HUMAN HEALTH SUBCOMMITTEE

Conference Call Summary
Friday, October 10, 2008
12:30 p.m. – 2:30 p.m. Eastern Time

Welcome

Dr. James Klaunig, Indiana University School of Medicine, Subcommittee Chair

Dr. James Klaunig, Subcommittee Chair, welcomed the Board of Scientific Counselors' (BOSC) Human Health Subcommittee members to the conference call and thanked them for taking the time to serve on the Subcommittee. He asked participants to identify themselves, reviewed the call agenda, which included the Designated Federal Officer's (DFO) remarks, the charge to the Subcommittee, and two presentations from U.S. Environmental Protection Agency (EPA) personnel. A list of the Subcommittee members and other participants is attached to this summary, along with the agenda for the conference call.

BOSC DFO Remarks

Ms. Heather Drumm, EPA, Office of Research and Development (ORD), DFO

Ms. Drumm thanked the Subcommittee members for their participation and reviewed the Federal Advisory Committee Act (FACA) procedures and rules that are required for all Board of Scientific Counselors (BOSC) Subcommittee meetings. As the DFO for the Subcommittee, Ms. Drumm serves as the liaison between the Subcommittee and ORD. It is her responsibility as the DFO to ensure that the Subcommittee's conference calls and meetings comply with all FACA rules.

The BOSC is a Federal Advisory Committee that provides independent, scientific peer review and advice to EPA's ORD, and as such, is subject to the rules and requirements of FACA. All meetings and conference calls involving substantive issues—whether in person, by phone, or by e-mail—that include one-half or more of the Subcommittee members must be open to the public, and a notice must be placed in the *Federal Register* at least 15 days prior to the call or meeting. The Subcommittee Chair and DFO must be present at all conference calls and meetings. All Subcommittee documents are made available to the public. Ms. Drumm reported that no requests for public comment were submitted prior to the call, but the agenda allows time for public comment at 2:15 p.m. She will call for public comments at that time, and each comment should be limited to 3 minutes.

The information for this conference call was entered into the federal docket management system (http://www.regulations.gov, Docket ID EPA-HQ-ORD-2008-0649). During this conference call, items will be discussed according to the agenda, and a summary of the call will be made

available to the public after certification by the Subcommittee Chair of the Subcommittee. The Chair must certify the summary within 90 days of the call or meeting. The summary then will be posted on the BOSC Web Site (http://www.epa.gov/osp/bosc).

Ms. Drumm has worked with EPA officials to ensure that all appropriate ethics regulations have been satisfied. If any Subcommittee member discovers a potential conflict of interest in relation to any topic discussed, Ms. Drumm must be informed. This conference call was convened specifically to provide an overview of the ORD and of the Human Health Research Program (HHRP). All Subcommittee members should have received a binder with background materials prior to this call. The presentations were sent to members via e-mail. As this conference call will be a matter of public record, Ms. Drumm asked the Subcommittee members to identify themselves before speaking.

Materials Overview

Dr. Sally Darney, EPA, ORD, National Program Director (NPD) for Human Health Research

Dr. Darney explained that the binders the Subcommittee members had received contained the materials relevant to this call, and that they would be receiving materials pertaining to the second call (to be held December 1, 2008) in early- to mid-November. At the face-to-face meeting to be held January 13-15, 2009, at Research Triangle Park, North Carolina, the majority of time will be spent directly on posters, and EPA will send poster books to the Subcommittee members at the beginning of January. The bulk of HHRP's accomplishments can be found in the poster book. Written materials in the ORD overview section of the binder provide background for Dr. Teichman's presentation, and the written materials in the HHRP overview section provide background for Dr. Darney's next presentation. The Multi-Year Plan (MYP) is an important document that describes the rationale for how the plan is organized and the program's Long-Term Goals (LTGs). In discussing program performance, it will be noted that the sections on goals and Annual Performance Measures (APMs) are intended to be living documents to be updated annually, so the details are not critical, but the structure of the plan is important. The MYP was revised after the 2005 BOSC program review.

The other materials originate from the Mid-Cycle Review Report and can be found on the HHRP Web Site (http://www.epa.gov/hhrp/resources.htm). All previous peer review materials including abstracts and posters can be accessed on that site. Dr. Darney advised Subcommittee members to pay close attention to the 2007 Mid-Cycle Report, because it raised some issues that the HHRP has been addressing since that review. The poster and abstract materials, bibliometric analysis, decision document analysis measures, partner survey report, and summaries of leadership contributions will be provided to members in mid-November. These materials will provide the Subcommittee with documentation for the items members are asked to address in the charge: program relevance, progress, importance, and impact. Some of these materials will be provided on a CD to spare members from carrying heavy notebooks to the meeting and to make it easier to link and review materials electronically. Tab E in the binder lists the materials on the CD, including a list of the grants that have been funded by this program, which will link to the grants Web site. The bibliography of the publications will include electronic links to abstracts on PubMed, and in many cases to the full article. The biographical sketches provide an introduction to the approximately 100 scientists contributing to the HHRP. The other items on the list refer to some important documents that also can be found on the Program Web site. Dr. Darney asked the Subcommittee members to notify the DFO it there are other materials that they would like to

receive electronically before the next conference call.

