
# REGION/ORD WORKSHOP ON CUMULATIVE RISK ASSESSMENT

November 4 - 8, 2002
Dallas, Texas

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# FOREWORD

The *ORD/Regional Cumulative Risk Assessment Workshop* was the eleventh in a series of Regional Science Topic Workshops sponsored by the Office of Science Policy (OSP) in the Office of Research and Development (ORD) at the United States Environmental Protection Agency (EPA). Other workshops in this series included:

- *Asthma: The Regional Science Issues*
- *Communicating Science: Waves of the Future Info Fair*
- *Fully Integrated Environmental Location Decision Support (FIELDS)*
- *Non-Indigenous Species*
- *Pesticides*
- *Endocrine Disruptors*
- *Emerging Issues Associated with Aquatic Environmental Pathogens*
- *Aquatic Life Criteria*
- *Critical Ecosystems*
- *Air Toxics Exposure Assessment*

The objectives of the Regional Science Topic Workshops are to: 1) establish a better cross-Agency understanding of the science applicable to specific region-selected human health and/or ecological topics, and 2) develop a network of EPA scientists who will continue to exchange information on these science topics as the Agency moves forward in planning education, research, and risk management programs.

Each year, EPA regions identify priority science topics on which to conduct workshops. The workshops address the science issues of greatest interest to the regions on the selected topic area. Each workshop is planned and conducted by a team of regional, ORD, and interested program office scientists, is led by one or more Regional Science Liaisons (RSLs) to ORD, and is facilitated by a regional chairperson. Participants maintain the cross-Agency science networks they establish at the workshops through planned post-workshop projects and activities such as identifying collaborative research opportunities, creating information sharing mechanisms (e.g., interactive web sites), and developing science fact sheets for regional use.

For additional information on a specific workshop or on the Regional Science Topic Workshop series in general, contact David Klauder in ORD's Office of Science Policy (202-564-6496).

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# EXECUTIVE SUMMARY

The *ORD/Regional Cumulative Risk Assessment Workshop* was held on November 4 - November 8, 2002, in Dallas, Texas. The workshop was co-chaired by Region 6 and ORD/NCEA, with support from ORD/OSP.

The workshop was organized into five sessions:

*I. Introduction and Overview*
*II. Planning, Scoping, and Community Issues*
*III. Approaches to Cumulative Risk Assessment*
*IV. Putting It Together*
*V. Policy Implications*

Scientists from EPA (regions; Office of Research and Development; Office of Pollution Prevention and Toxics; Office of Air Quality Planning and Standards; Office of Pesticide Programs; Office of Policy, Economics and Innovation) and invited speakers from a government laboratory and a private association presented methods, current research, and case studies on cumulative risk assessment.

The workshop structure was generally based on the structure of the new Risk Assessment Forum report, *Framework for Cumulative Risk Assessment* (EPA/630/P-02/001A). The first day was given to an introductory presentation on that Framework, along with a discussion of expectations for the workshop both from participants and from ORD, who expected to get research recommendations. The second day of the workshop focused on planning and scoping, problem formulation, stakeholder interactions, and generally "setting up" the assessment. The third day's content was the most technical, dealing with what is known about how parts of the assessment may be done, including case studies of ongoing assessments. Day 4 brought together the various pieces and discussed some of the ways the results might be presented. The final day featured a panel that discussed some of the issues in the science-policy interface. Three breakout sessions focused on stakeholder involvement (Session II), case studies and the development of research recommendations (Session III), and case studies and "putting it together" (Session IV). The closing remarks and discussion at the end of the workshop generated a list of action points and research recommendations (see Session V). Planned outcomes include follow-up of the issues raised at the workshop with ORD and the regions, and continued communication about cumulative risk issues. Most participants found the workshop useful, according to the workshop evaluations; many expressed interest in getting additional information about performing cumulative risk assessment and about linking cumulative risk assessment with enforcement and policy.

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# SESSION I: INTRODUCTION AND OVERVIEW

Co-chairs: Mike Callahan (Region 6) and Linda Teuschler (ORD/NCEA)

***PLEASE NOTE:*** *Slides from the Workshop presentations are available at:*
http://epa.gov/osp/regions/workshops.htm

Mike Callahan (Region 6) greeted participants and introduced Region 6 Administrator Gregg Cooke, who welcomed participants on behalf of Region 6. A videotaped welcome address from Paul Gilman, Assistant Administrator for Research and Development, was then presented.

## Welcome from Region 6 – Gregg Cooke (Regional Administrator, Region 6)

At a recent strategic planning workshop in San Francisco, CA, the Assistant Administrators and Regional Administrators identified cumulative risk as something that will have an impact in the future. It is already having an impact; for example, slides discussing regional risk issues are often noticed by the public in Agency presentations. The Texas state legislature requires the State to address cumulative risk, and Texas is relying on EPA to give them the tools to respond to this challenge. There is no particular right way to do it, and there are conflicting views. EPA's current methodology is all that is available, and it may "hit the front lines" sooner than expected. Workshop participants should focus on the tremendous challenge of explaining cumulative risk to the public in a manner that makes sense.

**Welcome from ORD –** Paul Gilman (Assistant Administrator, ORD) (by videotape)

Participants in this workshop are engaged in a very important activity. The workshop is driven by real-world actions and will hopefully have a real influence on EPA's evolving views of cumulative risk. The credibility of the cumulative risk approach depends on sound science at EPA. Establishing a better relationship with regional partners is key: these workshops are critical to the regions knowing what ORD is doing, and ORD is looking for input from the regions to drive the research agenda. The workshops provide a setting to integrate science across the Agency and between EPA and other agencies, and allow opportunities for collaboration, critical science uncertainties, and needed science products to be identified. Three expected outcomes of this workshop are: (i) to identify existing and ongoing work, (ii) to discuss issues and develop an understanding of limitations, and (iii) to identify information gaps where ORD could conduct needed research. Participants need to develop a sense of what can be done with cumulative risk and to integrate it into Agency activities. Communities can have difficulty understanding the basis for EPA's activities, so it is very important to get an "on the ground" perspective from the regions in putting together work on cumulative risk for the Agency.

## Keynote Address: "Everyone Agrees It's Important, but Will Cumulative Risk Assessment Make a Difference?" – Margaret MacDonell (Argonne National Laboratory)

Three questions can be asked about cumulative risk assessment: Why does it matter? Who cares? Where are we? Cumulative risk assessment encompasses a variety of issues, including national environmental programs [e.g., the National Environmental Policy Act (NEPA)], waste sites (Superfund), pesticides [under the Food Quality Protection Act (FQPA)], air (e.g., in Region VI), water [disinfection byproducts (DBPs)], ecology and sustainability, cities (cumulative hazard and risk studies), the workplace, food safety and nutrition, medicine, equity and economics, and homeland security. In cumulative risk assessment, we are looking for outcomes that are greater than expected, e.g., situations where, according to a mathematical humorist, "1+1=3 for very large values of one." Everyone – townspeople, workers, cultural groups, planners, environmentalists, policy makers, politicians – cares about cumulative risk, because people want to know if they are safe and if their quality of life is acceptable.

Cumulative risk assessment has been applied to many things, including human health, for workers and the public. Issues include risk drivers and regional differences, ambient conditions, changes over time (trends vs. adaptive responses), and scientific and technical advances (e.g., fingerprinting, gene therapy). Environmental cumulative risk assessments have also addressed a range of issues, from cleanup to protection and preservation, and a range of levels, from the individual to the ecosystem to the planet. Cultural factors, such as susceptibility, vulnerability, and equity, as well as relevant economic issues, including cost-effectiveness and willingness to pay, also are involved.

The "bottom lines" for cumulative risk assessment include: spending limited resources wisely; translating science to risk guidance and policy in the face of perceptions (e.g., inaccuracy and overkill); reflecting all stressors and factors in true risks; and dealing with over-conservative uncertainty considerations. The cumulative approach offers hope for more realism. For instance, equity in communities is important because traditional risk assessments based on individual sources ignore multiple impacts on the same person. An example would be the observation of more cervical cancer deaths in the southeast U.S., which is not attributable to higher risk, but to poorer access to health care.

Cumulative risk assessment is assessing risks of "integrated multiples." The environmental analyst's dilemma is that environmental processes are difficult to understand and predict and environmental management decisions are difficult to make. In terms of issues to address, both biological and statistical significance are important, and not always equivalent. Variables can be considered as binary (e.g., the presence of an enzyme) or as a continuum (cholesterol level); it can be useful to not consider a variable as a discrete, finite value. Another difference is

between hypothesis-driven reductionism and understanding the real world; the lab is not exactly like the real world (e.g., the biosphere project "failure" illustrated that).

Current (traditional) approaches have limitations. They are usually overly protective, e.g., the reference dose (RfD) concept reflects the extreme for every effect. This forces conservative risk management. For example, the Clean Air Act (CAA) is intended to protect asthmatics. The reference concentration (RfC) is a conservative bounding value, but it only considers a single contaminant acting alone, which may not reflect an asthmatic's response to multiple chemicals. There is no easy method; new knowledge is needed.

The issue of susceptibility also adds to the complexity of cumulative risk assessment; susceptibility can be genetic, environmental, and constitutional (i.e., age, gender, health status). It is also necessary to think about multiple exposures; this can be done through considering whole mixtures, groups of similar mixtures, dose addition using an index chemical, and the interaction-based hazard index (exposure level/effective dose), which uses weight of evidence judgments. Workplace studies can give information on agents that have combined effects, dose-additivity, and key combinations for targeted interventions, including mixed exposures, mixed effects, and mixed stressors.

In dealing with uncertainty, the traditional approach has been to ignore it, mention it, wave it away, or treat it qualitatively, e.g., to say the results are okay within an order of magnitude. Sometimes no information is given on uncertainties; sometimes conservative estimates are used, and the result is treated as "correct." Problems arise when there is a spurious degree of certainty, because the public expects precision. Risk assessors need to try to give people knowledge.

Streamlining is key. For instance, work could be done to develop effect groups, to streamline the number of major categories, and to reduce overlaps. Toxicity data can be organized by target organ. Effects can be grouped for a given route of exposure (the "body picture") to improve community understanding. Uncertainty is an opportunity to rise to the occasion, to meet the need. Partnerships are also key. Many have identified cumulative risk assessment as an issue; there is a need to do organized and complementary research. Participants should focus on an assessment of these needs.

**Questions and Comments**

Question: Is there some transition for people to begin working on cumulative risk assessment? Is it something that is only talked about in a workshop setting? Where is this being done?

Response: Some people are still talking about it and some are doing it. As to how you transition from traditional risk assessment to cumulative risk assessment, it tends to be a step function. One doesn't decide one day to be a cumulative risk assessor. It takes

something to make it happen. You start with no idea about how to approach it, so you invent something. If you're not doing cumulative risk assessment now, you can expect somewhere in the future that you will get a problem that will need this approach. (Callahan)

## Workshop Overview and EPA Framework for Cumulative Risk Assessment –
Mike Callahan (Region 6)

The Framework Document for Cumulative Risk Assessment (1) was sent out electronically to those who registered early enough. A framework is a general description of issues, but unlike guidelines, it is not a protocol for how to do a risk assessment [Slide 4]. We do not have enough knowledge now for guidelines, even though people would like to have them.

***What is a cumulative risk assessment?***

Cumulative risk assessment asks, "What is the probability of damage?" rather than, "What is the harm?" or "What are the adverse effects?" [Slide 5]. In order to have a cumulative risk assessment, one must have more than one stressor or chemical [Slide 6]. Calculating risks for 30 chemicals is not a cumulative risk assessment; one has to address what it means when those exposures are combined. Cumulative risk assessment can be qualitative; it does not have to be quantitative [Slide 7]. The goal of cumulative risk assessment is to address and answer questions related to the probability of harm to human health or to the environment from multiple stressors acting together [Slide 8]. Cumulative risk assessment is a tool, just like every risk assessment [Slide 9]. It is not going to be appropriate to every task; it is most useful when addressing the risks from multiple stressors acting together.

**A brief history.**

The 1997 planning and scoping memo (2) was an early look at the questions of: What do we mean by cumulative risk? What kinds of things do we consider? Who needs to be involved? [Slide 10]. The Science Policy Council called on EPA to move beyond planning and scoping; the Risk Assessment Forum's planning panel has been working on the Framework since 1999. Following consultations with the Science Advisory Board (SAB), external meetings with scientists and the public, and an external peer review in June of 2002, the one remaining step for the Framework is approval by the Science Policy Council.

**Issues.**

Issues facing cumulative risk assessment include process issues, such as identifying the participants; technical and scientific issues; and policy issues [Slide 11]. Policy is particularly important to the states, as evidenced in their comments on the Framework. Policy issues include interpreting the definition; Agency priorities; stakeholder fairness; defining acceptable risk (e.g., if the $10^{-6}$ *de minimis* value is still appropriate for cumulative risks); the types of additional stressors and risks included (e.g., biological factors or only factors for which EPA has a legal mandate); and legal issues [Slide 12]. The issue of whether to do a cumulative risk assessment rests on whether the cumulative risk assessment gives enough added value for the decision

maker. These policy questions will need to be answered if cumulative risk assessment is to become a commonly used tool.

***How is cumulative risk assessment different from traditional risk assessment?***

Features of cumulative risk assessment can include multiple chemicals or stressors, non-chemical stressors, a population focus, stakeholder emphasis, attention to vulnerability, and consideration of both human health and ecology, sometimes together [Slide 14]. Chemical-focused risk assessment addresses sources, fate, transport, and exposure routes and pathways, usually in several populations, while cumulative risk assessment considers stressors and chemicals that affect a population segment or subpopulation [Slide 15]. Cumulative risk assessments can also take into account vulnerability of a population and how it affects risk [Slide 17]. The Framework uses basically the same paradigm as the 1983 "Red Book." (3). However, traditional risk assessment uses exposure groups, dose-response groups, or toxicity groups; in cumulative risk assessment, they are not done separately.

Workshop participants should think about what kind of research is needed to bolster current knowledge [Slide 18]. How do we combine risk assessment on biologicals with risk assessment on chemicals? When do we learn the real importance of factors like lack of access to health care? When do those factors affect decisions and make them better? In terms of combining different risks, the questions are: How do you and can you? Can the risk of dying in a car crash and the risk of cancer from an industrial chemical be combined? [Slide 19]. How should common denominators, like similar mode of action, quality-adjusted life-years (QALYs) and disability-adjusted life-years (DALYs), or loss of life expectancy, be applied? [Slide 20]. Can one biomarker be a biomarker of exposure for a number of different chemicals? Can it integrate so that you do not have to calculate individual risks and add them up?

The approach of doing an index of different risks (e.g., cancer, liver impairment, etc.) for each group of chemicals to form a profile for the community or population can be considered [Slide 21]. Another approach (taken from Appendix I of *Science and Judgment in Risk Assessment*) is to define different types of risk to derive a line above which "something bad" is going to happen; this also merits consideration.

There are not many examples of cumulative risk assessments with outstanding uncertainty analyses [Slide 22]. When risks are calculated on a geographic area, and exposures are assigned to each of, e.g., 4 million people, management's first question is, "Is it statistically significant?" The idea of statistical significance is derived from the sampling that has been done for years in risk assessment; with a sample size (n) of 4 million, "everything is statistically significant." Things are different in cumulative risk assessment, and it is necessary to determine what kind of analysis would be useful.

In terms of future plans, the report from this workshop will contain recommendations to ORD [Slide 23]. The Framework will be published in late 2002 or early 2003. Case studies and issue papers will be developed. Guidelines development will start in 2002 or 2004; the exposure guidelines took six years, and the cancer risk assessment guidelines even longer. It is impossible to predict when cumulative risk assessment guidelines could be finished.

**Questions and Comments**

Question: What have you done so far and what do you plan to do after publication of the Framework?
Response: The people on the Risk Assessment Forum Technical Panel on Cumulative Risk Assessment will keep their Assistant Administrators apprised. Since there were several meetings with the Science Policy Council and there are no "musts" in the document, there should not be a problem. The Framework gives an array of issues that at least should be considered when doing a cumulative risk assessment. If a program ignores them, that program could be vulnerable to some criticisms later, but it should not have an affect on how any program office does things.

Question: Have studies been done to follow people around the country, or just where they live?
Response: ORD has done both to get at exposure.

Question: What are the Regional Administrators looking for in how to approach this?
Response: That depends on the Regional Administrators and the extent to which they get involved. Regional people can contribute to the research agenda. If they are silent, people will ignore the topic and hope it goes away.

Works Cited

(1) USEPA, 2002. *Framework for Cumulative Risk Assessment.* Risk Assessment Forum, Washington, DC. EPA/630/P-02/001A

(2) USEPA, 1997. "Guidance on Cumulative Risk Assessment, Part 1. Planning and Scoping." Science Policy Council, U.S. Environmental Protection Agency, Washington, DC. Attachment to memo dated July 3, 1997 from the Administrator, Carol Browner, and Deputy Administrator, Fred Hansen, titled "Cumulative Risk Assessment Guidance-Phase I Planning and Scoping."

(3) NRC, 1983. *Risk Assessment in the Federal Government: Managing the Process.* Committee on the Institutional Means for Assessments of Risk to Public Health, Commission on Life Sciences, National Research Council. National Academy Press, Washington, DC. ISBN 0-309-03349-7

**Research Planning for Cumulative Risk Assessment –** Linda Teuschler (ORD/NCEA)

Research planning goals are targeted research ideas, not a "laundry list." Some goals are to: identify program office and regional needs; identify available tools and methods; address special issues; discuss approaches, tools, and experiences; and collect information to identify future research needs and directions [Slide 2]. Major themes will be discussed on Days 2-4 of the Workshop; on Day 5, a summary of ideas will be generated [Slide 3].

The results of the workshop's research planning efforts will go to ORD and will mainly be used by the National Center for Environmental Assessment (NCEA) [Slide 4]. NCEA's function encompasses completing risk assessments, describing risk information, developing guidance and tools, and promoting research on new technology and applications [Slide 6]. There are many influences on ORD's research planning, including the programs, the regions, and academia, and the planning frequently evolves [Slide 9]. ORD has developed a research strategy with goals to be carried out by its team.

It is important for workshop participants to know that cumulative risk assessment is in the law [Slide 10]. The Food Quality Protection Act (FQPA) specifically requires the assessment of multiple pesticides through all pathways acting through a common mechanism of toxicity; the Safe Drinking Water Act Amendments (1996) call for the study of complex mixtures; and the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA, 1980) also includes "mixture" in its definition of contaminant. These laws drive resource allocation in ORD. There is not a top-down legislative push for cumulative risk assessment. It is needed in the regions and on the front lines in the communities. The ORD Strategic Plan incorporates cumulative risk assessment into two of its goals: clean and safe water and sound science [Slide 12].

Single chemical risk characterization follows the familiar risk assessment paradigm [Slides 13, 14]. Risk characterization for mixtures can be represented using a dose-response plane for different amounts of two chemicals, with a single exposure route and single critical effect, but a joint dose-response [Slide 15]. The risk assessment paradigm for mixtures is more complex, including all the issues of single chemicals, plus interactions and effects from total dose; characterization of unidentified material; degradation and interactions; toxicologic judgment about similar mechanisms of action; and interdependent dose-response and exposure assessment [Slide 16]. In cumulative risk characterization, still more complexity arises with the inclusion of more stressors, more pathways, and more time [Slides 17, 18]. The risk assessment no longer deals with a single effect, but with multiple effects, e.g., addressing developmental and reproductive effects early in life, and cancer 30 years later. Looking at a problem like this, it is evident that the problem needs to be scoped into manageable pieces in order to identify where

the impacts are. The risk assessment paradigm for cumulative risk assessment includes the potential for multiple effects from exposures by multiple routes and the roles of non-chemical stressors.

**Questions and Comments**

Question: The Agency would say that we do top-down research. I am struck that cumulative risk assessment is asking for bottom-up research. The regions and program offices are saying that this is what they want. Is it worthwhile to push it back to top management?

Response: Paul Gilman is the most receptive Assistant Administrator I have seen in terms of focusing on the regions and their research problems. His level of participation is unheard of. The regions have historically said they can not get into this process, and that none of our regional needs get listened to. Here is a vehicle – an open door into the system. People signed up from all 10 regions for this workshop; it should be used as an opportunity. It is not totally bottom-up; some level of management knows it is coming.

Response: The bottom-up element has to reach a level in the regions that will get Gilman to make commitments. At the FY04 budget meetings, he was disappointed because he did not hear about science from the regions. Gilman says that he is prepared to deliver, but the regions have to tell him what they need. There is a disconnect between regional staff scientists and management. This workshop is a place to say what you need.

**Discussion of Issues and Expectations for the Workshop –** Mike Callahan (Region 6)

Participants introduced themselves and gave short statements of their expectations for the workshop. Specific outcomes that participants hoped to get out of the workshop included the following:

- To learn about tools, including exposure modeling;
- To see if cumulative risk assessment better reflects reality than do other methods (because the closer we can get to reality, the better);
- To understand how human health risk assessors do cumulative risk assessment;
- To find ways to add in the things that are different;
- To see how we can apply ideas to practical settings to answer community questions;
- To hear the bigger picture (what other regions and offices are thinking);
- To get education on the state of the science;
- To find out how to apply cumulative risk assessment at the state and local level (to go from research to application);
- To find out what others are doing;
- To support development of cumulative risk assessment techniques in the Agency;
- To learn how to integrate exposures from non-Superfund sites into Superfund risk assessments;
- To learn about the use of cumulative risk for potentially susceptible life stages (e.g., in the Children's Office);
- To evaluate how well this approach works for meeting the objectives of the workshop series;
- To have discussion of a clear Agency message regarding the realities of cumulative risk assessment;
- To learn about technical and policy issues in order to assess civil rights in the context of cumulative risk;
- To get practical tools and communication methods to translate cumulative risk assessment to the lay community;
- To learn the status of cumulative risk in the regions;
- To facilitate getting regional input into the research process;
- To work toward practical, real-life research priorities;
- To hear about efforts toward allaying public concerns;
- To have a dialogue on how to move forward to assist the people who trust EPA;
- To learn how to communicate multiple stressors to the public;
- To learn to be more competent in determining corrective action needs;
- To understand the state of the art and get information about how cumulative risk is being used in environmental justice.

