Office of Research and Development's (ORD)
Human Health Risk Assessment (HHRA) Program
Mid-Cycle Progress Report to the Board of Scientific Counselors (BOSC)

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The U.S. Environmental Protection Agency's (EPA) Office of Research and Development (ORD) relies on its Board of Scientific Counselors (BOSC) to conduct independent expert reviews of its environmental research programs every four to five years. The Human Health Risk Assessment (HHRA) Program Subcommittee of the BOSC met in Washington, DC on November 14-16, 2007, and the BOSC Executive Committee provided a final report in May, 2008. The principal charge to the BOSC reviewers was to evaluate ORD's HHRA Program from a program assessment framework relative to program relevance, structure, performance, quality, leadership, communication, and outcomes. A second priority was to provide a summary assessment and performance ranking for each of the three long-term goals identified with the HHRA Program. A set of specific charge questions was used to guide the Subcommittee through the review, producing a number of recommendations with regard to the program.

On May 27, 2008, ORD received the BOSC's *Review of the Office of Research and Development's Human Health Risk Assessment Program at the US Environmental Protection Agency*. In that report, the BOSC concluded that the Program's goals are fully consistent with the Agency's strategic mission and with the Program's multi-year plan (MYP). The products from LTG 1 and LTG 3 are critical to EPA's regulatory mission and form the foundation for regulatory decisions and policies in a variety of program offices and regions. The BOSC also found that: 1) Integrated Risk Information System (IRIS) assessments are critical to a number of goals and objectives listed in EPA's 2006-2011 Strategic Plan; 2) IRIS serves as the internationally recognized standard in chemical risk assessment for other federal, state, local and international regulatory bodies and the private sector; 3) LTG 3 is aligned with the requirements for assessment of criteria air pollutants as mandated by the Clean Air Act (CAA), and the importance of the HHRA Program in meeting CAA requirements could not be overstated; 4) the research conducted under LTG 2 focuses on critical needs and that good strategic choices have been made to concentrate research in areas that are likely to result in marked improvements in risk assessment; and 5) the HHRA Program has been highly responsive to the needs of the program offices and regions who strongly value the work and expertise of the HHRA, both in providing risk assessment products (IRIS assessments, provisional peer reviewed toxicity values-PPRTVs, and integrated science assessments-ISAs) and in supporting emergency responses to crises like the 9/11 terrorist attacks on the World Trade Center and Hurricane Katrina.

The BOSC, however, raised concerns regarding the rate of production of assessments, the 10-year life span of IRIS assessments, the review cycle of IRIS assessments and the potential effects of removing older IRIS assessments from the database. The BOSC report's recommendations and HHRA Program's original response are outlined below, along with an update on progress made in responding to the recommendations.

Recommendation 1: NCEA should assess what needs to be done to increase the Program's ability to produce more IRIS and PPRTV assessments per year, not only to meet their own stated objectives but also to satisfy the needs of their clients. This could either be in the form of a recommendation to the Agency for more resources, or the development of a more streamlined process.

Original Response: The HHRA Program agrees that there is a need to provide more IRIS and PPRTV assessments per year and that there are both process requirements and resource limitations that affect productivity. For example, one prime limitation relates to the extensive reviews required for IRIS assessments and the additional demands on staffing and resources to conduct and respond to these reviews. On April 10, 2008, EPA Deputy Administrator, Marcus Peacock announced an update to the IRIS process for development of new assessments and reassessments and recommended the expeditious implementation of changes. The HHRA Program is implementing the revised process to meet current commitments and is revising the chemical prioritization and selection process to better reflect client office assessment priorities and associated resource requirements.

In addition, an IRIS Update Process is being developed that will include an updated literature search and re-evaluation of the qualitative and quantitative determinations in IRIS assessments greater than ten years old. This new process is integrated with the current Literature Screening Project which has identified existing chemical assessments where either no new data are available or new data are available for updating values. Application of new analytical methods (e.g., benchmark dose, PBPK modeling) will also be taken into consideration where appropriate as part of the re-evaluation. In some cases, significant new data may warrant advancing assessments into the queue as a new IRIS assessment. The update process will include peer review by a Federal Standing Science Committee as well as a Standing External Peer Review Panel. This IRIS Update Process will process 8-12 chemicals at a time to maximize throughput of updated assessments.

The HHRA Program is addressing the concerns raised by the BOSC to assess what needs to be done to increase the program's ability to produce more PPRTV assessments per year. The program has recently undertaken improvements in the standardization of document development and enhancements in the peer review and clearance processes. It is anticipated that these efforts will decrease the time required for the production of PPRTV assessments and increase the number of PPRTVs available to the program office.

Original Action/Timeline: The HHRA Program is implementing changes addressing development of new IRIS assessments and reassessments, is revising the chemical prioritization and selection process to address client office needs, has initiated development of a process for updating older assessments on IRIS and begun efforts to enhance and streamline the PPRTV process. The next update of the HHRA MYP will reflect any significant changes in these programs and new metrics agreed upon with the Office of Management and Budget (OMB). Progress regarding these efforts will be discussed at the mid-cycle review of the HHRA Program.

Updated Response: No changes to the ORD action.

Current Progress: The HHRA Program has taken several steps to meet this recommendation. The FY 2010 enacted budget includes additional resources for the IRIS program. Further, the process used to develop IRIS assessments was revised in May 2009 (www.epa.gov/iris/process); the new process allows for more rapid completion of assessments while retaining transparency

and opportunity for Agency and Interagency comments, as well as vigorous independent external peer review and public review and comment. The table below illustrates how the new process has greatly improved the ability of the IRIS program to provide high quality human health risk information to EPA's programs and regions in a timely fashion. After the announcement of the new process, the fourth quarter of fiscal year 2009 began. More final assessments were posted on IRIS in that single quarter of one year than in each of the previous three years. Thus, the HHRA's IRIS program has quickly demonstrated progress under the new process and will continue to show significant results in 2010 and beyond.

