication of temporal variability. Measures of intra individual temporal variability do not necessarily tell the complete story, as individuals may vary in concert, because of factors such as seasonal changes. It is also useful to examine the stability of individual's position or rank in the population exposure distribution to determine how this stability influences predictive ability of various exposure distribution parameters.
Goal/Objective:	To examine the importance of temporal variability and evaluate sources of variability in exposure factor measurements of an individual over time. To examine this variability on stability of an individual's rank or position in exposure factor population distributions.
Significance of Project:	It is important to understand the temporal variability in individual's measurements to assessment of potential bias of cross-sectional studies as estimates of exposure factor population distributions. A clear understanding of temporal variability will be useful in deciding when and where cross-sectional studies are appropriate for estimation of population exposure distributions and what modifications may improve these studies in a cost-efficient manner. This work also would provide highly relevant information on estimating the upper tails of the distribution.
Suggested Approach:	(1) Identify feasible and relevant variables from NHEXAS for study.. (2) Develop/assess methods for examining temporal variability and stability of individuals (3) Use mixed models to develop repeated measure/temporal correlation estimates and consider automation of methodology for examination of large numbers of variables.
Data or Input Needs:	The entire NHEXAS date set; especially the Maryland NHEXAS longitudinal data.
Feasibility (of analyses with current NHEXAS databases):	Feasible for variables where longitudinal data are collected for at least some individuals. Focus is likely to be on the Maryland study, with confirmation/validation use of Region V and Arizona NHEXAS studies.

Research Outputs

(1) Develop methods for examining temporal variability and stability of individuals

(2) Apply mixed models to develop repeated measure/temporal correlation estimates

(3) Final outputs:
- •Determination of factors influencing temporal variability in individuals exposed to environmental pollutants
- •Identification of limitations of cross-sectional population exposure surveys and recommendation of optimal spatio-temporal survey designs for future NHEXAS-type studies

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-8.

SPATIAL AND TEMPORAL VARIABILITY PROJECT

Project Name:	**ST-06. Spatial and Temporal Variability in Multichemical Exposure**
Short Project Description:	Project will better characterize the magnitude and variability in exposure to multiple chemicals measured in all environmental media by the three NHEXAS studies for different locations of the country. Both within- and among-study variability will be examined, and analyses will be conducted to determine whether exposure to one chemical in a given class is predictive of exposures to other compounds in that class or other classes.
Goal/Objective:	The goal of this project is to provide information that will improve the efficiency (e.g., cost-effectiveness) of future exposure, risk assessment, and epidemiologic investigations of health risks of cumulative chemical exposure. This study will provide some of the first information on multichemical and multipathway exposures required for cumulative risk assessments.
Significance of Project:	The need to assess risks of cumulative chemical exposures is well recognized within the scientific and regulatory communities. Little information is available for such assessments. Analysis of the temporal and spatial aspects of the NHEXAS data is important to reduce uncertainty in the exposure estimates for these assessments.
Suggested Approach:	The suggested approach is to examine multiple chemical exposure, first for each route of entry and second for aggregate exposure. This approach should be limited to two or three chemical classes, but utilize all of the NHEXAS data even if a compound was not collected in all media (e.g., VOCs). Analyses will be performed on measurements of environmental concentrations, exposure, and biomarkers (related to internal dose). Investigators should determine the appropriate chemical classes for study.
Data or Input Needs:	Concentration, exposure, and biomarker measurements from each NHEXAS study.
Feasibility (of analyses with current NHEXAS databases):	The feasibility of the proposed project is high for analyses of data within the Maryland study. Some limitations are anticipated in the types of samples available from the Region V study. (Longitudinal samples were not collected for Arizona.)

Research Outputs

(1) Initiate investigations within each medium and combine data across media where feasible for each study

(2) Complete single-route and aggregate analyses of cumulative exposure

(3) Final outputs:
- •Compare findings among studies
- •Report findings, write reports and manuscripts on cumulative chemical exposure

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project EA-5.

SPATIAL AND TEMPORAL VARIABILITY PROJECT

Project Name:	**ST-07. Development and Evaluation of Models for Interpreting and Quantifying Inter- and Intraindividual Variability in Pesticide Exposure/Dose Using NHEXAS Data**
Short Project Description:	Analyze cross-sectional and longitudinal biomarker and exposure data for pesticides considered in NHEXAS (such as chlorpyrifos and atrazine) to develop and test population-based pharmacokinetic (i.e., pharmacostatistical) models that explicitly discern and quantify intra- and interindividual variability in human doses.
Goal/Objective:	To develop, test/evaluate, and make available to EPA and the scientific community at large, a mechanism-based computational tool for characterizing and quantifying inter- and intraindividual variability (i.e., cross-sectional and longitudinal variability) in pesticides exposure/dose of human populations.
Significance of Project:	Quantitative characterization of inter- and intraindividual dose (and corresponding exposure) to common pesticides will reduce the uncertainty in, and thus improving, relevant dose/response studies and corresponding risk assessments. The mechanistic approach to be developed and evaluated should be applicable to a wide range of exposure situations and U.S. population segments.
Suggested Approach:	(1) Develop general formulations for population-based (pharmacostatistical) models of selected pesticides considered in NHEXAS (primary candidates are chlorpyrifos and atrazine) that explicitly incorporate/describe inter- and intraindividual variability of biological uptake/distribution/fate. This step primarily should consider existing "individual-based" "classical" (compartmental) models, as well as the possibility of formulating simplified population physiologically based models. (2) Perform analyses of appropriate NHEXAS data components to develop parameterizations for the above formulations (the Maryland study database being the primary candidate because it contains extensive longitudinal data); assess and interpret magnitudes of different types of variability. (3) Test the population pharmacostatistical model, with parameterizations derived as in the step above, with relevant independent data from other NHEXAS components to evaluate its ability to reproduce variability observed in these studies. (4) Review the available literature for other relevant data sets that may exist on dose variability for the pesticides of concern and extend the model evaluation to include these data sets. (5) Finally, evaluate the new model/method for its applicability to children's exposure to pesticides (using the NHEXAS Minnesota study data) and derive recommendations for appropriate model refinements/modifications and possibly additional data collection that would help to extend the model to children's exposure.
Data or Input Needs:	Pesticide exposure- and dose-related data from all three NHEXAS studies; other exposure/dose-related data from these studies (from both monitoring and questionnaires), such as activity patterns and additional literature data
Feasibility (of analyses with current NHEXAS databases):	At a minimum, it should be feasible with the collected data to at least evaluate the applicability of a population-based pharmacokinetic model for pesticide dose estimation to multiple regions and population segments of the United States. In some cases, biological half-life considerations may influence the modeling choices. In the best case, a widely applicable tool will be available; in the worst case, data needs for characterizing nationwide variability to dose will be identified.

SPATIAL AND TEMPORAL VARIABILITY PROJECT ST-07

(cont'd)

Research Outputs

(1) Data analysis/evaluation
Comparison and evaluation of existing approaches for individual-based pharmacokinetic modeling of the selected pesticides

(2) Final outputs:
- Tested operational population-based model with explicit descriptions of inter- and intraindividual variability
- Peer-reviewed manuscript

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-14.