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# SESSION II: PLANNING, SCOPING, AND COMMUNITY ISSUES

Co-chairs: Edward S. Bender (ORD/OSP) and George Bollweg (Region 5)

## Planning, Scoping and Problem Formulation in Cumulative Risk Analysis –

Edward S. Bender (ORD/OSP)

EPA has spent a great deal of time organizing activities around the risk assessment paradigm [Slide 2]. Risk assessments have proliferated and are becoming more and more complex [Slide 3]. Risk management and stakeholders were identified in the two major National Research Council reports; the Presidential Commission clarified that risk assessment includes both analytic (science) and deliberative (stakeholder) aspects. Environmental justice is also an important facing EPA. The Agency is no longer looking at the same risk assessment paradigm.

Planning and scoping and problem formulation should be done for every risk assessment, to help clarify the assessment's relationship to decision making [Slide 6]. Risk characterizations of 50 to 100 pages provide more uncertainty than clarification [Slide 7]. If planning and scoping were done initially, risk characterizations would be shorter, and there would be fewer apologies and regrets. Planning is a part of the original guidelines, and scoping has been added to make sure the size is right [Slide 8]. The steps of planning and scoping include determining who needs to be involved, and the scope (e.g., national vs. international) of the assessment [Slide 9]. It is important to identify and categorize concerns [Slide 10].

The planning dialogue starts with the people who might be affected, in addition to the risk assessor and risk manager [Slide 11]. It also includes dialogue with stakeholders about their concerns, values and potential impacts, and with economists, to understand social science and decision making. It is important to identify the problem, the charge, and what the risk assessment is answering. Scoping questions may be one of the most important things to consider in communicating risk assessment; they help identify what the parties are expecting [Slide 12]. Public involvement is important because it helps in determining the right questions to ask [Slide 13].

The conceptual model is the place where we start to think about important relationships that exist [Slide 15]. Hypotheses about how to combine various stressors are developed. Developing a conceptual model includes defining the goals and assessment context; delineating scales and boundaries; inventorying land uses and activities; describing potential stresses and sources; identifying contaminant release mechanisms; describing exposure pathways; identifying stressor-receptor co-occurrences; identifying health and ecological endpoints; determining health

and ecological measures; developing risk hypotheses; and ranking the relative importance of potential risks [Slides 16, 17].

Societal drivers create a stress regime that can be identified and modeled [Slide 18]. One can look at what exists now and what may exist in the future. When one looks at an assessment, the next question is how to follow up on risk management decisions. A conceptual model of mercury illustrates how detailed chemical and environmental information can be presented for a lay audience [Slide 20]. There are several pathways for generating methyl mercury, and several opportunities for identifying fate and transport. Environmental pathways can help the risk assessor identify where mercury could be a concern for human health.

It is necessary to start thinking about how to fill in data gaps and to set a basis for framing a particular analysis [Slide 21]. Carrying forward assumptions and reflecting agreements that may be made through dialogue helps to inform risk management. The workshops have taught that it is important to focus on the product, i.e., the risk assessment [Slide 22]. This helps the assessor to make some decisions about data needs, the approach (e.g., site-specific monitoring), and public input. It also helps to assure that information to evaluate risk management options is included. The analysis plan is not static; through the course of the study, modifications will be made to incorporate important new information. The process will save resources and improve risk characterization.

Stressor-stressor interaction ranking is one technique for making decisions about what to present in a risk assessment; for example, it was used in an assessment of fishery effects in the Great Lakes to identify stressors (and interactions between stressors) on fish spawning areas [Slide 23]. An impact matrix is another way to examine the effect of stressors on criteria, such as human health, aesthetics, biota, and economics; in the lake example, the impact matrix identified high adverse impacts on all areas except human health [Slide 24]. This tool allows assessors to portray why they are interested in a particular set of information.

Desirable outcomes of planning and scoping include clear understanding of the assessment questions and potential outcomes [Slide 25]. It is important for risk assessors to identify the factors thought about during planning and scoping, and to acknowledge that stakeholders might be disappointed in the outcome because they were expecting relief. If the public does not understand what the Agency is doing, they will think that it is doing nothing and will become frustrated.

Today, participants will hear case studies of what has been done and what can be done to identify research needs [Slide 26]. Many of the things that are not known are not in the nature of science, but in the area of decision making. There is a series of islands of information; scientists need to build bridges between them to get to the assessment of risk and inform the risk manager. We need to apply the best information we have now to the decisions we face; to

recognize critical aspects of problems for specific analyses; to evaluate stressor interactions; and to engage key stakeholders and do it soon.

The following web sites are useful references:

http://www.epa.gov/osp/spc.htm, for policy guidance and planning and scoping lessons;

http://cfpub.epa.gov/ncea/raf/index.cfm, for the Risk Assessment Forum;

http://www.epa.gov/pesticides/cumulative/; and

program and regional web sites.

**Questions and Comments**

Question: What kinds of decisions are you looking at?
Response: We want to expand the envelope. Economists make the fundamental assumption that people use rational decision making. Risk assessments aren't the only thing that risk managers are looking at. It's time to say that the Agency needs to understand the environment in which decisions are being made, how science interacts with other things, and how people make decisions and choices.

Question: In terms of stressor interactions, there is a mountain of information. Where do you think we are?
Response: We are trying to get you to start thinking about it. We are pretty good about interactions between two chemical stressors and families of stressors, and we are really good about understanding how a particular chemical acts. There are higher-order operations here. We can work the problem from two ends: first, by looking at impacts, epidemiology, evidence of adverse effects, and then, by moving toward that through lab studies and specific analyses. The challenge is to get closer. We will always use a broad-brush approach. We will not ever be able to understand every interaction intimately. Cumulative risk assessment allows us to understand the broad significant trend, and all its implications to risk management.

## Environmental Justice Considerations – Reginald Harris (Region 3)

In order to do any risk assessment properly, it is necessary to get out and know the community; risk assessments all require special judgments and knowing who you are dealing with. The Chester, Pennsylvania Risk Study illustrates this idea. Citizens of Chester approached the Regional Administrator with their concerns that the city had more than its fair share of hazardous chemicals and health effects, and, specifically, about the addition of more facilities [Slide 4].

The Regional Administrator committed to a complete evaluation of the issue, and to a determination whether adding additional facilities would have an adverse effect on the people of Chester [Slide 5]. EPA personnel met with concerned citizens; through the meetings, the two groups came to understand one another, and eventually developed an approach based on everyone's knowledge. The process showed that the citizens can understand the science, if they are appropriately challenged.

Several characteristics of the community are key to understanding the particular problem [Slides 7, 8]. Most of Chester's housing is located very close to industrial facilities; waste piles were scattered throughout the city; the city had been prosperous until major industries left in the 1950s. Politically, Chester is a Democratic city in a Republican county. In terms of health endpoints, Chester is "on the wrong side of the trend" (e.g., lower birthweights, higher cancer mortality) for every major health index. Citizens initially expressed concern and frustration about smaller issues, e.g., trucks idling on the roadways, but beneath that was concern about the public health and about multiple sources and stressors. Without listening to the community, EPA would not have known that some 75 men regularly subsistence fished in the Delaware River to supplement the diets of their families, catching four species for which advisories had been issued.

EPA and the community worked together to develop an overall plan for the assessment. Per the Regional Administrator, no new ambient data were collected; EPA used existing sources on fish, water, sediments, soil, etc., combined with modeling, to create a comprehensive risk assessment on cumulative risk and potential impacts [Slide 11]. Some 42 or 43 facilities, all located in close proximity to where people lived, were considered; processes were taken into consideration for oil refineries, incinerators, paper plants, and rotary kilns to find out the potential chemicals that were being used, byproducts, end products, and production information [Slide 13].

EPA used data from studies of various media that were being done in the Chester area [Slide 14]. The Agency learned that there were still private wells in the area; 68 were located during a very labor-intensive effort. The wells were fortunately not being used for drinking, because the ground water was heavily contaminated. Based on experience with the Baltimore lead study, Pennsylvania State public health personnel were brought in. The inclusion of public health outcome data made the study bigger, but was important because it allowed more problems to be

addressed, and because the citizens appreciated it.

A Superfund risk assessment for all pathways, all facilities, and mobile sources was done. For the water supply, a potential long-term risk was identified for disinfection byproducts. When EPA explained that without disinfection, there was an increased mortality risk in young and old age groups, the citizens understood the risk associated with disinfection byproducts and accepted it. Modeling showed no major risk associated with exposures from air. For noncancer risks, a few hazard quotients (HQs) above 1 were calculated. However, significant risks of $10^{-4}$ to $10^{-5}$ were associated with fish consumption.

In expanding the study, EPA asked the city to provide all its venous blood lead test results; this identified a serious public health problem. In a five-year period, 6,783 children were tested, and about half had blood levels in the range where lead poisoning is a concern; some were as high as 190 μg/dl. Sixty-seven percent of the children had blood lead levels above 10 μg/dl; for comparison, in the NHANES data set, the proportion was 3%, and in the heavily-polluted Jim Thorpe, PA facility, it was only 25%. Moreover, 6% of children had blood lead levels of 50 μg/dl or higher; in that range, they should be hospitalized for treatment. Traditional risk assessment gave no indication of this problem. The finding also brought the citizens closer to EPA because they felt that the Agency was trying to help. Initially, the citizens had believed that the industrial facilities were the most important problem, and through this assessment, learned that the city's lead paint removal practices were instead responsible for a serious problem for their children's health.

For respiratory cancer, the rate in Chester was higher than the rate in Philadelphia, and much higher than the state average, in both males and females. In males, the incidences of leukemia, prostate cancer, and all cancers combined were statistically significantly higher in Chester compared to the rest of the state, the county, and Philadelphia. In women, breast cancer incidence was low in Chester, which would be expected based on the community's demographics. However, the age-adjusted breast cancer mortality rates were high in Chester, and, in fact, were the highest in the State. This pattern suggests inadequate health care, e.g., misdiagnosis or not getting treatment, and vulnerability. It is important that the cumulative risk assessment suggested risks in the $10^{-6}$ to $10^{-4}$ range, but the public health data gave a completely different story.

In terms of actions and recommendations, Chester got $400,000 from Delaware County to treat childhood lead poisoning, plus money from the Centers for Disease Control. Truck routes were changed, voluntary compliance measures were instituted, and the proposed new facility never opened due to a legal challenge by the citizens.

The case study also shows that community involvement is possible. There is a tremendous wealth of information on both sides. Efforts must be coordinated; agencies all have useful information to share. In terms of environmental justice, EPA needs to understand that every

community is different, and every assessment is individual and special. Each community's circumstances must be dealt with, and something "out of the can" cannot address realistic concerns. Environmental justice is knowing who you are dealing with and recognizing that everyone is unique.

**Questions and Comments**

These questions were asked during the presentation:

Question: Did you make some cut of chemicals to look at?
Response: Like a Superfund risk assessment, we eliminated some chemicals.

Question: If a chemical was not likely to drive the risk you dropped it?
Response: Yes. And we got the citizens to understand that if it was not driving the risk, we would not carry it forward. We spent a lot of time explaining the rationale and getting feedback.

Question: The citizens' concerns are short-term. Did you look at chronic [endpoints]?
Response: We looked at chronic [endpoints]. We were aware of complaints of odors and episodic releases. The State agreed to place an on-site inspector who would take reports and investigate them with a mobile monitoring station.

Regarding the data on lead:

Question: Do the states have the data?
Response: Yes, it is there. You have to know how to ask. One way is through a letter to the health officer, with a promise to maintain confidentiality.

Question: Could you estimate the proportion [of lead exposure] from ingestion vs. burning?
Response: We could not tell specifically. There was not enough information from the city. There were no records. Most of it was incidental ingestion of lead dust. Burning [off old paint] only occurred with abatements, but there were no records, so we could not say where it was. With fumes, the particles were suspended, and much more bioavailable. We were shocked at how Pennsylvania was handling [abatement]. Maryland had stopped burning off paint a decade before.

Regarding the comparison between public health data and the risks identified in the assessment:

Question: What were the risks for air exposures?
Response: Air risks were related to trucks queuing for 8 to 10 hours a day. There were two spikes in those areas with risk exceeding $10^{-4}$.

Question: How did you reconcile the air data with the public?
Response: The public looked at it pretty realistically. They saw that the highest levels would be where the trucks were. There was nothing we could do based on environmental law. We worked with the state and city to change truck routes and to stop queuing. We negotiated with the state, telling them that the data show that this is the source and asking them to do something else. The state changed the hours that trucks could travel on streets in Chester.

Question: The air modeling showed that the facilities were not driving the levels. Did the citizens buy that [the facilities] were not driving risks?
Response: We were looking at everything. We said it still was an unacceptable risk, but there is also a risk from consumption of fish, drinking water, etc. The citizens thought that once the results came out, the facilities would go away. We had to continue meeting and working after that.

These questions followed the presentation:

Question: How did you get started?
Response: We met with the people who had made the request of the Regional Administrator, to find out what they saw, thought, and felt. We set up another meeting with the EPA people who needed to hear this, and with other citizens who had concerns. There was back and forth about what we could and could not do. People kept coming back. Ideas started to come up. There was a lot of venting in the first few sessions. We started learning on both sides, and established a dialogue.

Question: Were there demands for individual data? Did people want to know where they were personally?
Response: People could go and be resampled at any time. They should have received their own test results when they were done. The State made more testing available.

Question: Have lead levels gone down?
Response: The State released the results from the cohort, which showed a decrease, but more needs to be done. We are not seeing [µg/dl values in the] 60s or 70s any more.

Question: Is there a mechanism for follow-up to data that obviously show a problem?
Response: To the best of our knowledge, there was individual follow-up. There seemed to be a breakdown between the city health department and the state. That was corrected with a new health officer who developed a database for recording and reporting directly to the state. Nobody had looked at it as a whole, only individually [up until then].

**Using Cumulative Risk Assessment in a Community Setting –** Hank Topper (OPP/OPPTS)

Community concerns that risk assessors try to answer include: What is causing our poor health? Is something in the environment affecting our community's health? Do we have an unfair share of environmental risk? [Slide 3]. No one can truly do a total risk assessment; even cumulative risk assessment of all environmental stressors is a subset of total risk [Slide 4]. Most cumulative risk assessments include only a subset of those environmental stressors. In explaining the role of cumulative risk assessment to a community, the basic point is that environmental stresses are only one of many factors affecting community health, and the environment needs to be analyzed in the context of those other factors, which include diet, lifestyle, and occupational factors [Slide 5]. Communities want to explain current incidences of disease, while cumulative risk assessment applies to future risks [Slide 6]. Dealing with only one of many factors means that the community will not get the results it wants. However, cumulative risk assessment can provide crucial information and help build consensus.

EPA needs to be aware of other initiatives, such as the Healthy People 2010 goal of eliminating public health disparities [Slide 7]. EPA could consider partnerships with public health people. The entire process of cumulative risk assessment should be viewed as a way to reach the community goal of risk reduction [Slide 8]. By including the goal in the cumulative risk assessment, action can be started right away on the easier targets. Cumulative risk assessment is an educational tool in that it emphasizes work in voluntary settings; the goal is to have the community working together, with its own resources mobilized, to achieve reductions [Slide 9].

Working with partnerships is key in cumulative risk assessment; EPA has a long way to go toward this [Slide 10]. The community can provide information, such as locations of dry cleaners, that would not be available through other resources. Cumulative risk assessments also need to understand the community context, e.g., in Baltimore, a project was framed as a jobs and environment study instead of an air quality study, so that the data could be used to make the area attractive to development [Slide 11]. There are many obstacles to cumulative risk assessment: new information may not be welcome; the partnership approach is not the normal way of doing business; government agencies are accustomed to acting alone; and people in communities are uneasy about uncertainties and changes in science [Slide 12]. Only long-term efforts working with communities will demonstrate the value of cumulative risk assessment and partnership with EPA; some successful partnerships already exist [Slide 13].

More practical guidance and tools are needed [Slide 14]. The Office of Pollution Prevention and Toxics (OPPT) has turned the Baltimore screening method into a document; it is a step-by-step guide to help a community build partnerships, conduct scoping, and collect information for a cumulative risk assessment for air sources. It brings together EPA, state and local governments, schools, academia, and community groups. All the important decisions are done in partnership

in this model; it gives the community ownership of the product and is an educational process enabling the community to act. The Community Air Screening How-To Manual is currently undergoing internal peer review; completion is anticipated in five or six months. OPPT is also developing Internet graphic environmental modeling (IGEMS), which will enable communities to conduct air dispersion modeling [Slide 15]. OPPT is in partnership with the Department of Defense, the Office of Air and Radiation (OAR), and others to develop a curriculum for high school teachers to use the community assessment approach to teach science and social science. Stronger coordination within the Agency is needed to improve communication [Slide 16]. EPA could fill a role nationally that is now missing. At the state level, California is developing guidelines for neighborhoods to conduct cumulative risk assessments. EPA is just beginning to learn how to use cumulative risk assessment [Slide 17]. This approach presents an important opportunity to learn how to work with and empower communities.

**Questions and Comments**

Question: As more and more communities see opportunities to get their community modeled, etc. how would you prioritize who gets the money? Is it standard across the regional offices that they have to compete for money?

Response: The bottom line is that there is little money to be given out by the Agency. [The National Institute of Environmental Health Sciences, the Department of Energy, and the Department of Defense] give out more. There is no Agency coordination yet. Partnerships in a community do not need that much money if they can draw on resources in the community, e.g., as [the community did with] Johns Hopkins in the Baltimore case study. An interagency working group would be a great forum. It would be better if they had money to sponsor work.

## Cumulative Hazard Assessment for Ambient Air Toxics in Cook County IL and Lake County IN – George Bollweg (Region 5)

Today's case study will include no results, as they cannot yet be made public due to an agreement with participants [Slide 1]. In this study, the term "participant" will be used rather than stakeholder as not all participants are stakeholders, and vice versa [Slide 5]. The Cumulative Risk Initiative (CRI) resulted from a Toxic Substances Control Act (TSCA) petition filed in Region 5 [Slide 6]. Incineration was proposed as a fix for solid waste problems in northern Illinois and Indiana. The communities wanted the problem to be approached collectively, since people could be exposed collectively. The case study was initiated as a pilot project in 1997.

The two-county study area encompassed about 1,450 square miles, a large area in which to do a cumulative risk assessment [Slide 7]. There were eleven petitioner participants (all but one from Illinois), six state and local government participants, at least six EPA offices, and Argonne National Laboratory [Slides 8, 9]. Initially, there were serious trust problems; for instance, EPA needed to persuade the petitioners that the state and local agencies should be involved.

There were three phases to the project: scoping, conduct, and peer review/completion [Slide 10]. In the scoping phase, the non-petitioner public and industry were excluded; petitioners feared that involving industry would overwhelm the process or drive the assessment in the wrong direction [Slide 11]. The basic structure of the study followed the 1997 Science Policy Council (SPC) Guidance. The components of the CRI included an environmental loadings profile or multimedia pollution and emissions inventory, which cast a very broad net [Slide 12]. There were also petitioner workshops and meetings for planning and scoping.

Scoping for the CRI changed the approach from risk to "hazard." [Slide 13]. The original plan was to consider two neighborhoods, but the petitioners wanted the assessment to be relevant to the entire study area, despite its large size. Scoping also changed the focus from a cumulative risk assessment to a hazard assessment of outdoor air toxics, because air was the best documented of the media and was also most relevant to the entire area [Slide 15]. During scoping, determinations were made that the assessment would: rely on already available information, focus on EPA-regulated sources, focus on children, not link health data to releases, and exclude some diseases when data were inaccessible or missing [Slide 16]. The scoping process also excluded human exposure assessment, indoor air exposures, ingestion and dermal hazards, microbial agents, genetic susceptibilities, lifestyle hazards, and social hazards, to focus on things that EPA regulates [Slide 17].

The study assessed cumulative human inhalation hazard of EPA-regulated outdoor air toxics in the study area [Slide 18]. To assess impacts on children, Toxics Release Inventory (TRI) data were "overlaid" with the location of schools in the study area [Slides 19, 20]. The Risk

Screening Environmental Indicators (RSEI) weights from OPPT are toxicity data, applied to the TRI to generate toxicity-weighted emission numbers [Slide 22]. Those that show up consistently higher are identified. Comparison levels are applied to ambient monitoring data or model predictions. Assessment results are presented in formats that attempt to integrate the information [Slide 23]. Peer review occurred late in the project [Slide 24]. To complete the assessment, communication materials will be produced; the Programs, Region 5, and state and local agencies will agree on risk/hazard management steps; and the assessment will be made available to the petitioners and placed on the Internet [Slide 25].

Participants influenced the scope and direction of the assessment by defining the analytic and deliberative parameters, including exclusion of the non-petitioner public and industry, the focus on hazard instead of risk, the focus on children's health, and the focus on inhalation of air toxics [Slide 26]. Participants also influenced the design of the assessment, i.e., the use of existing data, and the inclusion of health information that was not connected with pollution. However, in the external peer review process, reviewers did not accept all of these scoping decisions and design constraints, even though those involved with the study did; other assessors need to be aware that this is a possibility [Slide 28].

In the deliberative part of the project, the lessons learned were that excluding stakeholders is risky, a big project has big management needs, and plans for closure are helpful [Slide 29]. On the analytic side, the large scoping effort was good, but the study was still difficult to complete, despite the exclusions. The long planning and scoping phase was well done and redirected the assessment; the technical and managerial needs of a project this size should not be underestimated; and it is sometimes necessary to acknowledge that certain data will just be presented, not combined, in an assessment [Slide 30].

**Questions and Comments**

Question: Was indoor air considered?
Response: Since 90% of people's time is spent indoors on the average, excluding indoor air removes a lot of exposure. The reason it was not done is lack of regulatory authority.

Question: Could a whole new target for cumulative risk assessment be city managers? They could build it in proactively into their planning, [instead of using] it when things crop up in response to a problem.
Response: Zoning is a big issue. The problem is often stupid planning, such as building sites next to where people will be. People worry about things [that are] next to where people live.

## Breakout Groups: Discussion of Stakeholder Involvement

Workshop participants signed up for one of four breakout groups to discuss topics related to stakeholder involvement. After the one-hour session, participants reconvened, and each group reported the conclusions it had reached to the workshop as a whole.