IRIS		Draft Assessments Start Interagency Review/Consultation	Draft Assessments Start Independent External Peer Review	Second Interagency Review/Discussion	Final Assessments Posted on IRIS
FY2006		11	1		2
FY2007		16	12		2
FY2008		5	12		5
FY2009	1st qtr.	3	0		0
	2nd qtr.	4	1		1
	3rd qtr.	2	2		0
May 21, 2009 New IRIS Process	4th qtr.	1	7		6
FY 2009 Total		***10***	***10***		***7***
FY2010 (Qu. 1-3)		5	7		3
FY2010 Projected					15

Additionally, we have developed an IRIS Logistics Team to coordinate all aspects of administrative support for the IRIS program. The development of this team has created efficiencies by centralizing logistical activities and relieving scientific staff of administrative burdens. This is a matrix managed team that includes project officers of contracts for IRIS document development, technical editing, and peer review; the NCEA Webmaster; the IRIS coordinator, who maintains the public tracking system for IRIS assessments, organizes listening sessions, and works with the chemical manager to develop project schedules; members of the NCEA Technical Information Staff, who develop and coordinate Federal Register Notices (FRN) and clearance for documents; the interagency point of contact, who handles all correspondence with interagency reviewers; and the NCEA communications director, who coordinates all communications dealing with IRIS draft and final assessments. Administrative support staff schedule, organize and administer IRIS-related meetings and briefings and coordinate with the EPA Science Advisory Board (SAB) and National Academy of Sciences (NAS) when these bodies conduct peer reviews of IRIS assessments.

NCEA has met extensively with EPA's program and regional offices to better understand their assessment needs. Additionally, NCEA is working with the California Environmental Protection Agency's (Cal/EPA) Office of Environmental Health Hazard Assessment (OEHHA) and the Agency for Toxic Substances and Disease Registry (ATSDR) under separate Memorandums of Understanding (MOU). It is anticipated that these efforts will eventually increase efficiency and assessment output. NCEA has also begun a project to update older IRIS assessments. Additional details are described in our progress under Recommendation #2.

We have taken steps to facilitate more efficient production of PPRTV assessments by: (1) developing a PPRTV review team within NCEA; (2) streamlining the information included in a PPRTV assessment to focus on pertinent data and decision-making sections; (3) educating EPA contractors about expectations for PPRTV assessment documents; and (4) batching assessment development and internal and external reviews. This has proven to be a successful effort. In FY 2009, NCEA produced 69 new PPRTV assessments. These 69 PPRTV assessments included a total of 140 new individual toxicity values (e.g., Reference Dose-RfD, Reference Concentration-RfC, Oral Cancer Slope Factor, etc.) that were added to the PPRTV database.

NCEA has also negotiated new program metrics with OMB. Specifically, NCEA's newly negotiated performance metric indicates the HHRA Program will complete health hazard and dose response assessments of high priority chemicals as interagency science consultation drafts or external peer review drafts with a program-defined value of 50 points applied to a 3-year rolling average. Additionally, the HHRA Program will post on the IRIS Web page completed health hazard assessments of high priority chemicals for public dissemination with a program defined value of 20 points applied to a 3 year rolling average. To account for differences in the level of complexity of assessments, the HHRA Program has also negotiated with OMB a tiering system that provides three different levels of complexity and associated points for reaching milestones for assessments. Tier 1 assessments are standard assessments that are expected to require a typical level of effort from NCEA scientists and be limited in controversy and the complexity of the science as well as the level of effort required for the assessment. Tier 1 assessments are assigned a point value of "1" for each major negotiated milestone met. Tier 2 assessments are more extensive in that they require more FTE effort, have a greater level of controversy or visibility, and are more scientifically complex than Tier 1. Tier 2 assessments are assigned a point value of "2" for each major negotiated milestone met. Tier 3 assessments are the most complex. They require an exceptional level of FTE support, are highly controversial and/or visible, and are exceptional in the complexity of the science involved in the assessment. Tier 3 assessments are assigned a point value of "5" for each major negotiated milestone met.

Additionally, the HHRA Program has begun a pilot project on advancing the next generation of risk assessment (NexGen) that will explore the feasibility of using advances in molecular and systems biology for developing health assessments. It is anticipated this pilot project will help pave the way for using high throughput data to develop rapid health assessments. This is a collaborative effort across ORD and with the National Institutes of Environmental Health Sciences (NIEHS), the National Human Genome Research Institute (NHGRI), and Cal/EPA.

Recommendation 2: Mechanisms should be considered for retaining IRIS assessments older than 10 years that have not been updated, rather than allowing these assessments to expire and be removed from the IRIS database and Web site. One option is to simply annotate them as such.

Original Response: The HHRA Program appreciates the support of the BOSC to retain IRIS assessments older than ten years that have not been updated on the Web site. The program has considered this recommendation and discussed with the programs offices and other interested partners the issue of whether to retain IRIS assessments older than ten years that have not been

updated or to remove them from the IRIS database and Web site. Older assessments will remain in the IRIS database and Web site and annotated as to the literature screening results until they undergo updating by the new IRIS update process or the traditional IRIS process.

Original Action/Timeline: Implementation of the IRIS update process is underway and progress regarding these efforts will be discussed at the mid-cycle review of the HHRA.

Updated Response: No change to the ORD action.