Dr. Klaunig mentioned the possibility that some of the CDs that members had received were corrupt; he advised all members to ensure that their CDs function properly. He noted that the only document on the CD is the *Report on the Environment*; and he asked Dr. Darney to send a link to that report.

ORD Overview
Dr. Kevin Teichman, Deputy Assistant Administrator for Science, ORD

Dr. Teichman thanked Dr. Klaunig for chairing the Subcommittee, and noted that this is a very qualified Subcommittee. The purpose of this presentation is to provide members with an overview of ORD, its role, mission, position within the Agency, organization, methods for strategic planning, and methods of performance measurement; the latter is where the BOSC fits into the process.

EPA is organized under the leadership of an Administrator and a Deputy Administrator. The Agency consists of the following program offices: Office of Air and Radiation (OAR); Office of Water (OW); Office of Solid Waste and Emergency Response (OSWER); and Office of Prevention, Pesticides and Toxic Substances (OPPTS). These are the primary organizations that write Agency regulatory and non-regulatory policies. (The HHRP is cross-cutting in nature, and not as targeted, for example, as EPA's Air Research Program within OAR.) ORD is directed by the Assistant Administrator for Research and Development, Dr. George Gray. Additional EPA offices include the Office of Enforcement and Compliance Assurance, the Office of International Affairs, the Office of General Counsel, the Office of Inspector General, and the Office of Environmental Information, which handles EPA's computer systems and is responsible in part for the *Report on the Environment*. The Office of Administration and Resource Management ensures proper staffing and infrastructure and the Office of the Chief Financial Officer manages the Agency budget. EPA's organization also includes 10 regional offices; therefore, there is a regional focus to Agency efforts as well as a national focus. Regional Administrators and Assistant Regional Administrators are political appointees who serve at the pleasure of the President; those currently serving will resign or continue in their positions in January at the choice of the new President.

EPA's mission is to "protect human health and safeguard the natural environment—air, water, land—upon which life depends." Agency program offices are responsible for writing policies and regulations and responding to the congressional deadlines in various legislative mandates by making national decisions. ORD provides the program offices the scientific information they need to write the regulations and other policies appropriately. Regional offices are the primary interface with the states, and they implement the regulations that come from the program offices. ORD has a responsibility to the regional offices as well, and provides them with the scientific information they need to implement Agency policies and regulations. ORD serves as a partner with the program and regional offices, but additionally provides scientific information to move forward the field of environmental science in general. The HHRP and the Ecological Research Program ensure that EPA can fulfill its mission in the short-term; they consider both immediate policy needs and those that may occur up to 5 to 10 years in the future.

ORD's mission is to provide the scientific foundation to support EPA's mission by:

- ✧ Conducting research and development to identify, understand, and solve current and future environmental problems.

- ✧ Providing responsive technical support to EPA's programs and regions.

- ✧ Collaborating with scientific partners in academia and other agencies, state and tribal governments, private-sector organizations, and nations (for example, the National Children's Study (NCS) in partnership with the National Institute for Child and Health Development).

- ✧ Exercising leadership in addressing emerging environmental issues and advancing the science and technology of risk assessment and risk management.

ORD has 1,858 full time equivalents (FTEs) (based on the President's budget request of 2009 still before Congress); a $551.3 million budget; a $55 million extramural research grant program* that funds the Science To Achieve Results (STAR) Program; and 13 laboratories, research facilities, and offices. ORD provides credible, relevant, and timely research results and technical support that informs EPA policy decisions.

ORD's organizational structure includes:

- ✧ Immediate Office of the Assistant Administrator
  - George Gray (political appointee), Assistant Administrator and Agency Science Advisor;
  - Lek Kadeli, Deputy Assistant Administrator for Management
  - Kevin Teichman, Deputy Assistant Administrator for Science.

- ✧ The heart of the organization is its seven laboratories and centers, which cover the full spectrum of risk assessment and risk management for health and ecological research and include:
  - National Health and Environmental Effects Research Laboratory (NHEERL), which studies effects.
  - National Exposure Research Laboratory (NERL), which investigates exposures.
  - National Center for Environmental Assessment (NCEA), which is responsible for risk calculation.
  - National Risk Management Research Laboratory (NRMRL), which is responsible for determining risk sources.
  - National Center for Environmental Research (NCER), which manages the STAR Program.
  - National Homeland Security Research Center (NHSRC), which has the primary responsibility for the decontamination of buildings and the area around buildings as well as protection of the water supply.
  - National Center for Computational Toxicology (NCCT), which applies genomics to assessing the toxicity of chemicals without testing as many animals.

- ✧ Support offices include:
  - Office of Resources Management and Administration (ORMA), which handles policies, procedures, develops the budget, and has an accountability group.

- Office of Science Policy (OSP), which is responsible for reviewing the scientific basis for the policies developed across the Agency as well as coordinating the interactions with the regions.

✧ National Program Directors (NPDs) manage programs distributed by subject matter.