### Breakout Group 1 – Problem Formulation

Group 1's charge was to consider issues such as bounding the analysis, developing hypotheses about possible cause and effect relationships, and recognizing who should be involved. A common, repeated theme of Group 1's discussions was that clarifying the purpose of the assessment is important. With respect to bounding or limiting the scope of the assessment, the group recommended developing a rationale that can easily be communicated later. They noted that when limiting the scope, it is important to not lose sight of the big picture. The most important research needs identified by Group 1 were having a clearinghouse for all [useful] data, developing a method for apportioning sources of exposure, and conducting more research to link cause and effect (e.g., fingerprinting releases or exposures and linking them to a source). When these were reported back to the workshop as a whole, there was discussion about what was meant by "all" the data, and about issues related to such a repository, such as cost and data quality.

### Breakout Group 2 – Stakeholder Involvement

Group 2 was charged with addressing issues including stakeholder participation, communicating cumulative risk to the public, defining fundamental principles of participation, and education / interaction. In their discussion of forming representative stakeholder groups, Group 2 identified a need to share information on determining what constitutes a representative group. The goal is community consensus on cumulative risk assessment, actions, and outcomes. Group 2 suggested interaction with non-governmental organizations (NGOs); building better cross-agency networks; extracting information from case studies; and developing an interactive web site or newsletter as ways to achieve this. A research need in this area is in how to develop a representative subset of the community to serve on cumulative risk assessment groups. Another research need identified by Group 2 was for better ways to communicate the limits of the science associated with cumulative risk assessment. What is needed is something easy to understand that qualitatively describes what cumulative risk assessment can and cannot do. Group 2 also called for a basic educational tool that could be used in giving communities an overview of their risks. The last research need identified by this group was for a compendium or clearinghouse of environmental health facts, such as chemical fact sheets, etc., with links to relevant case studies.

**Breakout Group 3 – Cumulative Risk Conceptual Models**

Group 3 was asked to consider topics such as sources, stressors and agents, pathways or routes of exposure, receptors, and endpoints, in the context of data sources, data quality and uncertainty, averaging periods, rationale, and defaults to fill data gaps. The group called for a template or consistent standard approach, e.g., a simple conceptual model that would be a starting point upon which other models could build. Group 3's second major idea was for decision matrix templates to train stakeholders to identify the most important issues and use them as input to a conceptual model. The third recommendation was for a national database with exposure data on various media, as models are currently limited when data are not readily available.

**Breakout Group 4 – Community Issues**

Group 4's charge was to consider environmental justice and special considerations for sensitive or highly-exposed subpopulations. Seven research areas were identified as important; the group voted on them and presented them to the workshop in order of importance. The most votes were cast for research into factors that make populations vulnerable. Developing verifiable public health indicators and identifying common elements in cumulative risk assessment case studies, such as those presented at the workshop, tied for second place in the voting. The remaining research areas that the group identified were: filling in data gaps for children (e.g., toxicity and exposure, adult-child differences); guidance on how to interpret available information; more attention to synergistic effects, which are at the heart of cumulative risk; and monitoring of real-life situations (such as pesticide runoff) to see if effects occur.

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# SESSION III: APPROACHES TO CUMULATIVE RISK ASSESSMENT

Co-chairs: Roseanne Lorenzana (Region 10) and Jane Gallagher (ORD/NHEERL)

## Health Risk Assessment of Chemical Mixtures – Richard Hertzberg (ORD/NCEA)

Conflict exists among work on mixtures, on cumulative risk, and on interactions among chemicals. The 1986 guidelines document on mixtures and the 2000 supplement (which includes interactions) lead to a sense in ORD that there is no need for more work on mixtures. This contributes to a fallacy, that if cumulative risk is equivalent to mixtures, then no additional work is needed, when there are actually many issues requiring work.

A mixture is defined as any two or more chemicals contributing to the same toxic effect [Main Slide 3]. The two chemicals can be in different media, have exposures at different times, or cause different effects when alone, but there must be some overlap in media, metabolic pathway, or target tissue. EPA's 2000 risk guidance on mixtures provides information on how to deal with substances like arochlor or gasoline, where the stability of the mixture and how the exposure will occur are known [Main Slides 5, 6]. The guidance allows opting out, or doing something qualitative, and thereby reaching a conclusion about the likelihood of health or environmental effects.

One common simplification when dealing with mixtures is the assumption of similarity [Main Slide 8]. Information on a similar mixture may be available, allowing it to be used as a surrogate. Surrogate mixtures can be close in composition, have the same mode of action (e.g., dioxin), or be a group of similar, chemically-related mixtures, such as arochlors or polycyclic aromatic hydrocarbon (PAH) combustion emissions. A second simplification is the assumption of independence of action, e.g., for carcinogens causing tumors in different organs [Main Slide 9]. The toxicity of one component of a mixture is assumed to not influence the toxicity of the other components.

Several types of additivity can be considered [Additivity Slide 1]. Dose addition, or cumulative exposure, allows the addition of doses by treating chemical 2 as the same as chemical 1; different potencies are addressed by adjusting the doses, e.g., if chemical 2 is twice as potent as chemical 1, a dose of chemical 2 is equal to two doses of chemical 1. Uncertainty arises when dose-response curves are not reliable; it is also necessary to have a good sense that the two chemicals are similar. Response addition, the method in the cancer risk assessment guidelines, is the addition of risks, with the assumption of toxicological and statistical independence [Additivity Slide 2].

Dose addition simplifies the assembly of dose-response curves [Additivity Slide 4]. It assumes the same mode of action as well as similarly-shaped dose-response curves for all the components

of the mixture and is best at low doses. When dose addition is assumed, a joint dose-response model can be built using single chemical data [Additivity Slide 5]. Dose addition is used in calculating the Hazard Index (HI), which is a summation of the estimated intake divided by the reference dose (RfD), to scale for toxic potency [Additivity Slide 7]. In application, a HI = 1 is generally not considered a concern; for a HI = 2, the level of concern depends on how good the RfD is. However, the regions are not consistent on how they take action based on HI values.

There is no good quantitative indicator of uncertainties for component-based approaches; considerable judgment is needed in mixture risk assessments, and the assessor should try to express the uncertainties whenever possible [Additivity Slide 8]. An interaction-based hazard index includes the questions: What are the toxicologic interactions? When should interactions be included? How can we quantify interactions? And, can we evaluate prediction accuracy [HI Slide 1]? An opportunity exists to make useful definitions for synergism; the HI is the default, no-interaction approach [HI Slide 2]. In the wake of the retracted Tulane research that showed unanticipated 1,000-fold interactions, attempts have been made to quantify interactions; there is much qualitative discussion, but little quantitative information, in the literature.

The formula for hazard index looks like that for dose addition; since it does not include interactions, it is not by itself particularly useful [HI Slide 4]. To quantify interactions, a weight-of-evidence approach, in which each hazard quotient is multiplied by a value reflecting the interactive effects of all the other chemicals, can be applied [HI Slides 5, 6]. The interaction adjustment can take into effect how the interaction changes with different proportions of the chemicals in the mixture [HI Slide 7]. When the weight-of-evidence scores are used, the farther away that the data are from human data, the less weight is placed on them [HI Slide 8]. More proof is also required for antagonism among mixture components [HI Slide 9]. For instance, at the Region 3 Palmerton site, the question was raised if the presence of zinc at the site allowed a reduction in the lead soil standard, since zinc inhibits lead and cadmium. However, since the data on this antagonism came from a study of testicular atrophy, but the lead regulation is based on neurodevelopmental effects in children, the determination was made that the lead standard should not be reduced.

Mixtures risk assessment and cumulative risk assessment will always be combinations of scientific information and judgment; however, there is concern that too many issues will be dismissed, because “we don’t know enough,” or “it’s not important” [HI Slide 14]. It is difficult to evaluate the accuracy of predictive methods; there are few good studies to say that interaction research or the HI work very well. An example of mixtures risk assessment is that for Picloram, where interactions, but not toxicity, occur in the kidney. In a mixture with 2,4-dichloro-phenoxyacetic acid (2,4-D), the exposure shifted in time to occur later. There was a 100-fold synergistic effect at low doses; the major interaction was lost, so this was not meaningful [HI Slides 16-19].

How often does synergism occur [HI Slide 25]? A review of the literature shows that it is not just positive reporting bias; a lot of studies show antagonism, or combinations of synergism and antagonism at different doses. There are very few inhalation studies of interaction, which poses a problem when dealing with air issues. Synergy magnitudes are not large; and must be taken in context, i.e., the route, dose, or test animal may not transfer to humans. There is some interaction data on over 600 chemicals; priority chemicals can be put into a decision approach, even if it is just using the HI as a decision trigger, although additional research is still needed.

**Questions and Comments**

Question: I can see how this would apply to Superfund. Are there applications to air (where there are so many more chemicals)?

Response: The best example is water. There are problems with ambient air exposure estimates, e.g., duration, order. If there were better exposure estimates, we could do a good job with air. This workshop should help in moving forward. We can look for common combinations that occur, e.g., in inner cities. Now, we are only looking at combustion products: diesel, wood, coal, cigarettes. We are doing comparisons now, such as the study at Lovelace. There are about a dozen chemicals that show up a lot in Superfund sites. For instance, iron is very high, which was a real surprise. To have a similar thing for air would be very good.

## OAQPS Case Study: Toxicologic Independence – Initial NATA National Scale Assessment – Deirdre Murphy (OAR/OAQPS)

The National Air Toxics Assessment (NATA) is one of the four primary components of the Air Toxics Program; it includes modeling at multiple geographic scales, such as the initial national-scale modeling attempt that will be discussed in this talk. The goals of the national-scale assessment have not changed since the planning and scoping document was developed in 1999. They include: to identify air toxics of greatest concern; to characterize contributions of different emission sources to exposure and risk; to prioritize collection of new data; to provide a baseline for tracking trends and measuring progress; and to assist in scoping for smaller-scale assessments [Slide 4]. The assessment is a backdrop that informs regulatory decision making.

The conceptual model developed for the assessment allowed consideration of everything that might be considered relevant, from which everything within the scope of the assessment was identified [Slide 5]. The initial assessment focused on outdoor sources and extrinsic (outdoor) background sources, but not indoor sources. The assessment was also restricted to chronic inhalation exposures, 1996 emissions data, 33 urban hazardous air pollutants (HAPs), and calculations at the level of census tract [Slide 6]. In choosing the HAPs, diesel exhaust particulates were added and dioxin dropped (because its risk was not driven by air exposure) [Slide 7].

The emissions inventories used in modeling, which are key to the quality of the assessment, included the 1996 National Toxics Inventory (NTI), the 1996 VOC in National Emissions Trends Inventory, and the 1996 Heavy Duty Diesel Rule Inventory [Slide 9]. Emissions estimates from sources were put into the HAPEM4 model. Dispersion was considered, but deposition was only minimally considered due to the assessment's restriction to the inhalation route of exposure [Slide 10]. For each cohort within each census tract, the model was used to predict breathing zone concentration for the simulation period; time activity data and microenvironmental factors were also included, and lifetime (70-year) exposure estimates were derived [Slides 12, 13]. There is a large data-management component to the assessment, with some 61,000 risk estimates calculated for each of 29 carcinogens and 61,000 hazard quotients (HQs) calculated for 27 substances with noncancer endpoints [Slide 14]. Cancer risks were aggregated in three ways: those based on human data, those based on animal data, and all carcinogens [Slide 15]. An interesting effect emerged for respiratory irritation, and a hazard index (HI) was calculated as the sum of eight HQs.

The data from the assessment can be summarized in charts that reflect the level of confidence in the exposure estimates, the cancer risk estimates, and the noncancer risk estimates [Slides 16-20]. The initial national-scale risk characterization showed that the national drivers of cancer risk were benzene, chromium, and formaldehyde, and that arsenic, 1,3-butadiene, coke oven emissions, and POM were important in some places (regional drivers) [Slide 21]. Acrolein was

identified as the single national driver for the respiratory irritation HI. Regional drivers included acetaldehyde, arsenic, 1,3-butadiene, formaldehyde, and manganese. The objective was to identify the air toxics of highest concern: there was higher confidence in the benzene values due to the newer risk estimate and better exposure data. A number of chemicals (hexachlorobenzene, lead compounds, mercury compounds, methylene chloride, PCBs, propylene dichloride, and vinyl chloride) were not found to be drivers or contributors [Slide 22]. However, these pollutants are not exonerated, for several reasons: the assessment included only inhalation exposures, and other routes may be more important; the resolution was low, and hotspots may not be identified; and only typical exposures, not individual extremes, were considered.

In conclusion, the Initial National-Scale Assessment does not answer all questions, but does help in identifying the air toxics of greatest concern; characterizing contributions of different sources to exposure and risk; prioritizing the collection of new data (e.g., what can be done to improve those areas where confidence is low?); and providing a baseline for assessment of trends and progress toward goals [Slide 23].

**Questions and Comments**

Question: The public views air toxics as a toxic soup, and wants us to address interactions. NATA shows that a few chemicals are driving risk, and not that the cumulative effect is great, so a focus on reducing those drivers may be a better approach.
Response: As a first step, that might be the general national approach. In particular areas, there might be some particular sources. It is perhaps logical to take care of the drivers, and then see what it means to cumulative risk when they are gone.

Question: The assessment does not include synergy?
Response: It is a straightforward summing. We assume [risks] are additive.

Question: [Can you provide] more information about the diesel component?
Response: Diesel particulates were included in the assessment. We did not quantify cancer risk, because the Agency has concluded there is insufficient information to do so; the ORD diesel health assessment document concluded it was a likely human carcinogen. We were unable to assign carcinogenic potency, and the dose-response is lacking. A study is under way to get those data. The possible range of upper bound risk is $10^{-3}$ to $10^{-5}$. Diesel particulate matter (PM) contributes to $PM_{2.5}$ noncancer concerns.

Question: Will there be changes in the future?
Response: Definitely. We are looking at concentrations distant from primary sources. We set those the same for all census tracts, but it has to vary. We were hoping in 1999 to have regional varying background concentrations, rather than a national background concentration. Initially, we did not have background concentrations for all pollutants.

Question: Where did you find background data?
Response: Through literature reviews and ambient concentrations observed at distant sites. The NATA web site shows the background concentrations we assumed and the references.

Question: Where does arsenic come from as a driver?
Response: There are a lot of different sources, including combustion and smelters. In addition to the significant soil sources, the sources are more diverse for air.

Question: Diesel was not a national driver in the assessment, but according to California it accounted for 75% of the risk in the Los Angeles area.
Response: We talked to the SAB about diesel for some time. The draft of the assessment had diesel as a driver. The SAB said that while we know a lot about diesel, we have some gaps, so the risks for diesel were not quantified.

Question: How good do you feel about the mercury numbers? In the 1999 study, mercury was included in the 2000 TRI. There were limited emissions data before.
Response: [Referring to the charts] We had low confidence in some part of the data going in. The TRI is at the bottom of our list [of data sources], but it would fill gaps. The emissions inventory group would be the ones to decide. We are trying to be consistent in not mixing data.

Question: Are you looking at how MACT (maximum achievable control technology) would impact the drivers?
Response: Yes, we want to project the impact. There are some comments on the web site, but no specific analysis yet. This is very important.

Question: What is the basis of your confidence determinations?
Response: The confidence in exposure was shown. There was also dose-response information. [The determinations were based on] marrying of exposure confidence with confidence in things like the RfD and the size of census tract, e.g., how large an extrapolation are you making? Some of it was qualitative. We tried to explain it as well as we could on the web site. We are hoping to have a more elaborate uncertainty analysis in the 1999 assessment.

Question: You said that ambient concentrations of metals were significantly underestimated; could you explain?
Response: Some had monitoring and modeling data. We were looking at locations for each chemical where we could do a comparison. For benzene, there was good agreement; for lead, cadmium, and chromium, there was not good agreement. Are we missing

particular sources of metals? Are we missing something in our modeling? There are a lot of places to look at, and we wonder about the inventory.

Question: There was no contribution from hexachlorobenzene. What sources were included?
Response: There might be negligible risks. We looked at the inhalation pathway and air sources, not at soil and incidental ingestion of soil or ingestion of fish. I do not know if the emissions inventory includes volatilization from pesticides. We are estimating some emissions nationally, but the cancer and noncancer risk calculated under the parameters of this study are low.

Question: Exposure modeling underpredicts personal exposures for many chemicals. How did you use personal monitoring data?
Response: Not very well. We took some to the SAB; it was not clear what we could say about it. Most monitoring studies are just a week; how do they compare with longer-scale averages? In the 1999 assessment, we want to do more elaborate things and get a look at subpopulations; we may do better with the monitoring data.
Comment: There should be a lot of information in the personal monitoring data.
Response: If you look at the web site, there should be information, [namely] what we took to the SAB in the external review document.

Question: You can push the envelope with a tool like this. Imagine looking at oral exposures, fish consumption, chemicals in fish. Could you overlay the analysis with highly exposed sensitive populations? Is this a tool that could come up with estimates to incorporate these other factors?
Response: To add an ingestion-related risk? We are trying to look at the non-air pathway. We know that air is not where it is happening. It is hard to see how to do that in a national-scale assessment. We are thinking about the options of how to do it. We need multimedia modeling [to address, e.g.,] how much in the fish came from the air. We could also try to add indoor sources, but that is stuff that comes from the outdoor air. We know that is a huge limitation.

**Biomarkers: Approaches / Status / State of the Science –** Jane Gallagher (ORD/NHEERL)

Biomarkers can be classified as markers of exposure, such as lead in blood or urine; markers of effect, such as polycyclic aromatic hydrocarbon (PAH) DNA adducts or induction of gene expression; or markers of susceptibility, such as elevated enzyme activities [Slide 5]. The great hope of biomarkers is that they will integrate exposure and effect to move toward an understanding of clinical disease [Slide 6]. The pathway from exposure to effect can be broken down further into steps including exposure, internal dose, biologically effective dose, etc.; biomarkers offer a way of filling in the steps [Slide 9]. In the risk assessment process, biomarkers can help identify subpopulations that may be at elevated risk; lower uncertainty by providing direct measurements; and provide insight into the shape of the dose-response [Slide 10].

Several factors influence the validation of biomarkers: significance, specificity, sensitivity, knowledge of background exposures in the general population (e.g., for DNA adducts), knowledge of confounding factors, and estimation of interindividual and individual variation [Slide 12]. Activation, detoxification, and elimination all interact with susceptibility and affect exposure responses [Slide 14]. Differences in cancer incidence in ethnic and racial groups illustrate differences in genetic makeup, although sociodemographic factors and other issues are also involved [Slide 15]. Genes impact functional aspects of metabolism and detoxification; the tendency is to look at many genes simultaneously to get at the role of genetics [Slide 16]. Challenges and limitations of biomarkers include that most have a baseline response that is observable in a population without a specific exposure to a toxic chemical; validation is lacking for most; and a biomarker may not measure all sources, or may measure other exposures that are not of interest [Slide 17]. Human DNA adducts are of interest because they are both a marker of exposure and a marker of effect; they can be used to characterize exposures from PAHs, nitrosamines, mycotoxins, aromatic amines, UV light, alkylating agents, and chemotherapeutic agents [Slide 18]. Some of the best research on PAH-DNA adducts from environmental exposures is the work by Perera and colleagues in areas of Poland where the air is highly polluted [Slide 21]. EPA often has to validate biomarkers in locations where exposures are significantly greater than exposures in the U.S., such as Mumford's work with smoky coal emissions in China [Slide 23]. A battery of endpoints is being employed to capture the net effect of exposure over several mechanisms of action or classes of chemical [Slide 25].

Another area of biomarker research is into the use of human surrogate cells or fluids and markers. These include nasal lavage fluid and cells, bronchoalveolar lavage fluid and cells, and blood plasma and cells [Slide 32]. A promising new surrogate is the infant fingernail; current research is extracting DNA and examining activating, detoxification, and repair genes [Slide 33]. Sputum has been examined for p53 antibody in cancer patients, as have buccal cells in persons exposed to arsenic [Slides 34, 35]. Nasal lavage has been used to study the effects of diesel

exhaust particulates (DEP) instilled into the noses of nonasthmatic subjects; the endpoint of interest is infiltration of inflammatory cells [Slide 36]. Breast milk is another fluid that can be studied for biomarkers; e.g., a pilot study of fractionated breast milk from 25 women found that 88% of samples were mutagenic in the Ames assay [Slide 38].

In biomarker research, the scales are beginning to tip toward looking at what people are exposed to – not just single tests, but an entire battery [Slide 40]. The availability of funding in genomics (the study of all the genes in a cell or tissue at the DNA, mRNA, or protein level) is driving research programs, and EPA is looking for a niche in this area [Slide 42]. Current research in proteomics is examining the profile of proteins in drops of blood over time. Other ongoing research on the toxicogenomics of water disinfection byproducts is looking at genes by their function [Slide 45]. Research in this area contributes to the interest in getting from exposure to effect and asks what happens at the target tissue level [Slides 46, 47].

The technology in this area is driving the science, and progress in this direction is inevitable [Slide 50]. However, the work is far removed from what people really do in the regions, and there is a struggle to make the work more applied [Slide 51]. One model already in use is Risk Screening Environmental Indicators (RSEI), developed by the Office of Pollution, Prevention, and Toxics (OPPT), which tracks potential risk-related impacts of chemical releases and transfers [Slide 52]. This model allows carcinogens, metals, high production volume chemicals, and priority chemicals to be considered [Slide 53]. It addresses cancer and noncancer effects, but not acute toxicity [Slide 58]. Regional drivers can be identified through chemical ranking by health score [Slide 61]. Priority ranks for industries can be calculated using toxicity factors and population impacts [Slide 62].

**Questions and Comments**

Question: Can you make some general comments about utility?
Response: Looking at lead and aflatoxin, they are good examples. The technology regarding parent compounds and metabolites is advancing fast. We will see success here.

Question: Other than the inhalation chamber studies with particles that you mentioned, what combination of stressors are you introducing?
Response: Most of our work focuses on PM, namely diesel, and comparison to other complex mixtures. We are looking at children in the cohort study, asking whether stored biomarker samples can be used to look at exposures from birth to age 21. We are trying to validate methodologies, e.g., for blood, toenail, buccal cells for arsenic. We are validating new methodologies like reactive oxygen species (ROS). These are very expensive methodologies, which is the biggest limitation.

Question: Is exhaled air another biomarker?

Response: NHEERL is looking into using exhaled air as a biomarker, but we are running into some difficulties. Swedish researchers are also looking at it. The problem is, what is on the breath indicates endogenous processes, and issues of background are important.

