

U.S. EPA Workshop on Research Needs for Community-Based Risk Assessment

**U.S. Environmental Protection Agency
Main Campus, Building C
Research Triangle Park, NC**

October 18–19, 2007

SUMMARY

INTRODUCTION AND OVERVIEW

The U.S. Environmental Protection Agency (EPA) Workshop on Research Needs for Community-Based Risk Assessments was held on October 18–19, 2007, in Research Triangle Park (RTP), North Carolina. The workshop brought together researchers from academia, private industry, regulatory agencies, and government to discuss ongoing and potential research on community-based risk assessments. The workshop also served as a stimulus for increased collaborations among the various researchers and agencies and resulted in improved knowledge of toxins in the environment. Approximately 85 individuals attended the workshop.

Ms. Deborah Segal, EPA, opened the meeting. She welcomed the participants, explained the logistics of the RTP meeting site, and introduced Dr. Hugh Tilson, EPA, National Program Director for Health.

DAY 1: OCTOBER 18, 2007

Welcoming Remarks

Hugh Tilson, U.S. EPA

Dr. Tilson welcomed participants to the meeting and to the RTP facility, which is one of EPA's greener facilities. He explained that there are many Office of Research and Development programs that involve human health, but the Human Health Research Program (HHRP) is the only crosscutting program that addresses multimedia and regional issues. The main objective of the HHRP is to reduce uncertainties associated with the risk assessment process by providing a greater understanding of exposures to environmental stressors and the basic biological changes that follow. The four Long-Term Goals (LTGs) of the program address crosscutting issues that most EPA offices and regions must manage. LTG 2, regarding characterization of aggregate and cumulative risk assessment, is the LTG most applicable to this workshop. EPA is increasingly being called to provide risk assessments for "super chemicals" and to determine how these interact with nonchemical stressors. There are several scientific questions driving research on cumulative risk, including those regarding available biomarkers, exposure models, and information about mode of action and exposure that can improve risk assessments. The question of how cumulative risk can be assessed at the community level has emerged in the previous 2–3 years. This workshop is important for participants to help EPA identify and address priority issues in this area. The program's goals regarding this issue are to: (1) develop tools and a framework to assess interaction of environmental chemical and nonchemical stressors at the community level, (2) support research on assessing exposure and health risk of tribes as a result of cultural practices, and (3) evaluate tools for use in assessing community risk.

Keynote Address: A Perspective on Community-Based Risk Assessments

Linda Sheldon, U.S. EPA

The fundamental concepts regarding community-based risk assessments (CBRA) are that: (1) not all communities are the same, (2) different communities can have differential risks as a result of exposure to environmental contaminants and other stressors, (3) the same community can have differential risks over time, (4) many of EPA's regulations do not consider these differences, and (5) many communities may be at higher risk because they are not adequately protected through environmental regulations and/or distribution of social benefits. Obvious environmental problems prompted the formation of EPA, and the Agency has addressed many environmental concerns successfully, but some communities still remain at risk. The Food Quality Protection Act defines cumulative risk as involving exposure to two or more pesticides, but it is important to consider nonchemical stressor impacts as well. For the purpose of this workshop, cumulative risk can be defined as the combined risks from aggregate exposures to multiple agents or stressors. Cumulative risk assessment is an analysis, characterization, and possible quantification of the combined risks to health or the environment from multiple agents or stressors.

Risk assessors must consider the following questions: (1) How do we identify the most important risks in these communities? (2) How do we assess the cumulative risk in these communities? (3) How do we develop appropriate risk mitigation procedures? (4) How do we demonstrate that we made a positive impact? During the past 3–4 years, the National Exposure Research Laboratory (NERL) expanded its aggregate risk research to include cumulative risk. In doing so, researchers then needed to consider multiple stressors and community conditions. Ecologists always consider communities (i.e., ecosystems) and the entire range of stressors and the condition of the ecosystem as a result of cascading effects. Ecologists have developed models and GIS tools that should be applicable to human health risk assessment; ecologists are valuable resources and potential partners for risk assessors.

During the recent International Society of Exposure Analysis (ISEA) 17th Annual Conference, a number of scientists, including Drs. Marie Lynn Miranda and Marc Serre, presented data on the application of advanced statistical, GIS, and modeling tools to understand exposure and risk. Dr. Miranda is applying spatial tools to CBRA research, and Dr. Serre is examining the spatial and temporal distributions of stressors in the community that allow estimates of pollutants in the community over space and time.

Science, tools, communication, partnerships, and trust are needed to advance CBRA research. To build the science, the source-to-health outcome continuum (environmental release, environmental concentrations, exposures concentrations, target organ dose, early biological effects, adverse outcomes) should guide the core research that is conducted to determine exposure and health risks. An emphasis should be placed on building the tools, including simple and low-cost monitoring methods, GIS tools, models for exposure, comparative databases, tools for interpretation, and primers for conducting assessments and using the tools. These tools must be developed for and used by the community. To build communication with the community, scientists must “keep it simple.” Researchers must listen to the community, hear its concerns, and know how the community is different and how this difference impacts community risk. Researchers should describe the science in simple terms, including the issues, what is known, and what can be changed. All researchers must be involved with the community at some level.

A paradigm shift for the Agency is the transformation from decision-making to providing technical assistance to help communities make decisions. Exposure and risk analysis has shifted from analysis done for the community to partnering in a deliberative process. Communities want to know what the possible exposures are and have concerns regarding exposures addressed; this often is more subjective than objective. CBRA is important because researchers have an opportunity to make a difference. It is hard work because CBRA is multidisciplinary, communities must be involved, and impact is an important issue. Technology exists that makes CBRA research possible, and it is improving steadily. This workshop is focused on bringing all of these factors together to improve CBRA research.

Summary of Session—“Exposure Assessment Methods in Community-Based Risk Assessment” From the International Society of Exposure Analysis (ISEA) 17th Annual Conference

Brad Schultz, U.S. EPA

Mr. Schultz summarized the session that he co-chaired with Dr. Valerie Zartarian at the recent ISEA Conference. The session started with a brief overview of the Community Action for a Renewed Environment (CARE) Program, which coordinates EPA program and regional offices and the Centers for Disease Control and Prevention (CDC) via a memorandum of understanding; the program also supplements EPA regulations to support community-driven risk assessment and risk management. One level of CARE research includes risk prioritization and the selection of risk reduction activities, whereas a second level involves risk reduction and quantification of effects. The session also included a CARE technical issues overview by the environmental health assessment co-chair, EPA Regions 1 and 6 case studies, the status of EPA cumulative assessment guidance, and an overview of EPA work on the National Children’s Study (NCS). A NERL principal investigator provided a summary of exposure tools research; collaborations with health scientists, risk assessors, and the CARE Program; NCS exposure assessment research; and research involving measurement methods and modeling. One attractive idea that was discussed was the use of Google Earth as a possible CBRA tool. Following these overviews, the session included a discussion regarding community needs and research needs for community-based cumulative risk assessment. Needs identified included: low-cost techniques for community monitoring; methods to assess the impacts on health following an action; information on nonchemical stressors and vulnerability; determination of the value of monitoring and modeling results; better methods to quantify local nonchemical information; tools to characterize dietary exposures at the community level for unique cultural groups; inventories and protocols for assessing nonchemical stressors; and research that is directly usable by the community or its local health or environmental department.

The important issues identified by session participants are as follows: (1) Community-driven assessment is of great importance. (2) Research results need to be usable by communities and their local health departments. (3) Cumulative risk assessment, including nonchemical stressors and vulnerability, is important. (4) Researchers should focus on the main contributors to risk and health impacts and recurring community questions to address cumulative risk. (5) Protocols for nonchemical stressors are needed, and low-cost measurements are important. (6) Dose-response for risk prioritization is important, including comparison with other chemical risks and nonchemical stressors. (7) Quantifying benefits is important for future applications by communities.

SESSION I: DATA NEEDS AND MEASUREMENT METHODS FOR COMMUNITY-BASED RISK ASSESSMENT

Development of Nanoscaled Sensor Systems for Detecting and Monitoring Environmental Chemical Agents

Desmond Stubbs, Oak Ridge Center for Advanced Studies

The Oak Ridge Center for Advanced Studies (ORCAS) is a nonprofit organization operating at the Oak Ridge National Laboratory as a Department of Defense and Department of Energy corporation. ORCAS is a “think and do” consortium of research universities, government, industry, and nongovernmental organizations (NGOs) that partners with local educational institutions to perform research. It focuses on critical issues with strong science and technology content. Problems are framed broadly, taking into account their scientific, technical, economic, social, and policy dimensions to develop research and integrated strategies for addressing those challenges. ORCAS attempts to ensure that its ideas and research are translated into action.

The organization held a workshop in April 2006 entitled “Nanotechnology Applications in Environmental Health: Big Plans for Little Particles” that introduced nanomaterials/nanosensors to the environmental

and ecological health communities. The workshop explored the “art of the doable” in terms of nanotechnology and fostered a discussion of the possible environmental health effects, exposure assessment, and ecological health applications. The result of the workshop was better informed communities with increased likelihood of beneficial interactions in the future. Additionally, Dr. Michael Strano, formerly of the University of Illinois at Urbana-Champaign, published a commentary, *The Case for Nanotechnology*, which provided a list of wants and needs of nanotechnology researchers, including low-detection limits, fluorescence-based techniques, and detection technologies based on nanosystems. The commentary also points out that shelf life varies as a function of the sensing layer, real-time detection is a common feature of nanosensing technology, and binding mechanisms for the sensor platform determine useful life of the technology. Following the workshop, researchers determined several factors that need to be included in a universal system, such as location and activity sensors, an electronic diary, wearable sensors, and portable sensors.

ORCAS and its partners are conducting research on several devices for use in exposure assessment, including passive radio-frequency identification (RFID) tags, an electronic nose (i.e., “dog-on-a-chip”), microelectromagnetic sensors, and interferometric optical sensors. The vapor phase sensor system currently being researched is a piezoelectric, surface-sensitive device. The surface sensitivity is important in vapor detection, and the devices can be used in an array to detect multiple chemical agents. In this system, antibodies to a selected chemical change the three-dimensional signal following detection. Antibodies are immobilized on gold electrodes as a result of their high binding affinity for the antigen. The multi-analyte, multicantilever detection system employs arrays of sensors on a single chip with selective coatings for application-specific programmable sensors. Eighty different chemicals can be detected on a single chip. An array of 300 chips can be formed on one wafer at a cost of \$3 per wafer. Built-in redundancies in this system allow comparison, and built-in telemetry provides remote sensing capabilities. The system was tested successfully via a chip implanted in the necks of rats that measured blood-alcohol levels.

The dog-on-a-chip technology was explored as a method for detecting trinitrotoluene (TNT), because the ability to detect TNT is key to reducing fatalities from the 100 million land mines scattered across the planet, tracking explosives materials, and addressing environmental concerns such as water and soil contamination. Two TNT analogs are musk oil and ammonium nitrate; the Transportation Security Administration’s current methods are unable to distinguish between TNT and the two analogs. ORCAS researchers used six TNT analogs to perform its proof of concept testing. Three-dimensionally plotting data points over time consistently and definitively distinguished TNT from the five other analogs. This method has the potential to be a universal platform to distinguish various analogs and provide useful data.

Discussion

A participant asked which monitoring device would be most useable in the community. Dr. Stubbs responded that all of the devices are sensitive devices that can be used in the community for acute sensing, but there is a saturation issue that must be considered with long-term use. The participant asked if the \$3 cost includes tailoring, to which Dr. Stubbs replied yes.

A participant asked if a library or inventory of chemicals that can be detected is available. Dr. Stubbs responded that an abstract had been published with the inventory, which includes mercury, pesticides, and explosives.

A participant asked if these devices could be used internally to detect stress steroids and endogenous chemicals. Dr. Stubbs responded that investigators currently are exploring internal human use. Assays have been developed but not tested, but this is the direction in which research is heading.

A participant asked for additional information on technologies that can be used for continuous monitoring. Dr. Stubbs stated that an algorithm to measure various factors over time can be built into these devices. Passive RFID tags allow the ability to retrieve data at any point in time. Using array technology also provides the advantage of monitoring over time; however, difficulties arise as a result of size and saturation issues. Researchers are working on a way to purge the device to manage these difficulties. Over-time, near-real-time, and real-time monitoring algorithms can be built into the selective layer.

A participant asked for comments on the known limits to the technology. Dr. Stubbs responded that as these are vapor-measuring devices, they are limited by vapor pressure. How analytes in solution are presented to the device is important. For example, the dog-on-a-chip cannot function in solution, but the RFID tag can be used in liquid by changing the configuration of the electrode. This, however, causes a loss of sensitivity.

A participant commented that the ability to detect the presence and the viability of pathogens is necessary and asked if the research has examined microbial detection. Dr. Stubbs answered that interdisciplinary research that includes microbiologists is necessary, and there has been some work completed on glyco-proteins in the cell wall. Chip researchers can collaborate with microbiologists to determine if there is a marker that can be used to indicate viability.

A participant asked what the ease of use is for the community and if these technologies are appropriate for those communities exposed to Superfund sites. Dr. Stubbs replied that the objective of developing these technologies was for this type of exposure. The devices are designed to be wearable, relatively inexpensive, remotely sensed, small, unobtrusive, and without the need for user literacy.

Data Collection Platforms for Integrated Longitudinal Surveys of Human Exposure-Related Behavior
Paul Kizakevich, RTI International

Dr. Kizakevich described research that addresses the need for an electronic diary that was identified following the April 2006 ORCAS workshop described by Dr. Stubbs. He explained that the need for integrated data collection is prompted by the various routes and modifiers of exposure. The overall objective of his research is to develop a personal data collection system that integrates data input streams for collection of human exposure-related behaviors, supports EPA human exposure assessment models, can be easily adapted for other human exposure assessment studies, and possesses sufficiently low burden that most members of the general U.S. household population will be willing to participate in the study for at least 1 week per season for 1 year. At a very basic level, the approach is to: develop diary methodologies for data collection; develop sensors and automation to reduce burden; evaluate methods in the general population; assess, improve, and enhance developments; reevaluate methods and technologies; and facilitate system use for future research studies. The researchers are exploring different methods of collecting data and evaluating these methods by collecting feedback from the population. Four types of diaries—paper, electronic menu, voice, and photo—are being explored via automated technologies such as global positioning systems for outdoor location and movement, wireless beacons for indoor residential locations, wireless Polar chest belts for heart rate monitoring, and accelerometers for movement and compliance monitoring.