ORD offices are located in areas with particular expertise in various environmental matters. Its four ecological divisions are located in particular locations necessary to accomplish their research (e.g., Duluth, Minnesota, contains the only freshwater research laboratory due to its location near the Great Lakes.) During the program review, the BOSC will hear presentations from EPA regional and program staff members.

ORD's research program evolves through input from a number of sources. Decision inputs come from:

✧ Programs and Regions, including Research Coordination Teams (RCTs).
✧ EPA Strategic Plan (updated every 3 years in addition to annual memos).
✧ Administration's priorities.
✧ Congressional mandates.
✧ BOSC reviews.
✧ Science Advisory Board (SAB), National Academy of Sciences (NAS), and other external advice.
✧ Stakeholders.
✧ NPDs, the Science Council, Management Council, and Executive Council.

Sources of ORD evaluation include:

✧ Program and regional office feedback.
✧ BOSC program evaluations (which feed into the Program Assessment Rating Tool [PART] reviews).
✧ NAS and other advisory bodies.
✧ PART reviews (the method used by the Office of Management and Budget [OMB] to evaluate programs across the government).

ORD's Executive Council makes decisions on what tasks ORD undertakes and how they will be accomplished. In planning the research program NPDs decide what research area-specific work is conducted and then Laboratory and Center Directors decide how ORD produces its research products (and what will be worked on by what staff members.)

In implementing the program Laboratory and Center Directors are responsible for developing ORD's research products and NPDs are responsible for communicating products to clients.

ORD's policy development and short-term research outcomes are subject to independent expert evaluation in the following areas:

✧ Focus: Outcome-oriented progress, and research and development (R&D) investment criteria.

- ✧ Evidence: MYPs, synthesis products, performance data, and partner feedback.

- ✧ Attribution: Sphere of influence that includes ORD and EPA partners.

ORD's strategic planning activity involves ORD's NPDs, who: (1) annually develop strategic research directions for their research programs, reflected in MYPs; (2) identify areas of growing, as well as decreasing, research emphasis; and (3) inform annual research planning and budgeting efforts. The MYPs are planning and accountability tools that address EPA's high-priority science questions and provide information to assist and support research decisions. The MYPs demonstrate how ORD programs contribute to Agency strategic goals and communicate research internally and externally available on the Web (see http://www.epa.gov/ord/npd).

The BOSC also is part of ORD's strategic planning efforts. The BOSC assigns a qualitative performance rating and provides a summary assessment of progress on each program's LTGs. The BOSC also provides a rating that incorporates elements of relevance, quality, and program performance (i.e., R&D Investment Criteria, as identified in the President's Management Agenda) as they relate to research outcomes.

Elements of the MYP include LTGs, Annual Performance Goals (APGs), and Annual Performance Measures (APMs). LTGs identify the timeframe to deliver work, determine ORD's role and the role of others, and feed into APGs. APGs (outcomes) identify the sequence to provide results, integrate research from all sources, and are based on APMs. APMs (outputs) determine who will accomplish the work (in-house Laboratory/Center or STAR research), and ensure that the work can be done with available resources.

Computational toxicology is an example of the complementary nature of cross-program and program-targeted research. ORD is conducting research toward understanding the toxicity of the conazole class of pesticides. While this research is providing a direct benefit to EPA's Office of Pesticide Programs, it also is serving as a proof-of-concept activity in ORD's ongoing effort to develop a generalizable capability to apply genomics-based computational approaches to environmental toxicology.

Cross-program research has broad applications and implications for multiple offices (human health, ecological program research). It covers issues that are persistent such that priorities remain fairly stable, but there is a continual need to improve the science to address the priority. Cross-program research applies emerging approaches and tools, serves as an incubator for innovative ideas to address long-standing issues, and offers double "bang for the buck" by selecting stressors to address a cross-program issue that also will inform a program-targeted effort.

Program-targeted research often has a single or primary client and may be legislatively mandated, with deadlines. This research has priorities that may shift based on changing program needs, and often employs established methodologies.

BOSC program evaluations help to determine if ORD is conducting the right science in the best way possible. They provide guidance for evolving the research/assessment program and evidence for OMB PART evaluations. Under PART, programs receive a numerical score and rating. In years past, EPA did not do well in these reviews, but due in large part to factors such as the

BOSC reviews, EPA has moved into the "moderately effective" range.

PART reviews evaluate program effectiveness in four areas: Purpose/Design, Strategic Planning, Program Management, and Program Results. The program receives a numerical score and rating (Effective, Moderately Effective, Adequate, Results Not Demonstrated, Ineffective). The results are based on annual and long-term performance goals with emphasis on outcomes (50% of the PART score). External program evaluations are addressed in both the Strategic Planning and Results sections (emphasis is on outcomes).

Dr. Teichman recommended that the Subcommittee members read the sections on R&D investment criteria rather than discuss them on the call. He added that the Subcommittee's review of the HHRP will be of great value to ORD, and it is much appreciated.