AGGREGATE EXPOSURE, PATHWAY ANALYSIS, AND CUMULATIVE RISK PROJECT

Project Name:	**AE-01. Aggregate Exposure**
Short Project Description:	This project will estimate aggregated exposures from all media and all pathways for a single chemical. Environmental concentrations, personal exposure data, biological levels, and questionnaire data from NHEXAS, supplemented by data from other sources, will be used in the assessments. Multimedia exposure models representing current state-of-the-science regarding chemical, environmental, and population dynamics will be employed. The project will determine the relative contributions of environmental media and routes of exposure to "total exposure" or dose for each NHEXAS study and compare results among studies. These analyses will help to identify critical exposure pathways, factors, and sources that contribute to high end exposures.
Goal/Objective:	(1) To utilize existing multimedia/multipathway exposure models to aid in the interpretation of NHEXAS data and to help identify critical exposure pathways, processes, factors, and sources that contribute to high end exposures. (2) To assess aggregate exposure and identify the important media, pathways, and routes that contribute the most to total exposure; (3) To identify or develop methodologies (or models) to use biological data in aggregate exposure assessment through analysis of the relationships among biological testing results (i.e., blood and urine samples), environmental concentrations, personal concentrations, and exposure/dose (4) To compare the approaches, data, and estimates used to apportion pathway-specific exposures used in the NHEXAS studies and to identify similarities and differences, and compare or pool results where possible.
Significance of Project:	(1) Addresses the important regulatory issues associated with single and multimedia exposures (e.g., air, water, contaminated soil, and food) (2) Advances exposure assessment methodology (multimedia and multipathway) (3) Helps the agency to prioritize resources to address the most important media or pathways, and to design intervention strategies to protect public health (4) Determines how the results (parameter estimates) from the individual NHEXAS studies can be systematically compared to each other or pooled to provide combined estimates of associations between pathway-specific measurements/estimates and aggregate exposure or dose. (5) Utilizes existing tools that assimilate or represent the current level of understanding of exposure processes to extract relevant and useful information from the NHEXAS studies.

AGGREGATE EXPOSURE, PATHWAY ANALYSIS, AND CUMULATIVE RISK
PROJECT AE-01
(cont'd)

Suggested Approach:	Ideally, this project should include at least one pesticide and one metal. For each chemical class, identify specific case studies that warrant investigation (e.g., elevated concentrations in multiple media, elevated exposure, sensitive subpopulations). (1) Identify or develop an aggregate exposure model to assess aggregate exposure for each individual. (2) Construct concentration and exposure factor distributions for each exposure variable using questionnaire and measurement data from NHEXAS supplemented by data from other sources where necessary. (3) Calculate aggregate exposure for each individual. (4) Compare aggregate exposure results to biomarkers. (5) Compare estimates of pathway or route specific exposures with total exposure or absorbed dose to identify pathway contributions to exposure. (6) Identify important contributors to high end aggregate exposure. Data on activity patterns, housing characteristics, and other exposure factors can be obtained from the questionnaire and assessed using a variety of methods that handle different data types (binary, integer, categorical, ordinal, and continuous). Potential methods may be based on regression trees, neural networks, factor analysis, or order statistics (i.e., statistics of extreme events). Fate and transport models and regression models may be used to assess contributions of sources such as industrial point sources, motor vehicles, smoking, pesticides and other consumer products used at the residence, building materials, and combustion sources. (7) For each study, examine sampling and analytical methods to determine if the resulting measurements are sufficiently similar to be compared. Compare results (parameters and error terms) among individual studies where feasible. (8) Pool data where measurements are similar to make generalized statements about exposure where feasible. (9) Evaluate uncertainties and limitations. Develop plausible explanations for NHEXAS results.
Data or Input Needs:	(1) Environmental concentration data in all media (2) Biological testing data (3) Questionnaire data (4) Information about sampling and analytical methods. (5) Supplemental data from other sources– Toxics Release Inventory, population density, pesticide use, absorption rates. (6) Coefficients (e.g., uptake rates, absorption rates, etc.)

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.1	0.5	0.5	3 (metals, VOCs, pest.)	1

Research Outputs

(1) Identify case studies, select models, and complete parameterization of case studies and complete initial analysis

(2) Final output: Journal article on cumulative exposure and risk to selected chemicals.

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Projects A-3, EA-11, M-6, and M-7.

AGGREGATE EXPOSURE, PATHWAY ANALYSIS, AND CUMULATIVE RISK PROJECT

Project Name	**AE-02. Comparison of children's' and adults' exposures to pesticides and other chemicals in the Region V, Arizona, and Maryland studies**
Short Project Description:	Compare children's and adults' exposures to pesticides, volatile organic chemicals, metals, and PAHs using biomarker and environmental data collected in the Minnesota Children's Pesticide Exposure Study, Region V Study, and Arizona and Maryland Studies. Data from the children's studies in Arizona and Baltimore may also be compared as they become available.
Goal/Objective:	To determine if children's exposures differ/do not differ from adults for pesticides and other NHEXAS chemicals.
Significance of Project:	Children have been identified as a potentially vulnerable subpopulation for exposure to pesticides and other chemicals (e.g., lead). NHEXAS data may be used to better understand differences between adults and children's exposures, and ultimately to determine if federal and state regulatory policies adequately protect children.
Suggested Approach:	(1) Determine what data may be compared (see limitations below). (2) Develop a set of consistent procedures for analyzing the data across studies to take into account among-study differences (e.g., methods for handling values below the detection limit; methods for handling non-normal distributions; methods for data sets with a large number of values below the detection limit). (3) Compare children's and adults' exposures (where appropriate). Focus on biomarker data (urine, blood), and then expand to diet, personal air, and other measurements. (4) Assess health risks for children and adults using appropriate toxicity values (e.g., RfDs, RfCs, cancer potency slopes). Compare health risks for adults and children.
Data or input Needs:	Data may be used from the Minnesota Children's Pesticide Study, Region V Study, Arizona Study, and Maryland Study. Data from the children's studies which are being conducted in Arizona and Washington may also be included (as the data become available).
Feasibility (of analyses with current NHEXAS databases):	Data among these studies may not be comparable because of differences in types of measurements (chemicals, media), detection limits, methods/strategies of collection, methods of analysis, and spatial and temporal factors. Consistent procedures for data analysis must be developed for comparisons to be valid. Data are available on children for metals and VOCs as well as pesticides. Also need to consider the effects of regional differences on differences between children and adults in different regions. Child subjects in the Region V and Arizona studies might possibly be used to address this, but there may be a limitation based on the number of children in those two studies (about 15%).

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.1	0.5	0.5	3 (metals, VOCs, pest.)	1

Research Outputs

Final outputs:
- Assessment comparing total exposure (dose) for children in Minnesota.
- Study of total exposure (dose) for adults in Region V or other appropriate studies.

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project A-8.

AGGREGATE EXPOSURE, PATHWAY ANALYSIS, AND CUMULATIVE RISK PROJECT

Project Name	**AE-03. Construction of an empirical multimedia/multipathway exposure distribution model including temporal variability based on NHEXAS data.**
Short Project Description:	The NHEXAS study collects data that can be used for the development of multimedia/multipathway exposure models and can also incorporate temporal variability in exposure factor measurements. Pre-NHEXAS models were based on data from studies that were often limited in scope to single media/single pathway. Using the NHEXAS data, the pre-NHEXAS models can be extended to include multimedia/multipathway correlation among variables, both among and within individuals. This project examines the issues involved in constructing this type of model based on the data available in the NHEXAS study.
Goal/Objective:	(1) Determine limitations of NHEXAS study design in construction of empirical multimedia/multipathway exposure distributions which includes temporal variability. (2) Construct empirical multimedia/multipathway exposure distribution model including temporal variability using NHEXAS data to extent possible. (3) Examine issues in constructing empirical models involving temporal variability, including development of methodology for estimating multivariate distributions
Significance of Project:	Project would extend empirical exposure distribution models to include temporal variability in individual exposure measures and development of multivariate joint and conditional distributions for use in empirical exposure distribution models. It will also highlight the limitations in the NHEXAS study design for construction of such models and provide information to improve future multimedia/multipathway exposure studies.
Suggested Approach:	(1) Use of NHEXAS Maryland data. (2) Assessment of data for use in development of multivariate exposure factor distributions. (3) Extension of pre-NHEXAS model framework to include multivariate distributions. (4) Estimation of parameters for empirical model exposure factors distributions
Data or input Needs:	NHEXAS study data. Pre-NHEXAS exposure models.
Feasibility (of analyses with current NHEXAS databases):	No feasibility issues beyond data and input needs.