Paper, electronic menu, and voice diaries were used to collect dietary data. Paper and electronic menu diaries and automated wireless beacons were used to collect consumer product data. For wireless beacon collection, a fob was assigned to inventoried products; fob-initiated time-stamps were recorded for each product-use event, and an accompanying electronic (PC Pocket) questionnaire was answered by the user. The fobs are a low-burden item to collect data, and the Pocket PC was designed with familiar Web-style menus for ease of use. Additionally, the Pocket PC measures the length of time that it takes users to operate the Pocket PC. Menus can be tailored to each individual user's activities. The photo diary is a

passive diary worn on the belt and takes pictures of the wearer's environment every 2 minutes. The user has the ability to delete photos before uploading to the EPA Consolidated Human Activity Database (CHAD); CHAD is used to categorize the locations in the photos. Another technology employed is locator beacons that are placed throughout the residence in study-designated rooms. The locator beacon syncs with the Pocket PC worn by the user and records the length of time spent in designated locations within the residence.

A pilot evaluation of the above technologies was employed to evaluate the technical performance of technologies and systems as well as participant and analyst burden for various diary modes. The study included 48 participants who for 7 days each used paper, electronic menu, voice, and photo data collection methods; agreed to heart rate and residential location beacon monitoring; and used wireless fobs to record product-use events. Participants represented a range of ages and education levels. Dr. Kizakevich showed examples of activity and dietary data, statistical integration of one individual's activity for 1 day, the top 15 activities reported by mode, and the top 10 food items reported by mode. Participant-reported compliance was underreported compared to the literature and may reflect a training issue. The perceived data-entry burden was greater than actual burden for activity and product-use data collection but lower for pesticide-use data collection. The data-coding burden was recorded as the amount of time the analyst needed to code the data.

The researchers concluded that the burden for menu-based activity and location data entry is low; however, several participants expressed difficulty with the menus. Activity and location reporting were lower than in previous studies. Participants liked using the voice diary, although technical issues affected recording quality. Although most participants liked the photo diary, some participants expressed privacy issues in their workplace. Because some participants reported avoiding activities and limiting diet to reduce entries for paper, voice, and menu diaries, further improvement in menu structures, prompting, and automation may help to improve compliance and avoid behavior modifications.

Discussion

A participant asked if the researchers were moving toward a plan to recommend any of these diaries or a combination of them and if the 7-day data will be available. Dr. Kizakevich responded that the data will be made available following the next round of monitoring. Originally the goal was to determine the best method, but now the plan is to release the data and let individual researchers use this knowledge to determine what method is best for their needs.

A participant asked if any consideration had been given to measuring exposures in children. Dr. Kizakevich replied that some of the diary methods could be simplified and made very specific for children. Activity sets can be tailored to children's activities. The voice method, combined with random prompting throughout the day, is a good method for children.

A participant asked if the resolutions needed to compute exposure for the different approaches had been calculated. Dr. Kizakevich answered that this had not been done in a formal manner. An advisory panel is providing guidance for the modeling studies, and this information may be available following the next round.

A participant asked how easy the sensors were for senior citizens to use. Dr. Kizakevich responded that this type of information has not been separated out, but one senior citizen who originally was confused by the technology became one of the best at using it.

A participant asked if a pictorial version would be available for children, those with language differences, or elderly individuals who cannot see words as well. Dr. Kizakevich answered that this has been discussed. All menu items are database driven and can be translated easily into other languages. One

problem with a pictorial approach is choosing pictures that have universal meaning so that there is no confusion. The platform is designed to be flexible enough to adapt to the needs of children and the elderly.

A participant commented that compliance as a function of education level could be investigated. He asked if there was a problem with care of the devices. Dr. Kizakevich responded that some were dropped, and battery longevity was a problem.

Assessment Methods for Community-Based Risk Assessment
Elaine Faustman, University of Washington

Three types of studies were examined to understand which pesticide exposures were occurring in children. The three types of studies were a community-based participatory research (CBPR) project, a longitudinal multiple sampling project aimed at understanding between- and within-family variability, and a longitudinal cohort study. The community was a unit of analysis as well as the individual. Researchers have only crude statistics of organophosphate and carbamate pesticide usage in various counties in Washington State, whereas the communities have better knowledge of usage. The study investigated four Washington State counties: Yakima, Benton, Franklin, and Walla Walla. Significant amounts of organophosphate and carbamate pesticides are applied each year to apples and potatoes, but the amounts vary each year and are unpredictable.

The CBPR project examined 12 communities, where community is defined as a town or a labor camp. The project utilized the Environmental Public Health Continuum adapted from Dr. Hal Zenick, which helps to facilitate understanding of potential sources and how these sources might lead to exposures at the individual, community, and/or population levels. The Continuum is a framework to educate the public regarding exposures and risks. Project researchers educated more than 6,000 community members at more than 250 events, such as community health fairs. Additionally, community members held more than 1,000 home health parties, and the overall number of participants in all levels of community activities was more than 18,000. Researchers handed out toys to children while teaching them simple things to help reduce their exposure to pesticides. Second and third grade students were invited to enter a drawing contest about methods to reduce exposure, and the winning entries were included in a calendar. Children also were taught handwashing songs. Following the interventions, children were asked evaluation questions to determine if they were receiving the message.

Another project received crucial input from the community regarding vehicle dust. As a result of the community's suggestion, the project model was changed, and this greatly improved the study. This underscores the importance of involving the community during the earliest planning stages. This project used chlorpyrifos metabolites as biomarkers of exposure to understand between-person and mother-child variability. A framework into which factors can be input is necessary to understand this variability. Quantifiable levels of two or more organophosphates in dust were found in 36 percent of homes and 42 percent of cars, and 60 percent of households (defined as home and vehicles together) had evidence of two or more organophosphates in collected dust. Results also indicated that 86 percent of children had quantifiable levels of at least one dialkyl metabolite, and 36 percent had quantifiable levels of both dimethyl and diethyl metabolites. Evidence of a take-home pathway was determined via the observation that workers who thinned crops were more likely than those who did not thin to have detectable levels of azinophos-methyl in their house dust and vehicles, and children of thinners also were more likely to have detectable levels. Contrary to expectations, workers who reported mixing, loading, or applying pesticides had lower incidence of detectable pesticide residues in their homes, vehicle dust, and in their children's urine; this may be a result of mandated safety training for this occupation versus thinners. These data were compared to National Health and Nutrition Examination Survey (NHANES) data, which showed that community farmworkers and their children possessed higher urine concentrations of metabolites versus the NHANES population. Farmworkers and their children also have higher concentrations when

compared to nonfarmworkers and their children within the same community. Year-to-year and crop-to-crop variability also existed. The take-home pathways that increased children's exposure to pesticides were examined so that effective interventions could be planned.

Two longitudinal studies of organophosphate metabolites were used to estimate within and between variability of 3,5,6-trichloro-2-pyridinol (TCP), the major degradation product of chlorpyrifos and chlorpyrifos-methyl pesticides. Multiple measurements in the same person across time permit estimation of both within- and between-person variability. TCP measurements below the limit of detection were treated as left censored in statistical analyses. Results indicated that this method has a poor ability to detect exposure to chlorpyrifos and chlorpyrifos-methyl pesticides. Sources of uncertainty for this method include stochasticity and parameter and model uncertainties. The collection design included three to five sampling events in each of the thinning, harvest, and nonspray seasons. Genotypes and gene expression are being examined in farmworkers versus nonfarmworkers and in parent-child pairs. Biomarkers of susceptibility, exposure, and effect are being determined. A viable framework that integrates these data is needed to educate the community; the methodology underlying this integrated framework tool is complicated. Ascertaining the genotype and phenotype for key chlorpyrifos metabolic genes will improve prediction of exposure response and at-risk individuals in agricultural communities. Determining polymorphisms is important as well. The community asks simple questions (e.g., Can I eat vegetables from my garden?) that have complicated answers; experiments must be designed to answer these relevant public health questions.

Discussion

A participant asked if study participants request and receive individual results. Dr. Faustman replied that all individuals receive their results with a detailed explanation.

A participant asked how researchers managed more complex questions, such as those regarding risk when it is not known, and how doctors in the community were involved. Dr. Faustman responded that pediatricians in the community already are associated with migrant clinics, and there are a lot of collaborations with community doctors. Study participants who are identified as having life-threatening conditions or those who researchers feel need follow-up (i.e., those participants whose risk is unknown) are sent to community doctors.

A participant asked what plans for gene expression had been made. Dr. Faustman answered that no analyses had been completed, but the profiles will be examined together. In this manner, variability should be explained and will be approached in an investigative framework.

A participant asked if drinking water was a possible exposure source. Dr. Faustman replied that her project examined one particular source, but the National Oceanic and Atmospheric Administration (NOAA) was performing similar studies in drinking water.

A participant asked how much has been done to intervene at different points in the cycle. Dr. Faustman explained that interventions are set up to educate people to change their clothes before entering their vehicle or house. The community knows the message, but researchers have not yet worked with the community to take the next step. The participant commented that the EPA framework can be used as a resource to assist with the interventions.

A participant commented that the researchers' plan of explaining all biological results could affect the design of the entire research project. Dr. Faustman explained that it is important to explain the individual results, and the community knows that the researchers are committed to them.

SESSION II: THE BIOLOGICAL IMPACT OF NON-CHEMICAL STRESSORS AND INTERACTION WITH OTHER ENVIRONMENTAL EXPOSURES

Social Stress, Stress Hormones, and Neurotoxins

James Herman, University of Cincinnati

Social stressors do not deprive an individual of essential needs such as oxygen, but these man-made stressors do affect human physiology. Stress responses can be anticipatory or reactive. Anticipatory responses are caused by possible threats to homeostasis and involve innate programs and learning. Reactive responses, caused by direct threats to homeostasis, are generated by reflexive pathways and are true emergencies. Stress responses are remarkably conserved and can be studied in mammals to construct meaningful predictions in humans. Behavior systems, the sympathoadrenal system, and the hypothalamic-pituitary-adrenal (HPA) axis mediate stress responses and release of glucocorticoids. Glucocorticoids are ligands; therefore, where receptors are present, physiological reactions can occur. These receptors are ubiquitous in numerous cell types throughout the body.

The HPA stress axis initiates a redistribution of physiological resources, the short-term benefits of which are energy mobilization and diversion, immune response limitation, and central nervous system (CNS) arousal. Constant stimulation of the stress response has several long-term consequences, such as metabolic disease, obesity, musculoskeletal atrophy, hypothalamic-pituitary-gonadal problems, immune dysfunction, depression, and possibly post-traumatic stress disorder (PTSD). The neurobiological consequences of stress are numerous. Stress-related affective disease states (e.g., depression, PTSD) affect 10 percent of the population in any given year. Stress exacerbates other affective disease states, such as schizophrenia and bipolar disease, and other organic disease processes. Stress hormone secretion can contribute to cell loss and cognitive decline in aging and dementia.

It is important to note that stress and glucocorticoids inhibit neurogenesis, and social stress produces a structural change in dendrites, causing them to shrink, in the hippocampus of nonhuman primates. These observations are consistent with glucocorticoid effects on memory and learning. Additionally, stress reduces neurotrophic factor expression in the cortex and hippocampus of rodents. Researchers also have determined that stress experienced by adults is not the only significant factor; stress experienced *in utero* can lead to depression-related syndrome. Stress can cause changes in the distribution of types of fat that affect obesity and diabetes; the percent of visceral fat is increased on recovery from stress. Following head trauma, glucocorticoids mediate resulting neurological effects; RU486, a potent glucocorticoid inhibitor, has been shown to be protective. Because stress is a predisposing factor in neurodegeneration, stress can be considered a risk factor for Parkinsonism. Stress is a predisposing factor in other neurodegenerative models, including epilepsy, stroke, aging, and Alzheimer's disease. Additionally, toxins have the ability to modulate circulating glucocorticoid levels; exposure to lead leads to elevated circulating glucocorticoids.

In terms of stress as a co-morbid condition, the implications for toxicology are immense. Stress enhances relapse of addictive behaviors (e.g., smoking, alcohol, other drugs of abuse), and social stress promotes abdominal obesity. Prenatal stress interacts with lead exposure to alter brain neurochemistry, behavior, and HPA axis drive. Finally, stress represents one of the "hits" in the multi-hit hypothesis of toxicity. In terms of risk assessment, it is important to note that substance abuse and obesity are prevalent in lower socioeconomic status (SES) populations, and these populations have disproportionate exposure to some environmental toxicants (e.g., lead). Environmental toxicants can modulate glucocorticoid secretion, which in turn enhances neurotoxic processes. Toxins can magnify stress on neurons, and stress can potentiate the effects toxins have on nerves. Therefore, stress and toxins can initiate synergistic effects on nerves.

Discussion

A participant asked if stressors accelerate disease state and aging. Dr. Herman responded that they did, and they also affect metabolic capacity. Another participant asked what effects result from diet, vitamin supplements, and exercise. Dr. Herman replied that antioxidants have been shown to be neuroprotective. Exercise is interesting in that it increases stress on the body while being performed, but decreases stress between exercise periods. It has been shown to have a number of positive effects on various processes.

A participant asked what measurement limitations exist. Dr. Herman answered that the ability to measure stress hormones in an at-risk population in real-time is not yet possible. Blood pressure and heart rate have daily variability and, therefore, are not reliable. Some hormones can be measured in saliva. The participant asked if baseline variability data are available. Dr. Herman responded that inter-individual variability is very high, and he is not aware of any available intra-individual data.

A participant asked if the degenerative process can be reversed after stress is removed. Dr. Herman explained that the best that can be done is to stop the degenerative process; it cannot be reversed.