Dr. Pellizzari asked whether the decision input occurs throughout the fiscal year or is sought at the beginning so it can be synchronized with the budgeting process. Dr. Teichman responded that each year the SAB requests that he and the NPDs defend the President's budget request. At that point, ORD cannot deviate from the President's budget request for the current year. Dr. Teichman has set up a different time for strategic planning discussions with the SAB that is not tied to review of an annual budget. Those meetings are open to the public. The NPDs make presentations on their research plans, and there is more robust input and open discussion. ORD meets with advisors throughout the year, but the best time to provide input is at the strategic planning sessions with the SAB, which have been very successful. Dr. Pellizzari asked if the BOSC's evaluation is timely in this sequence of events. Dr. Teichman replied that the BOSC evaluations are not locked into a given budget cycle, although the results will be effective for the following budget cycle. The BOSC process takes a significant amount of time. ORD knows which programs need to be evaluated, and by having three or four evaluated in a given year, the overall program is examined in a 4- or 5-year period. Reviews are timed to feed into the PART reviews conducted by OMB.

Overview of Charge/Rating Program Performance

Dr. James Klaunig, Subcommittee Chair, and Phillip Juengst, Accountability Team Leader, ORD

Referring to the draft program review charge located in Tab C of the notebook, Dr. Klaunig explained that the objective of the charge is to conduct a retrospective as well as a prospective review of ORD's HHRP. He recommended that members examine the draft charge on their own. It is important to recognize that there are four LTGs), and the Subcommittee will learn more about these during the December 1 conference call. The overall assessment is for the entire research program. Dr. Klaunig commended the presentation of the draft charge for defining the program assessment in terms of its components: relevance, structure and quality, coordination and communication, program performance, and scientific leadership. It includes a summary assessment and rating program for each LTG. The overall questions the Subcommittee is charged to consider include:

- ✧ How appropriate is the science used to achieve each LTG?
- ✧ How high is the scientific quality of the Program's research products?
- ✧ To what extent are the Program results being used by environmental decision-makers to

inform decisions and achieve results?

Elements to include when developing the program rating are listed, including accountability and appropriateness.

Dr. Blanc questioned whether the Subcommittee would have to translate the narrative rating categories into numeric scores. Dr. Klaunig responded that the Subcommittee will not be asked to translate the qualitative ratings into numeric scores. Dr. Blanc took part in another review process that was stimulated by the same OMB guidelines, and they were asked to give integer ratings. Dr. Teichman added that the BOSC does not determine numerical scores; OMB assigns a numerical score as part of its PART evaluation. ORD has stressed to OMB that when considering the BOSC reviews, OMB should focus on the narrative, which is richer than the rating.

Mr. Phillip Juengst, ORD's Accountability Team Leader, explained the rating process. ORD must develop meaningful performance measures for all of its programs to track outputs and outcomes, and one of the biggest challenges the office has faced over the years was finding quantifiable ways to measure its long-term outcomes. Based on meetings with OMB and the BOSC and some other agencies that employ quantitative survey tools, ORD developed this rating process as a more accurate and valid way of assessing the programs. The differences between the rating categories are based on the extent to which the BOSC believes the program is meeting all of its major goals or most of those goals. When goals are mentioned, it is the broad LTG level that should be considered, the equivalent of the APG level in the MYP. The Subcommittee must determine whether the HHRP is meeting those goals, and offer its perceptions on the relative speed and quality of the work to achieve progress toward the LTGs. The real focus is on the R&D investment criteria: quality, relevance, and performance are not just about ratings for ORD. The review is intended to serve two purposes: (1) to provide this rating, which helps ORD have a more definitive assessment of where the program stands, and (2) to provide the narrative content that informs ORD as to where to focus efforts to further improve the program and reach its goals.

In terms of the charge, under the program performance section there are four questions. The last question concerns the area of research efficiency. ORD has had discussions with OMB about this issue, and engaged the National Academies and other research agencies in these discussions because there were a variety of different approaches those agencies have taken to measure efficiency. A requirement that OMB has placed on agencies, and what came out of the dialogue with the National Academies, was that the focus should be placed on assessing investment efficiency, not process efficiency. Efficiency measures should examine how well ORD is investing its resources to achieve its program goals. In the "factors to consider," there is some discussion of portfolio management. This is not an examination at the level of detail of how much money is spent to develop an individual project, but at a broader level, what proxy ORD has been using to: decide how much to invest in one LTG versus another, determine research needs, and make mid-course adjustments as research and priorities evolve.

Overview of ORD's HHRP

Dr. Sally Darney, EPA, ORD, NPD for Human Health Research

Dr. Darney thanked the Subcommittee members for taking on the task of the HHRP review. She was pleased to see that the Subcommittee includes experts in toxicology and exposure with

fundamental and modeling expertise, complemented by experts in public health. She acknowledged the program work done by Dr. Hugh Tilson, the previous NPD for Human Health Research, who started the HHRP and shepherded it through the first full BOSC program review and mid-cycle review, and worked closely with the writing team for this conference call.