Current Progress: NCEA has decided that IRIS assessments older than 10 years will not be removed from the IRIS database. Additionally, a process for updating old IRIS chemical assessments has been developed and is nearing the implementation stages. The HHRA Program issued a FRN in October 2009 announcing the establishment of this IRIS Update Project. Additionally, the HHRA Program has developed a two-tiered peer review process consisting of a Federal Standing Science Committee followed by a Standing External Review Panel of the SAB under the Federal Advisory Committee Act (FACA). The SAB issued a FRN in March 2009 requesting the nomination of experts to serve on this committee. Committee members have since been identified and the panel has been established.

The intent of the IRIS Update project is to revisit all dose-response assessment values (RfDs, RfCs, Oral Cancer Slope Factors, and Inhalation Cancer Unit Risks) in IRIS with a posting date more than 10 years old. The values under current assessment by the standard IRIS process (on IRIS Track) and the values for pesticides not in active use are eliminated from the list of IRIS values greater than 10 years old. The remaining values are then prioritized for being updated. This prioritization takes into consideration several factors, including frequency of occurrence in National Priority List (NPL) waste sites, occurrence as hazardous air pollutants used in residual risk assessments, the presence of chemicals on the Contaminant Candidate List (CCL), and other intra- and inter-agency interests. From this list, smaller batches of assessments (~10) are selected for literature searches by a contractor. After the literature search, the path for development of a revised dose-response assessment value is based on whether new data exists or not and whether new values are proposed or not (binning).

Recommendation 3: The HHRA Program should continue to develop ties with NCCT, and should provide formal input to that program on the aspects of its research that will be of value to HHRA.

Original Response: The HHRA Program agrees with the BOSC's recommendation and is continuing to enhance communication and collaboration with NCCT. A number of such activities are underway including: 1) NCEA management and staff involvement in the development of the ORD Strategy for Toxicity Testing for the 21st Century; 2) formation of an NCEA-led cross-Agency workgroup on the analysis and application of physiologically based pharmacokinetic (PBPK) models for perchlorate that includes principal scientists from NCCT; and 3) NCEA scientists serving as internal Agency reviewers of DSSTox database. Examples of more informal collaborations are: 1) NCCT scientists' participation in NCEA sponsored workshops and conferences such as the State of the Science workshop on Issues and Approaches

in Low Dose-Response Extrapolation for Environmental Health Risk Assessment and the annual Toxicology and Risk Assessment Conference; 2) cross program sharing of information and resources, e.g., access to NCCT models and databases for SAR/QSAR screening approaches; 3) use of NCEA ARRAYTrack database and server by NCCT staff; 4) NCEA consultations with NCCT staff on the exposure communities of practice workgroup; 5) consultation on benchmark dose (BMD) methods and models development; and 6) cross-participation in program seminars (e.g., NCCT seminar on the virtual fetus held August 2008). In addition, efforts to enhance LTG1 assessment development include collaboration with NCCT on agenda-setting for the IRIS program and sharing assessment needs and prioritization information provided by clients with NCCT for consideration in prioritization of testing and evaluation in ToxCast. Future collaborations on the use of mode of action information in the virtual liver modeling efforts are also being discussed between scientists in both programs.

NCEA is continuing to build and strengthen expertise in the area of computational toxicology with staff participation in the upcoming Computational Systems Biology and Dose Response Workshop sponsored by the Hamner Institutes for Health Sciences. Dr. Rory B. Conolly of EPA's NCCT is one of the course advisors and trainers.

Original Action/Timeline: The HHRA Program has initiated and will continue to seek opportunities to further collaborate with NCCT to share data and information. In addition, NCEA is continuing to build and strengthen expertise in the area of computational toxicology. Further efforts will be discussed at the mid-cycle review of the HHRA Program.

Updated Response: No change to the ORD action.

Current Progress: NCEA has taken several steps to further develop ties between NCEA and NCCT. For example, NCEA scientists participated in the NCCT ToxCast meeting in May 2009. NCEA facilitated that participation by organizing a half-day seminar prior to the meeting to provide an overview of ToxCast and computational toxicology tools in preparation for that meeting.

Additionally, NCEA has developed a pilot project, which involves NCCT, to focus on the next generation (NexGen) of risk assessment. This is driven by 1) new scientific advances, particularly in understanding the gene environment; 2) challenges to current risk assessment practices as articulated by the National Research Council (NRC) in their 2009 report Science and Decisions: Advancing Risk Assessment; and 3) the European Union's Registration, Evaluation, Authorization and restriction of Chemicals (REACH) legislation that will require new testing and assessment of tens to hundreds of thousands of chemicals in commerce. In developing this program, the HHRA Program has worked with NCCT, as well as ORD's other labs and centers and EPA's program and regional offices. NexGen assessments will be developed at three levels of complexity to be responsive to the risk context. Category 1 would use reliable high and medium throughput assays and structure-activity analyses to conduct a screening assessment and rank chemicals for further analysis. Depending on the priority established in Category 1, the risk context and the available data, two levels of additional analyses could be conducted: assessments prepared for data poor chemicals based upon a relatively narrow context of use and

relying on standard practices (Category 2, e.g., PPRTV-like); or a broader, more complex assessment relying on state-of-the-science practices (Category 3).

The HHRA Program has provided information on chemicals of key concern to the NCCT program for inclusion in the ToxCast program. Included are those chemicals currently on the IRIS agenda or under assessment in the PPRTV program. Additionally, NCEA has developed a list of thousands of chemicals that appear on a variety of priority lists (Hazardous Air Pollutants-HAP, CCL, etc.) and compiled public health information (both exposure and toxicity) about each chemical. This information was also provided to the NCCT program. All of these chemicals will be added to Phase 2 of the NCCT's ToxCast program, per NCEA's suggestion.