A participant asked if there are factors that offset stress. Dr. Herman answered that data support that some factors can buffer some of the negative impacts of stress. Exercise and small natural rewards (e.g., sucrose snacks) improve the tone of the HPA axis. The participant asked if multiple stress factors worked together in a synergistic manner. Dr. Herman responded that intensity is a factor, and increased intensity causes increased wear and tear on the body.

A participant asked what is known about changes in stress response with recurrent acute stress. Dr. Herman stated that this was examined in a social stress model. Animals experiencing unfamiliar stress have increased stress response when compared to familiar stress. There is built-in habituation to similar stress and sensitization to other stress.

Intersections of Social Ecology, Neurobehavioral Development, and Environmental Contamination **Bernard Weiss, University of Rochester School of Medicine and Dentistry**

Dr. Weiss displayed a chart of rates of return to human capital investment originally devised by Dr. James J. Heckman, a renowned economist. This graphic illustrated the finding that an increase of opportunities at an early age increases benefits during later life, whereas delaying opportunities for youth decreases benefits. Abecedarian academic outcomes indicate that early investment in children increases college graduation rates and decreases the rate of children held back a grade. Rodent experiments showed that enriched environments initiated a change in brain biochemistry and subsequent behaviors; these enriched environments promote neurogenesis in a variety of ways. An important question is whether such effects are counterbalanced by exposure to environmental contaminants.

Dr. David Rall, a renowned environmental health scientist, introduced the concept of the overt effect when he posed the question about whether people would be aware of the toxic potency of thalidomide if the drug did not have overt consequences and instead reduced affected children's intellectual potential by 10 percent. Today, there are a wide variety of human exposures to neurotoxic agents such as heavy metals, pesticides, organic solvents, food and cosmetic additives, air pollutants and endocrine disruptors. Lead exposure is one example of the consequences of not being observant of mounting evidence and/or placing economic concerns above health. There is a direct correlation between increased blood lead levels and decreased IQ. Even a small shift in IQ distribution has significant effects on the population, with a 57 percent increase of those labeled "mentally retarded." Research indicates that blood lead increases reading-level deficits in children, and bone lead increases aggression and delinquency and decreases attention span. The academic and social costs of lead exposure are high, and from an economic standpoint, the cost to the U.S. of low levels of exposure has not been measured. It is the lower SES

groups that bear the brunt of the cost, including increased risk of drug dependency and jail time and decreased lifetime earnings. Low income has been correlated with increased blood lead levels, lower math scores, and increased antisocial behavior when compared to those in higher income levels.

One current perspective on lead is that there is no discernible threshold for lead toxicity. Neurotoxic effects grow more rapidly at low exposure levels, and behavioral disorders are at least as measurable as IQ deficits. Lead toxicity is a lifetime issue; its effects, including cognitive deficits and osteoporosis, persist with aging. The appropriate level of concern should be any value above zero, and lead exposure may diminish the effects of environmental enrichment. Environmental tobacco smoke (ETS) has a similar effect to that of lead. ETS and material hardship have a synergistic effect on the Bayley Mental Development Index, and children of mothers who smoked during pregnancy average a 3 percent drop in IQ. Using 1994 data and extrapolating back to 1964, this drop in IQ translates into a total earnings loss of \$720 billion for those 30 years. Insecticide use and prenatal exposure to polycyclic aromatic hydrocarbons (PAHs) also have similarities to lead and ETS exposure. There are commonalities between toxic exposures and social disadvantage; poverty is linked to high exposures to ETS and PAHs as well as lead and other developmental neurotoxicants. Social disadvantage embodies multiple dimensions. Income also affects relative risks of CNS disorders; increases in income and education decrease the effects of affective and anxiety disorders and substance abuse.

Many of the above issues can be linked to deficiencies in maternal care. Low mother-infant interaction is a risk factor for both social-emotional competence and verbal IQ in 4-year-old children. Maternal care has epigenetic consequences. A study on epigenetic changes induced by different styles of maternal behavior revealed that maternal fostering behaviors are nongenomically transmitted to the next generation of female offspring; daughters behave like their mothers. Other studies have shown that prenatal stress increases the effects of lead exposure; some are gender specific and involve altered male sexuality. Layered, cumulative risks exist in disadvantaged communities that deplete cognitive potential. Small changes can accumulate and have effects on the disadvantaged community that exceed effects seen in advantaged communities. A 3 percent rise in IQ would induce reductions in social risks and have enormous benefits on societal outcomes.

Discussion

A participant asked how a proposal to lower the level of concern of lead from 10 µg/dL to 2 µg/dL would translate in practical terms. Dr. Weiss replied that one example would be to remove lead-contaminated drinking water fountains from schools.

A participant asked how to deal with the increasing frequency of potentially contaminated products that are not being measured before import into the United States. Dr. Weiss stated that stabilizing or increasing the budgets of EPA and the Consumer Product Safety Commission would be a start.

A participant asked how decreasing the lead level of concern would be beneficial. Dr. Weiss stated that there is no apparent threshold for lead toxicity.

A participant commented that metals of concern change over time and asked if it would be necessary to address all metals at the same time to be proactive. Dr. Weiss replied that additional research is necessary for all metals and other potential neurotoxicants.

A participant asked about the hypothesis that small levels of toxicants are beneficial because they activate repair. Dr. Weiss explained that depending on the toxin, more negative effects may be seen at smaller doses than at moderate doses. Lead has no threshold, and alcohol has no fetal threshold. This 50-year-old doctrine should be re-examined.

Dr. Tilson commented that in terms of prioritization, quantifying risks so that communities can make decisions is necessary. A national calculation may be a good guideline, but some communities will deviate from this. Dr. Weiss added that disadvantaged communities have increased exposure compared to advantaged communities.

Social Environment as a Modifier of Chemical Exposures

Robert Wright, Harvard School of Public Health

Construction of the CNS, which begins *in utero* and continues throughout childhood, involves the production of 100 billion nerve cells and 1 trillion glial cells; these cells migrate, differentiate, and form synapses. Glial cells are the primary regulator of synapse formation. Synapses transmit signals between neurons. Environmental stimuli cause neurons to fire; neuronal/synaptic firing is a signaling process to mold the synaptic architecture of the brain. The brain builds its network in a partially stochastic manner. Synapses are made by the billions, and in some respects randomly, between neurons. Net gains in synapses occur from fetal life until age 2, and then the number of synapses in the human brain begins to decrease. Synaptic networks are created in a learned process. When synapses fire, neurotransmitters are released into synaptic junctions, which in turn release growth factors and provide a signal that this firing is an important neuronal connection; functional synapses release growth factors, whereas nonfunctional synapses do not release growth factors.

It has been demonstrated that environmental chemicals affect neuronal development. At “low” doses of blood lead (approximately 5–10 $\mu\text{g/dL}$), lead interacts with protein kinase C and stimulates neurotransmitter release; therefore, neurons fire in the absence of an appropriate environmental stimuli. Additionally, lead mimics calcium, a critical component of nerve signal transmission. Calcium enters neurons during depolarization, but lead blocks calcium channels. The net effect is that lead stimulates nerves to fire in a more stochastic fashion and also inhibits both appropriate and inappropriate neurotransmission. In this manner, lead decreases the efficiency of the underlying synaptic architecture.

Plasticity is the brain’s capacity to diminish the effects of toxic insults through structural and functional changes via processes similar to synaptic selection. Plasticity allows for new connections to be made that improve function following an insult. It has been demonstrated that social environment affects neurodevelopment as a result of chronic stress that impairs memory and learning capacity. The handling paradigm of rat behavior illustrates this point; rats that exhibit behaviors that stimulate stress in their offspring have fearful offspring with a brisk HPA stress response. Although the behaviors tend to cluster in family lines, researchers determined that environment, not genetics, plays a large role in influencing the behaviors. Prenatal and early life exposures increase the risk of late-life disease (e.g., hypertension and obesity), and the handling paradigm is an example of neuroprogramming.

Genes are influenced by histone methylation, which usually turns off genes, and histone acetylation, which usually turns on genes. Epigenetics refers to heritable changes in gene expression, such as histone acetylation and methylation, that do not involve changes to the underlying DNA sequences. Epigenetics plays an important role in synaptic pruning via environmental stimuli, and epigenetic marks within neurons change with synaptic activity. This “epigenetic opening” of synaptogenesis to the environment is maximal during childhood, and it is the source of the exceptional cognitive adaptability of humans and possibly the source of its fragility.

A study in rodents examined the effects of social environment and lead. Rats poisoned with lead during lactation (at levels seen clinically in humans) and kept in social isolation had less memory and learning function when compared to lead-treated rats raised in groups with social stimulation. This raised a question about whether reducing stress can be considered a treatment. One study examined mothers’ self-esteem when their children were 24 months old; covariates included blood lead, mother’s IQ and education, and child’s gender. The research showed that the effects of lead varied by mother’s self-

esteem; therefore, a positive social environment may mitigate the effects of lead. Another pilot study investigated *in utero* ETS exposure and respiratory outcomes and measured exposure to violence (ETV) and scores on the Wisconsin Card Sorting Test, a neurocognitive test. Children with *in utero* ETS exposure and ETV had significantly lower test scores than those without such exposures. This work led to the establishment of a new birth cohort that will study stress, lead, iron deficiency, and neurodevelopment from a holistic perspective. The long-term goals of that study are to: (1) identify factors that increase and/or decrease metal toxicity, (2) understand the biology of metal neurotoxicity, (3) prevent toxicity, and (4) treat toxicity after it has occurred by finding the appropriate intervention(s).

Discussion

A participant commented on the holistic framework of salutogenesis and the ability of some people in a normal population to overcome exposures. The positive factors that allow them to do this must be explored. He asked what Dr. Wright would like to see more of to further this type of research. Dr. Wright responded that he would like to see Superfund issues considered in risk assessments. Also, society as a whole can decrease the emphasis on economics. There is no budget for social interventions, but there is significant funding for pharmaceuticals. This inequality must be overcome.

Dr. Weiss agreed that interventions later in life are useful because neurogeneration still can occur in the aging brain. It makes economic sense to eliminate contaminants and intervene in cases of contaminated individuals because the plasticity of the brain is great.

A participant asked how EPA could contribute more to risk assessments. Dr. Wright commented that he understood that EPA faces budget cuts and undeserved hostility from the community. If enough research is completed that proves these concepts, the political climate may shift so that there is a mandate for EPA to receive the resources it needs.

SESSION III: STATISTICAL AND MATHEMATICAL MODELING FOR COMMUNITY-BASED RISK ASSESSMENT

Community-Based Risk Assessment—A Statistician’s Perspective **Louise Ryan, Harvard School of Public Health**

Dr. Ryan reported a past case about Cape Cod citizens living near a U.S. Air Force base who were concerned about excess cancer rates reported on the Upper Cape. There was clear evidence of multiple exposures, but the number of excess cases was small to moderate, the study power was limited by the total population, and no individual exposure assessment was completed. The data were very noisy, and smoothing of the data did not help. It was a very frustrating experience for researchers and the community. Another home allergen study completed in Boston with mother-child pairs found geographical variation in maternal serum immunoglobulin E, but geoadaptive modeling suggests a “hotspot” in the city that is confounded by race and poverty. Another study involves cardiovascular response to air pollution that will attempt to determine exposure levels at various points in the Boston area. The goal of the study is to relate predicted exposures to health outcomes (e.g., heart rate variability, arrhythmias, birth weight), and the latent variable formulation is promising. The similarities of these studies include sparse data, a clever combination of data from multiple sources, and the inclusion of spatiotemporal modeling in the study designs.

Mercury is an important human exposure of concern. A controversy arose as a result of conflicting conclusions from two large, well-conducted epidemiological studies. Both studies included prenatal enrollment, had reliable biomarkers of exposure, adjusted for similar important confounders, and measured similar outcomes. The National Academies of Science confirmed the quality of both studies and identified a third. When the focus was shifted from p-values to dose-response estimation, the studies were

less discrepant. Researchers now are using the data to focus on how methyl mercury relates to IQ because IQ has been monetized and relates to other endpoints. A summary of endpoints are available from the three studies and can be divided by domain (e.g., cognition, attention, motor). Graphical representation of all of the data shows that there is not much commonality between the three studies, but adding additional endpoints does show some similarities. Random effects formulation was used to express the data as a set of estimated dose-response coefficients, standard errors, and study and endpoint codes. There are not enough data to reliably estimate separate study and endpoint variance components, so a sensitive analysis was employed as assumptions were varied. This showed that one effect of mercury exposure was decreased IQ. Including the third study's outlying data point made the results appear concordant.

The researchers learned that uncertainty tends to be large when dealing with data collected in real-world communities, and there is a need to measure characteristics of the community in addition to individuals. There are major benefits to using statistical techniques (e.g., Bayesian) to synthesize information from multiple sources. Good tools, such as spatiotemporal and hierarchical models, exist. Researchers must be cautioned against over-interpreting model results and placing too much emphasis on p-values. Many sensitivity analyses must be performed. In the future, researchers should fine-tune spatiotemporal models and initiate work to adjust available tools for combining information so that they are able to handle multiple scales, levels of accuracy, and so forth. Researchers also should design studies about neglected topics. One such project is working on developing strategies for ingenious subsampling to maximize information and minimize cost; another project involves extensions to spatial setting. Spatial design in general is very interesting; including a spatial and a temporal piece allows space and time effects to be separated.

Discussion

Dr. Weiss commented that one of the differences between the two controversial studies was that one examined fish and the other examined whales, which are much more contaminated. The fish study separated the effects of polychlorinated biphenyls, and Dr. Weiss asked if it is possible to separate factors out when they truly are tangled. Dr. Ryan replied that if the characteristics of the studies themselves can be built, then separation of effects and confounding factors may be possible. If the unit of observation is the community, then more communities are needed. Hierarchical models, however, do not have the potential to do this.

A participant asked what was meant by measuring more characteristics of the community. Dr. Ryan replied that examples would be levels of community violence, racism, poverty, and so forth. The sample size is related more to the number of communities than to the number of individuals in the community.