The HHRP works closely with the RCT, which includes Program Directors and representatives from each of the laboratories and centers that contribute to this program:

- ✧ Sally Darney, ORD, NPD (Acting)
- ✧ Carlos Nunez, NRMRL
- ✧ Ross Highsmith, NERL
- ✧ Andrew Geller, NHEERL
- ✧ Devon Payne-Sturges, NCER
- ✧ Stan Barone, NCEA
- ✧ Jerry Blancato, NCCT
- ✧ Ray Putnam (Region 1)
- ✧ Marian Olsen (Region 2)
- ✧ Ravi Rao (Region 4)
- ✧ David Macarus (Region 5)
- ✧ Lesley Vazquez-Coriano, Santhini Ramasamy, Crystal Rogers-Jenkins, Kesha Forest, Sandhya Parshionikar, OW
- ✧ Michael Firestone, Office of Children's Health Protection and Environmental Education (OCHPEE)
- ✧ Scott Jenkins, OAR
- ✧ Jeff Evans, Anna Lowit, OPPTS.

The HHRP has employed the RCT to help direct its research. Dr. Darney explained that the objectives of this overview are to:

- ✧ Orient the BOSC HHRP Subcommittee to the HHRP, including its history and strategic future directions.

- ✧ Review the HHRP MYP 2006 for relevance, balance, and scope.

- ✧ Summarize changes in emphasis or direction in response to the 2007 BOSC mid-cycle review and other influences.

- ✧ Provide background and context for the second conference call on December 1 that will expand in more detail upon scientific progress and future plans.

The overarching goal of the HHRP is to help EPA protect human health. It is a cross-cutting program. Human health research develops the methods, models, and data to characterize and reduce uncertainty in the "critical links" across the exposure-to-effect paradigm and explore: fundamental determinants of exposure and dose; how those levels translate into disease; and the early signs and basic biological effects that result from exposure to environmental contaminants and lead to adverse health outcomes and health impacts. Linkages are critical to the big picture, and that is where much of the uncertainty lies. What is the best way to examine and evaluate source emissions in terms of how those emissions get transported into the environment? Another

uncertainty lies in how to measure whether a rule or law is protecting human health. The hope is that the HHRP will develop methods, models, and data that characterize the uncertainty in these pathways and reduce that uncertainty to the extent possible along the whole exposure-to-effect continuum. The HHRP explores fundamental determinants of both exposure and dose, and the basic biological changes or effects that result from exposure to contaminants and lead to adverse health outcomes. The program's goal is to help EPA increase public confidence that the Agency is protecting public health, and to assure partners in industry and business that the expenses that they incur enforcing or complying with EPA regulations is justified and based on sound science.

The four LTGs are explained in further detail in the charge. The HHRP hopes to help risk assessors and risk managers use the data methods and models that the program generates. Working within the LTGs, risk assessors and risk managers use ORD's methods and models to:

- For LTG 1: Understand and reduce uncertainty in risk assessment using mechanistic (mode of action) information. In this and all of the LTGs, there are APGs that lead to accomplishing that goal. Some mature in different years. APMs were projected in the 2006 plan, but each year that plan is revisited and the APMs are adjusted based on how the science has proceeded and the expertise at hand. The HHRP will give the Subcommittee a summary of where the program stands today; the 2008 report will be ready this month.

- For LTG 2: Characterize aggregate and cumulative risk in order to manage risks to humans exposed to multiple environmental stressors.

- For LTG 3: Characterize and provide adequate protection for susceptible populations.

- For LTG 4: Evaluate the effectiveness of risk management decisions. This deals with how EPA accounts for its regulations.

These goals are consistent with EPA's Strategic Plan, particularly in terms of its goal of ensuring safe communities.

The HHRP is a large program that deals with improving risk assessment, and dates back to the late 1990s. In 2003, thanks to Dr. Klaunig and others who participated in building this document, the Human Health Research Strategy document was released, and included two goals consistent with current LTGs. Drawing upon that research, in 2003, the first MYP was developed. The HHRP received its first BOSC program review in 2005. NCCT also was formed in 2005. Dr. Darney noted that NCEA previously had some goals in human health, but in 2005, NCEA developed its own Human Health Risk Assessment MYP. The HHRP views both these centers as partners and intermediaries between the HHRP and the program offices.

The HHRP MYP was revised in 2006. The BOSC mid-cycle review took into account some plans and goals of NCCT and a newly released document from the NAS, *Toxicity Testing in the 21st Century,* which points to a revolution in the way toxicity testing is conducted.

The HHRP conducts interdisciplinary cross-program research, and feeds products, models and data to the Clean Air, Endocrine Disruptors, and Drinking Water Programs, in addition to interfacing with the Land Program and its NCCT and NCEA partners.

The HHRP employs approximately 185 FTEs, of which 145 are scientists and science support staff in the ORD laboratories and centers. They represent broad expertise in air pollution, water pollution, and pesticides. Many of the staff members spend part of their time on human health goals and part on problem-specific goals. In terms of resources, approximately 25 percent of the program's funding is spent on extramural STAR grants. STAR funding has been relatively stable since 2003 at $16-17 million per year. Total program funding is approximately $60 million per year. There was some increase in 2008 to restore funding for basic research in human health and ecosystems. This money is not in the 2009 budget request. There is concern that the HHRP will have to adjust its goals in 2009 based on available resources. Also, flat resources across a number of years coupled with lower than expected retirement numbers and increased cost of equipment actually mean a decline in real dollars for research.