NCEA is also actively involved in an effort to expand the ToxRef database to include developmental neurotoxicity data. In collaboration with NCCT, NCEA has provided funding for data entry, and NCEA scientists are serving as advisors in developing the database structure and in assuring accurate interpretation of the data for entry.

NCCT and NCEA share postdocs through the Cross-ORD Postdoctoral fellowship program. Dr. Holly Mortensen works with both NCCT and NCEA. At NCCT, she has developed a toxicity pathway database that will be used to assess ToxCast assay results. This approach is in line with the NRC Toxicity Testing in the 21st Century's long range vision of moving toward a toxicity pathway perturbation based risk assessment approach. At NCEA, she is working on the use of genomics to inform intraspecies differences in response to toxic agents. She is currently co-authoring a manuscript on the use of 'omics data to inform susceptibility.

On several occasions, the Center Directors for NCCT and NCEA have presented jointly on the future of toxicology and risk assessment, including a briefing for the Senate Appropriations Committee staff on June 9, 2009. Other events where the importance of the two centers working together was presented include: The NAS' May 2009 symposium on toxicity-pathway-based risk assessment (http://dels-old.nas.edu/best/risk_analysis/symposium.shtml) and the BOSC's Computational Toxicology Subcommittee in September 2009.

NCEA and NCCT are collaborating through the EPA Risk Assessment Forum (RAF) to provide training for scientists in ORD on the application of computational methods in risk assessment, training for risk assessors on computational tools that are available for application in risk assessment (hazard and dose response), and training for decision makers on the implications of these new technologies.

Finally, several NCEA scientists have joined NCCT on detail assignments to the NCCT fellowship program. This relationship has been beneficial to both NCEA and NCCT and has led to additional collaborations between the two Centers and also between NCEA and other labs within ORD. This work will develop assessment applications for high throughput and high content data, methods and models. It will feed into and complement ORD's new integrated transdisciplinary research program on *Safe Products for a Sustainable World.*

STRUCTURE

The BOSC believes that the HHRA Program has a comprehensive and logical framework for producing high-quality risk assessments and for managing internal and external review processes. The consolidation of staff from multiple groups into a single core program under the HHRA rubric has facilitated communication and the adoption of standard practices and continuously improving processes. The interaction and cooperation between the HHRA Program and other ORD programs, program offices and regions is occurring at higher levels than previous interactions. However, the BOSC pointed out that while HHRA staff members have provided invaluable service to program offices, regions, states, etc. in responding to emergencies (e.g.. the 9/11 terrorist bombings, Hurricane Katrina) or assisting in difficult cleanup activities (e.g. asbestos cleanup in Libby, Montana), these high-value activities are not captured in the overall framework and HHRA MYP.

Recommendation 4: The BOSC considers the responsiveness of the staff members to national emergencies and the HHRA Program's contributions to particularly difficult cleanup sites as being of such high value that this should somehow be captured in the Annual Performance Goals (APGs).

Original Response: The HHRA Program appreciates the BOSC's recognition of the high value of the program's responsiveness and contributions to national emergencies or assisting in difficult cleanup activities. We agree with the recommendation that these contributions should be accounted for in a meaningful way within the overall framework of the HHRA Program. It is clear that HHRA staff expertise will continue to an integral part of such responses. The program also recognizes that one of the significant implications of responding to such events as national emergencies may be the reallocation of staff from key assessments or projects within LTG1, 2, and/or 3. As noted by the BOSC, it may not be plausible due to the unplanned nature of such events to fully account for or plan the resources needed to respond to such events or requests within an APG. The current APM/APG structure of ORD's MYPs is that APGs are major outputs that represent significant and timely milestones along a critical path toward the accomplishment of a LTG and that are planned over several years (three-five years). The program will however, work more closely with EPA's Office of Emergency Management (OEM) to be better prepared to respond to such events.

The HHRA Program has also started to implement procedures to better track these activities and the resources expended internally. Under its regulatory and program support activities, NCEA currently tracks monthly program office and regional requests for assistance and assignment of HHRA staff to cross-Agency regulatory workgroups. This system is being expanded to include emergency responses. In addition, NCEA is working with ORD's Labs and Centers and the Office of Science Policy to develop measures for support activities across ORD.

Original Action/Timeline: The HHRA Program has started to better track these activities and the resources expended both internally and across ORD. The program will also work more

closely with OEM to be better prepared to respond to such events. The next update of the HHRA MYP will include a section or description relating to these response efforts.

Updated Response: No change to the ORD action.

Current Progress: NCEA is tracking these emergency support activities and is holding discussions internally about how this should be described in the next version of the HHRA MYP. While it is impossible to predict the number and type of emergency response activities that may arise, we expect this tracking will give us a better idea of what level of commitment we could reasonably expect in the future for this type of support.

Over the past calendar year, NCEA has assisted with several high-profile support activities. In the summer of 2009, NCEA scientists provided extensive support to the Agency as it dealt with characterizing the risk of polychlorinated biphenyls (PCBs) in caulk in schools and other buildings. HHRA scientists developed a PCB exposure estimation tool and developed advisory limits for indoor school air concentrations. NCEA also provided support in 2009 to EPA's Region 5 and Office of Solid Waste and Emergency Response (OSWER), completing an evaluation of the University of Michigan Dioxin Exposure Study (UMDES). This evaluation provided perspective on how the UMDES results could inform Agency decision-making concerning dioxin in soils in Region 5. NCEA also provided rapid support to Region 7 as they dealt with an emergency situation involving hexavalent chromium. NCEA coordinated a conference call and presentation to provide information to Region 7 about the health effects of hexavalent chromium. As a result of this request, NCEA convened a meeting with other EPA programs and regions with an interest in hexavalent chromium to discuss accelerating an IRIS assessment for the chemical. Because of these meetings, NCEA has rapidly developed a draft health assessment document for hexavalent chromium that meets the identified needs of the programs and regions; that assessment is moving through the IRIS process at an accelerated rate. Also, NCEA served as a primary advisor to staff and scientists in the State of Hawaii, EPA's Region 9, and the Office of Air Quality Planning and Standards (OAQPS) regarding health risks associated with acute exposures to sulfur dioxide from volcanic activity, to support development of public health advisory levels and recommendations.