A participant asked if data were being collected to validate the model to ensure that the researchers were not underestimating exposure concentrations and exposures. Dr. Ryan replied that in developing a statistical methodology, agents to test possible underestimation are employed. Her colleagues are beginning to examine this, and it is a complicated issue.

A Multi-Site Time Series Study of Hospital Admissions and Fine Particles: A Case-Study for National Public Health Surveillance

Francesca Dominici, Johns Hopkins University Bloomberg School of Public Health

One broad goal of environmental health scientists is the creation of a national system for tracking population health. Currently, multiple government databases contain substantial amounts of information on the environmental, social, and economic factors that determine health. Research on population health could be rapidly advanced by integrating these existing databases and designing new statistical models that could describe major threats and their causes. These integrated databases and new analysis tools would create a national system for population health research.

Fundamental research topics regarding air pollution and health include determining if there is a risk at current pollution levels, how the risk can be estimated, how large the risk is, and what causes the risk. The objectives of a research project dealing with the health effects of fine air particles are to: (1) assemble a national database of time-series data for the period of 1999 to 2005 on hospital admissions rates for cardiovascular and respiratory diseases, fine particulates, and weather for 204 U.S. counties; (2) develop state-of-the-art statistical methods; (3) develop maps that illustrate relative risk of hospital admissions associated with short-term changes in fine particles; and (4) illustrate how integration and analysis of national databases can lead to a national health monitoring system. National data sources include: the National Claim History Files (NCHF), the Medicare Current Beneficiary Survey, EPA's AirData database, the NOAA Weather Monitoring Network, and the U.S. Census. The project is examining the 204 U.S. counties for which there are matched data. This national cohort is a national study of fine particles and hospital admissions in Medicare. Data include billing claims (NCHF) for everyone older than 65 enrolled in Medicare, date of admission/doctor's visit, treatment, disease, costs, age, gender, race, and place of residence (by ZIP code and/or county). The study design includes a large sample size to identify sample effects. Thus far, researchers have noted seasonality of hospitalization for chronic obstructive pulmonary disease in Los Angeles, California.

Multi-site time-series studies compare day-to-day variations in hospital admission rates with day-to-day variations in pollution levels within the same community. The study design avoids the problem of unmeasured differences among populations, and key confounders are the seasonal effects on infectious diseases and weather. Semiparametric regressions for estimating associations between day-to-day variations in air pollution and mortality and controlling for confounding factors are used for within-city analysis. Hierarchical models for estimating national-average relative rate and regional-average relative rate and exploring heterogeneity of air pollution effects across the country are used for between-city analyses. For any given city, the researchers attempt to estimate a small pollution effect relative to confounding effects of trend, season, and weather. Challenges include the strong role of other time-dependent factors, the high correlation between nonlinear predictors, and the sensitivity of findings to model specifications. Results have indicated that all effects are small but consistent across location. Respiratory data show a lag before the effects of air pollution occur. Determining the mechanisms, size, chemical components, and sources of particulate matter (PM) toxicity is the next step.

Multi-site time-series studies provide strong evidence of short-term association between air pollution and mortality, and preliminary results from Medicare data (1999–2002) indicate that current air pollution levels affect health. It is important to note that national datasets are powerful resources for assessing the health effects of air pollution, there are statistical models that can integrate information across space and time, and the national average estimates for the effect of PM are robust to various model formulations and statistical methods. Researchers need to be able to reproduce previous findings, test assumptions and robustness of findings, check methodology, and then implement and test new methodologies. One method by which researchers can share data and advance the science is to utilize the Internet to build databases and share methodologies from published papers.

Linking national databases and developing statistical methods that can properly analyze them are essential steps for a successful national public health tracking system. Because of the small risks to be detected and the large number of potential confounders, single-site studies generally display increased statistical error. A national system that routinely analyzes data from multiple locations in a systematic fashion is a promising approach for tracking population health. The explosion of information requires reproducibility and expertise in statistical methods and integration of complex databases.

Discussion

A participant asked if there are current methods that allow national data to be used to inform at the community level. Dr. Dominici replied that extrapolation across similar communities is possible.

The participant clarified that it is possible to borrow strengths of other characteristics that are more relevant and asked, if at some point, community-level data are too sparse to accomplish this. Dr. Dominici answered that much information may be available in some communities, but very little in others. The choice can be made to extrapolate the data and account for differential variations.

A participant asked if having multiple sites gives power to the data. Dr. Dominici responded in the affirmative. The participant commented that layers can be added, but it is limited by hospital admissions. Dr. Dominici replied that this is true, and in terms of linking data together, mortality data also can be acquired, and geographical resolution can be linked with other confounders. The participant asked if that meant that statistical methods are built in. Dr. Dominici replied that they were not at this point, but increased integration makes analysis easier.

A participant commented that this method appeared to work for communities in the range of a population of 1,000–30,000 individuals and asked what the role is for statistics in a community-based setting. Dr. Dominici responded that the goal is to be as practical as possible and link only community data with other available data. The participant asked if it is ever possible to state specifically what factors are responsible for what endpoints. Dr. Dominici answered that it is possible to address data in one community by using other community data to increase power. Dr. Ryan added that complexity depends on what factors are being examined. It is beneficial to reduce citizens' focus on cause and effect, and instead quantify how much risk people may have. A participant stated that context-driven data still are needed.

Dr. Cohen Hubal noted that one goal of this workshop is to identify tools and the gap between tools and answering questions at the community level. It is necessary to be aware of weaknesses and the characteristics of communities that are linked to increased risk of chemical exposure, as well as how more holistic techniques can be used to determine risks. What types of research can and should be done must be determined. One outcome of the workshop should be to determine how research can be done to move forward to answering CBRA questions in a better way.

Risk Assessment/Risk Communication: Understanding the Community
Thomas Schlenker, Public Health Madison-Dane County

Accurate and valid risk assessment cannot be performed unless there is an understanding of the community and communication between the community and researchers. A current CBRA involves human exposure to lead and the associated health risk and will analyze sources, pathways, routes, populations, internal dispositions, endpoints, and risk metrics. There is an enormous history related to lead, which was recognized as a risk by Benjamin Franklin more than 200 years ago. There is much research about lead, and national lead strategies involving EPA and the U.S. Department of Housing and Urban Development have been successful. Substantial funding is available for lead research.

When communicating with communities, it is necessary to tell a story about the “life” of lead in the body to engage them instead of merely providing data and scientific jargon about internal disposition of lead in blood, bone, and the CNS. Community research must involve the knowledge of how people live and their housing, SES, and behavior patterns. In Milwaukee, Wisconsin, community members and the media were focused on lead in water, which was a large distraction because researchers were attempting to focus on other routes of exposure. Policymakers, confused by the media, confounded the problem. Researchers eventually performed a simple study that indicated that there was no correlation between the age of the house and lead in water; this allowed them to focus on the issue of lead in paint. It has been established that increased exposure to lead causes a decrease in IQ; in one cohort, Dr. Herbert Needleman also determined that children not exposed to lead had a seven times higher rate of high school graduation than children with lead exposure.

Manganese is considered beneficial in small doses. In Madison, Wisconsin, manganese in water is a concern because manganese is precipitated out of the water by chlorine and settles into pipes. When there is a change in hydraulics, the manganese re-enters the water and enters homes as a thick, brown sludge. Researchers in Madison used the same model to examine manganese as was used to examine lead. EPA's 2003 *Health Effects Support Document for Manganese* established the health reference level for manganese to be 300 µg/L; in 2004, EPA's *Drinking Water Health Advisory for Manganese* established a lifetime health advisory level, which is much more useful as it defined the concepts of short- and long-term exposure. In the Madison case, one well was perceived as the worst offender in terms of manganese exposure, but two different wells a great distance from the perceived offender had higher levels of manganese. Brown water had unsafe levels of manganese, and some clear water with no visible signs of manganese also had unsafe levels. Additionally, manganese is present in infant formula; foods such as nuts, grains, tea, and soy; and over-the-counter supplements. The predigested form of infant formula contains manganese at the maximum health reference level. Human endpoints for exposure to manganese are generally unknown, but long-term effects are associated with Parkinson's Syndrome and Attention Deficit Hyperactivity Disorder.

Discussion

A participant commented that models that are developed to bring exposure risks to the community level must be understood by community stakeholders and asked how researchers can approach the need to take complicated models and move them into a context where they can be trusted and understood by the community. Dr. Schlenker replied that providing examples of how it has been or can be used at the community level would be best. It is helpful to have community guidance and advice. A participant added that community members do not need to have a technical knowledge of the models to understand the scientific narrative if it is explained in simple terms. Dr. Faustman noted that helpful guidance is available to assist in determining what information is needed to answer community questions.

DAY 2: OCTOBER 19, 2007

Perspectives, Issues, and Needs in Community-Based Risk Assessment **George Bollweg, U.S. EPA**

This workshop's definition of CBRA is "a model that addresses the multiple chemical and nonchemical stressors faced by a community, while incorporating a community-based participatory research framework and a transparent process to instill confidence and trust among community members." The National Research Council's 1996 *Understanding Risk* was the first well-organized approach to this type of research. It recognized that not just technical experts perform risk assessments and established steps for synthesis and implementation. CBRA researchers should consider including an evaluation step at the end of each research project. The 1997 *Presidential/Congressional Commission on Risk Assessment and Risk Management, Volume 1*, identified risk management in addition to risk assessment and stressed the importance of the problem/context step of the process. The 2003 EPA *Framework for Cumulative Risk Assessment* provides a useful, streamlined process. Traditional assessments focused on chemical stressors, whereas a new focus is population-based assessments, which emphasize that toxicity is influenced by factors surrounding an individual and not by the toxicant alone.

Different CBRA participants have different needs. Community members need timely answers, whereas researchers need timely publications. Industry participants need to persuade affected parties that risks are "acceptable," and EPA managers need to address Agency management priorities. Additionally, state and regional risk assessors need to conduct credible assessments that address participant needs. Community assessment can require substantial, multidisciplinary commitment and follow-through. Integrated human health risk assessments are necessary that combine the various EPA programs having different focuses and different methods of doing business. For example, the Air Program combines metrics for criteria and

noncriteria pollutant hazards or risk, but some programs may find that combining metrics results in excessive information loss, hidden incompatibilities, subjectivity, interpretability and communication problems, false precision, and so forth.

What may be considered “background” exposures are in the foreground for those exposed; fragmented EPA programs that have a single focus may not consider this. Exclusion of background stressor exposure or susceptibility results in incremental assessments that are irrelevant to some participants. This can be solved by addressing site-specific background susceptibility and/or stressor exposures or, if site-specific information is lacking, deriving a reference human exposure profile to which incremental exposures could be added.

Methods for choosing participants from the community are needed. Additionally, “getting the right science” and “getting the science right” are equally important. CBRA problem formulation must include background (pollutant and/or nonchemical) stressor exposures. What questions the community and the researchers want answered must be considered during the CBRA planning and scoping process. Organizational and political influences (e.g., levels of review, executive branch process control) on EPA’s Integrated Risk Information System (commonly known as IRIS) productivity should be evaluated; the levels of review have become too lengthy. The limits of Haber’s Rule also must be addressed. In cases where a community’s health is determined to be poorer than national averages but is not addressed in EPA exposure and toxicity estimates, an epidemiological investigation is necessary. The problem is how to evaluate this in a CBRA context, and if the assertion is true, how this situation can be addressed. CBRA research needs to examine synergistic or antagonistic toxic effects, determine the feasibility of an all-species hazard index, ascertain the appropriateness of using old datasets for future predictions, establish attributes of successful and unsuccessful deliberative processes, and determine if a formal evaluation step should be included in EPA risk assessments.

CBRA attempts to address real-world human susceptibility, exposure, and risk with inclusive, often resource-intensive deliberative processes. Some conceptual approaches and tools are available, but CBRA needs to process multiple, diverse participant input to better identify and formulate problems; help unify fragmented disciplinary “silos”; and acquire needed science to address questions and issues of participant concern.

Discussion

A participant asked what a graph of return on EPA investment in single agents versus mixtures would look like. Dr. Bollweg responded that he did not know, but it would probably depend on an individual’s needs, as some are exposed to single toxicants and some to mixtures.

A participant asked from a cost perspective whether it is better to create a healthy exposure profile or a reference exposure profile. Dr. Bollweg answered that the purpose of the reference exposure profile was to include items that normally were excluded. It is specific to areas and exposures (e.g., dust exposure of individuals living near roads).

A participant noted that comments from communities near contaminated sites show that the communities instinctively understood that their present condition is not good in terms of health and wellbeing. He asked whether Dr. Bollweg purposely excluded the need to satisfy regulations and laws from his presentation. Dr. Bollweg replied yes, because although difficulties have arisen as a result of permit requirements, the situation, especially with Superfund sites, is improving. There is a need to satisfy the goal of the Superfund as well as the conflicting needs of the community; CBRA may be able to integrate these differing needs.

A participant commented that local health departments need to be involved in CBRA projects and asked how to go about securing their participation, as well as the participation of other agencies. Dr. Bollweg answered that resource commitment is important. Also, determining the availability of data is important because some agencies are not authorized to share certain data. Prior knowledge that obtaining information is a complex and complicated process may decrease frustration.

Overview of Breakout Groups

Yolanda Sanchez, Association of Schools of Public Health (ASPH) Fellow, U.S. EPA

Ms. Yolanda Sanchez reiterated the definition of CBRA that Dr. Bollweg introduced in his presentation. The three breakout session themes follow the three session topics of the previous day: (1) data needs and measurement methods for CBRA, (2) biological impact of nonchemical stressors and interaction with other environmental exposures, and (3) statistical and mathematical modeling for CBRA. Each breakout group should: (1) identify tools and approaches that may be applied to conduct CBRA, (2) discuss how to incorporate community-based information into traditional EPA risk assessments, and (3) evaluate the research needs for CBRA. To facilitate dialogue in the breakout session, the organizing committee produced charge questions that have been included in the workshop materials.

CONCURRENT BREAKOUT SESSIONS

Breakout Session 1: Data Needs and Measurement Methods for Community-Based Risk Assessment

Moderator: Elaine Cohen Hubal, U.S. EPA

Recorder: Jennifer Hurlburt, The Scientific Consulting Group (SCG), Inc.