The HHRP's products are broadly applicable to many partners and stakeholders, including:

- ✧ EPA Program Offices (OAR,OPPTS, OW, OSWER)
- ✧ EPA Regions (States) and Tribes
- ✧ EPA's OCHPEE
- ✧ Other Federal Groups:
    - National Institutes of Health (NIH)/Centers for Disease Control and Prevention (CDC) – Interpretation of biomonitoring data; public health priorities and impact; diseases (asthma, autism);
    - NIH/National Institute of Child Health and Human Development (NICHD) – Participation in the National Children's Study (Intercultural Cancer Council with the National Institute of Health and Environmental Sciences (NIEHS) and the CDC); (Application of methods and models);
    - NIH/NIEHS – Centers for Children's Environmental Health and Disease Prevention since 1998
- ✧ International: World Health Organization, Organisation for Economic Co-operation and Development, and the International Programme on Chemical Safety
- ✧ NCCT and NCEA have moved from participants to partners with the HHRP.

Dr. Darney provided the following summary of the LTGs:

LTG 1, Mode of Action (MOA), is led by Julian Preston, who will give an overview on the December 1, 2008, conference call.

LTG 1 research:

- ✧ Methods and models to characterize MOA: cancer vs. non-cancer; oxidative stress pathways; neuroendocrine MOAs;
- ✧ Linkages between pharmacokinetic (PK) and pharmacodynamic (PD) models;
- ✧ MOA information to address extrapolation in risk assessment;
- ✧ MOA models and biomarkers are used in LTG 2 (Cumulative Risk) and contribute to NCCT's computational toxicology goals;
- ✧ Strategic direction: Increasing emphasis on systems approaches;
- ✧ Responsive to *Toxicology Testing in the 21st Century*.

Investigators in this group have partnered with NCCT to create a white paper on how to address

these issues. A large part of this program involves how the laboratories can contribute data and models that help NCCT to meet its objectives. This is largely an intramural effort; the other LTGs have an interface with NCER grantees.

LTG 1 research in partnership with NCCT (25% of the FTE effort) involves:

- ✧ Using toxicogenomics to explore MOA(s) of action of conazole pesticides;
- ✧ Linking PK and PD models for use in risk assessment (extrapolations);
- ✧ Identifying and using toxicity pathways; and using a systems approach to create the Virtual Liver and Virtual Embryo.

LTG 2, Cumulative Risk, which is led by Linda Sheldon and Ross Highsmith, accounts for 31 percent of the FTE effort. Goals include developing biomarkers of exposure and effect for use in cumulative risk assessment; developing source-to-dose models for cumulative risk; and creating tools for cumulative risk of chemical mixtures and for identifying and assessing communities at risk.

LTG 2 research:

- ✧ Elucidates determinants of exposure including life stage (informs LTG 3, NCS);
- ✧ Uses biomonitoring and observational studies to learn about exposure factors and test biomarkers (informs LTG 3 and 4, and NCS);
- ✧ Contributes to NCEA's Exposure Factor Handbooks used by program offices, regions, and states;
- ✧ Builds models: SHEDS-Multimedia exposure model for use in risk assessment by OPPTS and states (goal this year);
- ✧ Contributed to two NCER workshops on community risk assessment and biomarkers (2007).

LTG 3, Susceptible Populations, accounted for 38 percent of the FTE effort for 2008. Devon Payne-Sturges is leading this research, which focuses on life stage research (includes long-term exposure effects from pregnancy and lactation, children, and aging factors in older Americans); methods for longitudinal research (using the Children's Environmental Health Centers and NCS); and research on asthma (induction vs. exacerbation and factors such as age, biological, and inflammation.)

Within LTG 2, the children's health research includes susceptibility/vulnerability based on exposure – changes with place (home/school), and other factors (behaviors, activity, socioeconomic status [SES]). Within LTG 3, the children's health research includes susceptibility based on life stage (*in utero*, infant [breast milk], toddler, child, adolescent); possible long-term effects of *in utero* exposures (epigenetics), genetic factors, and asthma.

LTG 4, Evaluation of Risk Management Decisions, accounts for 6 percent of the FTE efforts.

Andrew Geller and Rebecca Calderon serve as LTG leads. This goal involves various approaches used to evaluate risk management decisions informed by LTGs 1, 2, and 3 (biomarkers, biomonitoring, and community risk assessment). In addition, this group is responsible for the health chapter for the *2008 Report on the Environment*.

In response to the 2007 BOSC mid-cycle review, the LTG 4 research effort was increased, and has since produced the following:

- ✧ *Framework for Assessing the Public Health Impacts of Risk Management Decisions*, 2007.
- ✧ "Accountability" pilot projects underway in collaboration with Region 1.
- ✧ Environmental Health Outcome Indicators grants, 2007.
- ✧ NCER Workshop held January 2008.