NCEA has maintained a consistent level of support and visibility to EPA's programs and regions. Through high profile, timely, and high quality support as identified above, as well as through established programs like the Superfund Technical Support Center and the PPRTVs, NCEA has become the "go to" organization for high quality and rapid scientific support.

NCEA has enhanced this visibility by conducting outreach to EPA's regional offices through one or two day regional visits. These visits typically consist of both informal discussions and formal presentations on a variety of topics. The goals of the meeting are to inform the regions of NCEA's products and capabilities, better understand regional issues and concerns, and strengthen ties at the management and staff levels. So far, NCEA has visited Regions 2, 3, 6, 8, and 9 with very successful results. Additional visits are being planned.

Finally, NCEA is currently helping the Agency respond to the Gulf oil spill emergency by providing information on the potential toxicity of constituents in crude oil and the dispersants used in cleaning up the spill.

Recommendation 5: The BOSC recommends that, in addition to the goals of 16 new IRIS and 50 new or revised PPRTV assessments per year, goals be established for increasing the number of assessments. The BOSC recognizes that it may not be possible to do more, given current staffing and budgetary limitations, but there is clearly a significant demand for these products.

Original Response: The HHRA Program agrees that there is a need to establish goals for increasing the number of assessments beyond that of 16 new IRIS and 50 new or revised PPRTV assessments per year. However, as noted in response to Recommendation # 1, there are both process requirements and resources limitations that affect productivity. The HHRA Program is implementing the revised process to meet current commitments and is revising the chemical prioritization and selection process to better reflect client office assessment priorities and associated resource requirements. Further, the HHRA Program is developing a process for the update of IRIS assessments ten years and older.

The HHRA Program is also addressing the concerns raised by the BOSC to increase the program's ability to produce more PPRTV assessments per year and has initiated significant modifications to protocols for the development of draft documents. In addition, the HHRA program has initiated a process for the evaluation of PPRTVs with sufficient data to develop into IRIS assessments. Two PPRTV assessments (vanadium pentoxide and cobalt) are being evaluated and modified for entry into the IRIS review process. PPRTV assessments are also being evaluated for use in the IRIS Update Process.

Original Action/Timeline: The HHRA Program has begun a number of efforts to streamline and increase the number of assessments produced per year such as: 1) the development of an IRIS Update Process; 2) significant modifications to the PPRTVs development process; 3) the modification of PPRTVs with sufficient data for entry into the IRIS process; and 4) PPRTV assessments are being evaluated for use in IRIS Update Process. An assessment of the programs' effectiveness, productivity and resource needs will be made as part of the implementation of these efforts. Consultations are also ongoing with OMB on new measures and metrics for the program.

Updated Response: See response to Recommendation #6 for updates on modifying PPRTV assessments to IRIS assessments.

Current Progress: The HHRA Program has taken several steps to meet this recommendation. The FY 2010 enacted budget includes additional resources for the IRIS program. Further, the process used to develop IRIS assessments was revised in May 2009; the new process will allow for more rapid completion of assessments while retaining transparency and opportunity for Agency and Interagency comments, as well as vigorous independent external peer review and public review and comment. The table provided in the response to Recommendation #1 illustrates how the new process has greatly improved the ability of EPA's IRIS program to

provide high quality human health risk information to EPA's programs and regions in a timely fashion. After the announcement of the new process, the fourth quarter of fiscal year 2009 began. More final assessments were posted on IRIS in that single quarter of one year than in each of the previous three years. Thus, HHRA's IRIS program has quickly demonstrated progress under the new process, and will continue to show significant results in 2010 and beyond.

Additionally, we have developed an IRIS Logistics team that coordinates all IRIS-related administrative support. Additional details are provided in the response to Recommendation #1.

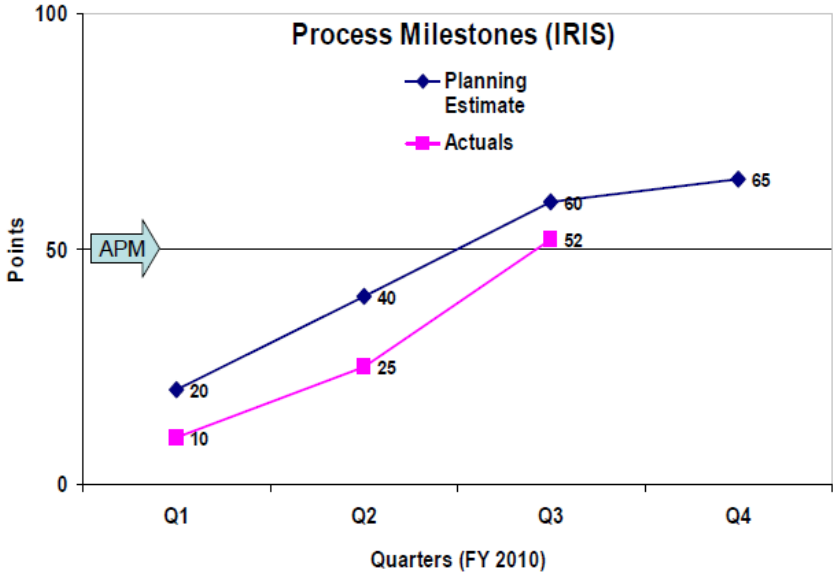
We have met extensively with EPA's program and regional offices to better understand their assessment needs. Additionally, we are working with Cal/EPA and ATSDR under separate MOUs; we expect these efforts to eventually increase our efficiency and assessment output.