Attendees: See Addendum

Dr. Cohen Hubal showed slides depicting two different conceptual models and a list of vulnerability factors to help facilitate thoughts about data needs and measurement methods. Important questions for the group to address are: (1) Are data currently available? (2) What are the data sources? (3) When is it necessary to collect data in the community? (4) What are the characteristics of the environment and of the individual environmental indicators that researchers must consider?

One issue that is confusing to many, including scientists and those conducting assessments, is how to link individual-level environmental exposures to community-level factors. The actual assessments are conducted on the individual level, but one method to connect the two is to group the individuals together for the analysis of the community-level factors, as they were in the distribution curves from Dr. Faustman's study.

Dr. Faustman asked Dr. Cohen Hubal about the Conceptual Model for Considering Vulnerability in Cumulative Risk Assessment. She wondered about the best method to incorporate the information from Session II: The Biological Impact of Non-Chemical Stressors and Interaction with Other Environmental Exposures into this type of model. For example, where do the potency factors enter for a given stressor, whether it is chemical or nonchemical? Dr. Cohen Hubal responded that that particular model was not intended to represent exposure length. The model's focus was on classification of all of the different factors; there are many issues (e.g., temporal aspects) that must still be addressed in the study.

Mr. Matthew Lakin, EPA, spoke about the distinction between vulnerability and susceptibility. One school of thought is that vulnerability and susceptibility are two different things. Susceptibility includes the biological factors that make a person more predisposed to some type of effect or adverse outcome. Vulnerability includes the environmental characteristics that might lead to a higher level of exposure. These appeared to be only one category in the displayed conceptual model. Dr. Cohen Hubal explained that in that particular study, susceptibility was categorized as a vulnerability.

Dr. Alesia Ferguson, University of Arkansas for Medical Sciences, mentioned that a speaker the previous day had mentioned a theory related to resilience. Would resilience be considered a vulnerability or a susceptibility? Mr. Kent Thomas, EPA, answered that resilience would be considered a susceptibility. Resilience occurs on two levels: (1) at the individual level, resilience is lessened as a person ages, so repeat exposures may be more harmful to older individuals; and (2) at the community level, the community as a whole may have less resiliency to recover from exposures. Dr. Cohen Hubal explained that in her study, susceptibility was defined as genetic susceptibility or developmental stage susceptibility. She explained that researchers traditionally have studied the source-to-outcome paradigm, but this breaks down when multifactorial issues are examined. She maintained that researchers need to move from a pathway focus to a focus that includes other issues that are present with these exposures. Dr. Faustman did not agree that the framework necessarily breaks down with these issues. She has worked with engineers who use some interesting vulnerability diagrams, and many issues are involved. For example, community location or conditions are important factors. Dr. Cohen Hubal commented that a researcher could define a system as a community and then specifically examine particular individuals or particular sources, depending on how the boundaries are drawn. If the intent is to identify multiple factors, the researcher must draw the boundaries to ensure that all the inputs and outputs are considered.

Dr. Cohen Hubal explained that she presented the conceptual models as examples to stimulate discussion. What are the important factors at the individual and community levels? Mr. Thomas explained that four categories of data are needed for a cumulative risk assessment: (1) physical environment, (2) social environment, (3) chemical environment, and (4) health (as an outcome or as a risk factor). Dr. Ferguson asked if data needed to be defined to represent risk quantitatively. Mr. Thomas replied that in terms of a screening-level assessment, researchers are able to determine some of the major stressors in the community. The next step is to work toward understanding the relative risk associated with these stressors.

Dr. Cohen Hubal asked if the participants knew of publicly available data that could serve as a starting point for researchers. Dr. Danelle Lobdell, EPA, responded that the data available depend on the research question and on the community. Dr. Faustman asked if any of the participants knew of an example of a known stressor other than air pollution that had been linked to specific communities. Dr. Dina Schreinemachers, EPA, replied that data on various toxicants are available in four states. She suggested that researchers start with ecologic studies and then move to subject-based studies. A series of multilevel, multidisciplinary studies is needed. Dr. Faustman mentioned that the CDC conducts surveillance projects in partnership with universities across the country. Dr. Socoby Wilson, University of South Carolina, added that he recently submitted a proposal to EPA to develop national health indicators.

Dr. Cohen Hubal asked those with experience working in communities if they often found the data they needed when they began their work. She asked for examples of the types of data found and whether the data were general or community-specific. Are there efficient, cost-effective ways to obtain these data? Dr. Ferguson responded that it depends on the chemical of interest and the location. For example, some states collect extensive lead-related data, whereas others collect no lead-related data. Mr. Thomas suggested that researchers start by determining the community's data needs. The next step is to determine what data are available. Dr. Mari Eggers, Montana State University, added that it would be helpful if there were guidelines detailing where different types of data could be found. Mr. Lakin said that he and his CARE Program colleagues currently are drafting guidelines, but there is a lack of data on many topics, and even if data exist, access often is an issue. Dr. Ferguson suggested that data be extrapolated from one community to another. Mr. Lakin added that this approach would involve quantifying the differences between the communities (e.g., accounting for a higher smoking rate in one community). Dr. Faustman suggested compiling a list of available data. Mr. Lakin agreed that a list could be helpful, but added that the ultimate goal is to identify quantitative relationships. Dr. Ferguson mentioned the study conducted by Dr. Zartarian as a potential model; Dr. Zartarian and her colleagues identified 100 factors and performed a stacked quantitative analysis. Dr. Wilson suggested developing spatial indices. He mentioned some other

potential models, including the social vulnerability index and a project in California related to risk and environmental health disparities. Mr. Lakin noted that there still is difficulty in linking the information to environmental risks.

Dr. Wilson pointed to the importance of collecting qualitative data as well as quantitative data. Quantitative data alone will miss many important issues, such as the effects of living in a stressful environment. Mr. Lakin agreed that there is value in both quantitative and qualitative data. Mr. Thomas noted that people often do not understand the risks associated with environmental stressors. The perceived risk might be very different from the actual risk. Dr. Ferguson pointed out that perceived risk still is very important, and Mr. Thomas clarified that he was not discounting perceived risk. Dr. Pamela Rao, Farmworker Justice, commented that, as a social scientist, her work always begins with the people in the community; their perceived risks are the starting point. Mr. Lakin asked Dr. Rao if she thought better information on community cohesion, sense of identity, and other factors linked to perceived risk were needed. She agreed that better data are needed and emphasized the importance of starting with qualitative data; without qualitative data the work will have no direction.

Dr. Cohen Hubal asked the participants to share their thoughts on measurement methods. Dr. Faustman commented that GIS data are very useful. GIS data can be used to ensure that areas are not missed in risk assessments. Alternatively, researchers need to be careful when using these data to determine specific risk areas. For example, a 1-mile radius might be identified as an area of concern, but what about the people living just outside of that 1-mile radius? Dr. Wilson pointed out that this is where the qualitative data is useful. Dr. Rao emphasized that research cannot be performed at a distance; it must be done in the community.

Dr. Ferguson asked if there is a point at which there are too much data. Mr. Lakin thought that a better question might be: What is the right amount of assessment? In his work, Mr. Lakin has found that the answer depends on the community. Dr. Cohen Hubal added that the information collected would be based on the community's concerns and conditions present in that community. Dr. Rao suggested starting with the research question. Mr. Thomas pointed out that from EPA's perspective, the question is: Where does the chemical and biological pollutant risk fit into that context? Mr. Lakin stated that it would not be inappropriate to begin a risk assessment by focusing on specific chemical stressors; that can be one of the solutions offered to the community, and if the community identifies other problems, others can be brought in to address those issues.

Dr. Faustman warned that risk comparisons can be dangerous. It is important not to ease the pressures on industry; they are responsible for keeping the environment clean. Dr. Cohen Hubal noted that there are still many compounds in the everyday environment about which little is known. Dr. Lobdell offered lead as an example; it is still not known if any level of lead in the blood is safe.

Dr. Faustman gave an example of a multifaceted problem that would require a multidisciplinary approach: the loss of traditional diets in Native American communities. This loss has resulted in serious health problems for this population. Loss of salmon, a staple of the Native American diet, from the waterways has contributed significantly to this problem. This loss can be represented with data. One aspect of improving the health of Native Americans involves ensuring that the waterways are clean to allow salmon to thrive. This problem requires that various agencies work together.

Mr. Thomas noted that some of the studies presented the previous day had indicated that the effects of exposure could be magnified because of certain attributes and vulnerabilities. What data are needed to understand those vulnerabilities? Dr. Rao asked if he was referring to taking the analysis to the chemical or environmental level. Mr. Thomas clarified that he was referring to the understanding that in a community there are multiple risks, and many of them have little to do with chemical and biological exposures.

Dr. Cohen Hubal asked Dr. Rao about a comment she had made earlier about the difficulty of measuring and characterizing the location of certain groups (e.g., migratory farmworkers) and their related risk. What are the limitations? What measurements are needed? Dr. Rao clarified that she was referring to cumulative risk issues that are not dependent on the individual's geography. Given that, Dr. Cohen Hubal asked how a researcher could define, track, and characterize the community. What should be measured? Dr. Rao responded that in many cases the data needed are not readily available. In her work with pesticides, she and her colleagues have had to use sales records and other clues to gain a better understanding of farmworkers' exposure. Dr. Wilson noted that different data are available on the national and local levels. The CDC has performed much work collecting environmental public health data, and EPA has state-level environmental indicators in areas such as air and water. Dr. Wilson added that the data frequently must be collected at the local level.

A participant asked if there were any case studies of comprehensive cumulative risk assessments that could be used for guidance. Dr. Faustman replied that there are some good examples, including *Community Risk Profiles and Understanding Risk*. Dr. Ferguson commented that as the risk assessments become more advanced, multidisciplinary approaches are needed. Mr. Lakin commented that, from a research needs perspective, taking a community-based participatory research approach is one method by which to ensure a multidisciplinary approach. He stated that more demonstration projects are needed to advance the work in this area. Dr. Wilson mentioned a book called *Street Science* by Jason Corburn that includes examples of community groups using EPA's exposure risk model.

Dr. Schlenker explained that most of his work involves starting with a health outcome and moving backward to find the cause. For example, in Madison-Dane County, as in the nation as a whole, the infant mortality rate (the rate of infant deaths occurring before age 1) for African Americans was more than twice the Caucasian rate. Since 2000, however, the African American infant mortality rate has steadily decreased in Madison-Dane County and is now comparable to the rate for Caucasians. What changed? Dr. Schenkler said that answering that question would involve qualitative research comparing the African American mothers currently in Madison-Dane County to African American mothers in other counties or comparing them to the group of mothers experiencing the high infant mortality rate.

Mr. Lakin mentioned the public availability of certain data, such as the mapping information available through Google Earth. The availability of this information makes it more difficult to mislead the public, but there still is a need to further expand these types of tools in terms of community access to data and interactivity. Dr. Faustman cautioned that with the current accessibility of certain data, researchers must be careful to protect people's privacy. In one case, for example, breast cancer data were mapped by house in a neighborhood, allowing everyone in the neighborhood to see who did and did not have breast cancer. Mr. Lakin thought that address-level data could be very useful in risk assessments.

Dr. Lobdell reminded the group that risk assessments must take into account the realities of the people living in those areas. For example, a factory may be a major polluter, but if the livelihoods of the people in that area depend on that factory, they may not want to address the pollution problem for fear that they might lose their jobs. Dr. Wilson added that many people do not have any other employment options. Dr. Faustman emphasized that communities should not feel as if pollution control is their burden; it is industry's responsibility. Dr. Ferguson said that for health outcomes, it is known that multiple stressors can contribute to health outcomes, even independent of one another. Thus, a chemical stressor could be removed, and the community could still have the same health outcome. If EPA finds that the chemical stressor is not the major problem in a community, then other agencies will need to be involved. Dr. Faustman suggested that other agencies be included from the beginning. Mr. Lakin pointed out that EPA's Ecological Program focuses on many of these multifactorial issues (e.g., how urban sprawl affects the environment); much of this work is performed in partnership with other agencies.

Dr. Wilson suggested using the environmental justice framework. He gave an example of a community in North Carolina that blocked the building of a highway by submitting a complaint to the Department of Justice arguing that their civil rights would be violated if the highway was built because they would not be able to access basic amenities. Are there other innovative approaches like this that could be used to affect change? Mr. Lakin agreed that this was one way to approach the problem. He asked what the research needs are. What is the missing component in terms of current scientific understanding? Dr. Wilson responded that, in this case, the community performed its own cumulative risk assessment. Mr. Lakin encouraged the other participants to think about ways to reproduce this type of success story in other communities.

Breakout Session 2: The Biological Impact of Non-Chemical Stressors and Interaction With Other Environmental Exposures

Moderator: Carrie Knowlton, ASPH Fellow, U.S. EPA

Recorder: Kristen LeBaron, SCG, Inc.

Attendees: See Addendum

Ms. Knowlton explained that the group's first charge was to identify tools and approaches that could be applied to CBRA. Mr. Gary Bangs, EPA, noted that some researchers have obtained access to difficult-to-access datasets. Perhaps a preconstructed, integrated database could be made available by those researchers who have broken barriers. Mr. Ravishankar Rao, EPA, added that Census data could be included. Ms. Kathy Sykes, EPA, mentioned the Interagency Forum on Aging-Related Statistics and noted that there may be a parallel dataset with families and children. Mr. Michael Callahan stated that there are many data in the literature about stress-causing impacts, the effects of violence on asthma, and other topics that EPA normally does not study. Dr. Robert MacPhail, EPA, agreed that there is a significant amount of data on psychoneuroimmunology topics.

Ms. Kacee Deener, EPA, asked if data on biological stressors or social stress in combination with environmental stressors were available. Dr. MacPhail responded that data on both, but primarily on biological stressors, existed. Ms. Deener asked if data on toxins other than lead were available. Dr. Peter deFur, Virginia Commonwealth University, commented that other toxins were included in a background paper.

Mr. Rao noted that some common data are available that may address community concerns. Mr. Bangs shared Mr. Callahan's concern that the right data may not be considered, and some data related to stressors, housing, measurement endpoints are not necessarily found in PubMed. Dr. Weiss stated that the number one factor in health risk is poverty.