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.1	0.3	1.0	3 (2 pest., 2 metals, 2 VOCs)	2

Research Outputs

(1) Development of methodologies for multivariate distributions
(2) Estimation of distribution parameters from NHEXAS data
(3) Development of framework for empirical distribution model
(4) Running and analysis of model
(5) Multimedia/multipathway exposure distribution model including temporal variability
(6) Empirical multivariate distributions and associated uncertainties based on NHEXAS data that can be used by other modelers
(7) Report/journal article assessing results of model analysis

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Workshop Project M-17.

AGGREGATE EXPOSURE, PATHWAY ANALYSIS, AND CUMULATIVE RISK PROJECT

Project Name:	**AE-4. Cumulative Risk from Exposure to NHEXAS Chemicals**
Short Project Description:	Assess cumulative risks of various health effects associated with multichemical exposures measured in NHEXAS
Goal/Objective:	(1) To test whether the distributions of concentrations co-vary across subjects for different chemicals or not. (2) To identify groups of chemicals that vary together across the population and/or that cluster together in the upper percentiles of exposure (e.g., upper 10^{th} or upper 25^{th}, depending on availability of data) and analyze questionnaire data for ability to predict whether a person falls in the upper tail of the joint distributions. (3) To prioritize pollutants and pathways as to their contribution to cumulative risk of various health effects to focus pollution control and other public health activities on higher risk contributors. (4) To assess cumulative risk resulting from exposure to multiple chemicals of similar action/toxicity.
Significance of Project:	A key question in addressing risks is whether the distributions across people in exposures to chemicals A, B, C... are independent of one another or whether the distributions are correlated. Are there individuals who fall in the upper tails of more than one chemical distribution? If so, this could have important implications for risk assessment. The results of this project will assist public health agencies (national, state, and local) in effectively and efficiently targeting resources to control pollutants and pathways of higher risk. This project, in conjunction with the Aggregate Exposure Project, will start laying the foundation for agency efforts in cumulative (multistressor) risk assessment. Examples where results of this project will be useful include assessments of pesticides with similar mechanisms of action under FQPA, assessments of multiple exposures to air toxics, and the recently begun effort to develop agency guidance for cumulative risk assessment.

Suggested Approach:	• Construct bivariate correlation matrices for all chemicals (using pooled data across study if possible) for NHEXAS media and carry out factor analysis to identify groups of chemicals that vary together across the populations. • Dichotomize exposure distributions into >X percentile or not and analyze whether assignments are correlated across chemicals • Characterize chemical groupings, if any, and use regression analysis to identify predictors of high exposure. • Develop cumulative risk assessment of chemical exposures for individual study participants measured in NHEXAS projects. One approach is to identify chemicals with common endpoints and/or mechanisms of action and use toxic equivalency factors to sum the risks. Some common metric for risk must be found to combine exposures of chemicals with varying toxicities. Approaches should conform to Agency guidance and scientific understanding for assessment of mixtures of stressors. Calculate a weighted index of "cumulative" exposure using the absorbed dose estimated from NHEXAS data • Characterize relative contributions to cumulative risk of individual pathways and pollutants per participant and describe distributions across study populations. Report relative contribution of individual pathways and pollutants for representative low-end, average, and high-end NHEXAS subjects. • Develop relative ranking of pathways and pollutants in terms of contribution to cumulative risk; identify key driving pathways and pollutants. • Compare across studies.

AGGREGATE EXPOSURE, PATHWAY ANALYSIS, AND CUMULATIVE RISK PROJECT AE-04

(cont'd)

Data or Input Needs:	Exposure measurements from NHEXAS studies Population descriptions (e.g., body weights, ages, food intakes, etc.) from NHEXAS studies Toxicity data Data on possible synergistic or antagonistic interactions among chemicals
Feasibility (of analyses with current NHEXAS databases):	Limitations include number of pollutants for which quantitative dose-response values are available. Initially, the project would probably consider those chemicals with common health endpoints and/or modes of action. Also assumptions on nondetects will have to be made (e.g., evaluate using nondetects set to zero versus set to ½ DL versus omitting large nondetect chemicals from analysis). Cumulative risks would be assessed for variety of health endpoints.

Research Outputs

(1) Intermediate steps:
- •Collect toxicity data and identify appropriate set of chemicals for study
- •Select appropriate models and parameterize models; complete initial
- •Complete initial descriptive analysis including bivariate correlations
- •Complete multivariate analysis of co-variance

(2) Final outputs: Report and publication on multivariate analysis of co-variance. Weighted exposure indices for 1 to 3 sets of chemicals, depending on data availability. Multipathway, multichemical assessments with estimates of total risk. Comparison of multichemical risk via single pathways with total risk for selected NHEXAS compounds. Comparison of risk via single chemical with total risk from selected NHEXAS compounds.

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Projects A-1, A-6a, and EA-12.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT

Project Name:	**M-01. Compare Pre-NHEXAS Model Results with NHEXAS Measurements**
Short Project Description:	Compare pre-NHEXAS model results for benzene, lead, and chlorpyrifos with NHEXAS measurements. Update pre-NHEXAS models with information from the measurement data.
Goal/Objective:	Assess validity of pre-NHEXAS models by comparing with measurements. Improve these models based on data to better predict exposures.
Significance of Project:	If models and data compare well, this provides a validated model for use in predicting human exposures to these pollutants. This then can be applied to populations outside of the NHEXAS study region. Differences between measured and modeled results can be used to improve model predictions and provide information on limitations in the use of disparate studies. Overall, this comparison will provide confidence in using models to estimate multimedia exposures.
Suggested Approach:	(1) Compare environmental concentrations as predicted from pre-NHEXAS benzene, lead, and chlorpyrifos models with corresponding measurements, with special attention to high-end concentrations. (2) Extend pre-NHEXAS models to go from exposure to dose and compare NHEXAS biomarker measurements to this version with special attention to high-end measurements. (3) Examine different parameters to determine possible reasons for discrepancies between models and measurements. This should include comparison of measured and modeled time/activity diaries and concentrations in air, food, water, and other media. In addition, algorithms for calculation should also be examined. (4) Determine if model predicts better/worse for a certain population subgroup, based on location, age, race, sex or other factors. (5) Improve model estimates based on results of tasks 1 through 4.
Data or Input Needs:	Questionnaire and time/activity data, environmental concentration data, and analyte concentrations.
Feasibility (of analyses with current NHEXAS databases):	Pre-NHEXAS model code, documentation, and their results should be made available. Questionnaire data and concentration data that correspond to the pre-NHEXAS models will be available.