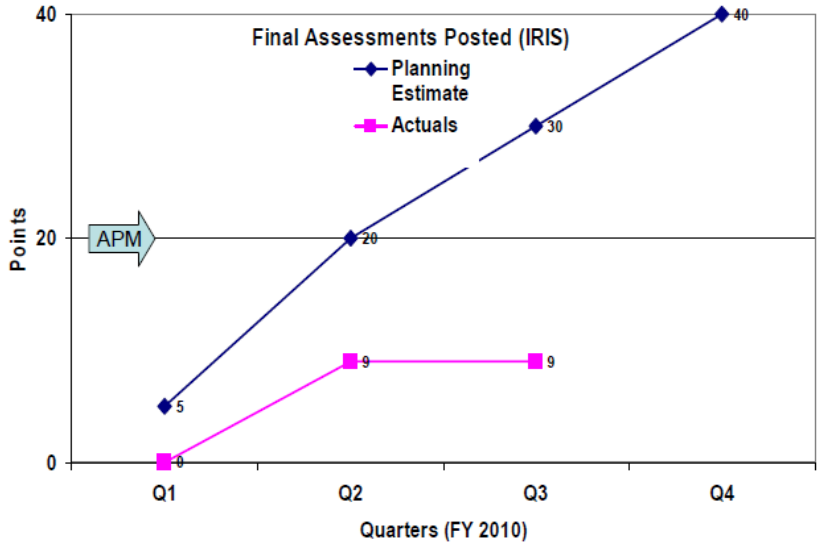
We have also begun a program to update older IRIS assessments. Additional details on this program are described in our progress under Recommendation #2.

We have taken steps to facilitate more efficient production of PPRTV assessments by: (1) developing a PPRTV review team within NCEA; (2) streamlining the information included in a PPRTV assessment to focus on pertinent data and decision-making sections; (3) educating EPA contractors about expectations for PPRTV assessment documents; and (4) batching assessment development and internal and external reviews. This has proven to be a successful effort. In FY 2009, NCEA produced 69 new PPRTV assessments. These 69 PPRTV assessments included a total of 140 new individual toxicity values (e.g., RfD, RfC, Oral Cancer Slope Factor, etc.) that were added to the PPRTV database.

NCEA has also negotiated new program metrics with OMB. Specifically, NCEA's newly negotiated performance metric indicates the HHRA Program will complete health hazard and dose response assessments of high priority chemicals as interagency science consultation drafts or external peer review drafts with a program-defined value of 50 points applied to a 3-year rolling average. Additionally, the HHRA Program will post on the IRIS web page completed health hazard assessments of high priority chemicals for public dissemination with a program defined value of 20 points applied to a 3 year rolling average. To account for differences in the level of complexity of assessments, the HHRA Program has also negotiated with OMB a tiering system that provides three different levels of complexity and associated points for reaching milestones for assessments. Tier 1 assessments are standard assessments that are expected to require a typical level of effort from NCEA scientists and be limited in controversy and the complexity of the science required for the assessment. Tier 1 assessments are assigned a point value of "1" for each major negotiated milestone met. Tier 2 assessments are more extensive in that they require more FTE effort, have a greater level of controversy or visibility, and are scientifically more complex than Tier 1. Tier 2 assessments are assigned a point value of "2" for each major negotiated milestone met. Tier 3 assessments are the most complex. They require an exceptional level of FTE support, are highly controversial and/or visible, and are exceptional in the complexity of the science involved in the assessment. Tier 3 assessments are assigned a point value of "5" for each major negotiated milestone met.

The following charts illustrate the HHRA Program's progress in meeting these program metrics.





Recommendation 6: The BOSC recommends that well-developed PPRTVs be considered as a source of prioritization in the development of full IRIS documents. This should assist the HHRA Program in meeting its goal of producing 16 IRIS assessments per year, but also should facilitate the accomplishment of stretch goals for completing additional assessments.

Original Response: The HHRA Program fully agrees with the BOSC recommendation that well-developed PPRTVs be considered as a source for the possible development of IRIS assessments. As noted in the response to Recommendation # 5 above, the HHRA Program has initiated this effort and currently PPRTVs for vanadium pentoxide and cobalt have been selected for modification and entry into the IRIS process.

Original Action/Timeline: HHRA management is routinely evaluating new and renewed PPRTVs for potential development of new IRIS assessments or updating existing IRIS assessments. Thus far PPRTVs for vanadium pentoxide and cobalt have been selected for modification into IRIS assessments.

Updated Response: In late 2008, the program made a decision to focus resources on ongoing assessments that were at or beyond the Agency review step of the assessment development process in order to accelerate the agenda. The specific examples chosen from the PPRTV program were in the earlier stages of assessment. The feasibility of using PPRTVs for development of IRIS assessments continues to be explored.

Current Progress: NCEA has looked at the possibility of using the PPRTVs for cobalt and vanadium pentoxide as sources for IRIS assessments. In 2008, NCEA decided to focus assessment efforts on those chemicals on the IRIS agenda that were further along in the assessment process. Those chemicals at the earlier stages of work, or for which work had not yet begun, were temporarily put on hold so staff could focus their efforts on completing those assessments that were further along in the process. Cobalt and vanadium pentoxide were in this group, called "Table 2", in the earlier stages of assessment.