Ms. Knowlton asked participants to identify models and technologies in addition to data sources. Mr. Michael Wright, EPA, suggested an examination of group-level effects separate from individual-level effects. Mr. Callahan noted that the Tool for Health and Resilience in Vulnerable Environments, an index of social capital commonly known as THRIVE, is one available tool.

Dr. deFur asked if models in this context were defined as computer-predicted or conceptual. Ms. Knowlton replied that she interpreted the question as computer-predicted, but conceptual models could be considered if necessary. Dr. Robert Hubal, RTI International, explained that one possible method is high-performance computing that simulates community impacts after an event. Dr. deFur added that some comparative behavioral science technologies may be useful, as well as some in the strict ecological sciences. Behavioral science may be a closer topic area that will not necessitate too many interpretations. Dr. MacPhail asked if the ecological science technologies were nonhuman-based. Dr. deFur responded that this was the case and that he was referring to the topic of experimental ecology in which the science examines large animal populations and ecosystems that have population changes as a result of stress (e.g., fragmentation of the ecosystem). These data can be indirectly translated into human systems.

Dr. MacPhail commented that field research provides the opportunity to perform mesocosm studies and gain control over stressors. Dr. deFur agreed that mesocosm studies have potential.

Mr. Bangs asked if social coping models were available that examined the addition of stressors and what factors lead to a failure or breakdown of coping at either the individual or the community level. Dr. Weiss stated that there is a large amount of information in medical and social science literature about the effects of stress on behavior and biology, but there are very few islands of data that have examined the joint effects of these types of displacements and chemical exposure.

Mr. Nigel Fields, EPA, commented that not many researchers were working on these types of effects. He mentioned the Broken Windows Theory, which explores social problems in the community that increase stress, and the Weber Theory, which states that African American women over time experience different impacts on their health than women of other races, and these impacts affect their children as well. There are a number of social models and theories that can be explored.

Dr. Weiss noted the difference between health and conceptual models. A given population has certain parameters and then is stressed by a chemical exposure; the biological basis for this effect has not been examined. This is a whole new field. He cited the example of a Montreal group that is examining an epigenetic model and maternal exposure to chemicals.

Ms. Knowlton summarized that social and environmental information need to be integrated. Dr. deFur commented that much of the research is attempting to address different questions. Dr. Weiss stated that the research addresses nonchemical stressors that are not usually considered by EPA. Mr. Bangs described a workshop in February 2007 that discussed microbial insult of nonimmunocompetent individuals and how these individuals respond. Dr. deFur described work that examines specific contaminants, how the contaminants affect community by source, and how disease affects response.

Dr. MacPhail noted that the stress experienced by home caregivers has not been examined and this phenomenon will increase over time. It is possible that environmental factors could be involved. Stress could result in accelerated aging in the caregiver. Ms. Sykes added that premature death also could be a result.

Mr. Ross Highsmith, EPA, added that epigenetic studies could be added to the toolbox. Mr. Wright suggested that simulation-based techniques and approaches across disciplines could be included.

Ms. Debbie Lowe Liang, EPA, asked if there was a deadline for providing suggestions and input to EPA about these topics. Ms. Deener responded that EPA would accept input for the next month. Ms. Liang asked if input from individuals who did not attend the workshop was acceptable. Ms. Knowlton responded that is was.

Ms. Knowlton moved the discussion to the second charge question and asked the group to consider how CBRA could be added to traditional EPA risk assessments.

Ms. Deener stated that the community can be important in identifying the exposure pathway. Ms. Sanchez, ASPH Fellow, added that the community also can identify exposure sources. Dr. Highsmith commented that they can describe lifestyles that may be outside of expectations. Mr. Wright noted that unique diets could be identified by the community. Ms. Liang stated that community input regarding social stresses is important.

Dr. deFur noted that several methods are presently in use at EPA. The 2003 EPA Community Involvement Conference, which might have identified successful methods regarding community focus

groups and meetings, could be a potential resource. Existing social structures (e.g., church) can be used as a gathering tool to obtain community input.

Dr. Weiss described a Web-based system for CBRA that he developed 10 years ago as the result of an EPA initiative. The reference for the resulting publication is: Weiss B. A Web-Based Survey Method for Evaluating Different Components of Uncertainty in Relative Health Risk Judgments. *Neurotoxicology* 2001;22(5):707-721.

Mr. Fields cited the Casa de Salud in Massachusetts as an example of building community infrastructure and knowledge. Researchers worked with the community and set up house parties to address household chemicals and asthma. It took approximately 3 years to escalate, but it has become a significant health movement focusing on a variety of health topics, such as diabetes, HIV/AIDS, and so forth. The mayor has incorporated it into the city's mainframe. Originally, this was a large, disenfranchised population that did not know how to be included, but has increased its involvement. Additionally, Drs. Barbara Harper and Anna Hardy are exploring nontraditional routes of exposure during religious rites.

Dr. MacPhail asked if the group's definition of community included a cross-section with all ages, races, gender, education, and so forth represented. Mr. Callahan indicated that this was not necessarily the case. Mr. Bangs stated that the community of interest includes affected individuals, and this might be a very specific group. Dr. deFur added that geography might be one classification.

Dr. Weiss advised that the term community must be defined. He is involved in a community advisory board that has varied members from industry, academia, and county health, who cover all constituents of the community. The community provides input so that the board can determine the environmental health needs. EPA could construct a paradigm in which community representatives are approached and included in an advisory board. Dr. deFur stated that EPA facilitates such committees at cleanup sites. Ms. Sanchez asked if Superfund sites were included. Dr. deFur stated that cleanup sites include both Superfund and non-Superfund sites, as well as states mandated with the Comprehensive Environmental Response, Compensation, and Liability Act (commonly known as CERCLA). There has been mixed success with this approach, and he is not aware of any studies regarding why certain attempts succeed or fail.

Ms. Knowlton asked participants to consider how the information obtained from the community can be used.

A participant asked about the CARE Program. Ms. Knowlton replied that the CARE Program provides communities with tools to determine their most important stressors and technical assistance to implement programs to reduce their own environmental problems. It does not use traditional risk assessment methods.

Mr. Callahan stated that if new information (i.e., community input) is being placed into an old framework (i.e., EPA traditional risk assessment process), then stakeholders and researchers must determine a method to make EPA decision-makers realize that it is in their best interest to consider it, or this will not happen. Dr. deFur agreed that this problem must be solved at the beginning; the same holds true for motivating the community. The inertia of encouraging citizens to be involved and inducing decision-makers to care must be overcome. Dr. Weiss suggested identifying community members who are active and approaching them. Mr. Callahan stated that decision-makers need a reason for change to happen; this is how to attract them.

Dr. Hubal stated that specific, real-time data can be gathered from individuals in the community; EPA managers can be shown the real-time data to drive policy decisions that need to be made. One method may be an interactive survey. Dr. Highsmith cautioned that some individuals and communities have been oversurveyed. It may be possible to find people in the community who have better questions.

Ms. Deener suggested increasing the level of trust between communities and EPA. Dr. deFur agreed that researchers must know the community, or the whole effort will fail. Mr. Fields added that understanding the linkages and social cohesiveness is necessary. Some communities provide services and support for each other; these services make the group functional. It is necessary to characterize the connections and know who provides what services to whom. Dr. deFur summarized this as assessment of social capital.

Mr. Bangs stated that the needs of the EPA risk manager and the needs of the community must be satisfied, or the effort is a failure.

Dr. deFur suggested changing and reshaping the risk management process so that it is not so rigid and stepwise, so that new types of information or processes can be inserted. Currently, the process does not work if it becomes necessary to work backward. The source-to-outcome paradigm cannot be used because the research is not starting with the source.

Ms. Knowlton asked the group to consider ways that this discussion could be expanded to include nonchemical stressors. Dr. Weiss stated that nonchemical stressors have biological effects. This can be the baseline with which to start. Having national standards that may not apply to all communities is not effective. Some communities will be more susceptible because of current health standards. Ms. Sanchez commented that within the environmental justice movement, the issue that equal exposure does not equate to equitable exposure has been argued for more than 15 years. Dr. Weiss wondered if it had been argued on a biological basis.

Mr. Bangs replied that a common complaint is that there is no metric. Ms. Sanchez thought that Dr. Faustman currently was involved in a water quality standards decision that affects a tribal community and whether or not the community should have lower standards because of their lifestyle. Mr. Bangs and Dr. deFur asserted that the states of Oregon and Washington had lowered standards; there is a precedence for this type of decision based on community lifestyle.

Dr. MacPhail stated that local newspapers have good knowledge of their own community. They are able to collect and disseminate information that might be useful.

Dr. deFur commented that a review board, composed of community members with local knowledge, needs to be instated because local knowledge can be a modifier of quantified data. The local community might have a different perspective than what statistics indicate. Mr. Fields agreed and cited the example of a community in which political leaders did not know the practice of Santeria existed; the practice was a source of mercury exposure that would have been otherwise unknown without local knowledge.

Ms. Liang commented that the technique might not work with national standards, but community advisory boards could help EPA determine the most impacted communities. Dr. MacPhail agreed that these boards could help identify at-risk communities, but they will not be able to help researchers understand why the communities are at risk; that is a scientific question. Mr. Callahan stated that community knowledge often is surprising. Ms. Knowlton added that community members know their own health and nonchemical stressors. Dr. MacPhail said a distinction between “identify” and “understand” must be made.

Ms. Knowlton asked the group to consider the third charge question, which asks participants to evaluate research needs for CBRA.

Dr. Highsmith stated that many factors result in stress. The two questions to consider are: Is there a relative potency of stress? What is the relevance of stress to susceptibility? Susceptibility appears to be an issue because it changes how exposures affect susceptible individuals. Mr. Callahan thought that by

taking the approach of relative potency, it is similar to saying that stress is a carcinogen. A different approach must be taken.

Dr. deFur stated that there are decades of clinical and laboratory research on stress response. The largest gap is that no one has asked questions that are specifically applicable to the issues being discussed. Data about stress and about certain environmental contaminants are available, but there are no data regarding how to combine this information or about what factors make individuals or groups more vulnerable. The question of vulnerability can be answered indirectly by gathering data from the individual parts and overlaying or combining them. The research question that has not been asked is what makes individuals in the community more vulnerable; in this regard, community is defined geographically or demographically. He thinks of vulnerability as a specific exposure concentration and of susceptibility as having a biological basis. Dr. Highsmith clarified that vulnerability means sensitivity and that susceptibility is a biological term. Mr. Callahan responded that the 2003 *Framework for Cumulative Risk Assessment* defined vulnerability, susceptibility, and sensitivity. Sensitivity and susceptibility are biological, whereas differential exposure, differential ability to recover, and differential preparedness are not.

Dr. deFur commented that social capital can crumble as a result of changes in infrastructure; therefore, this is one topic that can be considered.

Ms. Deener asked about the usefulness of laboratory animal studies versus community or epidemiological studies. Mr. Callahan replied that epidemiological studies in small communities are not useful because there is not adequate power. What is needed is a combination of laboratory research and community studies. Dr. MacPhail stated that the most beneficial features of laboratory research are the ability to control stressors and to collect tissues and other samples. Stress markers in the brain can be linked to urine and blood, which in turn can be linked to the community.

Dr. Hubal commented that the military is studying PTSD in returning soldiers; this could be a potential source of data. This is a specific community that can be studied, and laboratory data are available because the military is starting to collect them. Dr. MacPhail added that the military is collecting baseline, predeployment data so that comparisons can be made. This community is exposed to many stressors, so it might become too prohibitive to study all of them. Dr. deFur stated that the myriad combinations also make it prohibitive.

Dr. MacPhail stated that it is necessary to have a simplified design that can measure complex systems.

Ms. Knowlton asked the group to consider the second part of the charge question regarding important methodological gaps for incorporating nonchemical stressors into traditional EPA risk assessments.

Mr. Bangs commented that a holistic approach is needed. Ms. Deener speculated whether a discussion about incorporating nonchemical stressors into traditional EPA risk assessments can occur if the basic questions are not known. Mr. Fields commented that one gap includes determining what amount of epigenetics and other research will be studied before moving into the community.

Dr. deFur stated that research that tests assumptions is needed, especially the source-to-outcome paradigm. Mr. Callahan commented that the cumulative risk paradigm does not use the source-to-outcome paradigm, so this does not need to be addressed. Research is needed to determine which chemical stressors are important. Dr. MacPhail asked if a ranking for stressors had been investigated. Dr. deFur replied that such a ranking was published in the May 2007 issue of *Environmental Health Perspectives*. Ranking items such as psychosocial factors could change the quantification component or increase efficacy at the receptor level. Ranking also can change the dose-response curve in many ways that could result from vulnerability. There is no mathematical distinction between the ability to respond and the ability to recover, but there is a biological difference.

Mr. Bangs commented that basic biological and epigenetic research about multistressors, as well as a more ecological approach to risk assessment and risk management, is needed. Mr. Callahan agreed that this is how cumulative risk assessment must be done. Dr. deFur commented that specific ecological activities must be considered, and eventually cumulative risk must be a combination of both human health and human ecological risk assessment.

Mr. Callahan stated that there must be a plausible link between cause and effect (i.e., more than random data) for decision-makers to act. Dr. MacPhail added that regulators must realize that this is an exceedingly complicated issue.

Breakout Session 3: Statistical and Mathematical Modeling for Community-Based Risk Assessment

Moderator: Pasky Pascual, U.S. EPA

Recorder: Mary Spock, SCG, Inc.

Attendees: See Addendum

Mr. Pasky Pascual thanked participants for attending the session and asked them to introduce themselves. After the introductions, he noted the need to formalize and quantify data for use in decision-making. There should be a difference between the analytical component in the model and the modeling form itself, because the latter is what informs communities about their risks. If the modeling form is transparent, community members can follow the narrative of the science without needing to understand the analytical component behind it. Duke University is conducting interesting research in this area and has produced very simple, accessible modeling forms that lay people can understand, despite the sophisticated set of analytical techniques behind the models.