**Revised Cumulative Risk Assessment: Organophosphorous Pesticides –** Anna Lowit (OPP/OPPTS)

The Food Quality Protection Act (FQPA) mandated cumulative risk assessment for pesticides (by 2006). This makes the Office of Pesticide Prevention (OPP) different from other EPA offices. [Slide 4]. OPP reached out to stakeholders and achieved a high degree of public participation [Slide 5]. The Science Advisory Panel (SAP) provided advice on dose-response and hazard, exposure assessment, and other methodological issues [Slides 6-8].

The cumulative risk assessment started with the determination of a common mechanism group, the organophosphorous pesticides (OPs) [Slide 10]. The first paper on OPs was done in 1999, using cholinesterase (ChE) inhibition in the brain and peripheral nervous system as the common endpoint. All the OPs are ranked by their ChE inhibition potency compared to an index chemical; exposure equivalents of the index chemical are summed up in the cumulative risk assessment. [Slide 11]. The index chemical is methamidophos, the most structurally simple, and not the most potent, of the OPs [Slide 12]. Unlike other OPs, its ChE inhibition is highly characterized; male, female, adult, and juvenile animals show equivalent sensitivity, and potency levels are identical for blood and brain.

FIFRA provides enormous amounts of data on brain ChE inhibition; female rats are used because they are more sensitive [Slide 15]. The data used are for durations of exposure of 21 days or greater [Slide 16]. Monitoring data suggest that several years ago, human exposures occurred on a regular basis. Since OPs act in an irreversible way, ChE will stay inhibited until the molecules "turn over." Because exposures are continuing, the body comes to some unknown steady state at about 20-30 days, which is best reflected by studies of 21 days or more. Dermal and inhalation data were used [Slide 17]. As a measure of relative potency, the $BMD_{10}$ for oral administration was used; this is the dose at which ChE activity is reduced by 10% compared with the background level of ChE activity [Slide 18]. The data quality was insufficient to allow modeling of BMDs for dermal and inhalation exposure, so comparative effect levels (CELs) were used. The $BMD_{10}$ was used as a point of departure for modeling [Slide 19]. Two 2-year and two 90-day studies were used for modeling; the agreement among the data was exceptionally close [Slide 20]. The studies could be combined because both represented steady state conditions; this allowed all the available data to be used [Slide 21]. The literature does not allow the question of whether dose-additivity is a good approach for modeling ChE data to be answered; science and judgment play a role, e.g., if dose-response curves are not the same shape, should relative potency factors be calculated [Slide 22]? The potency of OPs varies over five orders of magnitude [Slide 23]. Confidence is high in the points of departure for the methamidophos $BMD_{10}$ because the lower limits are close to the central estimates [Slide 25].

The FQPA also provides for an additional 10X safety factor; this is an unusual requirement [Slide 27]. Intended for protection of children, the additional 10X factor results in a starting

safety margin of 1,000. FQPA safety factor guidance is structured around three areas of analysis that are taken into account in doing a cumulative risk assessment: the completeness of the toxicity data, the degree of concern for pre- and postnatal toxicity, and the completeness of exposure data [Slide 28]. The analysis focuses on common mechanism of toxicity and effects in the young [Slide 29].

The food assessment component included 22 OPs; residues on many major foods were analyzed under the assumptions of a national diet and no seasonal dietary variation. [Slide 32]. Separate assessments were conducted for children 1-2 and 3-5 years of age and adults 20-49 and 50+ years of age (because there are no OPs in baby food, there is no exposure for children less than 1 year, and teens were considered to generally eat like adults) [Slide 33]. Monitoring data for residue concentrations came from the USDA Pesticide Data Program [Slide 36]. Children's foods were targeted, and included fresh fruits and vegetables, canned and frozen vegetables, grains, dairy products, and some processed foods (e.g., peanut butter) [Slide 37]. FDA monitoring data were used for eggs, seafood, and meat [Slide 38]. Residue estimates were found for almost 97% of the diet of children in the cumulative assessment [Slide 39]. Information on individual consumption came from the Consumption Survey of Food II [Slide 41]. The Dietary Exposure Evaluation Model (DEEM-FCID™ from Novagen Sciences) was used to back-calculate pesticide residues using recipes [Slide 42].

When exposures are considered for the population age groups of interest, the highest exposures are seen in children aged 1-2 years [Slide 43]. Using the DEEM model, the individuals who made up the high ends of the distribution were examined; this allows checking for errors, or for unusual characteristics, such as someone who eats three apples per day, or the "squash baby," reported to eat one pound of squash [Slide 44]. Relatively few chemical or crop combinations were found to play a major role in the OP cumulative risk assessment [Slide 45]. The most significant chemicals in the top 0.2 percentile of exposure for children age 1-2 were dimethoate / omethoate, azinphos-methyl, acephate / methamidophos, methamidophos, phosmet, and phorate [Slide 46]. Approximately half of the exposure in the highest percentile was due to dimethoate / omethoate, which is still in risk mitigation, so exposures are highly likely to decrease. The three most significant foods were uncooked fresh grapes, pears and apples [Slide 47].

The drinking water assessment, which was less important because there was the least exposure by this route, looked at daily distributions of residues and was done on a regional scale [Slide 49]. The highest water and home exposures were seen for Florida, where there is high pesticide use year round [Slide 50]. The assessment found that drinking water was not a major contributor to total cumulative risk [Slide 53]. The residential exposure assessment started with 17 OPs with residential or public area uses [Slides 55, 56]. Of the uses identified as still important, DDVP, used as pest strips in home closets and cupboards, was identified as a risk driver for indoor use in the residential exposure assessment [Slide 57]. This is the only remaining indoor use of OPs and is in risk mitigation [Slide 64].

The three assessments were put together into a cumulative risk assessment; it is important that the estimated exposures were integrated or combined in an internally consistent manner to develop region-specific pictures of risk [Slide 67]. Potentially exposed persons needed to be tracked on a daily basis to preserve appropriate linkages [Slide 69]. DEEM™ / Calendex™ was used to provide a probabilistic assessment with appropriate matching [Slide 70]. Time-sensitive residential and water exposures were integrated with exposures from food and potency factors to allow the data to be viewed across time and across percentiles of exposure [Slide 71]. Food was a driver for risk, because residential exposures are gone except for inhalation exposure to DDVP, which is also a driver [Slide 73]. The cumulative assessment considered food, water, and residential exposures probabilistically; it reflected realistic pesticide use based on pest pressures, weather, activity patterns and other factors, while preserving temporal and spatial characteristics. [Slide 75]. The result of the assessment is a time-based exposure profile of exposure (total or for various pathways) at any selected percentile [Slide 76]. In terms of risk characterization, the OP cumulative assessment represents state of the art advancements in risk assessment methods. [Slide 77]. Under the FQPA, the next common mechanism groups to be assessed include the N-methyl carbamates, the triazines, and the chloracetanilides [Slide 78].

**Questions and Comments**

Question: There has recently been concern over the disposal of birth control patches, that is, whether they can leach into streams and lakes. Is the same true for pest strips? Do they become an ecological contaminant?
Response: I am not sure that has ever been looked at.

Question: If residential exposures are no longer considered, what does that mean?
Response: Existing risk assessments show that chlorpyrifos is a problem. Assessments are being done on what is left [post-mitigation] to be sure it is not a problem.

Question: Are there pesticide use data from the USDA for agriculture data on purchase or use agriculturally?
Response: There are data on purchase.

Question: Was the variability in food exposures mostly from variability in residue or in the diet?
Response: Both. The residue data have many zeros because there were so many that were nondetectable. That creates variability. There is also interindividual variation in consumption.

Question: How do you address the nondetectables?
Response: For a single chemical., we used half of the detection limit. In the cumulative risk assessment, it defaulted to zero. This could be an area to look at. There is some sensitivity analysis to be done.

Comment: Imported apple juice has lots of pesticides.
Response: This assessment includes both imports and exports. There are 5,000 pages on the EPA/OPP web site, including that information.

Question: [Regarding safety factors]
Response: We are using three criteria: how well we characterize exposure, the completeness of the database, and pre- vs. postnatal toxicity. We feel that we are doing the best we can to characterize. Each [criterion] is [approximately] a third of [the protection factor of] 10. For the common mechanism, we think our database is really complete. For pre- and postnatal exposures, the concern is the common mechanism. How we looked at ChE data was that several years ago, OPP called for data on developmental neurotoxicity studies to be supplemented with ChE data. We only received six of those studies. A combination of the existing data, the literature, and NHEERL data suggests that three-fold is a reasonable average. This is a point that the SAP discussed in depth: is it adequate, underprotective, [or if you] can not make an average. We hope more developmental neurotoxicity studies will come in; we are still working on it.

**Traditional Tribal Lifeways Paradigm –** Vivian Parker (California Indian Basketweavers Association)

Indians in California are concerned about pesticide use, particularly about the millions of pounds used on national forest lands. Through the Tribal Science Council, EPA has a tremendous reputation with the tribes for being a leader in environmental justice. Each region has tribal coordinators and environmental liaisons. Since some tribes are only now hiring their environmental coordinators, the potential to make progress is huge at this time. A subcommittee of the Tribal Science Council has developed an alternative to risk assessment based on the Native American perspective of wellness and health. Health is a strong aspect of traditional Indian culture, and has spiritual as well as physical, mental, and emotional components.

Mohawk tribe member James Ransom has been key to the development of the alternate paradigm. The canoe is key in the Mohawk culture, and is used as a symbol, a "holder of culture," in the paradigm. In the traditional tribal lifeways paradigm, the tribes plan to go into tribal communities, do interviews with elders and traditional practitioners, and get the information that forms the "canoe" (or "basket" for California tribes). The information includes the tribe's relationship with the land, which is inseparable from Native American culture. Furthermore, because they are intertwined, if the land and water are not healthy, the people are not healthy. The process involves a return to listening to traditional practitioners. The stories will be validated by going back to the tribes to get agreement that the stories are correct. Validation will be followed by analysis to see how applicable the stories are. The tribes would like for EPA to analyze the paradigm. There are no particular timelines at this time; it may take a year or more to accomplish.

**Questions and Comments**

Question: Is validation done by a tribal person? The same one who collected the story? How are stories recorded?
Response: Yes, probably by several people. The stories will probably be collected by tape recorder, then the stories will be written down.

Question: Will the analysis be taken back to the original contributors?
Response: Yes, there will be a lot of validation and consensus.

Question: What will the input be?
Response: There are many indicators. Related to the California tribes, the Klamath River salmon situation is a horrible natural catastrophe due to reduced water flow to support farming in the desert. For the California tribes that use salmon, it is integral to what they are – they have the first salmon ceremony, a world renewal ceremony – and they feel that they can not exist without salmon. They have stories about what is

healthy for them and for the environment. By documenting the stories and relating it to wellness, we can get some sort of paradigm.

Question: How will you define wellness and wholeness? Everyone has different ideas of what they mean.
Response: The stories will define wellness. It has to do with balance, the health of the land, and the spiritual connection with the land.

Comment: Lifespan is an indicator of health, and people are living longer now.
Response: That is not true for Native Americans.
Question: Are there separate health statistics for Native Americans?
Response: I am pretty sure that they have the shortest life expectancy in U.S.

Question: Diabetes is rampant among Native Americans. Is it environmental? What is the tribes' view?
Response: I can not speak for the tribes. A lot of people are changing their diet. There is a movement to restore the traditional diet, but those who are separated from connections with their people have to learn it from the beginning. [Native Americans] are trying to do it for health reasons. The basketweavers association was started in 1993 by elder masters. Part of their work is trying to restore traditional ecological techniques, such as to use burning to restore basket plants; to allow access to plant populations; and to protect plants and people from pesticide effects.

## Breakout Groups: Discussion of Case Studies and Development of Research Recommendations

Workshop participants signed up for one of four breakout groups to discuss topics related to the case studies and research recommendations. After the one and one-half-hour session, participants reconvened, and each group reported the conclusions it had reached to the workshop as a whole.

### Breakout Group 1 – Toxicology of Mixtures

Group 1 was asked to address understanding the toxicology of combinations of chemicals and how this impacts the ability to conduct a cumulative risk assessment. The group identified a need for a way to translate mixtures guidance, that is, a more user-friendly guide. There is such a wide range of judgment and so many procedures that there will be problems in consistency and reproducibility among users. Like the indirect exposure model translated for RCRA, the group suggested developing a default value (a range or a number), with documentation or a rationale to be used as a starting point, because there is too much leeway in the mixtures guidance. Second, Group 1 called for identification of common mixtures to which people are exposed, such as urban air toxics, water, food, and soil pesticides. They noted that it might be necessary to do some research into how best to define common mixtures. The group said that mixtures that are toxic enough to merit mixtures guidance treatment should be identified, although this process would be labor-intensive and costly. They suggested putting a bound on uncertainty, e.g., a factor of 5, as a bounding estimate for the kind of interaction that could occur with that mixture. While formulas are in the mixture guidance, a program office needs to turn it into a rule and make it mandatory. The third area identified by Group 1 was that the concept of mixtures seems different enough from single chemicals that it might be worthwhile to consider mixtures exposure guidance, including issues like bioavailability, guidance on how mixtures are different from single chemicals, and perhaps the development of a vulnerability factor for particulates (which might sensitize people to other exposures).

### Breakout Group 2 – Risk Assessment Approaches

Group 2 was asked to look at what methods work and what methods do not work in cumulative risk assessment. The first point the group noted was to identify sources of pollutants that are associated with an activity so that assessors know what to look for and what the risks are. The second point was to determine what specific chemical, associated with a group of stressors, tends to drive or dominate the hazard. The third was to develop a systematic way of looking at health information or integrating public health with risk assessment; since human health tends to drive the process, that information needs to be used. Other areas identified by Group 2 were: a method of presenting results and uncertainties to the public; a method of bounding uncertainties; and updating or adding data to existing mixtures toxicity databases. In terms of what does not

work, Group 2 noted that we do not have complete understanding of what cumulative risk is, and that there is at the very least the appearance that various groups are not all doing it in the same way. Also, improvement is needed in learning how to group things, e.g., a way to have a characterization without the need to do extensive literature reviews. Another concern is that the programmatic/regulatory structure does not allow crossover, so the process is not completely transparent to the public.

**Breakout Group 3 – Biomarkers**

Group 3 was asked to consider the use of biomarkers in cumulative risk assessments, including technical challenges. In terms of research needs, the most votes were cast for using a battery of assays associated with a variety of endpoints, which allows one to get farther out on the continuum from exposure to disease. The disease process is so complex, Group 3 said, that we have to get away from hypothesis-driven research and get at the impacts (cancer and noncancer) that cumulative exposure might have. Research could also go back retrospectively to identify indicators that might be predictive of an outcome. The second highest number of votes was for the pragmatic recommendation of more research to aid in identification of chemical-specific biomarkers that would allow "fingerprinting," or linking to a specific exposure or site; mechanisms also need more research. The third area identified was research to validate the use of surrogate cells and to investigate if there are more biomarkers in blood and urine at the target level. The group also recommended mining existing databases as they relate to exposure and effects markers; by looking collectively, i.e., at multiple endpoints, more can be learned about disease. It was noted that Group 3 members from the regions supported using a battery of assays (the Agency's long-term direction), rather than chemical-specific markers, which are more feasible and allow identification of drivers.

**Breakout Group 4 – Cultural Factors**

Group 4 considered cultural factors that affect exposure assessment and identification of endpoints in cumulative risk assessment. The group noted that culture is much bigger than risk. Many of the things that define culture are outside normal monitoring considerations, e.g., exceptional dietary exposures (to food types, parts of animals), genetic characteristics and disease prevalences, and ceremonial practices that have toxic exposures. Among its research recommendations, Group 4 noted that some very specific scenarios have not been considered, and identified a need to look at real field exposures, e.g., residues, and what they mean to people who are exposed. They noted that there are lots of indirect exposures, such as to natural foods, and recommended validation of the assumptions made in the various models. Group 4 said that research was needed to address the point at which a population's lack of heterogeneity alters the way toxicity factors are developed. Other research questions include the characterization of latent effects that might be carried over into multiple generations, how higher prevalence of one disease (e.g., high blood pressure) affects vulnerability to other stressors; and improved data on contaminant exposure from environmental media (e.g., in a population where people eat moose

liver). The group did not rank these factors, which they felt would affect risk calculations. They recommended thought into developing advice to be entered into the risk management process, and highlighted problems, such as that singling out a population could be considered discriminating against them or identifying them as an exception. Finally, the group raised the issue that cultural impacts, such as a culture's success over time, could be risk assessment endpoints.

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# SESSION IV: PUTTING IT TOGETHER

Co-chairs: Audrey Galizia (Region 2) and Jim Cogliano (ORD/NCEA)

## Vulnerability – Mike Callahan (Region 6)

EPA has not done a lot of vulnerability analysis in the human health area. Vulnerability is not the same as susceptibility and sensitivity: it includes those concepts, but is bigger. The dictionary definition is "open to being wounded." [Slide 2]. In application, a vulnerable person can be hurt by something that would not hurt a person in the general population, or would hurt them less [Slide 3]. Vulnerability can be due to susceptibility and sensitivity, differential exposure, differential preparedness, and differential ability to recover [Slide 4].

There is a shade of difference between susceptible (especially liable to being affected by something) and sensitive (highly responsive to certain agents); they are also both different from vulnerability [Slide 6]. The higher incidence or severity of response in a susceptible or sensitive individual or population is generally outside the normal variability of the population [Slide 7]. When dose-response curves are done, some of the outliers, or actual measurements that are higher than the bounding estimates (e.g., a child that ingests 8 g of soil per day, when the mean is 100 mg/day) do not get taken into account; this raises questions about whether the dose-response curve fits when the population is at an extreme [Slide 8]. When biological events happen, they may all be in the tail of the dose-response curve, they may occur at certain vulnerable life stages, and they may occur in people with chemical sensitivities [Slide 9]. An example would be that toluene plus industrial noise results in much worse hearing damage than would be expected if the effects were just to be added. It is thought that toluene damages the ear in a way that makes it more sensitive or susceptible to the adverse effects of noise. Differential exposure can also affect response, e.g., a person at the low end of the exposure curve, with little background, might not show much of an effect with a particular dose; however, the same dose can produce a greater response in someone in the middle of the curve [Slide 11].

Vulnerability can also be thought of as the exposure to threat plus the inability to cope [Slide 12]. The ways in which households usually cope with famine (where famine is indicative of a crisis or emergency) can be used to think about how a community copes with stressors [Slide 13]. Typical mechanisms include using household stocks and assets, transferring from other family members, reducing food consumption, using other foods, getting assistance from the community, and finally, getting assistance from the government [Slide 14]. Households seek to augment their resources, and they often diversify their consumption; however, exposure to multiple risks can undermine households' capacity to cope with future crises, and if their resources are depleted, they may not cope as well, which can lead to a downward spiral of vulnerability [Slide 15]. The inability to cope changes risk, as illustrated by the breast cancer statistics for women in Chester, PA; despite the low incidence, the risk of death was increased

due to inability to access health care [Slide 16]. In terms of differential preparedness, or "coping," boarding up a house in a hurricane can reduce damage, flu shots will protect those in the population who get them, regular health checkups will prepare people (e.g., early detection), and general health status can help a person or an ecosystem to resist insults [Slide 17]. Differential recovery can be tied to already having a disease or to lack of access to health care, and means that people will not get over an insult as well [Slide 18].

EPA has not done vulnerability assessments per se. Perhaps they are not as important for single chemical assessments. There is a question about who is being protected (i.e., in the case of deliberate substance abuse, one hears, "We're here to protect the fools, but not the damn fools"), and we can only go so far in being protective. However, cumulative risk assessment is a different kind of risk assessment; if looking at a stressed community, such as Chester, PA, we need to think about things that change the risk for the community, and not assume they are like the general population. People will support doing vulnerability assessments if they can see concrete examples of where doing one really made a difference.

**Questions and Comments**

Question: If you are not looking at stressors like smoking and drinking [in an assessment], then how do you deal with genetics?

Response: Smokers are a huge percentage of the population. By the definition, they are a vulnerable population, e.g., nonsmokers could handle an additional insult, but the smokers possibly can't. They could be considered a vulnerable population and acknowledged in the write-up. People like to exclude smokers, but they are hard to ignore in community risk assessments because they are a quarter to a third of the population.

## Ecological Cumulative Risk Assessment – Glenn Suter (ORD/NCEA)

Ecological risk assessment is cumulative risk assessment; ecologists look at the environmental context and the potential for many interactions with a toxicant [Slide 2]. Unlike human risk assessors, they also have to integrate across multiple species. Ecological effects are large, e.g., not just a change in health status, but local extinction of multiple species. The broader mandates for ecological risk assessment, such as the Clean Water Act's requirement to maintain and restore designated uses, also force a cumulative approach.

An example of a novel, site-specific assessment involves the toxic risks of new smokes and obscurants being used in military training and testing; Department of Defense and Department of Energy lands where the training occurs have more endangered species than do lands for which agencies mandated to protect the environment are responsible [Slide 4]. Very heterogeneous activities have to be combined for this risk assessment, including releases of smokes and obscurants, effects from driving tanks and wheeled vehicles, and effects of firing ammunition [Slide 5]. The framework for the risk assessment reflects the risk manager's input, problem formulation and analysis of exposure and effects for all activities, and an integrated risk characterization [Slide 6]. A framework is developed for each activity, such as effects on wildlife [Slide 7].

A relatively simple example of a standard generic conceptual model of a situation, is one for the effects of tank maneuvers on desert tortoises [Slide 8]. Estimates of the number of tortoises killed are developed based on density and other factors; they are fed into the model to look at effects on tortoise abundance. Habitat effects, such as the crushing of plants, are also fed into the model. Plants are considered as a separate endpoint with their own exposure-response relationships. A logic diagram allows for examination of effects including spatial / temporal overlap among the activities [Slide 9]. If there is overlap, then the agents can be screened to determine if any are inconsequential. If none can be excluded, then mechanism of action is considered; for acute lethality of tortoises, the numbers killed by tanks, humvees, and mortars are simply added. Finally, a mechanistic model can look at how loss of habitat and acute lethality interact to affect the population, e.g., if the habitat is damaged to the point that the population cannot compensate for deaths through increased survivorship or fecundity.

When integrating heterogeneous effects, the common units problem arises, i.e., how do we express all those effects in a way that can be used by the decision maker? [Slide 11]. The ecological risk assessor can go to a higher level of organization, e.g., for a fish population exposed to both harvesting and toxicity, population abundance is a common unit for two very different factors. Integrative units, like "emergy" and "empower," and economic units (market value and service) are also used. An alternative is computational toxicology, which is used to combine heterogeneous effects at the molecular level, with integration to cumulative effects at the organismal level [Slide 12]

The approach of ecoepidemiology and risk assessment was applied to impaired ecosystems because conventional methods were not doing the job, e.g., not restoring the uses of water under the Clean Water Act [Slide 14]. The idea was to look at the ecosystem to see how it was responding, using methods like community surveys and media toxicity testing [Slides 15-22].