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.1	0.4	0.60	3 (pest, metal, VOCs)	2

Research Outputs

(1) Compare environmental concentrations from measured and modeled results
(2) Extend exposure model to dose and compare with urine/blood concentrations
(3) Determine which inputs/algorithms/population subgroups are responsible for discrepancies between model and measurements
(4) Final outputs:
- •Report on comparison between measured and modeled data
- •Improve model based on results

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-16.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT

Project Name:	**M-02. Comparison of NHEXAS Findings with National Air Toxics Assessment (NATA) Estimates for Ambient Air Levels and Exposures for Selected VOCs and Metals**[a]
Short Project Description:	Compare patterns and trends in monitored neighborhood ambient air levels of VOCs and metals to the annual average estimates of the same compounds derived through the NATA; evaluate the relevance of NATA predictions to the types of exposure situations characterized in NHEXAS.
Goal/Objective:	To evaluate the relevance of NATA predictions to the types of exposure situations characterized in NHEXAS; to identify gaps and potential improvements in both screening modeling methods for ambient air quality characterization and in data collection for exposure characterization.
Significance of Project:	The NATA study has attracted remarkable attention regarding its reliability to predict exposures actually experienced by individuals and populations. This project will help in understanding and characterizing both the relevance and the limitations of NATA (and potentially of similar approaches), as well as in identifying specific steps in improving exposure estimates to airborne contaminants through screening modeling approaches.
Suggested Approach:	(1) Extract ambient air concentration estimates from the 1996 database (or from the follow-up database utilizing more recent TRI emission data, depending on its availability at the time of project implementation) for a set of selected airborne VOCs and metals monitored in the NHEXAS studies and for the approximate locations of the monitors. (2) Incorporate both the NATA estimates (i.e., based on HAPEM4 and ASPEN model analyses) and the corresponding NHEXAS observations in a Geographic Information System linked with appropriate statistical/geostatistical software routines to ensure maximum usability, visualization, and analysis options for these data and estimates. (3) Perform qualitative and statistical comparisons of relevant ambient air concentration estimates/data from NATA and NHEXAS, with focus on identifying general patterns and trends. (4) Perform screening calculations of exposure for selected subsets of the NHEXAS components, using the NATA estimates as the starting point and utilizing partial information from the NHEXAS databases (such as activity patterns and other questionnaire-based information). Compare these results to personal exposure and biomonitoring measurements and estimates that utilize additional NHEXAS data. (5) Consider, evaluate conceptually, and, if possible, investigate through limited case-specific studies, potential improvements in NATA-type methodologies for screening ambient and exposure characterization.
Data or Input Needs:	For phase I (steps 1 to 3 of the approach), NHEXAS monitored selected VOCs and metals with corresponding geographical location information. NATA results are publicly available but certain additional information may need to be provided by EPA. For phase II (steps 4 and 5), access to more extensive information from the NHEXAS databases (e.g., activity patterns and household attributes).
Feasibility (of analyses with current NHEXAS databases):	The study is straightforward and feasible, depending only on on-time availability of NHEXAS data for Phases I and II (as identified in the Data Needs).

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT M-02

(cont'd)

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.20	0.2	1.0	2 (2 VOCs, 2 metals)	1

Research Outputs

(1) Report summarizing evaluation of the relevance of the NATA estimates for exposure assessments
(2) Final outputs:
- Evaluation of methodologies for screening exposure assessments for airborne contaminants
- Specific recommendations for improving screening modeling methodologies and data collection approaches
- Peer-reviewed manuscript(s)

[a]This is a two-phase project (Phase I - Year 1; Phase II - Year 2). Critical results evaluating the relevance of NATA estimates will become available from Phase I, whereas Phase II will focus on more exploratory aspects of the problem, leading to recommendations for methodological improvements in screening exposure assessments.

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-15.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT

Project Name:	**M-03. Develop Model Parameters from Qualitative and Quantitative NHEXAS Monitoring Data, Questionnaires, Time/Activity, and Survey Data**
Short Project Description:	Develop exposure model parameter (e.g., ingestion rates, emission rates, etc.) values, ranges, and distributions making use of both quantitative and qualitative data generated in NHEXAS. Exposure parameters should be developed in accordance with the current state of the art in exposure assessment and corresponding model input requirements. Specific emphasis should be placed on key exposure parameters common in multimedia exposure assessment and those that are likely to contribute to high-end exposures.
Goal/Objective:	Generate deterministic values and stochastic distributions for exposure model parameters, using available NHEXAS database. Exposure parameters that are selected should be relevant to exposure assessments that are based either on mechanistic, statistical, or empirical models.
Significance of Project:	Improve exposure parameter values and the utility of questionnaires for quantitative exposure analysis.
Suggested Approach:	Develop methods to interface available selected exposure models with qualitative and quantitative questionnaire data (e.g., time/activity patterns, identified sources and exposure pathways) for the purpose of deriving magnitude, ranges, and distributions of exposure parameters. The combination of artificial intelligence and statistical methods is one possible approach for the automated analysis of large data sets.
Data or Input Needs:	NHEXAS chemical monitoring data for all media (where available) and qualitative/quantitative data generated from questionnaires and other sources (e.g., local survey of potential sources).
Feasibility (of analyses with current NHEXAS databases):	The use of mathematical and computer methods to combine qualitative and quantitative data for the purpose of generating quantitative exposure parameters represent a new and challenging approach. The proposed approach is feasible given the rich NHEXAS database and existing state-of-the-art mathematical methods of quantifying descriptive data in the context of model development. Analysis may be limited by censored (e.g., nondetects) data for chemical measurements in some media.

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.20	0.4	0.50	3 (Region V, AZ, MD)	2

Research Outputs

(1) Development of methodology and demonstration of general test cases
(2) Final outputs:
- •Generation of distributions for exposure model parameters
- •Journal article describing improved exposure model parameter values.

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-3.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT

Project Name:	**M-04. Evaluate Implications of NHEXAS Results for Existing Chronic Exposure Assessment Methodologies**
Short Project Description:	Screening models (sets of algorithms) are used widely to make preliminary decisions for Superfund sites, pesticide regulations, and the evaluation of emissions to air and water. However, high quality and reliable multimedia monitoring data to validate these models are virtually nonexistent in the literature, and, as such, the opportunity to test screening models, even on a qualitative scale, is rarely available. This project will take the dose estimates from personal monitoring or biomarkers and compare the estimates to those produced from EPA screening methodologies (also referred to as Tier 1 or initial Tier assessments). Examples of these methods include recommended exposure models under the Superfund program and the residential SOPs.
Goal/Objective:	To improve the understanding of the strengths and limitations of existing screening models and identify opportunities for improving future models.
Significance of Project:	Screening models provide the basis for preliminary regulatory decisions for pesticides, hazardous waste sites, and the evaluation of releases to air and water. NHEXAS databases provide a unique opportunity to evaluate these models.
Suggested Approach:	This project would be performed in phases, (1) Determine how the NHEXAS data set would be used (selection of pollutants, interim findings, activity/dietary patterns, etc.). (2) Development of the strategy for developing model inputs and relating outputs to the data set. (3) Perform the evaluations. (4) Analyze the results to determine why the models did or did not match with the survey. (5) Publish a final report. A clear methodology should be established for the evaluation procedure that will be reviewed scientifically. A consistent strategy for dealing with data gaps should be established.
Data or Input Needs:	The complete data set (including the data from the questionnaires) should be available prior to the development of the specific model test sets. Participation from the relevant EPA program offices is desirable to confirm detail on how screening exposure models actually are used.
Feasibility (of analyses with current NHEXAS databases):	The project is feasible with the indicated data resources.

Research Outputs

(1) Development of a modeling strategy that addresses differences in the type of models and how data gaps will be addressed
(2) Application of screening level and refined multimedia exposure and dose models to selected pollutants
(3) Evaluation of differences among the results obtained from alternative chronic exposure modeling methods
(4) Final output: Develop final report and journal articles (s).