To better understand the Agency's needs, NCEA has proactively sought advice from EPA's program and regional offices in an effort to identify the highest priority assessment needs across the Agency for chemicals currently on the IRIS agenda. Those highest priority needs will be addressed through the IRIS program. Where needs have been identified as a lower priority, NCEA has consulted with the programs and regions to determine if a PPRTV would meet the identified need. This would allow the assessment to be completed in a more rapid timeframe and free up capability within the IRIS program for the highest priority needs. This exercise also helped us to set priorities for those chemicals on "Table 2" so as staff time becomes available as chemical assessments are completed, we can focus efforts on the highest priority chemicals first.

PROGRAM PERFORMANCE

The BOSC summarized HHRA's performance as making substantial and satisfactory progress on each LTG based both on the clearly defined milestones (APGs and APMs) and on providing the support requested in response to unscheduled emergency needs. The BOSC did note, however, that with respect to LTG 1, the APGs for every year include the completion of 16 high priority health hazard assessments and 50 new or renewed PPRTVs. This rate of completion will not satisfy the stated goal to have no IRIS entries over ten years old because there are now over 540 IRIS chemicals, and a renewal rate alone of 54 per year would be needed to achieve that goal.

Therefore, the BOSC reiterated their recommendation that NCEA should assess what needs to be done to increase the rate of assessment completion.

Recommendation: NCEA should assess what needs to be done to increase the program's ability to produce more IRIS and PPRTV assessments per year, not only to meet their own stated objectives but also to satisfy the needs of their clients. This could either be in the form of a recommendation to the Agency for more resources, or the development of a more streamlined process.

Original Response: See response to recommendations #1, 2, 5 and 6 above.

Original Action/Timeline: See response to recommendations #1, 2, 5 and 6 above.

Updated Response: No change to the ORD action.

Current Progress: See responses to recommendations #1, 2, 5 and 6 above.

PROGRAM QUALITY

The quality of the products of the HHRA Program was judged primarily on the basis of the global acceptance and use of the health assessments and the presentation of the research efforts completed and currently being pursued by staff scientists. The BOSC stated, on both counts, the very high quality of those products was evident. They also stated that IRIS assessments are considered internationally to be of the highest quality and reliability. The research efforts presented to the BOSC had a high degree of scientific relevance and merit. The review of criteria air pollutants has an excellent record of past performance.

Recommendation 7: In order to maintain the high level of quality that is evident in the HHRA work products, the BOSC strongly recommends that steps be taken to ensure the transparency of decisions made in the process of performing IRIS and PPRTV assessments and ISAs

Original Response: ORD appreciates the BOSC's recognition of the "very high quality" of its products and noting of the international status of IRIS assessments as being "considered to be of the highest quality and reliability" and agrees with the recommendation that steps be taken to ensure the transparency of decisions. As part of the new IRIS process announced on April 10, 2008 by EPA Deputy Administrator, Marcus Peacock, the program has begun chemical specific "listening sessions". Since the April announcement, the HHRA Program has conducted listening sessions for the carbon tetrachloride, cerium, beryllium, and tetrachloroethylene IRIS assessments. Protocols and standard operating procedures for the selection, prioritization and development of IRIS assessments are available on the IRIS Web site and the program is currently revising the chemical prioritization and selection process to better reflect client office assessment priorities and associated resource requirements. All external peer review meetings are announced in the Federal Registered and are open to the public.

The IRIS Update Process is currently under development. In developing the draft process, the HHRA Program has met with EPA's programs and regions, the EPA Science Policy Council and the Toxic and Risk Subcommittee of the Committee on the Environment and Natural Resources (CENR) for their input into the process. Agreements have been established to involve all interested parties and agencies in the prioritization and peer-review of updated chemicals assessments. The draft process includes both public notices through the Federal Register announcing chemicals under consideration and a request for available data and announcement of external peer review meetings. All external peer review meetings for the IRIS Update program will be conducted through a FACA process and will be open to all interested parties.

For PPRTVs, OSWER works with the HHRA Program to identify and prioritize chemicals for development. New contaminants are selected based on their frequency and level of contamination at Superfund sites and whether or not toxicity values are available from other entities like Cal/EPA or ATSDR. Existing PPRTVs are re-evaluated every five years and updated as appropriate.

As noted in the BOSC report and discussed during the face-to-face meeting, the Agency has developed a new NAAQS review process which includes the development of ISAs by the HHRA Program. The new process was developed by an internal EPA workgroup in consultation with the Clean Air Scientific Advisory Committee (CASAC), Congressional staff and interested stakeholders. The new process also includes extensive collaboration and consultation between ORD and OAR throughout the entire review. It incorporates additional steps for peer consultation with outside experts and stakeholders and includes an integrated planning step that guides the entire review. This integrated planning is achieved through workshops jointly sponsored by ORD and OAR to receive input from experts including members of CASAC who discuss key issues. The transition to the new process began in 2007 with the NOx and SOx reviews.

Original Action/Timeline: The HHRA Program is developing and implementing a new IRIS development process which includes extensive intra- and interagency and public involvement, revised approaches to chemical prioritization and accountability, and a new Update Process Also, as noted above, ISAs are being developed as part of the new NAAQS process which includes extensive collaboration and consultation between ORD and OAR and public involvement throughout the entire review. An update on the development of IRIS assessments, PPRTVs, and ISAs will be provided at the mid-cycle review.

Updated Response: NCEA has also developed and is using the Health and Environmental Research Online (HERO) system, which houses the scientific literature used to develop ISAs as well as IRIS and PPRTV assessments. Additionally, several steps have been taken to further increase transparency and communication.

Current Progress: In May 2009, the Administrator of the EPA announced a new IRIS process that is more streamlined yet retains a strong commitment to transparency through multiple opportunities for intra and inter-Agency review, external peer review, and public comment. Additionally, in March 2010, EPA announced the availability of the Health and Environmental

Research Online (HERO) database, which was praised by EPA as "a milestone in transparency" and a part of EPA's "open government directive to conduct business with transparency, participation, and collaboration." The publicly accessible HERO database (www.epa.gov/hero) provides an easy way to review the scientific literature behind NCEA's science assessments.