A number of STAR Requests for Applications (RFAs) fell within the HHRP. Integrated themes included:

- ✧ Centers for Children's Environmental Health and Disease Prevention, 1998, 2001, 2003, 2005, and 2009 (this is under LTG 3, but supports all LTGs).
- ✧ Decade of Children's Environmental Health Research, 2007.
- ✧ Children's Vulnerability to Toxic Substances in the Environment, 2001 (LTGs 2 and 3).
- ✧ Complex Mixtures, 2000 (LTG 1).
- ✧ Issues in Human Health Risk Assessment, 2001.
- ✧ Biomarkers for the Assessment of Exposure and Toxicity in Children, 2002 (LTG 3).
- ✧ Lifestyle and Cultural Practices of Tribal Populations and Risks from Toxic Substances in the Environment, 2002, 2007 (LTGs 2 and 3).

The following RFAs were initiated since the last program review. The HHRP worked closely with NCER to determine the best research for the programs:

- ✧ Application of Biomarkers to Environmental Health and Risk Assessment, 2004 (LTGs 1 and 2).
- ✧ Early Indicators of Environmentally Induced Disease, 2004 (LTGs 1 and 2).
- ✧ Interpretation of Biomarkers using Physiologically Based Pharmacokinetic Modeling, 2007 (LTG 2).
- ✧ Development of Novel Environmental Health Outcome Indicators, 2007 (LTG 4).
- ✧ Community-based Cumulative Risk Assessment (planned).
- ✧ Novel Approaches for Assessing Exposure for School-Aged Children in Longitudinal Studies (planned).

The HHRP will recruit for the NCS in 2009; however, to implement the HHRP's overall strategy, the program will have to consider the resources available. Funding is aligned with FTE elements. Because real funds are decreasing, the HHRP hopes to build upon existing data and partner with others (CDC, NICHD-NCS) to conduct field studies on exposure and community risk assessment and research to interpret biomonitoring data. The HHRP also will contribute to epidemiology studies and mine the data.

The HHRP will focus on research issues with which it can have the greatest impact with its unique capabilities and available resources. The program staff is looking forward to sharing

HHRP results and products with the Subcommittee and receiving its feedback throughout the review process.

Dr. Joel Schwartz noted that in the upcoming meetings he would be interested in learning about the following issues:

- ✧ LTG 1, in terms of thinking about understanding, quantifying, and reducing uncertainty in risk assessment (RA). Although computational toxicology and mechanistic studies are extremely important, statistical methodologies have been developed and are being developed to deal with RA. What is the HHRP doing with respect to that?

- ✧ Work has been conducted on methods to determine the quantitative value of information and methods to prioritize what research would do the most to reduce uncertainty in quantitative RAs. It would be useful to know if the HHRP is thinking about these methods when prioritizing efforts.

- ✧ This comment focuses on LTG 2 but cuts across some of the other goals. There was no discussion during this conference call of the role of epidemiology in doing quantitative RA, but in the past 20 years, it has played a greater role. In the past, quantitative RA for ozone exposure was extrapolated from chamber studies and exposure models were built, but this time in setting the ozone maximum, dose-response relationships from epidemiology studies played an important role. This extends beyond air pollution; other examples are the arsenic rule for drinking water and the examination of endocrine disruptors. The HHRP would not have to conduct its own epidemiology research; in fact, it is encouraging that the program plans to use data from existing studies because it is cost effective. To use epidemiology data for RA, however, there must be evidence in toxicology that demonstrates whether these associations are biologically plausible. The type of toxicology studies conducted for that are somewhat different than those conducted for RA and mechanistic toxicology studies. They are more qualitative, but examine systems and pathways, and it would be interesting to learn how the HHRP will be doing this.

- ✧ In terms of susceptibility, children were mentioned, but many studies suggest that diabetics are more susceptible to some environmental agents, and it would be useful to hear about the HHRP's efforts in that area.

- ✧ Finally, in terms of prioritizing the budget, is there a systematic method within categories that the HHRP uses to set priorities, and if so, what is it?

Dr. Klaunig responded that these issues will be covered as the individual LTGs are discussed in depth. Dr. Darney agreed that all of these topics will be covered, and added that it is helpful to hear what specific information the Subcommittee needs.

Dr. Blanc noted that he would like more specific information on the 2007 BOSC mid-cycle review and the written response from ORD. What were the most salient challenges that came out of the mid-cycle review? Dr. Darney noted that they included the concept of the framework for the whole program, improvement of the framing of LTG 4, and a question about how the HHRP interfaces with the international community; more information on all of these topics can be provided at the upcoming meetings.

Dr. Hal Zenick added that he hoped that, as the HHRP presented its programs, the Subcommittee would offer suggestions when they see integrative opportunities; this is particularly important given the budget constraints. This may not be captured explicitly in the charge, but is very important because the program has many new tools emerging. If the Subcommittee members noted where they thought the science could really make a difference, this would be invaluable to the HHRP during this period of limited funding. Dr. Klaunig said he thought this fit into the charge because the Subcommittee has been asked to review the program prospectively as well as retrospectively.

Public Comment

At 2:15 p.m., Ms. Drumm called for public comment. No comments were offered.