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-13.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT

Project Name:	**M-05. Evaluation of Existing Multimedia Models Using the NHEXAS Data Set**
Short Project Description:	High-quality and reliable multimedia monitoring data are virtually nonexistent in the literature, and, as such, the opportunity to test existing models, even on a qualitative scale, is rarely available. Several multimedia models have been developed, or are under development, that predict media concentrations in residential environments based on inputs such as source characterization and fate and transport, etc. Information available from the NHEXAS questionnaires, particularly those related to local source characterization, fate and transport, receptor characterization and activity patterns (supplemented by default values) should be analyzed and used in these models to predict media concentrations and personal exposures of the NHEXAS respondents. These predictions should be compared with the individual's exposures and microenvironmental concentrations monitored in NHEXAS. Examples of models that can be evaluated include, but are not limited to, TRIM, MEPAS, CARES, LIFELINE, and CONSEXPO, as well as other linked and nested compartmental models.
Goal/Objective:	• To improve the understanding of the strengths and limitations of existing multimedia models and identify opportunities for improving current and future models. • Identify the usefulness of the data set and determine how future NHEXAS studies could better meet the need for testing models.
Significance of Project:	Multimedia models provide the basis for regulatory decision for pesticides, hazardous waste sites, and the evaluation of releases to air and water. Currently, there are very limited opportunities to evaluate these models. NHEXAS provides a unique opportunity for such evaluations.
Suggested Approach:	This project would be performed in phases. (1) Determine how the data set could be used (selection of pollutants, interim findings, activity/dietary patterns, etc.). (2) Identification of the models, modeling strategies (e.g., linked and nested multimedia models) and the development of the strategy for developing model inputs and relating outputs to the dose measurements in the NHEXAS data set. (3) Model teams (preferably the developers of each multimedia model) perform the evaluations. (4) Analyze the model's prediction and NHEXAS findings to determine how and why the models did or did not match with the survey. (5) Develop recommendations on how future NHEXAS projects could be better designed to meet the evaluation needs of multimedia modelers. (6) Publish a final report/peer review publication. Tasks 1 and 2 could be performed by a panel of exposure assessment experts, through one or more workshops. Where possible, model owners should be involved in these workshops. A clear methodology should be established for the evaluation procedures. The selected models should be divided into modules, if possible, for estimating intermediate and final exposure results. Modules should include source characterization, fate and transport, receptor characteristics, activity patterns, and exposure assessment (Task 3). A consistent strategy for dealing with data gaps should be established. The model's predictions of interim findings (air and surface levels, hand wipe, dietary levels, activity patterns, etc.) also should be compared to the NHEXAS data set.
Data or Input Needs:	The complete data set (including the data from the questionnaires) should be available prior to the development of the specific model test sets. Models should be well characterized and model developers should participate in the project.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT M-05

(cont'd)

Feasibility (of analyses with current NHEXAS databases):	The project should be feasible. Only existing models will be evaluated. Where appropriate, model developers will be included in the project team. Models of many source terms cannot be included in this exercise because they were not included in NHEXAS.

Research Outputs

(1) Selection of models for evaluation, development of a modeling strategy that addresses differences in the type of models and how data gaps will be addressed
(2) Application of selected models to the NHEXAS database
(3) Analysis and comparison of model results to NHEXAS study concentration, exposure, and biomarker measurements
(4) Improve the development and evaluation of existing multimedia, multipathway exposure models
(5) Final output: Report assessing the findings from the model evaluation study using the NHEXAS database.

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-2.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT

Project Name:	**M-06. Quantify Uncertainties in NHEXAS Data and Assess Contribution to Model Errors**
Short Project Description:	Provide uncertainty estimates within the NHEXAS database that is available to researchers and the public, so that uncertainty is addressed consistently and does not lead to redundant effort by modelers. Identify how the data uncertainties may impact modeling uncertainties and illustrate with case studies.
Goal/Objective:	• Provide consistent, understandable uncertainty estimates of the NHEXAS data within the NHEXAS database • Provide guidance/advice on applicability and use of various types of data in models to minimize inappropriate model construction.
Significance of Project:	The NHEXAS database will be used by many researchers and the public. Inclusion of uncertainty estimates/descriptions will avoid duplication of effort in calculating these values, will mean that the data uncertainties are treated consistently, and will alert the public and regulatory community of possible limitations in the use of the data.
Suggested Approach:	<u>Analytical Measurements</u> (1) Ensure that NHEXAS data are QA'd and flagged appropriately. (2) Ensure that NHEXAS data include Limit of Detection information. (3) Calculate standard errors for each analytical methodology (including sampling and analysis). (4) Tag uncertainty data to all NHEXAS data entries and provide a methodology for error estimation with the public database. <u>Survey and Time/Activity Information</u> (1) Provide qualitative assessments of data and their applicability for modeling by including meta data from field staff on reliability of individual household; include expert panel judgment of uncertainties of the methodology in general, including effects of sample size, inaccuracies of recall diaries, observer effects, time resolution effects, etc.; and compare survey results from NHEXAS with other data sources. (2) Include qualitative assessments in database. <u>Assessment of Model Uncertainties</u> Convene workshop of modelers to evaluate impacts of uncertainties for variety of analytes, with differing critical routes of exposure. Provide qualitative descriptions of uncertainties and caveats for inclusion in the database. Provide case studies to illustrate how errors impact modeling uncertainties.
Data or Input Needs:	Paced by the availability of the database, the NHEXAS data need to be quality assured to flag/remove inappropriate data. Duplicate sample data, split sample data, blanks, and other QA/QC information on the analytical measurements need to be included in the database. A description of the sampling and analytical methods also must be included.
Feasibility (of analyses with current NHEXAS databases):	The first part of the effort is quite doable, and should build on normal QA/QC procedures. This work is to insure that the synopsized uncertainty data also are made readily available for researchers and the public. The impact on modeling errors is much more likely to be case dependent, varying with each analyte and model used.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT M-06

(cont'd)

Research Outputs

(1) Review NHEXAS databases now under development for data to be included and make sure that QA/QC data and metadata on QC are in database for both analytical and survey data
(2) Calculate synopsis information from data sets now scheduled to be delivered in FY01
(3) Convene workshop or expert panel to provide qualitative description of uncertainties associated with survey information
(4) Convene workshop or expert panel to evaluate impact of uncertainties of modeling–prepare case studies for specific analytes/major routes of exposure
(5) Final output: Incorporate uncertainty estimates and case studies into public database

* **NOTE:** Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-4.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT

Project Name:	**M-07. Reconstruct Exposure and Dose Profiles from Biomarker Data Utilizing Questionnaire and Environmental Measurements**
Short Project Description:	The relationships among environmental measurements, time/activity data, and biomarker levels will be investigated with the goal of classifying exposure scenarios into steady-state cases (e.g., from long-term average exposures) and intermittent events. There are several assumptions regarding the route and timing of dose that need to be addressed in making these estimates, and the questionnaires and time/activity data will be used to make these determinations. There is the potential to focus on the exposures of children, in addition to the general population.
Goal/Objective:	To develop and evaluate a methodology that provides realistic estimates of the dose and exposure associated with a biomarker measurement as a function of the types of exposure that occurred.
Significance of Project:	Biomarkers can provide an indicator of total absorbed dose. However, making quantitative estimates of this dose requires several assumptions about the timing and route of the exposures, as well as the suitability of the model being used. The estimates of total absorbed dose may help to evaluate current exposure assessment models and assumptions (e.g., OPP's Residential SOPs) and to develop and test models describing residential exposure.
Suggested Approach:	• The total absorbed dose from a steady-state exposure will be modeled by a mass-balance, and the absorbed dose from discrete events will be estimated by an inverted pharmacokinetic model (in the case of compact classical compartmental models) or maximum likelihood optimization procedure (in the case of comprehensive physiologically based models). • These dose estimates will be linked to a range of possible exposures and environmental concentrations and then compared with those measured in the NHEXAS study. Differences will reveal areas of improvement for modeling methods and indicate additional information that will be useful to collect in future studies.
Data or Input Needs:	• Pollutant concentrations in solid-food, personal air, dermal rinse, surface press and wipe, urine (pesticide metabolite), and measurements. • Pesticide use from household screening, baseline, and follow-up questionnaires. • Time/activity and food consumption diaries. • Information on urine volume, creatinine concentration, time of last void, and body weight.
Feasibility (of analysis with current NHEXAS databases):	This project can be implemented in a 2-year time period assuming the availability of the NHEXAS database. Likely candidate chemicals are chlorpyrifos, lead, arsenic, and benzene. • The food diaries may not be coded to link with ranges of pesticide residues (by food type), which may limit the temporal resolution of the dietary data estimates. • There are concerns about applying model parameters (e.g., absorption and elimination rates) determined in a small number of individuals to the general population because of differences in personal characteristics such as age, gender, race, and health status.