Dr. David Reif, EPA, agreed that it is important to present data to communities in a manner that does not involve excessive technical language. How a solution to a problem is represented is more important than the underlying method used to reach the solution. One approach is to use easily accessible infographics, maps, graphs, and pictures.

Mr. Pascual suggested that the HB Model is a ready answer to the first question, which asked participants to identify tools and approaches that could be applied to CBRA. Mr. Schultz responded that HB is a tool that works well for spatial representation of levels, but does not incorporate some of the nonchemical stressors or human activity patterns that might affect nonspatial factors such as mixtures, activities, and community practices. Mr. Pascual recommended that the group parse the first bullet point and determine the various issues involved.

Dr. Paloma Beamer, University of Arizona, stated that researchers need better dose estimates and better methods for interpreting biomonitoring. Researchers must get closer to what they are measuring to access risk.

Dr. Janis Johnston, AAAS Science and Technology Policy Fellow, noted that researchers need to account for, quantify, and assess social variables, and these do not easily lend themselves to the process. For instance, if community members are asked to rank a variable from one to five, this creates noncontinuous data; however, if asked to rank a variable from one to 100, the task often seems too difficult and information may be lost. Researchers must decide how to determine which social and contextual variables are important and apply these to the model.

Mr. Pascual agreed that pertinent social variables must be identified in each case and then converted into measurable indicators to include in a model. Dr. Bollweg added that researchers must identify and parameterize variables.

Dr. Reif noted that if researchers have, for example, a suite of measured, quantitative airborne exposures and a suite of questionnaire data, then perhaps a decision tree is a useful approach. This would be an explicit representation of the interaction between a quantitative variable and a socioeconomic variable.

Dr. Beamer mentioned a paper by Ms. Rhona Julien published in the *Journal of Exposure Science and Environmental Epidemiology*, “Pesticide loadings of select organophosphate and pyrethroid pesticides in urban public housing,” in which these types of classification regression trees were used to examine pesticide levels in Boston public housing.

Ms. Eloise Mulford, EPA, explained that Native American tribes tend to distrust models provided by EPA. A situation pertinent to tribes is the desire to return to previous diets that consist of more fish. Risk assessment, however, will examine their current diet, the majority of which might be store-bought groceries and not fish from a contaminated river. Researchers therefore must determine how to incorporate the tribes’ planned dietary changes into risk assessment models. Another variable has not been included in previous risk assessments for political reasons; Native American tribe members, unlike other Americans, cannot relocate to avoid contaminants. This variable increases risk for this population. Additionally, some tribes have only 100 or 1,000 members, and this is another variable often missed in risk assessment. Researchers must communicate effectively the risk of 1/1000 to a tribe of only 100 members. Dr. Reif responded that perhaps risk could be presented specifically in terms of the risk per 100 fish from the contaminated river.

Mr. Pascual noted that Ms. Mulford’s point was consistent with Dr. Johnston’s statement: As researchers attempt to formalize problem scoping, they must include the typically nonquantifiable values.

Ms. Mulford explained that tribal members tend to be process-oriented. They care about what is included in the input for risk assessment and also want to know how researchers use the input. Dr. Bollweg interpreted this as a communication challenge. “Black box” processes are not acceptable to tribes, so researchers must improve their ability to communicate complex ideas and the extremely mathematically complicated models behind them.

Mr. Pascual explained, that based on the workshop’s definition of CBRA, the session participants had been focusing on chemical and nonchemical stressors but needed to examine the two additional building blocks, participatory-based research and transparency. Research starts with a holistic perception of the problems, but analytical modeling tools (such as Analytica and Stella) can identify the primary factors of interest and allow researchers to choose arrows of association and causation.

Dr. Bollweg stressed that modelers must be able to explain their technically complex models in plain English. Mr. Pascual suggested that community members be engaged in building the models, using standard conceptual modeling tools to determine what factors are important. Dr. Beamer added that one of the goals of modeling is to develop a structure that can be applied from one community to another. Ms. Mulford added that researchers frequently explain only simple facts to the public, but the knowledge and understanding of communities should not be underestimated.

Mr. Pascual summarized the important needs that the group had identified:

- Better geospatial characterization of the communities.
- Greater ability to deal with multiple scales (temporal, spatial, or data from multiple sources).
- Greater ability to deal with mixtures versus single insults.
- Better measures of physical variables (e.g., dose).

- Greater ability to identify which social variables to measure and to turn those variables into something quantifiable.
- Better measures of quantified social variables.
- Greater ability to explain models and/or to build them in collaboration with the community to ensure transparency.

Dr. Tilson asked how researchers can validate complex models to ensure they are working. Mr. Pascual commented that working with communities starting from model conception would be useful because different people have different versions of reality. If researchers chart out important variables in a group, they can ascertain that the versions of reality match in a qualitative, consensual manner. Mr. Pascual added that he prefers using Bayesian mathematical approaches to examine the likelihood of the model against data that emerge over time. This provides a formal way to test the ability of the model to capture reality.

Dr. Reif stated that the usual method researchers use to build risk assessment models involves prespecification. This approach works if the community has identified a problem, but if the problem is not known, researchers must measure a number of variables and use an empirical model. He wondered if communities would be amenable to research that determines what is important based on what the collected data show. The important issues might not be those the community initially thought were important, so the strength of the model must outweigh prior conceptions about the problem. Mr. Pascual added that under this premise, when in the laboratory, the goal is to capture all possible data. In the community setting, however, data are expensive, and this approach may not be possible. Dr. Reif explained that there would still be an underlying hypothesis that what researchers are measuring is relevant; determining how factors are important differs from the determination that they are important.

Mr. Pascual added that another significant set of research needs involves verifying and increasing the credibility of models.

Mr. Schultz noted that when communicating with communities regarding dose, interpretation of what the dose means in terms of effect is important. Mr. Pascual added that when building exposure models, researchers must link the dose to both the effect and the source.

Dr. Winona Victory, EPA, mentioned that researchers should consider using data collected by the CDC's Environmental Public Health Tracking Program, which is attempting to link environmentally measured situations with health records. Mr. Pascual agreed that pooling data is beneficial when combining data from multiple sources.

Ms. Segal advised that regarding CBRA and nonchemical stressors, dose-response will shift when other factors are considered. Different communities will show different dose-responses and effects based on socioeconomic disparities.

Dr. Beamer noted that exposures cannot occur without activities that lead to them, and there has been insufficient examination of these activity patterns, such as lead exposure as a result of hand-to-mouth activities, which might be higher in poorer children with fewer toys.

Mr. Pascual mentioned that a key point regarding national models had been raised at previous sessions. The basic approach of HB is to say that there is a common model that applies nationwide, but the value of HB is in viewing the model not as fixed but as stochastic; if data from a certain community are entered, the value can change. There may be a common model with parameters that vary from location to location.

Researchers then can determine why they vary. HB models are single models working on many scales, not numerous different models.

Dr. Johnston advised that when researchers display a map, often some Midwestern states have no data listed, and the people living in those areas will perceive the model as irrelevant. Dr. Roy Whitmore, RTI International, stated that researchers conducting a community-based study from one of those areas could still incorporate data from that area into the model, but would need less local data if using related data from other geographic areas. This concept could be explained to the community.

Mr. Schultz asked for clarification on whether Mr. Pascual suggested that researchers use HB methods for the whole process (from chemical concentration to the health effects) or specifically for estimating localized concentrations. Mr. Pascual explained that he was working on a project that was attempting to link societal behaviors and physical changes and determine the valuations, but this was not entirely based on HB methods. One specific set of issues is related to combining data over several dimensions. He asked for assistance from the group on accounting for the interactions of multiple stressors.

Dr. Reif noted that when combining multiple data types, decision tree-based models could be effective. The approach is nonparametric, so these models are not affected by sample size, as are many others. They also are easy to interpret. Dr. Tilson agreed that this approach is reasonable and asked if research had been conducted using physiological measures of stress, such as steroid hormones, in subpopulations to determine if stress is a factor. Dr. Victory noted there was a study that examined cortisol levels and exposure to violence. Ms. Segal mentioned studies by Dr. Cory-Slechta evaluating the interaction of lead and corticosteroids. Dr. Tilson added that many nonchemical stressors will produce a fairly generic stress response.

Dr. Beamer suggested that researchers incorporate physiologically based pharmacokinetic (PBPK) and physiologically based pharmacodynamic (PBPD) models into CBRA. For instance, if there is a known hormone level shown under stress, researchers could incorporate this with another variable with a physiological basis.

Mr. Pascual added that socioeconomic factors are difficult to desegregate at the individual chemical level and wondered how researchers could handle this issue. Dr. Reif explained that each individual would have a decision tree, and if, for example, there were five causes leading to a particular outcome, community members could be partitioned into five groups. Mr. Pascual stated that the particular behavior activity could serve as a proxy to estimate exposure to mixtures. Researchers might only be able to study the effects of mixtures on a cellular mechanistic level. Dr. Beamer explained that this is why more pharmacodynamics of the PBPD models, as well as data to validate them, are needed. There is a relationship between physiological and sociological responses, and researchers can use mathematics to describe physiological factors.

Dr. Tilson noted that, regarding the interaction of chemical and nonchemical stressors, if the stress of the environment produces a response, there will be a differential response to chemical stressors in that population, which offers some biological plausibility about the interaction. Dr. Beamer added that models also can incorporate the unique physiologies of different communities.

Mr. Pascual stated that the group had not discussed incorporating community-based information into the research. Dr. Reif raised the point that when science is presented to the public, what appears to be a decent weight of evidence to the scientists (such as a 95% confidence interval) is not seen as such by community members, because the concepts of uncertainty and variability are not widely understood. Scientists must communicate these concepts so that people understand that the data do apply to them; how to best accomplish this is unclear.

Dr. Bollweg responded that people simply want to know if a stressor is safe or not; they do not want to be given a number. Researchers do not get questions in an objective form, however, and part of the job is to convert these subjective questions into testable variables.

Dr. Victory noted a use for this concept at the local governmental level. For example, during a presentation on manganese in the water supply in Wisconsin, there were questions raised on how the information was ascertained and what indicated that the water was or was not safe. The data should be user-friendly and easy to locate. Researchers have a great deal of information, but it may not be accessible to the affected communities.

Ms. Mulford agreed that communities want to know not only whether the water is safe, but how scientists determine this. Dr. Whitmore stated that the answer to whether or not something is safe is not always “yes” or “no.” Mr. Pascual agreed that the binary approach does not always work. Using an analytical hierarchical process, researchers might not be able to put a number on what people prefer, but they can decide in an ordinal way what factors are important, weigh different options, and analyze the tradeoff. Communities need to know that scientists frequently do not deal in certainties. In one study, Mr. Pascual worked with fishermen in the Philippines, and decision-making was conducted in the form of a board game. Fishermen learned about the stochasticity of decision-making by playing the game 10 times and making strategic decisions that led to various outcomes.

Ms. Mulford explained that if agencies list options for tribes in terms of pollution cleanup standards, the answer they receive may be that none of the options are sufficient, and only zero pollution is acceptable. A better approach with a community is for the Agency to ask where they should begin to cleanup, and honor that preference.

Mr. Pascual summarized that the four main areas the group had discussed were: (1) selecting the proper analytical tools; (2) using these tools to link exposure back to emissions and forward to effects; (3) taking better measurements on the physical and social sides to feed into the analytical tools; and (4) building up credibility and learning better ways to verify the models used (i.e., “meta” issues).

Dr. Bollweg pointed out that in terms of modeling exposures to mixtures, there are some new methods, such as toxicity testing prioritization using high-throughput methods. Researchers can learn which mixtures (and what concentration of these mixtures) are found repeatedly in large areas. Dr. Reif added that this is being done for toxic gas, and researchers are attempting to extend the method to other domains. Dr. Beamer offered that combining PBPK with Bayesian methods might be a way to integrate some of the issues discussed.

Mr. Pascual suggested that shared, mapable ontologies for organizing data gathered at multiple levels is critical to ensure that information can be shared and located easily using semantic search engines. Dr. Reif added that communities should be able to organize data themselves using a desktop tool. Whoever within a particular community establishes a formal ontology for data sharing can be a contact person at the community level. Ms. Mulford agreed that a tool that the community can operate themselves would be beneficial for tribal communities, many of whom do not like to share data. Dr. Whitmore added that this approach may encourage them to share data, and the National Institutes of Health have developed some relevant data-sharing protocols.

Mr. Pascual concurred that, for example, if Maricopa County in Arizona can see a benefit from using New York data, the community may feel a sense of reciprocation. Shared ontologies allow different versions of reality to be mapped to each other.

CLOSING SESSION

Breakout Reports to the Group

Breakout Moderators

Drs. Cohen Hubal and Faustman summarized the salient points of Breakout Group #1 (See Appendix A, Data Needs Outline). The group identified data needs, especially contextual information. Data needs are driven by community needs. Data access is an issue; existing data may not always be obtainable. A list of available tools would be beneficial. The differences between vulnerability and susceptibility must be explained to the community. Development of indicators and metrics is needed as well as translation of indices to risk. Several options for applying existing tools and developing new tools exist. Detailed case studies are needed, but completion of demonstration projects could address this. One important point is that EPA needs to partner with other agencies, universities, NGOs, and advocacy groups. Communication and the responsibility of a formal report-back to the community are critical, and ethics, training, and education also need to be considered. Additionally, tools and approaches from other fields also should be examined and adopted to CBRA as appropriate.