In ecoepidemiological inference, surveys, assessments, tests, and analyses are combined to ask if there are cumulative effects in the community [Slide 23]. The idea is to actually determine the cause in a general sense; it is published in a stressor identification guidance document for how to do site-specific causal analysis. The most conclusive characterization of a cause would be to eliminate something (e.g., if the effect occurred both upstream and downstream of a source); the strength of evidence approach uses the broadest available information [Slide 24]. Case-specific information is considered in comparison to other situations with similar effects, and in reference to biological knowledge (e.g., dose-response, diagnostics), and then consistency and coherence are considered, e.g., are the signals from all the lines of evidence pointing to a particular cause? [Slide 25]. The CADDIS (Causal Analysis / Diagnosis Decision Information System) is being developed as a web-based system that will allow people to do these analyses and produce defensible results.

In summary, ecological risk assessment differs from human health risk assessment through its generally broader concerns, including indirect toxic effects (such as loss of food and shelter), consideration of nontoxic agents (like habitat alteration), and the possibility of shifting to an integrative level of organization; and its heavier reliance on epidemiologic approaches, which are routine in the ecological side because of the large effects (like dead fish) that are encountered and the ability to manipulate subjects [Slide 26]. Lessons for health risk assessment include: using ecological sentinels (which are more exposed and often more sensitive), using epidemiology when possible (in a weight of evidence context), testing whole materials or media, and using human ecology to integrate (because human welfare is more than health) [Slide 27].

**Questions and Comments**

Question: What is an example of whole materials or media?
Response: If you are concerned about mixtures of pesticides in the food supply, you could consider testing the mixtures that occur in fruits or vegetables, rather than just adding up the individual pesticides, to see if the models give the right answer. The same could be done with drinking water. This is very expensive.

Question: Please expand on using epidemiologic data for human health. There are different kinds: what were you focusing on?
Response: Not on any particular kind. In the literature and in documents from the Agency, the tendency is, if epidemiology is looked at, at all, it is in isolation. For example, a study does not have sufficient power, so therefore we will go back to the RfDs. I suggest keeping weak epidemiologic results, and making them work with the toxicity

data in the weight of evidence. The toxicity data can be used in a more sophisticated way. The Office of Water (OW) is trying to respond to a report on the use of biosolids. Some have said that we'll just do a risk assessment for the chemical constituents of biosolids, but a National Research Council (NRC) panel was formed due to complaints from people in communities. It seems that even a qualitative epidemiologic approach would be a place to start to find what has happened to people.

Question: Every time there is a mixtures training course, the suggestion is made to develop a whole mixtures approach. It has not happened for 16 years. These suggestions are great in terms of taking new approaches and getting out of the comfort zone. How do we do it? Any ideas?

Response: On the ecological side, it was obvious that the old methods were not working. We can see that. There will need to be some realization on the human health side that the methods are not working. It is not sufficient to say that based on our scientific knowledge we know that things are failing. We have to show them.

Comment: It is a loop. We have to do the studies, but we can't. How do we jump start it to make people see that change is needed?

Comment: The current methods do not work; the evidence is out there in communities with health disparities. The most impacted communities with poor health show deterioration in the last 20 years; that should be evidence enough. The government, not just EPA, needs to do something different.

Response: This is a large box, that includes more than just EPA.

Comment: The combining of human health and ecological research – bringing in human ecology. Can you give more insight into what we are trying to accomplish?

Response: It is frustrating to perceive that we are doing a really good job on ecological risk assessment, but are having little impact on decision making. One way to get more attention for ecology is to integrate it with human health, for instance, through services of nature and human well-being. The World Health Organization (WHO) has an integrated human health and ecological framework. Goal 4 of ORD's Strategic Plan is more integration across health and ecology. Actually changing the way things are done is very difficult to do, due to organizational inertia and stove-piping. You need someone more knowledgeable about the culture of the Agency.

Comment: Developing ecological sentinels for urban environments – going where the people are – might be an effective way to start.

Response: Work to date on respiratory pathology in urban birds has not had much influence.

Question: Ecological risk assessment focuses more on indicators of populations, while human risk assessment tends to look at individual indicators and add them up. Do you have any suggestions for measurements for healthy populations?

Response: The tendency is to look at highly vulnerable individuals. You might do a better job of protecting by looking at the whole human population, looking at distributions for air contaminants, food contaminants, and seeing how the distributions compare, or by framing the decision in the context of alternatives. For instance, ocean dumping of biosolids was outlawed over 10 years ago without considering if this had the greatest risk, or if the risk was greater for land application or incineration.

Question: Aren't you looking at different questions? For instance, in human health, there is concern about cancer. But in ecology, cancer at an older age, when an organism is past its reproductive time, does not affect the population.

Response: We do not have the same demographic impacts in humans that we have in plants and animals. Cancer is a concern in animals; the frequency of lesions in fish is included as an endpoint in Superfund ecological risk assessments. It is a big concern for people, such as the fishermen who see these fish; people bring up the canary in a coal mine analogy.

## Combining Risks: Implications for Uncertainty Analysis – Jim Cogliano (ORD/NCEA)

One of the relevant topics in combining risks is response addition, in which the probability of response from multiple exposures is the sum of the probability of response from each individual stressor; it relies on the assumption that the stressors behave independently from each other in their toxicokinetic and toxicodynamic properties [Slide 3]. Another is dose addition, in which doses of multiple stressors are weighted by relative potency and summed; this approach assumes that the stressors behave similarly, but not independently [Slide 4]. A constant proportionality between effective doses of the stressors is assumed. When dose-response curves are nonlinear, dose addition is particularly important; because the response depends on the overall level of exposure, e.g., the addition of a dose higher on the curve can have a greater effect than addition lower on the curve [Slide 5].

There are two types of dose-response estimates: (i) a model that characterizes risk as a probability over a range of (low) environmental exposure levels, and (ii) a safety assessment that characterizes the safety of one lower dose (e.g., reference dose) with no explicit characterization of risks at other doses [Slide 6]. In a cancer bioassay or occupational study, the use of upper and lower bounds on the dose-response allows uncertainty to be addressed [Slide 7]. Safety assessments are typically done for noncancer effects, and assume a nonlinear dose-response at low doses [Slide 8]. The NOAEL becomes a starting point, that is, the point of departure, from which the safe dose is estimated. It is divided by uncertainty factors to address interspecies differences, human population variability, and environmental vs. laboratory conditions to calculate the reference dose (RfD) for the general population, including sensitive, but not hypersensitive, subpopulations.

Current practice for adding cancer risks is to use response addition [Slide 9]. Risk of cancer is calculated by multiplying the slope factor by the dose; risks are then added to obtain cumulative exposure. Slope factors are plausible upper bounds for addressing uncertainty; they have been criticized for compounding conservativism in assessments. To investigate this issue, two questions can be asked about adding plausible upper bounds: Does the sum of upper bounds yield an **improbable** estimate of the overall risk? Does the sum of upper bounds yield a **misleading** estimate of the overall risk? [Slide 10]. When plausible upper bounds are added, the law of large numbers means that the distribution of risk (between zero and the upper bound) will approach normality [Slide 11]. There is an imperceptibly small probability that all the risks will be at the upper or lower bounds; the overall risk will be in the middle of the distribution, somewhere between zero and the sum of the upper bounds. The sum of the upper bounds becomes increasingly **improbable** as an estimate of the overall risk, but the sum is **not misleading** as an estimate of overall risk, and it can be adjusted to yield more plausible upper and lower bounds on the overall risk [Slide 12].

For noncancer risks, a safety assessment (RfD or RfC) is generally used [Slide 15]. These are combined using a hazard index (HI) based on dose addition. If the HI is greater than 1 for Superfund, a more refined assessment will be done to get at the common target organs or systems, then a judgment will be based on the HI for the organ. FQPA assessments are more restrictive, and require there to be a common mode of action for the chemicals being combined. Issues of harmonization include how to add oral and inhalation doses when the target organ is not the site of contact; the body does not discriminate by route of exposure, and once in the system, the chemical's effects are the same [Slide 16]. Also of issue is how to include effects that are not the critical effect for a particular chemical. RfDs focus on one effect; for most, there is not information to calculate safe levels for other effects, although there is some pressure to consider having RfDs for secondary and tertiary effects of chemicals.

Future applications of dose addition include chemicals with a common mode of action; multiple chemicals operating in the same manner could be considered on the same dose-response curve [Slide 17]. Another is common metabolites. The perception is that toxicity is due to a specific chemical, when, in reality, metabolites can also be toxic. As for exposures via multiple routes, the body does not discriminate among the sources of metabolites; there can be cumulative exposure to chemicals to which one is not exposed directly.

Trichloroethylene (TCE) is one example of multiple sources of exposure to toxic metabolites, namely trichloroacetic acid (TCA) and dichloroacetic acid (DCA) [Slide 18]. Humans are directly exposed to TCA and DCA because they are byproducts of drinking water chlorination, and indirectly exposed because they are metabolites of some chlorinated solvents. The risk from TCE exposure is thus related to not only its own level, but to the level of direct and indirect exposure to the metabolites, i.e., where one starts on the dose-response curve makes a difference in the risk. The TCE example is also complicated because cumulative exposures can alter metabolism [Slide 19]. There are two metabolic pathways by which TCE is broken down. A metabolite of one pathway is associated with liver cancer in animal and human studies; a metabolite of the other pathway is associated with kidney cancer. Variation in the levels of the enzymes in these two pathways across the human population results in different susceptibilities related to the amount of TCE that goes down each pathway. The Science Advisory Board (SAB) commended EPA for considering metabolic interactions, and recommended a 5-fold modifying factor be used to account for differences in the levels of metabolites related to concurrent exposures [Slide 20]. Populations of particular concern are people exposed to drinking water with toxic metabolites and dry cleaning workers exposed to perchloroethylene (PERC), which is also metabolized to TCA, putting them higher on the exposure curve for TCA.

**Questions and Comments**

Question: Dry cleaning sites are leaking PERC. Can the environmental breakdown products yield exposure to multiple solvents?

Response: There is probably no single-exposure solvent site; they are all multiple. The risk assessment approach may not be right. You may have to break down the solvents, and add the metabolites together to see if they are above the toxic dose. Then you get into alcohol and other factors. These are complicated problems. But this is a clue to why there are interactions when everything is below the allowable level or the RfD.

Question: Are you making an argument for doing cumulative risk assessment on a single chemical?

Response: TCE inside the body is no longer just one chemical, but a family of a dozen. So inside the body, TCE is a mixture, and it is this mixture for which we do a cumulative assessment. You can use pharmacokinetic models to predict its breakdown in the body. In 20 years, we will have those for other chemicals. We are currently in an awkward situation, looking at slope factors in isolation. There are 19 other solvents where we do not have the same level of study as we do for TCE. Perhaps some sort of modifying factor might be appropriate.

Question: [Regarding the chloroform nonlinear dose-response.]

Response: The TCA dose-response curve has been shown in some studies to be linear. For DCA, there is more evidence for it being nonlinear. It rises very steeply when you get to a certain level. In a population that can metabolize to that level, with higher exposure, you might have higher internal DCA levels than you thought. How is DCA causing cancer? There are lots of pieces to get at. For risk assessment, we know enough information to be uncomfortable with the current methods, but we do not have the methods to make it better.

Comment: There is also the air pathway. TCE and other chemicals are very common vapors in hazardous waste sites, and even in offices.

Response: That is a good point. With our methods for adding RfD and RfC, it is not clear how to get the same internal doses. There are different equivalents for TCA and DCA. It is not clear how to get equivalents for oral and inhalation exposures. There are the same tumor sites with both routes of exposure in rats. The metabolism is different. When it is ingested, it goes through the liver and is metabolized. Inhalation means that TCE gets into the bloodstream and is distributed in the body. A person can be exposed to TCE through the shower or by using White-out.

Question: You raised the difficulty of cumulative risk, knowing some things about some chemicals but not others, knowing something about chemicals and other exposures. We need to address this. The issue of consistency has been raised over the last few days, [as has] the characterization of co-exposure to non-regulated things; we do not have a procedure for that. Should we put them in when we do not regulate them?

Response: This is a good area for discussion. For instance, one approach could be to say that the RfD is the safe dose for exposure to a chemical alone, without any other exposures. For TCE, we suspect that there is interaction, and we introduce a 5-fold data-derived factor from modeling. We tell the risk manager that other exposures are common, and that people are likely to have these other exposures to solvents all the time. The approach may differ for other chemicals.

Question: What is the basis of the modifying factor of 3?

Response: We knew there were effects that we would expect. The pharmacokinetic modeling is being published now, and will be out there by the time the TCE assessment is published. Based on judgment, there was not enough information to go to [a factor of] 4 or 5.

## Use of Other Metrics for Combining Risk – Chris Dockins (OPEI/NCEE)

Economic metrics address how to combine multiple risks in a way that reflects individual welfare changes. A very simplified linear process can be used to show the steps that lead to summary economic metrics: emissions to environmental concentrations to exposure to health risks to economic metrics. This approach does not illustrate feedback loops, such as behaviors like smoking and drinking [Slide 3]. Economic metrics are related to individual welfare, and can then be summed to estimate "social" welfare; they are distinct from community-wide scales, and their individualistic focus does not capture broader values, e.g., how my welfare is improved when your health is better [Slide 4]. The metrics combine disparate risks (e.g., cancer and noncancer) into a single measure [Slide 5]. Economic metrics are founded on how individuals value desirable things; those values are based on three key principles: consumer sovereignty (individuals generally know what is in their interest and act accordingly); constrained tradeoffs (individuals make tradeoffs between desirable things because resources are limited); and rationality (the tradeoffs individuals make are systematic, given their preferences) [Slide 6].

"Health effect" can be defined in three ways, only the first of which is fully accommodated by economic metrics: as something that affects well-being and functioning (i.e., disease or death); as an indicator of other effects on well-being, but with no direct effect itself (a change in hormone level); and as something with neither a direct or indirect effect on well-being (a change in organ weight) [Slide 7]. Economic metrics require well-defined endpoints [Slide 8]. They (and the models based upon them) also require a set of probabilities to represent expected changes in risk to an individual [Slide 9]. Information on the timing of risk reductions, particularly when there are lags, is also needed; timing affects the present value of costs, and people have a positive time preference for risk reduction now, rather than later [Slide 10].

Economic metrics include: cost of illness (in $); health state indices [in weighted years, such as disability adjusted life years (DALYs) and quality adjusted life years (QALYs)]; and willingness to pay (WTP) for risk reduction (in $) [Slide 11]. WTP addresses aggregate welfare and is used in benefit-cost analysis, and QALYs / DALYs are used in cost-effectiveness or cost-utility analysis [Slide 12]. To look at cost of illness, each health effect is converted to a dollar equivalent based on lost production and health care costs; it is clearly defined and measurable, but has some limitations (it is not necessarily based on individual preferences, does not include pain and suffering, and the price of health care may not equal the costs) [Slide 13].

QALYs and DALYs conceptualize health using longevity and health-related quality of life [Slide 14]. DALYs measure the burden of the condition compared with optimum health and longevity (based on a standard of Japanese females); increments of life are lost based on health risks [Slide 15]. More weight is given to the productive ages, with a peak at age 25; this does not necessarily correspond to people's opinions about when a loss would be most damaging [Slides 16, 17]. For QALYs, well-being is defined by a health profile over time, but income is not included [Slide

18]. Total QALYs are the sum of values of health-related quality of life multiplied by the duration in that state of health [Slide 19]. The ideal outcome following an intervention is longer life of higher quality [Slides 20, 21]. For something less than the ideal, e.g., shorter life but higher quality or longer life but lower quality, the net QALYs following an intervention could be positive or negative [Slides 22, 23].

Assumptions of the QALY approach include: a constant proportional tradeoff (quality does not depend on time) and risk neutrality over the lifespan (lotteries on longevity are evaluated solely by life expectancy) [Slides 24, 25]. To measure quality, surrogates are derived from surveys of "community preferences," including visual ratings of gain in welfare; time trade-off questions (years in ill health vs. years in perfect health); standard gamble questions (e.g., the risk of death one would accept to return to perfect health); and person tradeoff (extending the life of healthy people relative to non-healthy people or relative to improving quality for non-healthy people) [Slide 26]. To aggregate QALYs, the metric used is the sum total QALYs gained or lost over the affected population [Slide 29]. Equity (interventions for the young are preferred to the old; life extensions for the healthy are preferred to those for the non-healthy) and economic criticisms (the assumptions are restrictive and do not reflect actual preferences, and concern about data quality) are other considerations related to QALYs [Slide 30].

The WTP metric defines well-being in a general utility function that includes health and all other goods [Slide 31]. With WTP, the essential tradeoff is between wealth and health, e.g., if you are ill, how much wealth are you willing to give up to get to a healthy state [Slide 32]. Willingness to accept (WTA), what cost would you accept to accept a higher risk of illness, is a related metric. WTP is one's own WTP for one's own risk reduction and is affected and constrained by income; it is not a measure of compensation for experiencing health effects [Slide 33]. WTP assumptions include that individuals are willing to trade off health risks and wealth, and that they perceive risk accurately and behave in their own best interest [Slide 34].

To measure WTP, economists look at situations where people trade off risks and dollars, e.g., accepting additional wages to work risky jobs, paying more for safety devices and safer vehicles; they also use surveys where individuals state what they would pay for a given risk reduction [Slide 35]. Economists also break down estimates by mortality and morbidity, rather than by cancer or non-cancer [Slide 36]. The aggregate metric is total WTP for a set of health risk reductions; the value of statistical life for mortality and morbidity estimates for non-fatal illnesses are assumed to be additive [Slide 37]. Equity considerations (WTP is related to income; whether age or health status affects valuing of mortality or morbidity) and economic criticisms (the effect of risk perceptions; the focus on "self") also apply to WTP [Slides 38, 39].

There are few head-to-head comparisons of QALYs and WTP [Slide 40]. An example using reductions in fine PM, which combined mortality reduction and chronic bronchitis reduction,

calculated 132,855 QALYs gained, with a WTP of $48.7 billion. Costs were $4.2 billion, or $31,000 per QALY gained, for $44 billion in net benefits [Slides 41, 42].

The choice of economic metric is based on what the analyst wants to do, e.g., if it is a comparison with costs of a policy, then WTP would be used, and on what the analyst is prepared to accept in terms of assumptions and data. [Slide 43]. Economic metrics assume that causality and dose-response issues are resolved [Slide 44]. The specific population focus of cumulative risk assessment implies the need for population-specific measures, especially WTP. However, WTP applies only to risk changes, not to the characterization of a given risk level [Slide 45].

**Questions and Comments**

Question: With West Nile virus in Chicago, communities were faced with a tradeoff between spraying for mosquitos and concern about pesticides. Has that kind of situation been studied?

Response: We want to include risk-risk tradeoffs. How individual communities do it has not been studied. Given a set of assumptions, we can say how we would work through it systematically. We want to reach a conclusion on maximizing health, but I am not familiar with how it would be done on a community basis.

Question: When asking people about tradeoffs, do you get different answers from sick people vs. people who are answering in the abstract?

Response: A fundamental question is who you ask, that is, a healthy person or a person in that health state. You would expect very different answers. What is the policy question you are asking? If it is affecting persons already at risk, then ask them. Some say people adjust to chronic conditions, and after an initial decrement, they are essentially as happy as before.

Question: If you can only talk about your own health [in valuation exercises], how do we find out about children?

Response: A children's health valuation handbook is coming out soon. The first assumption is to go to the parents, but that is incomplete. If you go to only the parents, what component are you missing in the public sense? Children have benefits to all. The handbook details the missing components, but we do not have a good handle on how to get to that. You can ask for private (self) and public (program) willingness to pay. The answers do not always align for acting in a public or a private context. Economics does not handle children well.

Question: Agencies have had to combine risk assessment and economics. Both have uncertainties. Can you compare which has more?

Response: Often, the risk assessment is more uncertain. That may be because we are not taking a complete look on the economic side. There can be a 10-fold range between the low and high economic estimates. In a lot of contexts, risk assessment is less certain, but for economics, our coverage is spotty. When we are interpolating, we do not have any better handle.

## Cumulative Risk Index Analysis – Gerald Carney (Region 6)

Under the National Environmental Policy Act (NEPA), Region 6 was examined on a watershed basis to ask when saturation is reached for a typical industry, such as concentrated animal feeding operations (CAFOs). Planning and scoping was well-suited for this approach; the CAFO cumulative risk index analysis (CRIA) is an ambitious attempt to start putting economic data with landscape (e.g., GIS) and human health information [Slide 2]. Key issues in cumulative risk include legal definitions, e.g., for the mobility of compounds through soil, which differ for the Resource Conservation and Recovery Act (RCRA) and Superfund; how to use the available data; and the potential to examine many environmental criteria with available technologies [Slide 3]. Issues of risk characterization include transparency (e.g., not having models within models), clarity, consistency, and reasonableness [Slide 4].

Planning and scoping is important to the process; in dealing with CAFOs, industry and citizens were involved [Slide 5]. The conceptual model for CAFOs looked at impact on a watershed basis. Data were presented in different formats, e.g., census block, watershed, and county, and there was sometimes a concern about how to integrate them [Slide 6]. The assessment looked at when the numbers of CAFOs were starting to saturate the region [Slide 7]. The Region 6 Risk Characterization Implementation Plan (RCIP) identifies levels of analysis, and it was determined that this project fit into the category of screening [Slide 9]. In the screening approach, vulnerability criteria were ranked on a 1-5 scale as to environmental concern, and impact criteria were also ranked [Slide 10]. The watershed vulnerability assessment endpoints included wildlife, economic status, and many others [Slides 11, 12]. Some of the judgments included determining what is valued wildlife and what is not, and deciding that an economically-stressed area would be ranked higher than an area that is at the state average. Everything is ranked on the 1 to 5 basis. Adding the scores for all the items of interest gives a score that is informative about the particular site; because this is a screening tool, a high score tells that more investigation is needed.