EVALUATION/REFINEMENT OF CURRENT EXPOSURE MODELS AND ASSESSMENTS PROJECT M-07

(cont'd)

Research Outputs

(1) Obtain and merge needed databases
(2) Analysis of questionnaire/activity data to group by types of exposure
(3) Review metabolite data by individual to identify intermittent and steady-state patterns
(4) Solving and programming the models
(5) Incorporation of the model in an estimation methodology
(6) Uncertainty analysis
(7) Final output: Journal article on approaches to estimate dose from a biomarker and exposure information

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-9.

DESIGNING EXPOSURE STUDIES PROJECT

Project Name:	**DES-01. Survey and Statistical Aspects of the Design of an Exposure Field Study: Lessons Learned from the NHEXAS Pilot Studies**
Short Project Description:	A review, revision, and updating of the discussions, analyses, and conclusions which provided the original foundation for the NHEXAS design as presented in the Callahan et al. paper (JEAEE, 1995) will be conducted in light of the NHEXAS pilot studies experience. The hypothetical calculations would be replaced with calculations based on actual NHEXAS data. In addition, the analytical and statistical hypotheses that were generated in the design of the NHEXAS pilots will be reviewed to determine which hypotheses were testable and which were not.
Goal/Objective:	The objective of the project is to provide directly relevant and specific guidance for the sample and survey design aspects of a national-scale multichemical, multimedia exposure field study.
Significance of Project:	The Callahan paper influenced the design of the NHEXAS pilots. Its revision will provide scientifically relevant, specific, and current guidance for the design of a full national NHEXAS, and also for other regional or national human exposure field studies, especially multichemical, multimedia studies.
Suggested Approach:	Callahan et al. (JEAEE, 1995) discussed the statistical and survey design issues involved in designing a population-based environmental exposure study. It made a number of design recommendations – about the optimal selection of Primary and Secondary Sampling Units (PSUs and SSUs) and households, about screening strategies, about the selection of target household member, etc. Many of these recommendations were based on calculations of hypothetical intraclass correlations, design effects, and variances. There is now a wealth of data available from the three NHEXAS pilot studies that is germane to these survey design issues. This project would involve a review of the discussions, analyses, and conclusions in the Callahan paper in light of the NHEXAS experience. The hypothetical calculations of design effects and intraclass correlations would be replaced with calculations based on actual data, and the conclusions and recommendations revisited. These analyses would be repeated for different pollutants and classes of pollutants to determine if different conclusions would be reached for different pollutants. In addition, the analytical and statistical hypotheses that were generated in the design of the NHEXAS pilots will be reviewed to determine which hypotheses were testable and which were not. Testability would be measured through the calculation of the statistical powers of the tests. Tests with high powers would be deemed testable, whereas tests with low power would be deemed not testable. Through a review of the data, the reasons for the ultimately testability will be determined. These calculations will lead to conclusions regarding the testability of the hypotheses, and the optimal design of future environmental exposure studies.
Data or Input Needs:	For each household in each of the three NHEXAS pilots, the following data are needed: the PSU and SSU containing the household; the design stratum containing the household; and the data on each pollutant/medium sampled.
Feasibility (of analyses with current NHEXAS databases):	The current NHEXAS data files have the necessary data to perform the calculations. At worst, there are potentially small or empty cells in the survey designs that might force combining cells or qualifying the conclusions.

DESIGNING EXPOSURE STUDIES PROJECT DES-01. (cont'd)

Estimated Level-of-Effort				
Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.2	0.5	0.5	1	1

Research Outputs

(1) Gather data sets; plan, review, and approve the statistical analyses

(2) Perform the statistical analyses

(3) Final output: Report with recommendations for the optimal design of a national-scale human exposure study

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project LL-1.

DESIGNING EXPOSURE STUDIES PROJECT

Project Name:	**DES-02. Evaluating Modeling Considerations for the Design of Future Exposure Field Studies**
Short Project Description:	In conducting field studies, usually a study is designed, monitoring data and other related data are gathered and then statistical analyses performed to interpret the data. However, from a model development, model application, or model evaluation perspective, the data gathered may be insufficient, particularly for inferential purposes. Future NHEXAS studies should accommodate the needs of existing or modified multimedia models. To achieve this, the model parameters should be understood and incorporated in the study design. Sample parameters include those related to time/activity patterns, contact rates, and dermal and dietary exposure (e.g., surface coverings in residences, contact times with these surfaces).
Goal/Objective:	To establish a procedure wherein modeling considerations are accommodated in the early stages of the design of future NHEXAS studies.
Significance of Project:	The power of any future NHEXAS study lies in interpreting the measurement results within the risk assessment/risk management paradigm used by EPA to select actions designed to protect the public. This interpretation can be done effectively only through modeling the exposures and the changes resulting from the risk management actions. It is critical that future NHEXAS field studies incorporate modeling considerations in their design from the very inception to ensure their usefulness for protecting human health and the environment.
Suggested Approach:	The results of the NHEXAS pilot studies can be used to identify a multimedia exposure assessment methodology, either currently implemented in a model or that can be later modified. This methodology can be used to establish the parameters to be monitored in future studies.
Data or Input Needs:	All available data from NHEXAS pilot studies.
Feasibility (of analyses with current NHEXAS databases):	This project is immediately feasible and should be undertaken early in the design process for any future NHEXAS or large-scale field study.

Estimated Level-of-Effort

Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.3	0.3	0	1	1

Research Outputs

(1) Determine model parameters to be monitored

(2) Final output: Demonstrate use of poststudy data

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project M-5.

DESIGNING EXPOSURE STUDIES PROJECT

Project Name:	**DES-03. Scaling Up: Evaluation of the NHEXAS Pilot Fixed Costs, Coordination and Communication Strategies, and Degree of Standardization**
Short Project Description:	This project evaluates the NHEXAS pilot start-up expenditures and cost implications for various scales of coverage. The evaluation also will address the effectiveness of coordination approaches that were used and their application to a full scale survey, and communication approaches as results were shared with respondents and with local, state, and federal officials and organizations. A key component of the analysis will be the evaluation of approaches that were standardized explicitly and a determination of whether or not the degree of standardization was adequate.
Goal/Objective:	This project will transfer the experience of the pilots to compare and contrast the implementation and communication strategies of the three consortia to determine which strategies or components worked well and which components need improvement and standardization for the most cost-efficient full survey possible.
Significance of Project:	A national-scale survey must utilize the most cost-effective approaches. Experiences gained coordinating and standardizing implementation procedures for the pilots provide valuable information for the design of future large-scale projects. Communication is a component of human exposure assessment that often is given low priority by project planners and sponsors, yet it is an important component of the overall package of benefits that are provided to the respondents and that serves as a significant component of the incentives used to promote participation. In addition, timely reporting of values that exceed nominal thresholds is a mandatory component of all human exposure research.
Suggested Approach:	(1) Interviews will be conducted and pilot documentation collected addressing coordination, communication, and degree of standardization of management and staff from the involved agencies and consortia. (2) Cost information will be collected. (3) The processes used in the three pilot studies to share individual results with the respondents will be reviewed and compared. The respondents may be interviewed to determine how well they understood what was provided and what questions were not answered. In a focus group setting, the same data information using each of the three study processes will be tested to allow direct comparison of approaches and determine the best means of sharing data. (4) Interviews with the local and state agencies that received notification from any of the three studies for measured values exceeding state or local reporting thresholds will be held. The process by which the data were shared, what each agency did after receiving the data, and the range of thresholds reported by the states, and their role in release of data and dissemination of results will be reviewed. (5) The reporting mechanisms for the three studies will be reviewed for common approaches. The utility of the reports will be assessed. Attempts will be made to determine what means of data reporting are of value to different levels of users, and to develop a basic format to be used in reporting composite data to subjects. (6) Recommendations will be made for an optimum scale-up strategy and a communication evaluation manual will be developed.
Data or Input Needs:	Cost data; available documentation; NHEXAS database; copies of material used by each member of the consortium to provide results to the respondents and data to local, state, and federal agencies

Feasibility (of analyses with current NHEXAS databases):	Feasible; all information ultimately available. Communications assessment may proceed immediately without access to the NHEXAS database. Recontacting participants and state and local representatives may be problematic.