Ms. Knowlton summarized Breakout Group #2's discussion (See Appendix B, The Biological Impact of Non-Chemical Stressors and Interaction With Other Environmental Exposures Breakout Session Responses). The group discussed scientific and social data that are not integrated and debated the pros and cons of local versus national databases. Participants examined the role of communities in improving data on nonchemical stressors to be used in EPA's traditional risk assessments, including modifying quantitative data and identifying sources and pathways of exposure, activity patterns, and important social stressors and health endpoints. Existing CBPR literature, the 2003 EPA Community Involvement Workshop, and Dr. Barbara Harper's work on Native Americans and treaty rights offer potential models for involving communities. Existing models from the fields of ecology and the social sciences can be built on to incorporate the information gained from national databases and local community input into a risk assessment framework. Participants also suggested that local standards should be developed to accompany national standards, and representatives from the most impacted communities should be present on national advisory boards. Expanded community involvement may not increase the understanding of interactions between chemical and nonchemical stressors, but it will help make associations that drive research. In terms of gaps in knowledge and methodology, more community-based studies and laboratory research are needed to better understand the relationship between environmental and social stress. More research also is needed to determine the most important nonchemical stressors and identify biomarkers of stress and its interactions with chemical exposures. The basic assumptions of the source-to-outcome paradigm must be tested, and researchers must look beyond biological effects and dose-response relationships to incorporate a more ecologic approach, including risk perception and social/economic effects.

Dr. Reif and Mr. Pascual provided the summary of Breakout Group #3's session (See Appendix C, Statistical and Mathematical Modeling). Interpretable solutions exist for answering the question that the community is asking (i.e., translation of results). Credible results are needed, and explanations that underestimate the community's ability and desire to understand must be avoided while respecting the need for nontraditional or advanced methods. Diverse data types, such as environmental, biological, and social, should be included in statistical modeling. The group discussed how to identify relevant data that can be converted to an understanding of indicators, which in turn must be associated with chemical stressors. Data does not need to be stored in one manner as long as it is hierarchical. Analytical issues include how to manage multiple scales and stressors. A general model can be adapted by geographic location and include multiple sources. The Hierarchical Bayesian Model requires more research to increase its ability to add data from multiple sources and scales. One approach to answering the question of mixtures may be to use desegregation techniques to classify lifestyles that serve as proxies for

exposures. It is important to ensure that linkages are appropriate in models. A certain level of transparency is necessary for credibility, and involving the community in building the model will help accomplish this. The preferred outcomes of stakeholders must be identified, and the most important mixtures must be identified and prioritized.

Closing Remarks

Michael Callahan, U.S. EPA

Mr. Callahan commented that he is encouraged that a workshop such as this was organized and noted the quality of the presentations. He provided a brief history of cumulative risk assessment, stating that the first cancer risk report in 1976 has become simplified over the years, and too much emphasis has been placed on some assumptions. Many documents and reports during the subsequent 30 years have provided a revisiting of these assumptions. The Cumulative Risk Technical Panel has commissioned a series of papers regarding issues, case studies, and research needs in cumulative risk assessment. CBRA should be considered a wise investment because communities have begun to request it, EPA's relevance with the public is at stake, and issues of fairness are involved. Environmental justice groups have determined that CBRA is a good tool for communities. Communities are not asking for total risk reduction, and some parts of the assessments the communities desire can be accomplished now.

Some communities perceive that risk assessment does not work for them as a result of items such as cascading effects, nonconventional stressors, and potential losses being omitted from past risk assessments. Physical and spiritual losses that may not be identified in a traditional risk assessment but are important are loss of land, language, spirituality, extended family relationships, sense of belonging, autonomy, rights, self-sufficiency, social structure, connection to land, culture and tradition, identity, history, cultural pride, community, and trust. EPA managers are concerned that including these items contributes to "mission creep," but even under the narrowest view of EPA's mission (i.e., identifying harm as a result of chemical exposures) these factors constitute harm. Public needs are a part of EPA's priority, and EPA needs to respond to the public's question in such a manner that demonstrates understanding and the desire to help.

Vulnerability is the state of being open to harm as a result of the inability to cope with a hazard because of biological susceptibility, prior exposure or disease state, or lack of the resources for resilience. Vulnerability can mean that the exact same exposure can result in widely different effects; equal exposure is not equitable. Three levels of coping exist: (1) nonerosive, (2) erosive, and (3) failed. Risk assessors consider the first two stages but rarely consider the third. This third stage needs to be considered, and communities have known that for quite some time. The third stage provides some range of vulnerability.

CBRA can begin with screening methods that determine important nonchemical stressors and factors that contribute to vulnerability. CBRA is not an all-or-nothing process; it starts step by step. Investment in CBRA is important because demands for it will increase, it will enhance the Agency's relevance and credibility, and it can be entered into in a modest, step-wise manner.

Discussion

Dr. deFur asked what the next step was to continue this discussion on a larger scale and to increase participation by individuals from other parts and outside of the Agency. Mr. Callahan replied that a bottom-up approach was the key; other groups will follow as more dialogues occur.

A participant commented that CBRA is necessary, but quantification is extremely difficult. He asked if quantification is necessary to mitigate risk. Mr. Callahan responded that it is not.

A participant stated that tribes deal with stress in different manners to mitigate final risk. Mr. Callahan agreed that tribal examples are unique, and decision-makers must be aware of the unique harms facing tribes. A participant agreed that community values must be included and prioritized. Mr. Callahan answered that this is what comparative risk assessment is (i.e., how risk is ranked according to values).

A participant suggested that communication within EPA be improved, because frequently after the condition of the environment has been determined, the environment has changed.

A participant agreed with the concept of placing stresses in an economic context because communities need to know the economic consequences of risk. Mr. Callahan noted that poverty is a correlate and may be one way to quantify various issues.

Ms. Segal thanked the presenters for their excellent presentations, which received many favorable comments from attendees. She thanked Dr. Cohen Hubal, Ms. Knowlton, and Dr. Reif for organizing the breakout sessions and Mr. Pascual, Mr. Bangs, Dr. Meta Bonner, Mr. Schultz, and Mr. Lakin for their assistance in organizing the workshop. She recognized Mr. Fields as the impetus for the workshop, and thanked him for his guidance. He and Ms. Deener contributed to the original proposal for the workshop.

Dr. Cohen Hubal thanked Ms. Segal for her organization of the workshop.

The meeting was adjourned at 1:05 p.m.

APPENDIX A: DATA NEEDS OUTLINE

1. Data needs—contextual information
 - a. Based on scoping
 - b. Community-level concerns
 - c. Contextual experts needed
 - d. Community-driven versus community-based
2. Data access
 - a. Guidance on available sources
 - b. Multi-agency
 - c. Surveillance (e.g., CDC, multi-university, environmental health tracking)
 - d. Indicators
 - e. EPA/National Institute of Environmental Health Sciences Children's Centers
 - f. Databases that are available and accessible
 - g. GAPS AT THE LOCAL LEVEL—AND ACCESS (e.g., NHANES)
3. Definition of community
 - a. What important factors characterize similarities/differences among communities (when is extrapolation appropriate)?
 - b. What factors are important for characterizing vulnerabilities that may interact to increase risk from chemical exposure?
 - c. Geography is not always a defining factor (Not all communities geographically bound, may have shared exposures, vulnerability factors)
4. Development of indicators and metrics
 - a. How much data are needed, when do you have enough, when does too much limit interpretation?
5. Translation from indices to risk
 - a. What available social indices may be applicable for EPA cumulative risk assessment?
 - b. How can these indices be translated in a quantitative way to assess risk?
 - c. Importance of both qualitative and quantitative indices
6. Application of existing tools and developing new tools
 - a. Geographic information systems have tremendous power but significant limitations in interpretation (often because of data limitations)
 - b. Linking with risk
 - c. Make tools available and accessible to community (Google Earth-ish)
7. Multidisciplinary teams

8. Case studies
 - a. Review, compile
 - b. Lessons learned
 - c. Use available tools
9. Demonstration projects
 - a. Exposure-based (highly exposed)
 - b. Outcome-based (specific health issues)
 - c. Population-based (particularly vulnerable group)
 - d. Solutions-based (identification of positive trend, understand why)
10. EPA needs to partner!! (Responsibility)
 - a. National Institutes of Health
 - b. CDC/Agency for Toxic Substances and Disease Registry
 - c. Department of Housing and Urban Development
 - d. Departments of Transportation, Agriculture, Education, etc.
 - e. State and local level
11. Partner for context
 - a. Universities
 - b. Non-governmental Organizations
 - c. Advocacy groups
12. Communication
 - a. Scoping
 - b. Interpretation
 - c. Methods of dialogue and interaction
13. Ethics
 - a. Balance accessibility with confidentiality
 - b. Research needed on de-identifying data to improve access for analysis
 - c. Data ownership
 - d. Report back
 - e. Honor and build off of existing relationships in community!
14. Training/education
 - a. Attract more representatives of minority communities to field
 - b. Education in academia on how to work with communities and conduct CBPR
 - c. Communities need introduction to RA—basic training on environmental health and RA
15. Mining other fields

APPENDIX B: THE BIOLOGICAL IMPACT OF NON-CHEMICAL STRESSORS AND INTERACTION WITH OTHER ENVIRONMENTAL EXPOSURES BREAKOUT SESSION RESPONSES

The following was recorded from the session flipchart.

1. Identify tools and approaches that may be applied to conduct CBRA. (*Workshop participants: We will touch on this question briefly during the breakout session, but if you know of additional research programs or studies that contribute to the body of knowledge, please e-mail them to the facilitator at knowlton.carrie@epa.gov before or after the workshop.*)

- What data are available on biological impact of nonchemical stressors and the associated interaction with environmental exposures?
 - Census data
 - Interagency Forum on Aging-Related Statistics
 - Extensive social/economic data, just not commonly used by EPA
 - Must make a distinction between local data and national databases
 - Stress and caregiver studies give insight into biological effects of stress
- What models exist to help us understand interactions of nonchemical stressors and environmental exposures?
 - THRIVE social capital index
 - Social coping models
 - High-performance computing
 - Epigenetics
- What techniques (i.e., measurement, modeling) can be borrowed from other disciplines to quantify the effects of nonchemical stressors?
 - Computer simulations
 - Methods from social epidemiology
 - Behavioral sciences
 - Ecology (community structure, disturbance)

2. Discuss how to incorporate community-based information into traditional EPA risk assessments.

- How can community-based participatory research frameworks be most useful for identifying important exposures and risks?
 - Modifiers of quantitative data
 - Sources and pathways of exposure

- Lifestyle/activity pattern
- Social stressors/poverty
- Must demonstrate CBRA to be an improvement on traditional risk assessment
- Increased participation → more data
- What methods have been successfully used to collect community-based information regarding nonchemical health issues? Are these methods transferable to any community?
 - Review existing literature and outcome of EPA's community involvement conference
 - *Neurotoxicology* has published an article on a Web-based community risk assessment tool
 - Barbara Harper's work on Native Americans and treaty rights
 - Use of advisory boards representative of communities
 - Create models based on lessons learned
 - Real-time surveys (e.g., sensor technology) can lead to increased participation
 - Need a fundamental change in the risk assessment process
 - Need to look at biological endpoints, not single chemicals
- How can community knowledge be incorporated into EPA's risk management process?
 - Can lead to standards based on local conditions, as opposed to national standards
 - Lead to community-driven programs, designed by and implemented by communities
 - Local media can become involved to disseminate information
 - National risk management and standard setting can incorporate community advisory board with representatives from most impacted communities
- What is the role of community knowledge in understanding the interaction of multiple stressors?
 - Community knowledge may not help us understand interactions but will help make associations that drive research

3. Evaluate the research needs for CBRA.

- What are the most significant gaps in our understanding of the biological impacts of stress and interactions with environmental exposures?
 - Need research on effects of combination of stress and chemical exposure
 - What makes certain communities more vulnerable?
 - Community epidemiological studies need to be combined with animal data and laboratory research

- Biomarkers
- Need to look beyond biological effects at risk perception and social/economic effects
- Need to know which nonchemical stressors are most important
- What are the important methodological gaps for incorporating nonchemical stressors into traditional EPA risk assessments? How can this information be used in risk assessments?
 - Need to test basic assumptions of source-to-outcome paradigm
 - Need an ecologic approach beyond dose-response

APPENDIX C: STATISTICAL AND MATHEMATICAL MODELLING

- Interpretable solutions
- Answer the question the community is asking (translate results)
- Credible results
- Avoid the “black-box” explanation, but respect the need for nontraditional or advanced methods
- Include diverse data types (environmental, biological, social . . .)
- Data sharing (ontologies)
- Can analysis be a two-way street?

ADDENDUM: BREAKOUT SESSION PARTICIPANTS

Breakout Session I

Name	Affiliation
Eggers, Mari	Montana State University at Bozeman
Faustman, Elaine	University of Washington
Ferguson, Alesia	University of Arkansas for Medical Sciences
Hu, Chih-yang	Louisiana State University
Cohen Hubal, Elaine	U.S. EPA
Kizakevich, Paul	RTI International
Lakin, Matthew	U.S. EPA
Lobdell, Danelle	U.S. EPA
Rao, Pamela	Farmworker Justice
Schlenker, Thomas	Public Health Madison-Dane County
Schreinemachers, Dina	U.S. EPA
Thomas, Kent	U.S. EPA
Watkins, Timothy	U.S. EPA
Wilson, Sacoby	University of South Carolina

Breakout Session II

Name	Affiliation
Bangs, Gary	U.S. EPA
Callahan, Michael	U.S. EPA
Deener, Kacee	U.S. EPA
deFur, Peter	Virginia Commonwealth University
Fields, Nigel	U.S. EPA
Highsmith, Ross	U.S. EPA
Hubal, Rob	RTI International
Knowlton, Carrie	ASPH Fellow, U.S. EPA
Lowe Liang, Debbie	U.S. EPA
MacPhail, Robert	U.S. EPA
Rao, Ravishankar	U.S. EPA
Rouse, Tonesia	U.S. EPA
Sanchez, Yolanda	ASPH Fellow, U.S. EPA
Sykes, Kathy	U.S. EPA
Weiss, Bernard	University of Rochester
Wells, Sharon	U.S. EPA
Wright, Michael	U.S. EPA

Session III

Name	Affiliation
Beamer, Paloma	University of Arizona
Bollweg, George	U.S. EPA
Johnston, Janis	AAAS Science and Technology Fellow, U.S. EPA
Mulford, Eloise	U.S. EPA
Pascual, Pasky	U.S. EPA
Reif, David	U.S. EPA
Schultz, Brad	U.S. EPA
Segal, Deborah	U.S. EPA
Tilson, Hugh	U.S. EPA
Victery, Winona	U.S. EPA
Whitmore, Roy	RTI International