The approach was applied to enforcement targeting for 403 watersheds in Region 6; each environmental, socioeconomic, or enforcement criterion was ranked on a 1-5 scale, the scores were added, the watersheds were ranked, and watersheds with high scores were targeted, that is, industries within them were evaluated [Slide 14]. A watershed compliance score was based on eight criteria covering violations in any of the major programs; the thinking was that if there is a lot of noncompliance, then there is more vulnerability, e.g., more chances of a spill [Slide 15]. An example is a watershed in Houston, TX where there is a concentration of industry, which scored 81 out of 100 in the ranking process. Because any criteria can be selected, the model can also be applied to environmental justice concerns, as it was for a Houston site that was a RCRA concern [Slide 19]. There were a high number of economically stressed residents nearby; that ranking was combined with other socioeconomic factors, like education and income, to produce a list of apparently impacted areas for further analysis [Slides 20, 21]. An example of an

application of the approach to human health was conducted in Galveston, TX in an area with over 400 TRI sites; health risk and environmental justice index scores were calculated. [Slide 22]. Each TRI release was assessed for its potential health risk based on factors like bioaccumulation potential, amount, media to which released, and potential toxicity. The highest score was in Texas City, TX which would not have been predicted based solely on the number of industries there [Slide 25]. The CRIA approach gave EPA information to back the decision and the information was understandable to the mayor of Texas City.

CRIA has also been applied to highway construction projects; these incorporate information from Fish and Wildlife, including endangered species information, as well as socioeconomic criteria, and look at highway alternatives to pick the best route [Slide 29]. For example, CRIA was used to validate a decision by the Oklahoma Department of Transportation for a highway from Tuttle to Mustang, OK [Slide 31]. Three alternatives were evaluated to find the one with the least impact, i.e., the one that traversed less wildlife habitat and fewer streams and had less socioeconomic impact. Advancements have been made in considering disruption to wildlife habitats and fragmentation [Slides 33, 34]. Additional criteria have been developed for highway segment evaluations [Slides 35, 36, 37].

Region 6 uses CRIA frequently, is careful how it is used, and seeks a lot of input. As a final illustration, the location of a site near the home of one of the workshop participants was provided, and a potential environmental justice index was considered. This exercise illustrated the extent of the regulatory information available for CRIA, and illustrated some of the factors to be looked at from various perspectives.

**Questions and Comments**

Question: Do you have a database or do you plug it in?
Response: It is all automated. Our goal is to have everyone in the region able to access it. The analysis took less than an hour, but more time would be needed for the program people to make sense of it.

Question: What are the land use data for an area of rapid growth and how that would be affected?
Response: There is a high level of fragmentation from roads. You have to make decisions. If you rank from good to bad, do you protect an area that is more fragmented or an area that is less fragmented and more pristine? The easy answer is to protect both, but how do you do it?

Question: Is there a way of doing case-specific weighting?
Response: We decided years ago that we would not weight anything. There is a lot of overlap in the data here. If we started weighting one over the other, it would introduce bias. We wanted it to be flexible. Weighting is done by some programs when they take the data. We did not know how to weight the comparisons, so we decided not to.

Question: Do you document which data are correlated, so that if someone wants to weight, it is not double-counted?
Response: That relies on the user to put it together with the rationale they choose.

Question: Because the index approach hides or collapses information, as a user, do you have the sense that it is conservative health-protective?
Response: This is much more accurate when it is directed toward potential exposure, and not really good for health outcomes. It is a screening tool. It allows us to look at a place and ask for level 2 and level 3 analyses. It would be ultraconservative if [we were to] extrapolate it to potential disease.

Question: Is screening done to find bad areas or not to waste resources?
Response: It is the former. We look for [rankings of] 4s and 5s. There is no bottom-line added number. We have to go in and use our expertise. [The tool] tells us where to go next.
Comment: The book goes through the criteria, and tells what a "1" is equal to. An index like this does not have to hide information. The spreadsheet showed the numbers and the index. From the sense of cumulative risk assessment, I really like that he goes through and puts different stressors into different categories. You can rank categories, or look across the stressors and see a profile of the area. You can think beyond this specific application to how this might be applied, especially for chemical and non-chemical stressors. It really shows how much information is out there – there is a lot more information out there than assessors dream of. (Callahan)

Question: About reproducibility, if you submit the same rankings to five different risk assessors, who use their judgment on what to pick in the total ranking, how consistent is the usage?
Response: We have not done that. We have, as often as possible, validated some of the results, such as for lead abatement in Houston, [where,] after doing our outreach, we got blood lead data to validate it. If you look at enough parameters and judge them correctly, it will point you in the right direction.

## Breakout Groups – Discussion of Case Studies and Other Aspects of "Putting It Together"

Workshop participants signed up for one of four breakout groups to discuss topics related to the case studies and other aspects of "putting it together." After the one and one-quarter-hour session, participants reconvened, and each group reported the conclusions it had reached to the workshop as a whole.

### Breakout Group 1 – Risk Characterization Methods

Group 1 was charged with addressing population-based risk assessment, identifying and accounting for uncertainty in cumulative risk assessment, and integrating risk information across scientific and non-scientific disciplines. The group noted that it would be helpful if the risk characterization methods included something that would be more complete and useful for the cumulative risk process, e.g., when to use it and when not to use it; how to set up a tiered approach; and something to work through in a case-by-case method. This would also include assistance on the quality of the data, identification of where the appropriate data are, and a mechanism and methodology for data review. Finally, there should be new ideas for bringing the cumulative risk process into the decision tree, i.e., to understand how to do that would help get to the next step. The group suggested consideration of a supplemental guidance book on risk characterization appropriate to cumulative risk assessment, and a checklist for contributing factors, which, in addition to traditional chemicals and stressors, would include social and economic factors that are new to risk assessors, who need to determine how they fit in. The group also noted that this is a complicated topic, no matter the audience, and suggested that it would be helpful to work out new risk communication strategies and guidelines. Group 1 drew the following ideas from the presentations: to understand coexposures of chemicals or stressors that interact in detoxification pathways (such as chemicals with the same mode of action, like drinking water disinfection byproducts); to learn more about cumulative uncertainties that are aggregated over cumulative risk assessment (how many things are we adding together? how do they impact the uncertainty of the risk assessment?); and to examine the potential usability of and perception issues related to metrics like QALYs, DALYs, and WTP in cumulative risk assessment.

### Breakout Group 2 – Combining Risks

The charge to Group 2 was to consider ways to express cumulative risks, disparate risks, choice of metrics, and ranking systems. Group 2 called for a new approach to combining risks. The group identified questions related to combining risk, such as whether chemical and non-chemical stressors should be combined, and how to draw the distinction between voluntary and nonvoluntary exposures. As an example, the group cited a water risk assessment, and asked what would be the decision point for incorporating non-chemical stressors. They raised the

issues of site- and stakeholder specificity, and commented on the need to stay within EPA's jurisdiction. Group 2 also called for formal ties with other agencies. They recommended that guidance not be given unless it is clear what difference it makes. Having lots of options that are implemented differently at the state level is less helpful to the regions. The group commented that everybody is for better science, but that something that is easy to implement is what is needed. Group 2 also said that it would be helpful to establish subpopulation-specific human background body burdens for chemicals. They also suggested that if information on secondary and tertiary effects that is not put into IRIS exists, it should be made available, as should subpopulation dose-response curves. However, the group said, an analysis might need to be done first to be certain that making the information available, particularly in an accessible format like IRIS, is really going to be beneficial to risk assessors.

**Breakout Group 3 – Integration of Approaches**

Group 3 considered the similarities and differences among ecological, human health and tribal / socioeconomic / quality of life approaches, noting that the latter is a much more holistic approach that treats man as a part of nature. Human health is more focused: the receptors and stressors are more defined, and interactions are standardized on a site-specific basis. Group 3 said that the ecological approach is kind of a cumulative approach, as it is more community-based. Human health assessment is more focused to man or a single receptor. Group 3 recommended expanding health risk assessment to include quality of life, and to get beyond the chemical type of assessment. The group identified the lack of information available for quantifying welfare and indicators of socioeconomic status as a factor holding this back. Group 3 said that research is needed on indicators and on acceptable and unacceptable levels of impacts on those endpoints. The group also identified as a problem the lack of direction for acceptable levels of risk in the ecological and socioeconomic approaches, noting that only NEPA has direction on how to look at this. Questions remain about how to incorporate this, and there is no mandate to force EPA to look at it. Group 3 suggested broadening the focus of human health assessment to include the overall welfare of the culture. They also noted that the indices being used mean different things to different people, and are hard to reconcile and hard to use as a basis of decisions. They called for more research on ecological impacts on human health and the economy, so that the information can be tied into a more holistic type of approach. Other research needs identified by Group 3 are more cost-benefit analysis, particularly including cultural and holistic approaches, guidance on how to present GIS information and use it as part of the assessment process; evaluations of the replicability of regional cumulative risk models; making more information about regional modeling resources more widely available; consideration of how to extrapolate back from quantifications of ecological changes on human health and the economy; and consideration of the best indicators to use to assess the welfare of the population, community or subpopulation being studied.

## Breakout Group 4 – Vulnerability

Group 4 did not convene. The group was planned to address data gaps and methodologic difficulties in conducting a vulnerability analysis, capturing vulnerability factors in the risk characterization, and overcoming the traditional absence of vulnerability in risk assessment.

# SESSION V: POLICY IMPLICATIONS

## Policy Panel

**Moderator:** Mike Callahan (Region 6)

**Panelists:** Jim Cogliano (ORD/NCEA), Chris Dockins (OPEI/NCEE), Barbara Harper (Tribal Consultant), Reggie Harris (Region 3), Rick Hertzberg (ORD/NCEA), Anna Lowit (OPP/OPPTS), Glenn Suter (ORD/NCEA)

In introducing the panel, Callahan said that today, participants would talk about policy, which had been off-limits during the rest of the workshop, and make comments about what EPA needs to do. He noted that none of the panelists can speak for the Agency on policy, but he asked them to speak about their own personal opinion on where cumulative risk fits in.

### Barbara Harper (Tribal Consultant)

There is a transition in EPA's risk assessment characteristics, but there is nothing about cumulative risk in the EPA strategic plan [Slide 2]. The breadth of what we consider in reviewing any risk assessment is human, ecological, and cultural health; the ultimate message is that a healthy culture and healthy people need a healthy environment [Slide 3]. With reference to six questions from the "lessons learned" document, a population includes quality of life and socioeconomic factors, but the concept is not consistently carried through the rest of the document into the endpoints [Slide 4]. It was good to see the statement that risk = proportion x vulnerability x magnitude. Proportion is an important environmental justice concept, but because the absolute numbers of tribal populations are small, they will always be 100% affected, and will "lose" compared to the general population [Slide 5]. The concept risk = toxicity x exposure x sensitivity needs to be considered in the context of clustering of risks in tribal populations [Slide 6].

Other issues that need to be considered are the time frame (many generations, all important, may be affected by persistent contaminants); the spatial boundary concept (reservations or homelands may be large, even though the number of people is small); and integration (an explicit step is needed to trigger integration for holistic evaluation of risks) [Slide 7]. Ecological and cultural "boxes" need to be added to the flow chart usually used to illustrate risk assessment; for the tribes, risk characterization does not happen until the integrating step at the end, where the ecosystem stories come into play [Slide 8]. Getting people

to think holistically can be difficult; we could spend infinite resources studying a piece and miss the whole; it is only if you ask the people what it means to them that you get the complete picture [Slide 9].

Cultural ecosystem stories or dependency webs are a way to think about a resource or area and describe all the reasons it is important to people, including human health, economics, natural resources, language, and intergenerational transfer of knowledge [Slide 10]. By collecting all the reasons, unanticipated things that will affect decisions will be identified. This helps the community design the assessment. The Agency for Toxic Substances and Disease Registry (ATSDR) guidance manual for mixtures seems to be a lot of money put into something that may not make a difference in decisions [Slide 11]. Finally, the tribes are not stakeholders, but sovereign nations, and their trusteeship is a Federal obligation that can not be waived [Slide 12].

**Questions and Comments**

Question: What does trusteeship mean?
Response: The Federal government has to protect natural resources so that they are safe and of good quality to use in the original manner that tribes used them. They must be safe for subsistence use, e.g., of good quality for basketmaking. It is a core principle that tribes litigate on when they have to.

Question: You discussed cultural toxicity. Are there written materials on it?
Response: There is a big literature on Quality of Life. Those metrics are used because they fit anybody. As for what metrics you would use in a tribal setting to reflect cultural well-being, a research project would be nice. We are not totally starting from scratch. [Another question is] can a culture be a receptor, or is it a byproduct of real risk.

**Jim Cogliano (ORD/NCEA)**

Do we think that cumulative risk should be and will be addressed by the Agency over the next few years? What we have heard this week says that cumulative risk should be addressed. Examples from this week show interactions, etc., and tell us things should not be looked at individually. EPA should go beyond the idea of adding up the chemicals we regulate (through dose addition, etc.) to consider interactions with other stressors. The data we have seen say that we should be doing that, e.g., toluene and noise might not be considered in current assessments. There is the potential for differential effects in different populations. TCE and its interaction with solvents might fit in the current approach, but not its interaction with alcohol or acetaminophen. However, those data are there and should be taken into account.

In terms of health vs. chemical basis, we sometimes see things we would not expect, which points to interactions. Aspects of vulnerability are not recognized in risk assessment, e.g., what

is the recovery or capacity of the population to respond. This may be important in cumulative risk assessment. A population where there is an excess incidence of disease points us to something going on, perhaps an interaction among several factors. It is very clear that EPA should move beyond the current approach, by broadening chemical assessments beyond laboratory studies of effects of one chemical, to interactions with other chemicals and with other factors. Will EPA do that? Just about every project is worthwhile. Which office or which person would do them? There are lots of programs that address cumulative risk in a certain way; this will be difficult to change. For instance, in pesticides, multiple chemicals used on different crops are linked. Common mechanism of action (MOA) is a restrictive form of cumulative risk assessment. A more expansive definition would be the interaction of a step of two different MOAs, such as for noise and toluene. Lots of programs in Washington deal with one chemical at a time, or sometimes a group, like trihalomethanes, but this is not as expansive as dealing with interactions. Does this kind of information go into the hazard index instead of the RfD? If so, EPA would have to change the guidance. Watching what happens with TCE is a good test case of where cumulative risk assessment will go. It is a fairly limited application, including only other chemicals, not the broader universe of other stressors, such as alcohol, socioeconomic status and access to health care. That will require changes in program offices before it will be implemented.

We want to get the practice of cumulative risk assessment to meet the need. We can develop clear test cases of chemicals or groups of stressors that act in a more than additive way. We can do simple dose addition very well; we need to move beyond it. We can find cases with interactions that are not covered in current risk assessments, incorporate them into the scientific portion, and then, after we do it a few times, it will be more accepted. Changes take a while, e.g., as for risk assessment for children. The Agency has been wrestling with bioavailability for years, and will do so for cumulative risk assessment as well. We need to find a test case where the actions together are much greater than the sum of the individual actions.

**Anna Lowit (OPP/OPPTS)**

From the Program Office point of view, cumulative risk assessment is case-by-case. There are a variety of regulatory requirements and community pushes for action. We have to be flexible. Pesticides have common mode of action as a regulatory mandate; the air program may have to pare down chemicals from the Clean Air Act list; screening can be used to identify at-risk communities, as in the example from Texas.

What influence **should** cumulative risk have? A lot – but how much will depend on regulatory requirements and the pressures behind the assessment. How much influence **will** it have? A tremendous potential if we play our cards right. If programs do not require cumulative risk, then we can use interactions with communities and other agencies to get a strong push for action to use cumulative risk. The big “take-home” message is that the very best thing we can do is go

out and talk to people: community organizations, stakeholders, tribal organizations, environmental groups, and even the "dumpers." The more people who can sit at the table in a respectful way, the better. We are still figuring out where we are going. Meetings, program office participation, and ORD participation may be one of the best ways to push forward.

**Questions and Comments**

Question: Is there a way we could improve the process of getting regional- and ORD-initiated projects into the program offices?
Response: You could have co-leads on a project, rather than one entity in control. (Yurk)
Response: That does not really work with regional people, even 10 percent. (Hertzberg)
Response: To get cumulative and community initiatives, under reinvention, there used to be meetings to discuss. It might be practical to get the regions to ask the program offices for more assistance. It might get on the agenda. (Topper)

**Glenn Suter (ORD/NCEA)**

Cumulative risk assessment depends on laws and regulations in a particular area. The Clean Water Act says that we need to do cumulative assessment. The law says that the Agency shall assure the biological and chemical integrity of waters, and the ecologists have been running with it. Working at the holistic or cumulative level in communities gets beyond EPA's powers as an agency to take regulatory action.

EPA has been facing a problem under the Clean Water Act because it only has the "permitting hammer," and needs more, like good physical structure of the stream, controlled silt load, and riparian vegetation, which requires that the Agency have more flexibility. States are required to designate uses for every water body, e.g., if one use is as a cold water fishery, there can be no point sources on the stream, and if the state has not achieved that use, it needs to go into the watershed and determine why not. It could be logging practices causing silt loading; if so, then the Agency has to work with the Forest Service to restore the designated use. If the land owner is not Federal, it becomes more complicated. EPA is working with USDA to develop best farming practices, showing farmers it is in the interest of self and the community to not till up to a stream bank, for instance.

A mechanism to which people are going is the establishment of watershed councils or community organizations to adopt watersheds; these approaches mobilize people who will do what needs to be done. With the right legal mandate, EPA can do all the things that people have said this week are difficult or impossible. Without a mandate, such as TSCA or FIFRA, people will continue doing the single chemical approach until the law changes or the people tell them to do something different.

**Questions and Comments**

Question: Considering that EPA has put out a State of the Environment Report, and the regions look strongly at NEPA, do you see any hope in that arena?
Response: That would be great. I do not know the policy associated with that. The Agency has resisted applying NEPA to their activities. If as an Agency, we did adopt NEPA, and accepted the mandates as part of EPA's mandates, this would give a mandate equivalent to the Clean Water Act's integrity mandate for everything EPA does. That would be great. It would clear obstacles in every path.

Question: Does it make sense for us to think about integrating ecology and human health?
Response: There are two motives to do so. One is increased efficiency. There are a lot of commonalities among vertebrates, particularly mechanistically. The same is true with transport and fate modeling. Those efficiencies are easy to argue for. The other impetus is broadening the definition of human health to include quality of life or welfare. A deep integration of human and ecological risk assessment would involve translating environmental changes into changes for humans. It would seriously address services of nature and perceptions of nature. That will be much more difficult to sell, but could be much more important.

**Chris Dockins (OPEI/NCEE)**

From the perspective of economics and outside the risk assessment paradigm, the essential message of cumulative risk assessment is that chemical risks have a context, e.g., of other chemicals, stressors, community preferences, and community assets like the availability of health care. It is essential to recognize this. From economics, risks are only meaningful in how they affect well-being.

For metrics focused on health, some limited attempt has been made to distill that meaning, i.e., how important changes of risk are to populations. It seems that recognizing that and setting policies to consider the context of risk is essential. We have to understand interactions to do that effectively. In a broad sense, cumulative risk should be part of decision making. It is certainly a research imperative to ask the empirical question as to how much impact these things will have.

Combining metrics in terms of human welfare is limited, but it can be done in some framework. Economics should play a – not the – role in decision-making. Economics will matter a lot in the next strategic plan. OMB has asked for the social costs of achieving each goal; economists think OMB should also know the social benefits. We need to provide a more comprehensive assessment of benefits. To do so, we need to combine ecological risks and human health risks, and appropriately couch that in terms of communities. It could have a big effect on big

budgetary decisions. The better able we are to combine risks and understand the meaning of cumulative risk, the better off we are.

Whether this **will** this have an effect depends upon the decision context (statutory, historical, etc.). A decision is made on the basis of $10^{-4}$ or $10^{-6}$ for Superfund; how important are all the other factors, if they never make it into the decision process? We know enough about cumulative risk to be uncomfortable; it would be good if the decision makers knew enough to be uncomfortable as well. The increased demands for benefit-cost analysis mean that economists will try to combine information. There is more need to work together to try to understand what cumulative risk means. Avenues include the Risk Assessment Forum, which has now started an Economics Forum. We need to move from safety assessments to population risk estimates for noncancer effects; that is the only way to incorporate them into an economic framework. The onus is on economists to develop models that incorporate risks and to try to get a handle on their relationship to quality of life measures. We do not know how metrics feed into existing models.

**Questions and Comments**

Question: There are costs to reduce risks and to save lives. Your costs are based on benefits of not saving a life, or not improving the quality of life. Is this a different twist from how EPA does business?
Response: We need to work more closely with the regions on how the tools and frameworks can be informative.

Question: With cost-benefit relationships, we often hear of costs to old businesses due to environmental concerns. That generally means it is a new opportunity for business. Do you consider that?
Response: We should. We attempt to. It is an open question with economics, especially with regulation. Do the opportunities on the whole make us better off? It can affect the way people think about the problem.

**Rick Hertzberg (ORD/NCEA)**

Having been detailed to the Homeland Security Agency and commenting with that perspective, the Homeland Security research center has a two-year deadline. We never think about two years in ORD; it is a total shock. Most proposals were poorly done; they could not get out of the academic research mindset. In addition to the risk assessment part of the Homeland Security research center, there are also safe buildings and water security parts, which are headed by engineers, who are used to short deadlines. They are having to adjust their thinking to timetables of 2 years, and even to 6-9 months. Engineers have a tendency to take clean-up and detection as far down as they can go, whether or not it is toxicologically meaningful. There are efforts to

change this, e.g., when working with communities that do not have the budget, by setting realistic and cheaper priorities.

The risk assessment proposals up for immediate funding are in the safe buildings area and have the potential to address cumulative risk. They deal with acute and short-term exposures, e.g., in a terrorist incident, there would be immediate exposure, exposures of hours, weeks, or months for emergency workers, and short-term exposures with reoccupation. There is a range to do some validation. The RfD is a "nothing happens" level, so there is interest in a scientific sense to do back-calculations of exposure data and to ger real data to check the approaches. In terms of short-term limits, we are looking at the cost of a building not being occupied during cleanup. The population being protected in the building is different than the population outside; we will try to include the healthy worker effect. The public will also have an exposure, e.g., from an infected person, or through leakage of contaminants.