DESIGNING EXPOSURE STUDIES PROJECT DES-03

(cont'd)

Estimated Level-of-Effort				
Staff Time/Year				
PI	Scientist	Support	No. Tasks/Year	No. Years
0.4	0.5	1.5	1	1

Research Outputs

(1) Collect needed data and compare NHEXAS processes

(2) Complete local/state interviews

(3) Final outputs: Report recommending approaches for effective communication. Report recommending optimum scale-up strategy

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Projects LL-9 and LL-12.

DESIGNING EXPOSURE STUDIES PROJECT

Project Name:	**DES-04. Influence of Incentives, Response Rates, and Nonresponse Bias on Survey Design**
Short Project Description:	Analysis of NHEXAS recruitment procedures and incentives and their effects on response rates for various subpopulations will be conducted. Analysis of potential bias resulting from NHEXAS nonresponse based on information obtained from the descriptive questionnaire, and information/observations recorded by interviewers on noncontacts or nonrespondents for each study and for various subpopulations are important elements in the design of future studies.
Goal/Objective:	Determine the recruitment procedures and incentives that should be recommended for a national NHEXAS or other large field study. Determine the extent of nonresponse bias that can be expected at each stage of these studies.
Significance of Project:	Projected participant incentives and response rates will be a major consideration for OMB approval of a national NHEXAS. It will be necessary to project reasonably high response rates and to justify the incentives and procedures proposed to achieve those response rates.
Suggested Approach:	Contrast recruitment strategies, information provided to potential respondents, incentives, and response rates across (and within, where feasible) the NHEXAS pilot studies for subpopulations of interest. Compare recruitment procedures, incentives, and response rates with those from other studies collecting comparable data (e.g., TEAM and NHANES). Use the NHEXAS Descriptive Questionnaire data to compare characteristics or respondents and nonrespondents for each NHEXAS pilot study, stage of participation, and subpopulations of interest (e.g., race/ethnicity, gender, urbanicity).
Data or Input Needs:	Indicators from each NHEXAS pilot study of participation for each stage of the study: households contacted (no answer/refusals/number of contacts), descriptive questionnaire, baseline questionnaire, core monitoring, and sampling for each matrix and pollutant. Documentation of the recruitment procedures (including information provided, informed consent, approaches used for questionnaires and sampling, communications and contacts with press/community, etc.) and incentives used by each NHEXAS pilot study. NHEXAS descriptive questionnaire data. Incentives, recruitment procedures, and response rates for other studies collecting comparable data (e.g., TEAM and NHANES) Quality Systems Implementation Plans, protocols for survey sampling and training manuals for survey teams
Feasibility (of analyses with current NHEXAS databases):	Must complete QC on descriptive questionnaire data for each NHEXAS consortium. Must complete NHEXAS chemical analyses, set respondent flags, and QC those flags. Must document all NHEXAS respondent selection procedures for each stage of each study.

Research Outputs

(1) Secure necessary data; QA data

(2) Final output: Impact of response rates on survey design

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Projects LL-5 and A-11.

DESIGNING EXPOSURE STUDIES PROJECT

Project Name:	**DES-05. Cost-Effectiveness of Exposure Measures and Comparisons to Indirect Methods**
Short Project Description:	This project evaluates the cost-effectiveness of exposure measures for pollutants and pathways using decision analysis, value of information, and cost-benefit analysis techniques. Data from NHEXAS pilot studies questionnaires, environmental sampling, personal sampling, and biomarkers will be analyzed to assess the reproducibility, accuracy, limits of detection (LODs), ranges, interferences, uncertainty, and costs, for the purpose of evaluating direct measures relative to indirect methods based on existing data and models. From the analysis, identify methods that were unsuccessful and other methods (i.e., questionnaires, simplified or indirect sampling schemes) that could serve as screening tools in large-scale exposure studies to classify more highly exposed individuals and reduce costs.
Goal/Objective:	(1) Compare the costs and benefits of methods used to characterize multimedia exposures and examine their implications on sample size needs, sampling costs and burdens to the study subjects; (2) Evaluate the utility of low-cost screening methods for identifying households or subjects requiring more intensive monitoring and for providing data useful for exposure assessment (e.g., distributions). (3) Assess the cost and uncertainty differences among exposure models using screening level measurements, questionnaire information, nonprobability samples (i.e., purposive samples), and existing exposure-related data relative to the NHEXAS measurements and study designs.
Significance of Project:	Multimedia, multipathway studies are expensive to implement. Screening methods are needed to provide a low-cost approach that can identify highly exposed individuals and identifying which samples or media should be analyzed. In addition, screening methods with sufficient quantitative power may provide data adequate for exposure analysis and modeling. This study will identify the incremental differences in model performance associated with more detailed (sensitive and accurate) methods, and with representative population samples–relative to more focused stratified or specialized substudies. This study will provide information on how to minimize costs and prioritize resource allocations for the design of future NHEXAS and other large-scale exposure studies.
Suggested Approach:	(1) Identify screening methods, or methods and questionnaire data that could be used for screening, from the NHEXAS pilot studies and assess the ranges, reproducibility, accuracy (i.e., false positives/false negatives) and LODS for identified screening methods with more rigorous and expensive methods. (2) Determine which methods were successful (or could be successful) and those that were not. (3) Assess the cost and burden (participant and field staff) of methods used in the NHEXAS pilot studies and developed more recently, that show promise for use in future studies. (4) Compare exposure models derived from measurement with different sensitivities (e.g., questionnaires and screening measures with differences in analytical performance) with models using subject-specific chemical measurements, characteristics, and activities. (5) Develop methods selection criteria.

DESIGNING EXPOSURE STUDIES PROJECT DES-05

(cont'd)

Data or Input Needs:	(1) A listing of field and analysis methods with performance data used by each NHEXAS pilot study (2) Concentration, biomarker, questionnaire, and time/activity data (3) Information about the time and effort needed to implement each field collection or measurement method and any associated laboratory and analysis costs, particularly for paired low-cost/high-cost methods at homes where both were employed. (4) Exposure and intake models from each study
Feasibility (of analyses with current NHEXAS databases):	High, there are sufficient data groups to allow the proposed analysis. Some examples include, for VOCs, photoionization detector, and passive diffusion badges versus actively pumped sorbent tubes; for pesticides, immunoassay methods and analyses by gas chromatography with various detectors; for metals, XRF versus inductively coupled plasma (ICP) with various detectors, AES, and ICP/MS; for PAHs in air, real-time PAH monitor. Limitations include equivalency in terms of temporal and geographic variability, SES/demographic/population variability/representativeness, collection and analytical methods.

Research Outputs

(1) Compile listings of methodology and associated data (QC, range, LOD) from databases; obtain cost information and models from each NHEXAS study for comparisons

(2) Generate statistical comparison data sets of paired sample results, assessment of success and cost of potential screening methods

(3) Final outputs: Final reports and peer reviewed publications describing screening method assessment results, methods selection criteria, and model performance

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Projects LL-6, LL-8, EA-08, and A-11.