Preparation for the Next Call and Face-to-Face Meeting
Dr. James Klaunig, Subcommittee Chair

Dr. Klaunig reminded members that the next call will be held on December 1, 2008. He mentioned that there is a draft agenda for that call in the binder. There will be reports on all of the LTGs and time for questions and answers. Dr. Darney added that she will try to get the information to be discussed on that call to the members with as much lead time as possible, and she will send Web links via e-mail as well. The call is scheduled for 11:00 a.m. to 2:00 p.m. Eastern Time.

Ms. Drumm reviewed the draft agenda for the face-to-face meeting to be held in Research Triangle Park on January 13-15, 2009. The first day (Tuesday) will focus on LTGs 1 and 2; each will have a poster session overview, poster session, Subcommittee discussion/report out on the poster session, and a chance for questions and answers between Subcommittee members and EPA. There will be breakouts at the end of that day for the LTG 1 and LTG 2 workgroups. The second day (Wednesday) will include the same sessions for LTGs 3 and 4 with breakout sessions at the end of the day for the LTG 3 and LTG 4 workgroups. The Thursday session is a half day, and will include client testimonials, and time for the Subcommittee to discuss writing the report and discussing the ratings for each of the LTGs. There also will be time for a general report out to the HHRP staff.

Dr. Klaunig indicated that he will distribute the writing assignments via e-mail. He would like to have at least three Subcommittee members on each LTG breakout group, which means members would serve on more than one workgroup. He asked the Subcommittee members to examine the goals and identify their first, second, and third choices for the LTG workgroups they would like to join, and send those choices to him as well as Ms. Drumm and Ms. Houk. He will send a reminder e-mail to the Subcommittee members requesting this information. With the Subcommittee's permission, Dr. Falk and Dr. Klaunig will assign members to the LTG workgroups in the near future. Dr. Klaunig asked if the Subcommittee members had any other additional information needs.

A participant asked to receive a hard copy of the NAS Report *Toxicity Testing in the 21st Century*. Dr. Klaunig stated that Ms. Drumm would look into the possibility of getting copies for the members. Dr. Darney noted that the report was available for sale, but that they would see

what was available for the Subcommittee. A summary of the report is available to download for free on the NAS Web Site, and the health chapter, which is an HHRP project, also is free.

Hearing no further questions or comments, Dr. Klaunig thanked participants and adjourned the conference call at 2:36 p.m.

Action Items

- ✧ EPA staff will provide the poster and abstract materials, bibliometric analysis, decision document analysis measures, partner survey report, and summaries of leadership contributions to the Subcommittee members in mid-November. These materials will be provided to the members with as much lead time as possible prior to the December 1, 2008 conference call. Web links to the materials will be sent as well.

- ✧ Subcommittee members who would like to receive additional materials electronically prior to the December 1, 2008, conference call should notify Ms. Drumm so that she can request the materials from Dr. Darney.

- ✧ The Subcommittee members should verify that the CDs they received are functioning properly.

- ✧ Dr. Darney will provide to the Subcommittee more information on the challenges that came out of the BOSC mid-cycle review at the upcoming meetings.

- ✧ Dr. Klaunig will distribute writing assignments via e-mail.

- ✧ Members should examine the LTGs to identify their first, second, and third choices for the LTG workgroups they would like to join, and send these choices to Ms. Drumm, Ms. Houk, and Dr. Klaunig. Dr. Klaunig will send a reminder e-mail to the Subcommittee members requesting this information.

- ✧ Dr. Falk and Dr. Klaunig will assign Subcommittee members to the LTG workgroups in the near future.

- ✧ Ms. Drumm and Dr. Darney will determine whether hard copies of the NAS Report *Toxicity Testing in the 21st Century* are available for the Subcommittee members.

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APPENDIX A: Teleconference Agenda

HUMAN HEALTH SUBCOMMITTEE TELECONFERENCE AGENDA
October 10, 2008
12:30 p.m. – 2:30 p.m.

Friday, October 10, 2008

12:30-12:40 p.m.	Welcome - Roll Call - Overview of Agenda	 Dr. James Klaunig Subcommittee Chair
12:40-12:45 p.m.	BOSC DFO Remarks	Ms. Heather Drumm, ORD
12:45-1:00 p.m.	Materials Overview	Dr. Sally Darney, Human Health National Program Director, ORD
1:00-1:30 p.m.	ORD Overview	Dr. Kevin Teichman, Deputy Assistant Administrator for Science, ORD
1:30-1:45 p.m.	Overview of Charge/ Rating Program Performance	Dr. James Klaunig, Subcommittee Chair Phillip Juengst, Accountability Team Leader, ORD
1:45-2:15 p.m.	Overview of ORD's Human Health Program	Dr. Sally Darney, Human Health National Program Director, ORD
2:15-2:20 p.m.	Public Comment	
2:20-2:30 p.m.	Preparation for Next Call and Face-to-Face Meeting - Discuss Writing Assignments - Identify Additional Information Needs	Dr. James Klaunig, Subcommittee Chair
2:30 p.m.	Adjourn	