These assessments will be tightly community-based (in the rough sense of the word). They will focus on population characteristics; time will be a critical factor; the interplay between exposure levels and toxicity assessment will be tight. If there are airborne exposures, the inhalation pattern will not be standard. We expect dust, which is a cofactor that can affect breathing behavior as well as the respiratory tract. There are lots of changes in the population in an emergency situation. The emergency crew will be different; they will no longer be wearing standard emergency gear. This is totally foreign to EPA. We are collaborating with other agencies; there is a host of resources out there, and examples to tap into.

From the risk communication aspect, we are working with firefighters and emergency crew at the city level, trying to estimate acute and short-term exposure limits. We are asking what kind of information do you need with local people, so we do not have the error made of different agencies in the same situation giving different risk characterizations to their own workers and to the public. The decontamination process introduces more exposure to different kinds of things. For instance, raw chlorine used for disinfection yields byproducts; some are left as residuals to make sure the initial contaminant is not a problem. Exposure guidelines like acute exposure guideline levels (AEGLs) and temporary emergency exposure limits (TEELs) give an absolute safe, minimal (tolerable) level, and moderate toxicity. This gives building owners more flexibility in what they can afford for cleanup.

These assessments are not dealing with complex mixtures. Hopefully, there are at most 2 to 5 components, with interactions. This is nothing complex like PCBs or dioxins, unless it is something we can characterize as an entity in itself, like a (commercial) pesticide. Homeland Security is going to have an impact on this kind of assessment and prevention effort in a short time. Several case studies will show that cumulative risk can be done at a focused level, to include lots of factors, and to crank out a useful answer.

**Questions and Comments**

Question: Are you considering delayed effects?
Response: Where we know them. You can also have delayed exposure when everyone goes back to work, such as by resuspension. It can have either a delayed effect or a differential effect in a sensitized population.

Question: Are you looking at background or preexisting exposures?
Response: There is one proposal to use Landscan to map where people are and overlay exposures, such as copy machines, and account for them, although probably not for sick building syndrome.

**Reggie Harris (Region 3)**

The environmental justice and regional standpoint is a very different point of view than most other people here have. The pressures and responsibilities are quite different, and other considerations are more important. Necessity is the mother of invention. Looking at political realities, with an emphasis on states facilitating dialogue, there is an obvious need to do cumulative risk assessment. States in Region 3 demanded a cumulative risk forum so that they could explore it. In this Administration, what the states want, the states get. The Chester, PA study was a reality when the Regional Administrator said, "Let's do it." Other Regional Administrators will make those demands at some point in time.

It is not if, but when, will the next one occur. Partnership is very important. These things go outside EPA's charge. It would be irresponsible to stop at the boundaries and not do any more. We have to find inventive ways to get to the end of the road that is set by others. We need the help of other groups within EPA, states, and other agencies. There is a greater need for support within the Agency: the regions are in a difficult situation. They do not have the resources and manpower to take these on as projects; they are being strained by base activities. If there is a mandate, then there is a greater impetus to act. We should not be thinking about the "if," but rather the "when."

Concerning environmental justice, communities are a lot more aware and informed than they are given credit for. There is talk out there about cumulative risk assessment on the part of community groups and organizations. The next NEJAC meeting will focus on cumulative risk assessment. It is not a stretch to see that things will head in this direction. If demands are made, we will do it.

From the community perspective, in Chester, there were 149 children with elevated blood lead levels. The required medical interventions cost $800-$1500 a day for 30-45 days. That is a small snapshot of one set of interventions in a small community. Some children also needed

second and third interventions. In addition, children were eating unsafe fish and living in a community with the highest unemployment in the state, where health care providers had left the area because it was depressed, resulting in a lack of adequate care, where there were mobile sources from I-95 and trucks queuing up in the city streets. If you think about these things, it is a situation where we do not have a choice but to look at it and address it. It is the way we choose to address it that is the point of debate now. We find ways of getting things done. There are obvious inadequacies in what we have done and in what we do, but we need to continue along these lines and to work together, to come up with strategies.

**Questions and Comments**

Question: These things happen when you get a law in place. We are trying to balance the level at which groundswell from communities is going to impact what ORD does, compared to having a law.

Response: We are going to hear more. The states are beginning to ask. We are getting pressure from citizens who see this is a viable way to address it. We expect to see more, such as the NEJAC meeting. The regions do not have the money now. Region 3 could not pull staff off of everything else to do another Chester assessment now, but if the Regional Administrator and the states hear enough, there will eventually be a call for legislation.

## General Discussion

Mike Callahan invited the panelists to start the general discussion.

Comment: Concerning integration of human, ecological and cultural (quality of life), my experience is that EPA will talk about integrating the first two, but not about quality of life. We may need to do work here if we want to see progress. (Harper)

Comment: It is up to assessors to show that cumulative risk assessment will make a difference. (Cogliano)

Comment: As EPA people, we have been forbidden from lobbying Congress. We can say informally that cumulative risk assessment might be a good idea, and figure out where we are in the legislative playing field. (Lowit)

Comment: We have no mandate or knowledge. EPA is seen as the monolithic Federal government that is supposed to know everything that other agencies know. The public does not want to hear, "that isn't my job." How are we taking care of that issue? (Suter)

Comment: This ought to scare you: basically, if you do not do cumulative risk, the economists will do it for you. Where do we stand? (Dockins)

Comment: We are being forced by timelines to get out of the traditional ORD academic mindset of having 10 years to do an assessment. It is the same for Title 6 applications. We do not have years and years and years. A question can not sit for three years. Questions will get answered, but not as well. We do not have the time. (Hertzberg)

Comment: The regions need support from the Agency. Three years ago, in a meeting with the Regional Administrators and the Assistant Administrators, Mike Callahan said that communities are asking about cumulative risk: can we say, "we have no idea," which makes us irrelevant, or, "it's not the right question, we will revise the question and answer it," which is still irrelevant, or do we try to answer it or find someone who can answer it. If we do not get into cumulative risk, within 10 years it will be there and we will be irrelevant. (Harris)

All workshop participants were then invited to participate in the open discussion.

Comment: It is incumbent on us to offer a more clear description of what the scope of cumulative risk is. It is a lot of different things (from this week), from detailed two-chemical interactions, e.g., with TCE at the metabolic level; to looking at all the

data, and picking the relevant pieces to make an index; to developing quantitative estimates of risk based on emissions, etc. Most people say that it can not be one thing, we must tailor it to the need. Unless we can describe it so that it is understood by a lay audience, there is no chance of getting support to get it introduced into the standard Agency protocol. (Klauder)

Comment: Risk assessment generally is complex. Cumulative risk assessment is just two or more stressors acting together. We have been successful getting risk assessment into the mainstream of agency thinking. Why is it case specific? Every person identifies with a set of statutes or requirements. There is a series of principles that need to be applied and adapted to situations. The fact is that we chose to focus on community issues, because it brought in a unique perspective. We are not trying to turn [the Agency] around, but to broaden the perspective to environmental protection, not just chemical hazard and analysis. So, we start with asking "what's the problem." Even laws do not drive every decision: laws catch up with popular opinion. We are at a point where we are hearing what the future legislation will be. The principles are important (such as the framework document) – let's look at how they fit. There is not one set of instructions for a community. We have to be sensitive to the questions they are asking – we do not know the set yet. (Callahan)

Comment: To expand, from an outside-the-Agency perspective, we can focus on models and methods. It may go up to [the level of] guidelines, policy, and law. Sometimes we are proving that we "can" do something. Also, at the policy level, in some situations, the policy comes first, and gives the funding to fix the models. Who is doing the policy? Is there opposition to change? Policy is the "must" level. The third piece is the data (epidemiologic, laboratory, field) – sometimes it drives the whole process. To some extent, models and methods are at the program level. Policy includes FACA: we can lobby, we can write letters, and we want to. We do not see what decision opportunities there are at the present time. It helps if EPA says, "here is an important document." We could use a letter that says, "this is an important issue, because an opportunity is coming." It is a symbiosis; it helps to have an inside perspective on what will make a difference. (Harper)

Comment: The same comment [has been made] from academia and industry. Communication is not always good. We had the problem of defining cumulative risk when developing the framework. We wanted it to have a simple, all-inclusive definition, to have two lines to capture what we wanted it to do, but [also] enough details for someone at the policy or funding level to see that it is feasible. This can look impossible due to the complexities. At the case level, the risk is that people get locked in to [using the] feasible parts that are appropriate for [their] situation. If [the definition is] too accurate, it looks too immense and complex. (Hertzberg)

Comment: This is kind of like a traditional risk assessment with a broad view that narrows when [looking at specific] cases. (Callahan)

Comment: The regions have more power than you think, for instance, in Hanford, they negotiated a settlement with the stakeholders. If we have that flexibility in all the regions, we can do cumulative risk – planning and scoping, etc. – as a matter of course. We need to keep track of the cumulative risk efforts that work, and share [the information]. Then we will start seeing that the culture [has been] happening all the time, and is not new. (Hertzberg)

Comment: With respect to [Jeff Yurk's]'s demonstrations of [risk assessment] tools, would it be useful for all the regions to have that capability, such as for Jeff to go on the road and teach? (Callahan)

Comment: In Region 1, there are interesting things going on at the regional level, [which will] really matter to other regions. We will have to write reports. Can ORD help us by replicating the basic tools across the regions? To provide the basics to which the regions can add their own layers? This is incredibly important. (Castagna)

Comment: The regional offices deal with politics, the public, the media. [There are differences, for instance,] it is hard to have a one-size-fits-all implementation policy.

Comment: The tribes' relationship precedes the States' relationships with the Federal government. They look to EPA to help; they want a Federal line in the sand. They end up fighting with individuals who are not going to change. It would also help to have policy from Headquarters that trickles down into the regions, because things get lost. (Harper)

Comment: Part of the way of getting cumulative risk advanced is to advertise existing things, like tools, but also to talk more about things that are starting or going on that are dealing with some aspect of cumulative risk. [If we] advertise their effectiveness, it is part of the process of acceptance. We may be missing that cumulative risk projects tend to be narrow, e.g., to be strictly air; we need to do pilot projects that can address broader community issues, like Chester. This will demonstrate the usefulness of the approach to communities. If we can do one [cumulative risk assessment] in a really good way, it would be a big help. Cumulative risk is a nonpartisan thing: it comes under Democratic and Republican, environmental justice and local community capacities. It is not out of favor. It fits well with both agendas because community needs is a nonpartisan issue. (Topper)

Comment: There are other tools to do cumulative-type things: community profiling is one. There is lots that could be done that communities would like. (Harper)

Comment: We are trying to take back a list of proposals to ORD. Is it better to have someone look at a number of case studies and show how they differ from a simplified standard approach, or is it better to put the effort into new projects to show that [cumulative risk assessment can] be done? It will take a concerted effort to do, but it is possible. Which is more worthwhile? We hope the regions will do case studies. We are looking at ten years for the cumulative risk guidelines; that gives us more time to get case studies in. (Hertzberg)

Comment: That is a great idea. Several case studies have been done, but not so much has been done with comparing data. We could use more time to take an actual area, where we know there is a problem and where we have data, to try a case study using the best available approaches to do one area well, not many. (Kaleri)

Comment: It is like writing a term paper: before you start, you review the literature and figure out what happened before. You look at what was done, and get a sense of the state of the science. You take a look back before starting a new study. (Teuschler)

Comment: For that to really take hold, you will have to demonstrate that it makes a difference. Not just a different risk number, but perhaps better community acceptance. People need to know that it is not just being done because it is interesting, but because it makes a difference. We need to show value-added for costly, more expansive approaches. (Cogliano)

Comment: A synthesis or a lessons learned from existing studies would be extremely useful; it would demonstrate the aspects of cumulative risk assessment, and make it more concrete. (Dockins)

# Closing Remarks, Summary, Future Actions

### Research Needs – Linda Teuschler (ORD/NCEA)

The following list of research needs identified by the breakout groups (with some redundancies removed) was presented.

### Data Needs

- Need data on joint toxicity of mixtures.
- Need detection/monitoring data, exposure data for all media; need to know what is available.
- Need to fill data gaps for children, both toxicity and exposure, differential effects between children and adults, better exposure estimates for children, mode of action
- Need clearinghouse (library or inventory) of all types of data being gathered. Include a measure of data quality. Provide data in a consistent format.
- Identify common mixtures found in various media, e.g., air toxics, food, soils, pesticides. Decide which mixtures are toxic enough to merit evaluation using the methods in the 2000 Mixtures Guidance.
- Identify groups of chemicals associated with specific processes (C&D landfills, products of combustion processes, etc.). For each group, identify what toxicological mode of action or endpoint is most representative of the specific mixture. Indicate if there is a specific chemical driving the risk/hazard of the mixture. Target priority mixtures for toxicological evaluation.
- Address hypothesis that particulate exposure is a sensitizer for other effects (i.e., a vulnerability factor).
- Classify/categorize health effects to systematize the relationship between cumulative risk and public health outcomes. Consider public health surveillance methods. Prioritize disease outcomes using public health data. Develop tools to integrate environmental health and public health data.
- Need battery of assays and endpoints associated with health endpoints (disease) in humans.
- Conduct research to identify chemical-specific biomarkers (exposure vs. health endpoints).
- Conduct field studies of real life exposures (e.g., berries, venison, fiber plants). Develop parameters of alternative exposure scenarios (e.g., basketweavers).
- Establish human background body burdens/subpopulation-specific.
- Subpopulation dose-response curves on IRIS.
- More cost/benefit valuation that includes cultural and holistic factors.

**Method Needs**

- Need ways to consider background.
- Need ways to identify susceptible/vulnerable populations, factors.
- Need ways to communicate limits of science associated with cumulative risk assessment.
- Need "fingerprinting" of releases to attribute to sources or an exposure biomarker, to get at cause and effect.
- Need method for source apportionment for community exposures including fate and transport.
- Need decision criteria for what to include/exclude from the analysis.
- Need method to evaluate effectiveness of the final cumulative risk assessment to link to the original scoping.
- Need a method for presenting results and uncertainties of cumulative risk assessments to the public, including bounds on uncertainty.
- Explore how to incorporate joint action, other than additive, into a risk assessment. When is additivity correct to assume and what do we miss using this assumption and under what conditions?
- Explore how to incorporate non-chemical stressors and factors such as age-related sensitivities into cumulative risk assessment.
- Investigate the effect of homogeneity on toxicity factors. At what point does a population's lack of heterogeneity alter the way toxicity factors are developed?
- Investigate how higher prevalence of disease (e.g., high blood pressure) affects vulnerability to other stressors causing effects in the same system (e.g., kidney disease).
- Need to understand co-exposures that interact in detoxification pathways, e.g., chemicals with same mode of action that have co-exposures in drinking water.
- Investigate cumulative uncertainties that aggregate across cumulative risk assessment factors.
- Research into potential use of QALYs, DALYs, WTP, etc. in cumulative risk assessment, usability and perception issues.
- Expand health risk assessment to look at all stressors, like ecology does. Broaden human health focus of cumulative risk assessment to include "wellness" concepts – allows bringing in welfare and culture.
- Better ways to present GIS information to show impacts.

**Guidance**

- Need guidance on how to interpret available information (children and other susceptible populations).
- Need ways to share information on how to form and implement stakeholder groups. Must lead to community consensus on cumulative risk assessment, actions, outcomes.
- Convert 2000 Mixtures Guidance document to a User's Guide to promote consistency of

approach across programs and other users. Need ranges or defaults for using various methods with documentation and rationale. Guidance should have site-specific applicability.
- Write mixtures exposure guidance, e.g., include bioavailability, speciation.
- Risk characterization.
- Risk communication.

**Training**

- Need training on how to put together conceptual models, decision matrix templates, conceptual model templates, how to limit scope.

**Lessons Learned from Current Batch of Case Studies**

- Have case studies do summaries using a standard format to learn what does and does not work. Conduct retrospective analysis of case studies for what works/does not work.
- Break cumulative risk down into pieces, indicating what is working and where most uncertainty exists.
- Evaluate replicability of regional cumulative risk models.

**Questions and Comments**

Comment: [Workshop participants should] think about [potential] contact people for follow-up. (Hertzberg)

Comment: There will be a report [on the workshop], and establishment of a contact list. There will be follow-up. Eventually, there may be another planning group. (Callahan)

Comment: For the last word on the formal agenda, a suggestion is to convene the planning group again, go through the discussion conclusions, and let the planning group decide which look most promising, then invite participation [from others]. The slides will be up on the Internet within about a week and will be publicly accessible. The presenters and session moderators will review the draft report; it should take two to three months [to go through the] process. (Klauder)

# APPENDIX A: AGENDA

**DATE: November 4-8, 2002**
**LOCATION: Region VI Offices, Dallas, TX**
**Co-Sponsored by ORD Regional Science Program, NCEA-Cincinnati, and the Region 6 Regional Science Council**

## DAY 1 (Monday):

Session Co-Chairs: Mike Callahan (Region 6) & Linda Teuschler (ORD):
Co-Chairs for Course and Expo (all week): J eff Yurk (Region 6) and Eletha Brady-Roberts (ORD)

| | | |
|---|---|---|
| 7:30 - 8:00 | Registration | |
| 8:00 - 12:00 | Cumulative Risk Tools Course, Part 1 (Jeff Yurk/Region 6) | |

***1. Introduction and Overview***

| | | |
|---|---|---|
| 1:00 - 1:30 | Welcome & Introduction<br>Gregg Cooke, Regional Administrator, Region 6<br>Paul Gilman, Assistant Administrator for Research and Development | |
| 1:30 - 2:30 | Keynote Address (Margaret MacDonell, Argonne National Laboratory) | |
| 2:30 - 2:45 | Break | |
| 2:45 - 3:30 | Overview/EPA Framework for Cumulative Risk Assessment (Mike Callahan, Region 6) | |
| 3:30 - 4:15 | Research Planning for Cumulative Risk Assessment (Linda Teuschler, ORD) | |
| 4:15 - 5:00 | Discussion of what cumulative risk issues people have and what expectations they have for this workshop | |
| 5:00 - 6:00 | Social Mixer/Poster Session (Eletha Brady-Roberts/ORD) | *Fairmont Hotel* |

## DAY 2 (Tuesday):

Session Co-Chairs: George Bollweg (Region 5) & Ed Bender (ORD)

***2. Planning, Scoping, & Community Issues***

| | |
|---|---|
| 8:20 - 8:30 | Issues for the Day (Bollweg/Bender) |
| 8:30 - 9:30 | Planning, Scoping and Problem Formulation in Cumulative Risk Assessment (Ed Bender/ORD) |
| 9:30 - 10:15 | Environmental Justice Considerations (Reggie Harris/Region 3) |
| 10:15 - 10:30 | Break |
| 10:30 - 11:15 | Using Cumulative Risk Assessment in a Community Setting (Hank Topper/OPPT) |
| 11:15 - 12:00 | Cumulative Hazard Assessment for Ambient Air Toxics in Cook County, IL and Lake County, IN (George Bollweg/Region 5) |
| 12:00 - 1:00 | Lunch |
| 1:00 - 2:00 | Discussion of Stakeholder Involvement (Breakout groups) |
| | Breakout Group #1<br>Problem Formulation: Bounding the analysis, developing hypotheses about possible cause and effect relationships, recognizing who should be involved |
| | Breakout Group #2<br>Stakeholder Involvement: Stakeholder participation, communicating cumulative risk to the public, defining fundamental principles of participation, education/ interaction |
| | Breakout Group #3<br>Cumulative Risk Conceptual Models: Sources, stressors/agents, pathways/routes of exposure, receptors, and endpoints in context of data sources, data quality and uncertainty, averaging periods, rationale and defaults to fill data gaps |
| | Breakout Group #4<br>Community Issues: Environmental justice, special considerations for sensitive or highly exposed subpopulations |
| 2:00 - 2:50 | Report Back with Research Recommendations and Future Steps |

| | |
|---|---|
| 3:10 - 5:00 | Cumulative Risk Tools Course, Part 2 (Jeff Yurk/Region 6)<br>Posters (Eletha Brady-Roberts/ORD) |
| 6:30 - 7:30 | Demonstrations of Risk Tools, Part 1: Land Scan (Budhendra Bhaduri, Battelle-Oak Ridge) |

## DAY 3 (Wednesday):

Session Co-Chairs: Roseanne Lorenzana (Region 10) & Jane Gallagher (ORD)

***3. Approaches to Cumulative Risk Assessment***

| | |
|---|---|
| 8:20 - 8:30 | Issues for the Day (Lorenzana/Gallagher) |
| 8:30 - 9:15 | Toxicology of Mixtures (Rick Hertzberg/ORD) |
| 9:15 -10:15 | OAQPS Case Study: Toxicologic Independence (Deirdre Murphy/OAQPS) |
| 10:15 - 10:30 | Break |
| 10:30 - 11:15 | Biomarkers Approach: Status/State of Science (Jane Gallagher/ORD) |
| 11:15 - 12:00 | OPP Case Study: Toxicologic Similarity (Anna Lowit/OPP) |
| 12:00 - 1:00 | Lunch |
| 1:00 - 2:00 | Traditional Tribal Lifeway Paradigm (Vivian Parker, California Indian Basketweavers Association) |
| 2:00 - 2:30 | Break |
| 2:30 - 4:00 | Discussion of Case Studies (break out into subgroups) & Development of Research Recommendations<br><br>Breakout Group #1<br>Toxicology of Mixtures: Understanding toxicology of combinations of chemicals and how this impacts our ability to conduct a cumulative risk assessment<br><br>Breakout Group #2<br>Risk Assessment Approaches: What methods work and what methods don't work in cumulative risk assessment<br><br>Breakout Group #3<br>Biomarkers: Use of biomarkers in cumulative risk assessment, technical challenges |

| | |
|---|---|
| | Breakout Group #4<br>Cultural Factors: Factors that affect exposure assessment and identification of endpoints in cumulative risk assessment |
| 4:00 - 5:00 | Report back with Research Recommendations and Next Steps |
| 6:30 - 8:30 | Demonstration of Risk Tools, Part 2: RAIMI System and Biomarker Tools (Jane Gallagher/ORD; Jeff Yurk/Region 6) |

## DAY 4 (Thursday):

Session Co-Chairs: Audrey Galizia (Reg. 2) & Jim Cogliano, (ORD)