DESIGNING EXPOSURE STUDIES PROJECT

Project Name:	**DES-06. Optimizing NHEXAS Pilot Information and Methods To Move to a National-Scale Exposure Field Study**
Short Project Description:	A thorough evaluation will be performed of single- and multimedia pollutant issues and regulatory initiatives for the purpose of contributing to the design of a national-scale exposure field study. The information obtained in the pilot studies and other source and effects information will be utilized to prioritize the selection of pollutants and pathways leading to exposure. Included would be an evaluation of the ability of each consortium to achieve the objectives or hypotheses originally proposed for each type of investigation. This project will capture and integrate the knowledge gleaned from the analysis, interpretation, and evaluation of the experiences in undertaking the NHEXAS pilot studies for assisting in designing and planning the next generation of NHEXAS-type or other major field studies.
Goal/Objective:	(1) To compile the results and conclusions from the analyses conducted by the NHEXAS studies and evaluate the successes and failures in achieving the original hypotheses; (2) To document the successes and shortcomings of the NHEXAS pilot studies based on the outcomes of implementing the Strategic Analysis Plan; (3) To build a knowledge base on the current and emerging scientific and regulatory issues associated with pollutants and their occurrence in multimedia; (4) To build a knowledge base on the prevalence of xenobiotics measured in biological samples from human populations; (6) To develop strategies for optimizing exposure information that permit effective management and reduction programs; (7) To link the above information to support moving forward, as part of the input to the design of the national-scale exposure field study.
Significance of Project:	The products and outcome of this effort provide justification and a defensible scientific basis to design and implement a national-scale exposure field study.
Suggested Approach:	(1) Obtain completed significant analyses on the databases and information content obtained by each consortium and from the implementation of the Strategic Analysis Plan. (2) Utilize a multidisciplinary team to conduct an overall evaluation of the NHEXAS pilot studies; (3) Identify a team of scientists to work with the program offices, other government agencies, states, and other stakeholders to acquire the knowledge base for selecting and prioritizing pollutants and pathways and for identifying innovative exposure reduction strategies. (4) Evaluate the success and completeness of the above in workshops composed of EPA and extramural scientists, other professionals, partners and stakeholders. Incorporate the output from the workshops to refine and augment the knowledge base to be used for designing the national-scale exposure field study.
Data or Input Needs:	The analyses conducted to achieve each study's hypotheses and objectives and the results from the implementation of the Strategic Analysis Plan. The project initiation is contingent on having sufficiently completed products from other projects in the Strategic Analysis Plan. Information is obtained from the analyses conducted, program office activities and initiatives, NHANES, other exposure and health-related studies (e.g., EPA/ORD STAR Grant Program, NIEHS, National Cancer Institute, Health Effects Institute, National Institute for Occupational Safety and Health, ATSDR), and state exposure data and pollution reduction initiatives.

DESIGNING EXPOSURE STUDIES PROJECT DES-06

(cont'd)

Feasibility (of analyses with current NHEXAS databases):	High, if the Strategic Analysis Plan is implemented in a timely manner, including the projects analyzing and documenting the lessons learned.

Research Outputs

(1) Evaluate information and summarize findings

(2) Identify strategies and conduct workshops

(3) Final outputs: Synthesis of information and transferring output to support moving to future large-scale exposure field studies

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project LL-3 and LL-4.

DESIGNING EXPOSURE STUDIES PROJECT

Project Name:	**DES-07. Cross-Studies Evaluation and Recommendations for Standardization of Data Management Procedures in Large-Scale Exposure Field Studies**
Short Project Description:	This project will analyze the data collection and automated survey management procedures developed for each NHEXAS pilot study from sampling, through sample analysis and to inclusion in the final database. The data QA/QC procedures and QC data will be evaluated, and the resulting database structures will be examined. The strengths and weaknesses of the three approaches will be noted with respect to ongoing EPA data management initiatives. NHEXAS pilot QC data will be analyzed, and recommendations for future studies will be developed. These recommendations will include areas that would benefit from standardization; for example, data transfer from analytical laboratories, database elements, QA/QC codes, information shells, etc.
Goal/Objective:	To have appropriate conventions and procedures for recording data and data quality and to increase the efficiency of future data collection efforts.
Significance of Project:	Management of large EPA databases as a valued resource is currently a high priority within EPA. Procedures and conventions used to manage the integrity of data are evolving but are essential to both primary and secondary data users. The NHEXAS studies are an excellent opportunity to analyze the procedures used by three different organizations to develop and populate study databases. Results of this project will be used for improving/optimizing data collection and storage for future human exposure studies and other EPA primary data collection efforts.
Suggested Approach:	(1) Assess the data management processes and conventions used in each NHEXAS pilot study. (2) Review the status of EPA efforts with respect to Reinventing Environmental Information (REI), specifically, current status of data standards (Chemical ID, Location ID, etc.), the Environmental Data Registry (EDR), the Environmental Information Management System (EIMS) and any other relevant efforts to insure the quality and accessability of EPA databases. (3) With stakeholder input (EPA program offices, involved Federal agencies, etc.), recommend application of EPA conventions and procedures for a future national-scale NHEXAS or other large exposure field database. Recommend conventions in areas where none exist. Conventions that document the limitations of the data are particularly important. (4) Analyze available quality control information (i.e., batch level laboratory QC information) and develop Data Quality Indicators that can be stored with the data for the benefit of data users.
Data or Input Needs:	Needed information for each consortium: data management plan/procedures; field data collection procedures; procedures for transferring the field, analytical, questionnaire/diary and related data into the final databases; data QA/QC procedures; and final database design. Each consortium also will need to provide an analysis of how well their procedures worked and problems encountered.
Feasibility (of analyses with current NHEXAS databases):	Data collection and processing SOPs are available from each consortium. The analysis of how well the procedures worked in each consortium will need to be done in the relatively near future, while the staff involved are still available. EPA-level initiatives in this area are active and ongoing.
Research Outputs	
(1) Collect and review NHEXAS SOPs and QA documentation (2) Final output: A data management strategic plan for future exposure studies	

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project LL-13.

DESIGNING EXPOSURE STUDIES PROJECT

Project Name:	**DES-08. Evaluation of NHEXAS Results To Derive an Optimal Set of QA/QC Activities for Human Exposure Field Studies**
Short Project Description:	This project will identify and evaluate the QA/QC across laboratories and consortia. This will include an analysis of the NIST and comparability study data. The project will develop an annotated inventory of recommended QA/QC activities needed to successfully conduct large-scale human exposure measurement studies. This will include all phases of the study from planning to final database development.
Goal/Objective:	The goal of this project is to provide an optimum set of QA/QC activities for future human exposure studies. This is needed to assure that the studies produce data of the required quality while keeping costs to a minimum.
Significance of Project:	Effective QA/QC is essential to produce high-quality data from the funds invested in any field exposure study. Because of the high cost of these types of studies, it is also important not to include unnecessary QA/QC that might increase costs. By examining the QA/QC used in the NHEXAS studies, guidance can be developed for this critical study component.
Suggested Approach:	(1) Identify the QA/QC activities performed by each consortium and laboratory, including the NIST standards and performance evaluations studies, the interlaboratory comparability study, QA documentation, reviews, audit reports, reviews of field performance, and QA samples. (2) Evaluate the success of each activity and the benefits it provided to the study. (3) Identify areas where data quality could have been improved with additional QA/QC activities or areas where excess QA/QC activities might have been employed. (4) Develop an annotated inventory of the recommended QA/QC activities needed to conduct a large-scale human exposure study.
Data or Input Needs:	Access is needed to the complete NHEXAS database and documentation, including all QA/QC information of each consortium and laboratory and the NIST and comparability study results and reports.
Feasibility (of analyses with current NHEXAS databases):	The study is feasible using data from the NHEXAS database. A mixture of laboratory, field and QA expertise is needed to evaluate information.

Research Outputs

(1) Review consortia documents

(2) Final outputs:
- •Consolidate information from documents and develop annotated inventory
- •Guidance document on optimal QA/QC for human exposure field studies

NOTE: Crosswalk to NHEXAS Data Analysis Workshop (EPA 600/R-99/077, 1999) Project LL-10.