***4. Putting it Together***

| | |
|---|---|
| 8:20 - 8:30 | Issues for the Day (Galizia/Cogliano) |
| 8:30 - 9:15 | Vulnerability (Mike Callahan, Region 6) |
| 9:15 - 10:30 | Ecological Cumulative Risk Assessment (Glenn Suter/ORD) |
| 8:30 - 9:30 | Implications to Uncertainty Analysis of Combining Risks (Jim Cogliano/ORD) |
| 10:30 - 11:00 | Break |
| 11:00 - 12:00 | Use of other metrics for combining risks (Chris Dockins, OPEI) |
| 12:00 - 1:00 | Lunch |
| 1:45 - 2:30 | Cumulative Risk Index Analysis (Gerald Carney/Region 6) |
| 2:30 - 2:45 | Break |
| 2:45 - 3:30 | Discussion of case studies and other aspects of "putting it together" (breakout) |
| | Breakout Group #1<br>Risk Characterization Methods: Population-based risk assessment, identifying and accounting for uncertainty in cumulative risk assessment, integrating risk information across scientific and non-scientific disciplines |
| | Breakout Group #2<br>Combining Risks: Ways to express cumulative risks, disparate risks, choice of metrics, ranking systems |

| | | |
|---|---|---|
| | Breakout Group #3<br>Integration of Approaches: Differences and similarities in approaches to cumulative risk in methods used in ecology, human health, and tribal assessments | |
| 3:30 - 4:30 | Report Back with Research Recommendations and Next Steps | *Texas Room* |
| 6:30 - ??? | Dinner at Sonny Bryans's Restaurant | |

## DAY 5 (Friday):

Session Co-Chairs: Mike Callahan (Region 6) & Linda Teuschler (ORD) *Texas Room*

***6. Policy Implications***

| | |
|---|---|
| 8:00-8:15 | Issues for the Day & Review (Callahan/Teuschler) |
| 8:15 - 10:15 | Policy Panel (Mike Callahan, Moderator; Panelists to be announced)<br>[Discuss policy implications, how cumulative risk assessment will affect our way of doing business in the future, current thinking of EPA policy folks. Question: Is cumulative risk assessment going to change the way we do business, or is it just a flash in the pan? Answer questions.] |
| 10:15 - 11:15 | Closing remarks, summary, future actions (Callahan/Teuschler/Galizia/Klauder) |

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# APPENDIX C: SLIDES FROM PRESENTATIONS

*These slides can be found at*
http://epa.gov/osp/regions/workshops.htm

| | | |
|---|---|---|
| 1. | *Workshop Overview* | **Paul Gilman** |
| 2. | *Keynote Address* | **Margaret MacDonell** |
| 3. | *Overview/EPA Framework for Cumulative Risk Assessment* | **Mike Callahan** |
| 4. | *Research Planning for Cumulative Risk Assessment* | **Linda Teuschler** |
| 5. | *Planning, Scoping and Problem Formulation in Cumulative Risk Assessment* | **Ed Bender** |
| 6. | *Environmental Justice Considerations* | **Reggie Harris** |
| 7. | *Using Cumulative Risk Assessment in a Community Setting* | **Hank Topper** |
| 8. | *Cumulative Hazard Assessment for Ambient Air Toxics in Cook County, Illinois and Lake County, Indiana* | **George Bollweg** |
| 9. | *Health Risk Assessment: Toxicology of Mixtures* | **Rick Hertzberg** |
| 10. | *Initial NATA National Scale Assessment* | **Deirdre Murphy** |
| 11. | *Biomarkers Approach: Status/State of Science* | **Jane Gallagher** |
| 12. | *OPP Case Study: Toxicologic Similarity* | **Anna Lowit** |
| 13. | *Traditional Tribal Lifeway Paradigm* | **Vivian Parker** |
| 14. | *Vulnerability* | **Mike Callahan** |
| 15. | *Ecological Cumulative Risk Assessment* | **Glenn Suter** |
| 16. | *Implications to Uncertainty Analysis of Combining Risks* | **Jim Cogliano** |
| 17. | *Use of Other Metrics for Combining Risks* | **Chris Dockins** |
| 18. | *Cumulative Risk Index Analysis* | **Gerald Carney** |
| 19. | *Tribal Perspectives on Cumulative Risk* | **Barbara Harper** |

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# APPENDIX D: FLIP CHART NOTES

## Breakout Session I: Discussion of Stakeholder Involvement (Day 2)

***Breakout Group #2-1***

*Problem Formulation: Bounding the analysis, developing hypotheses about possible cause and effect relationships, recognizing who should be involved.*

Attendees:

| | | |
|---|---|---|
| Cheryl | Bradley | Oklahoma Department of Environmental Quality |
| Gerald | Carney | Region 6 |
| Barbara | Driscoll | OAR/OAQPS |
| Clara | Lee | Region 6 |
| Roseanne | Lorenzana | Region 10 |
| Anna | Lowit | OPP/OPPTS |
| Margaret | MacDonell | Argonne National Laboratory |
| Michael | Sivak | Region 2 |
| Linda | Teuschler | ORD/NCEA |
| Anna | Treinies | Region 6 |
| Winona | Victery | Region 9 |

Problem Formulation

- Clarify purpose of the assessment
  - Determine what are the criteria that indicate a "problem"
  - Identify multiple uses
- Define the resources available to the project
  - Money
  - Time

  - Expertise that's available
  - Info that's available
- What are the possible products of the assessment; who will use them and how?
  - Risk management options
- How far to go to collect data/info to determine the scope
  - Hypotheses of causes and effects
  - What's "in" and what's "out" and the rationale for each
- How to limit scope without losing the BIG picture?
- Figure out regulatory boundaries
- What are the factors motivating the need to perform a CRA?
  - Who to involve
    - Who's interested
    - Who has vested interest
- Timing Issues:
  - When to establish partnerships
  - When to monitor to leverage resources
- Maximum use of resources with the right timing
  - Resource planning
- Recognition of differences in expectations
- Brainstorm the universe of outcomes
- Consider what the decision-maker needs
- Education & communication for justifications of limits of the scope
- What question is being addressed (what's the question)?
- What's the end purpose?
- What's the Cadillac version vs. the tricycle version?

Research Needs for Problem Formulation

- Clearinghouse (library inventory) of all types of data being gathered
  - Include data quality
  - Provide data in consistent format
- Retrospective analysis of case studies for what's worked/not worked
- Decision criteria for inclusion/exclusion
- Cause-Effect
  - "Fingerprinting" of releases to attribute to sources (or) an exposure biomarker
- Method for source apportionment for community exposures including fate and transport
- Method to evaluate effectiveness of the final CRA to link to the original scoping
- Method for limit the scope by identifying representative indicator

***Breakout Group #2-2***

*Stakeholder Involvement: Stakeholder participation, communicating cumulative risk to the public, defining fundamental principles of participation, education/interaction*

Attendees:

| | | |
|---|---|---|
| George | Bollweg | Region 5 |
| Kuenja | Chung | Region 6 |
| Jane | Gallagher | ORD/NHEERL |
| David | Klauder | ORD/OSP |
| Carrie | Paige | Region 6 |
| Clint | Rachal | Region 6 |
| Brad | Schultz | Region 5 |
| Henry | Topper | OPP/OPPTS |
| Beth | Walls | Region 4 |

Stakeholder Involvement

- Forming representative stakeholder groups

  Need: Ways to share information on how to do

  Implementation: Must lead to community consensus on CRA, actions, and outcomes

  How to get there:

  - Go to NGOs
  - Build better cross-Agency networks
  - Extract information from case studies
  - Interactive web site/newsletter
  - Research: How to develop representative subset of community to serve on CRA groups.

- What can CRA do/not do (current reality), so don't "over sell."
  - Needed - yes - ?? in part - see
  - Doesn't yet exist - ? "informed consent" course
  - How to do it.
    - Form cross-Agency workshop to develop statement/factsheet
    - First action - scour to see what exists, e.g., informed consent course
  - Research Need: How do you communicate limits of science associated with CRA.

- Educational Tools:
  - Community Risk - overview targeted at community level - Here's what we have learned about community risks. Use as a starting point for CRAs. What do we know about community stressors. Integrate what exists - use fact sheets and State of the Environment Report.
  - Require all A case studies to do summaries (using a standard format).
  - Environmental Health Facts - quarterly/annual publication/web site.
    - Interactive "click on" technology that describes what we know about building, stream, factory, air - link to specific case studies.

***Breakout Group # 2-3***

*Cumulative Risk Conceptual Models: Sources, stressors/agents, pathways/routes of exposure, receptors, and endpoints in context of data sources, data quality and uncertainty, averaging periods, rationale and defaults to fill data gaps*

Attendees:

| | | |
|---|---|---|
| Ed | Bender | ORD/OSP |
| Norman | Dyer | Region 6 |
| Kendra | Harmason | Louisiana Department of Environmental Quality |
| Rick | Hertzberg | ORD/NCEA |
| Ofia | Hodoh | Region 4 |
| David | Macarus | Region 5 |
| Phuong | Nguyen | Region 5 |
| Toni | Payne | Oklahoma Department of Environmental Quality |
| Mary | Wu | Region 8 |

Cumulative Risk Conceptual Models

- What experience have you had with conceptual models? What worked well, what did not?
- Wish list - conceptual
- What tools, methods or research would help to meet those wishes?
  - Data on mixtures joint toxicity
  - Detection/monitoring - what's available
  - Communicate joint efforts across EPA
  - Model validation
  - Background needs to be considered
  - Training regarding conceptual models, decision matrix templates
  - How to limit scope
  - Exposure data for media

- Template conceptual models
- Share information and results
- Data available
- Standard approaches
- Training, tools
- National data

***Breakout Group # 2-4***

*Community Issues: Environmental justice, special considerations for sensitive or highly exposed subpopulations*

Attendees:

| | | |
|---|---|---|
| Thomas L. | Baugh | Region 4 |
| Eletha | Brady-Roberts | ORD/NCEA |
| Kathy | Castagna | Region 1 |
| Brenda | Foos | OA/OCHP |
| Audrey | Galizia | Region 2 |
| Reginald | Harris | Region 3 |
| Vivian | Parker | California Indian Basketweavers Association |

Community Issues

Research Priorities:

- Development of verifiable public health indicators based on public health outcomes data (verify).
- Data gaps for children (toxicity and exposure)
  - Differential effects (adult vs. child)

  - Better exposure estimates for children
  - Mode of action
- Guidance on how to interpret available information (children and other susceptible populations)
- Synergistic effects (2+ chemicals)
- Identify common elements in CRA case studies (such as presented in workshop)
- "Real life" exposures (pesticide use, drift and runoff)
  - Monitoring for prevention
  - ORD to verify methodology
- Identify susceptible/vulnerable populations (factors)

# Breakout Session II: Discussion of Case Studies (Day 3)

***Breakout Group # 3-1***

*Toxicology of Mixtures: Understanding toxicology of combinations of chemicals and how this impacts our ability to conduct a cumulative risk assessment*

Attendees:

| | | |
|---|---|---|
| George | Bollweg | Region 5 |
| Brenda | Foos | OA/OCHP |
| Rick | Hertzberg | ORD/NCEA |
| Ofia | Hodoh | Region 4 |
| Michael | Honeycutt | Texas Commission on Environmental Quality |
| Clara | Lee | Region 6 |
| Carrie | Paige | Region 6 |

Toxicology of Mixtures

- Regional opinion: We can't implement Mixtures Guidance (with so much "judgement") - "deficiencies in available methods"
    - Reproducibility among users?
    - How can we use consistently?

  Need (1): Convert 2000 Mixtures Guidance to "Users Guide?" (Like IEM → HHRAP)

  Purpose:
    - Cross-program consistency
    - "Ranges," "Defaults," - documentation/rationale for both
- This Guidance should have site-specific applicability

  Need (2): Identify common urban air toxics mixtures (same for common water pollutant mixtures?) (Food?), soil pesticides, mixtures → asthma? (Is work in progress?)

- PAHs
- Phthalates

Which mixtures are toxic enough to merit "mixtures guidance type" consideration?

Need (3): Mixtures Exposure Guidance (e.g., that considers bioavailability, speciation)

Need (4): Particulate Exposure as a "sensitizer"

- Can this be addressed, generally? (A "vulnerability factor")?

What are we missing with status quo? (Additivity assumption)

***Breakout Group # 3-2***

*Risk Assessment Approaches: What methods work and what methods don't work in cumulative risk assessment*

Attendees:

| | | |
|---|---|---|
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| Cheryl | Bradley | Oklahoma Department of Environmental Quality |
| Michael | Callahan | Region 6 |
| Barbara | Driscoll | OAR/OAQPS |
| Anna | Lowit | OPP/OPPTS |
| David | Macarus | Region 5 |
| Torin | McCoy | Texas Commission on Environmental Quality |
| Phuong | Nguyen | Region 5 |
| Clint | Rachal | Region 6 |
| Michael | Sivak | Region 2 |
| Linda | Teuschler | ORD/NCEA |
| Mary | Wu | Region 8 |

Risk Assessment Approaches

*What do we need to know about approaches to cumulative risk assessment?*

*How can we incorporate joint action other than additive in a risk assessment?*

*Is additivity correct to assume?*

*What should we do about non-chemical stressors?*

- Break cumulative risk down into pieces

*What is working?*

*Where is most uncertainty?*

- Use genetic factors to sort out what is important - long-term
- Tools to integrate environmental health and public health data

  Need method.

  Epidemiology data problematic regarding exposure assessment.
- Write up white papers on issues.
- Prioritize what disease outcomes are important using public health data.
- Target priority mixtures for toxicologic evaluation - Use DoD sites for example.
- Inventory of what has already been done on what chemicals to target in toxicity studies.
- New spills vs. weathered mixtures
- Animal - Human extrapolation / Route to route extrapolation
- How to use biomarkers?
- Age-related sensitivities
- More PBPK modeling/data collection (PK)
- Uncertainty in fate and transport models - bioavailability, changes over time in chemical composition
- Classify/categorize health effects to systematize cumulative risk and relationship to public health (and public health surveillance methods)
- Clarify risk assessment methods for “mixtures” for consistency across programs.
- [Mixtures toxicity] database - review, and update priority mixtures
- Decision tree that represents method of doing cumulative risk for substances that have interaction or don’t

- Method of presenting results and uncertainties to public
  - Bounds on uncertainties
  - Identify groups of chemicals associated with specific processes (C&D landfills, products of combustion incinerators, etc.)
  - What toxicological mode of action/endpoint is most representative of the specific mixture?
  - Is there a specific chemical driving the risk/hazard of the mixture?
  - Long-term exposure to low levels of these mixtures
  - Identify any existing lifestyle sensitivities
- Method for evaluating relative importance of mixtures

***Breakout Group # 3-3***

*Biomarkers: Use of biomarkers in cumulative risk assessment and identification of endpoints in cumulative risk assessment*

Attendees:

| | | |
|---|---|---|
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| Audrey | Galizia | Region 2 |
| Jane | Gallagher | ORD/NHEERL |
| David | Klauder | ORD/OSP |
| Brad | Schultz | Region 5 |
| Anna | Treinies | Region 6 |
| Winona | Victery | Region 9 |
| Beth | Walls | Region 4 |

Biomarkers

*What do we need to know about approaches to cumulative risk assessment?*

*Needs?*

*Challenges?*

Chemical by chemical:

- Exposure biomarkers that identify a greater variety of chemicals.
- Mechanism information.

or

General - matching biomarker "profiles" with disease/health endpoints.

Question: How do we use this to "mediate" exposures?

Answer: EPA has necessary discretion Also, endpoints, like immune response, do focus on mechanism - than can target SPS of chemicals. Can couple with metabolite measurements in blood/urine - to help get at source.

- If you have "biomarker to health outcome" measure - you have what you need for risk assessment.
  - Chemical specific biomarkers.
    - "Mine" existing data (e.g., OPPT, FDA, NHANES, CDC, industrial chemicals)
    - Focus on most common chemicals at Superfund sites
  - Mid-sad -DNA adducts to SPS of chemicals
  - General profiles associated with health endpoints - unknown mix of stressors (including DNA adducts).
- Exposure and health endpoint biomarkers vs. archiving samples - is there a unique niche for EPA?
- EPA needs to tie in with other Agency epidemiology studies
- Do biomarker research with ongoing animal studies - to determine relationship between surrogate markers with target tissue levels.
- Biomarker Needs:
  - Exposure biomarkers needed that identify a greater variety of chemical and metabolites

- Battery of assay and endpoint covering the continuum
- Mechanistic information needed
- Archiving of biological and environmental samples and measurements as new technologies advance
- Validation of surrogate cells with target tissues responses

***Breakout Group # 3-4***

*Cultural Factors: Factors that affect exposure assessment and identification of endpoints in cumulative risk assessment*

Attendees:

| | | |
|---|---|---|
| Thomas L. | Baugh | Region 4 |
| Eletha | Brady-Roberts | ORD/NCEA |
| Kathy | Castagna | Region 1 |
| Reginald | Harris | Region 3 |
| Roseanne | Lorenzana | Region 10 |
| Toni | Payne | Oklahoma Department of Environmental Quality |

Cultural Factors

- Field studies of real life exposures (e.g., berries, venison, fiber plants)
- Exposures:
  - Indirect exposure model validation with real measurements.
  - Parameters of alternate exposure scenarios (e.g., basketweaving)

- Toxicity:
  - Effect of homogeneity on toxicity factors. At what point does a population's lack of heterogeneity alter the way toxicity factors are developed?
  - Characterization of latent effects carried across multiple generations (e.g., seven generations)
  - Culture as an endpoint of toxicity (e.g., loss or adverse effect on the culture)
  - How higher prevalence of disease (e.g., high blood pressure) affects vulnerability to other stressors causing effects to the same system (e.g., kidney disease)?
  - Data (contaminant) for environmental media contacted in the alternate exposure scenarios.

# Breakout Session III: Discussion of Case Studies and Other Aspects of "Putting It Together" (Day 4)

***Breakout Group #4-1***

*Risk Characterization Methods: Population-based risk assessment, identifying and accounting for uncertainty in cumulative risk assessment, integrating risk information across scientific and non-scientific disciplines*

Attendees:

| | | |
|---|---|---|
| George | Bollweg | Region 5 |
| Audrey | Galizia | Region 2 |
| Ofia | Hodoh | Region 4 |
| Anna | Lowit | OPP/OPPTS |
| Torin | McCoy | Texas Commission on Environmental Quality |
| Carrie | Paige | Region 6 |
| Linda | Teuschler | ORD/NCEA |
| Winona | Victery | Region 9 |
| Mary | Wu | Region 8 |

Risk Characterization Methods

- Guidance
  - When to use, not to use
  - Tiered approach (case by case?)
  - Why items included / excluded
  - Methodology on quality of data
    - Criteria
    - Identify appropriate data
  - Mechanism for data review and methodology

- Supplemental guidance on risk characterization
- Checklist of contributing factors
  - Social
  - Economic
- Risk communication strategy

- Research Areas
  - Understanding co-exposures that interact in detoxification pathways (e.g., chemical same MOA, co-exposure in OW)
  - Cumulative uncertainties that aggregate across CRA factors
  - Research into potential use of QALYs, DALYs, WTP, etc. in CRA usability and perception issues.

- Ideas
  - Risk characterization supplement
    - Uncertainties in cumulative risk
  - Guide/Method for quality of data - how to measure (methodology)
    - Criteria
    - Review
    - Identify usable / appropriate data
  - Consistent risk calculation (later)
  - Definition of cumulative risk (policy)
  - Paradigm to follow
  - Case by case basis
  - Guidance on when to use, when not to use
  - Tiered approach with explanation of why items included / excluded
  - Checklist of contributing factors

***Breakout Group #4-2***

*Combining Risks: Ways to express cumulative risks, disparate risks, choice of metrics, ranking systems.*

Attendees:

Not available

Combining Risks

- Look for different way of expressing risk
- Need weighting for non-chemical stressor - sensitivity analysis
- Establish human background body burdens / subpopulation-specific
- Beat IRIS → Give more implementatable information, secondary, tertiary effects
- Subpopulation dose - response curves on IRIS
- More refinement on exposure factors (life-stage sensitivity analysis)

***Breakout Group # 4-3***

*Integration of Approaches: Differences and similarities in approaches to cumulative risk in methods used in ecology, human health, and tribal assessments.*

Attendees:

Not available

Integration of Approaches

- Health
  - Typically only add individual assessment
  - Need to model eco
  - Need to expand health risk assessment to look at all stressors, like eco

- Ecological
  - Cumulative risk is the basic approach
  - Integration step is unique
- Socio-economic / quality of life - Tribal
  - Need research to quantify welfare / cultural socio-economic indicators for health and eco assessments.
  - Problem: little legislative directive (outside NEPA) to include culture / community health in risk assessment; i.e., lack of real drivers
  - Broaden "human health" focus of community risk assessment → "wellness." This allows bringing in welfare and culture.
- Indices
  - There are many eco and cultural indices - but because these are less "quantitative" than human health cancer / RfD risk assessment - health drives the decision.
  - Indices too "fuzzy" - Eco trying to move away from - more toward probable risk assessment → better chance of influencing decision.
  - More research on eco impacts on human health and economy.
- Research Needs
  - More C/B - valuation - that includes cultural
  - How environmental impacts impact cultural community health
  - More harmonization of health and eco
  - Better ways to present GIS information to show impacts
  - Evaluate replicability of regional cumulative risk models
  - Quantification of welfare and cultural indicators
  - Quantification of eco impacts on human health and eco

# APPENDIX E: PARTICIPANT EVALUATION SUMMARY

Meeting participants agreed that the information they gained from the workshop would help them better perform their job, especially the case studies, GIS Tools, and RAIMI model applications. Some attendees felt that the economic and tribal presentations were too vague and of less use to them. Though it was agreed that the presentations were effective in communicating regional issues and ORD science to address those issues, the majority of participants felt that the workshop should have contained more regional cumulative risk assessment issues such as the link to policy and enforcement, presenting the concept to decision makers, and a discussion of available EPA resources to make dissemination of technology and information more efficient. Interest was also expressed in presenting methods to identify, measure, and present relevant nonchemical stressors, as well as how to assess risks from the interaction of chemical and nonchemical stressors and how to use public health information in cumulative risk assessment.

Participants agreed that the presentations were sufficiently tailored to suit their information needs and that breakout sessions were effective in providing an opportunity to further explore the topics using the information learned. Some felt that breakout sessions should have been slightly longer and more focused. Suggestions for methods to facilitate continued interaction with contacts established at the conference included conducting additional workshops, preparing and posting a summary report and other follow-up material on a workshop web site, hosting a web-based message board, and creating and distributing a participant e-mail list. Overall, participants agreed that the meeting was useful and successful, and consistently offered positive feedback and praise to the organizers for a great workshop.

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