The database includes more than 300,000 scientific articles including the authors, titles, dates, and abstracts. In addition, through a simple keyword search, anyone can see information from the articles that were used to develop specific risk assessments. HERO includes peer-reviewed literature used by EPA to develop ISAs that support the NAAQS review. It also includes references and data from IRIS, a database that supports critical agency policymaking for chemical regulation, and from PPRTVs.

At the time of the BOSC review, EPA was in the process of implementing revisions to the NAAQS review process, and NCEA was developing ISAs for reviews of the NAAQS for nitrogen oxides and sulfur oxides. In the past three years, NCEA has completed the initial set of ISAs for oxides of nitrogen and sulfur (NOx- health effects, SOx – health effects, and ecological effects of NOx and SOx) along with ISAs for PM and CO, meeting several court-ordered deadlines along the way. In the process, NCEA has restructured the ISA to place a concise summary and integrative synthesis of the key findings at the beginning of the assessment, focusing on the key policy-relevant findings with figures that present the findings from across health studies relevant to pollutant concentrations to better inform decision makers. NCEA has developed a causality framework that has been used in all five ISAs, and provides transparency and consistency in the process of drawing conclusions and causal judgments. CASAC panels have lauded the implementation of the causal framework, the process for developing the ISA and the structure of the ISA; positive comments have been received during the peer reviews of draft ISAs for both PM and CO.

Also, in the recent draft dioxin report entitled, *EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments (*http://www.epa.gov/dioxin), there is lengthy discussion and accompanying schematics detailing the delineated study selection process for the identification of appropriate studies for TCDD dose-response analysis. In addition, in February 2009, to assist NCEA in responding to the NAS, NCEA convened a scientific workshop to identify and address issues related to the dose-response assessment of TCDD and to ensure that EPA's response to the NAS focused on the key issues and reflected the most meaningful science. This workshop was open to the public and included scientific experts from academia, industry, non-profit organizations, and government. These experts discussed potential approaches to TCDD dose-response assessment and considerations for EPA's response to NAS. As a result, the process used by EPA to determine key scientific approaches and decisions in the development of the recent draft dioxin report can be held up as a model for transparency and public participation.

NCEA has also been providing listening sessions for the public and stakeholders for chemicals on the IRIS agenda. Additionally, for high profile chemicals like formaldehyde, dioxin, and arsenic, NCEA has provided briefings for other Agencies and stakeholders at key points in the assessment process.

Finally, NCEA has taken steps to standardize assessment practices within the Center. Standard Operating Procedures for developing IRIS assessment documents have been written, and NCEA has started to convene regular science policy discussion meetings with staff to make sure science policy practices are consistent across assessments.

SCIENTIFIC LEADERSHIP

The BOSC found that: 1) there are important areas in which HHRA Program scientists have played leadership roles at both the national and international levels; 2) the HHRA Program is clearly recognized as an international leader in risk assessment in both methods development and implementation; and 3) the areas of impressive leadership are related to IRIS and Air Quality Health and Environmental Assessments. The report also states that, taken as a whole, the evidence speaks to a community of highly trained and productive scientists, many of whom are leaders in their field, who are providing leadership to the United States and international governments as well as scientific communities and are engaged in risk assessment science and in solving important risk assessment problems.

Recommendation 8: The HHRA Program should consider using available resources to recruit one or two additional senior scientists, especially into the LTG 2 program where efforts are underway to integrate emerging technologies into the risk assessment processes.

Original Response: The HHRA Program appreciates the feedback and recognition by the BOSC of the quality and extent of its leadership both nationally and internationally. The HHRA Program agrees with the recommendation to enhance that quality by recruiting senior scientists throughout its program and will look for opportunities to fill positions with senior leaders from both within the Agency and outside experts.

Original Action/Timeline: Recently, the HHRA Program recruited a senior scientist from NHEERL, Dr. Linda Birnbaum. In addition, ORD has obtained authority to hire experts and senior scientists under Title 42. The HHRA Program has initiated one recruitment action under this program and will announce an additional recruitment in 2009.

Updated Response: Dr. Birnbaum has taken a new job. She is now the Director of the National Institute of Environmental Health Sciences (NIEHS).

Current Progress: For the last three years NCEA has had the benefit of input from two senior statisticians who participate in the Oak Ridge Institute for Science and Education (ORISE) fellows program. Dr. Kenny Crump has been a leading investigator in the field of dose response modeling over the past 30 years. His participation in the ORISE fellows program has allowed him to contribute to important science issues faced by EPA in the area of quantitative risk assessment. In particular he has delved deeply into issues regarding application of biologically based dose response models for risk assessment needs. This effort has sharpened our understanding of the strengths and limitations of such models in advancing understanding of chemical risks. Dr. Crump is currently working on the quantitative application of genomics and

other high-throughput data in chemical risk assessment. Dr. Bimal Sinha, Professor of Statistics with University of Maryland Baltimore County, has worked with NCEA to advance statistical methods for several areas of quantitative risk assessment. These areas have included application of more robust statistical procedures in modeling data from pharmacokinetic studies, extension of methods for incorporating experimental error estimates in benchmark dose modeling, and analysis of exposure statistics data.

The HHRA Program has used the ORISE program to bring on board a few senior scientists to help address some of the complex scientific issues discussed in the 2009 National Research Council (NRC) Report, *Science and Decisions: Advancing Risk Assessment.* Additionally, scientists from the HHRA Program are actively engaged with scientists in academia, state governments, and industry, both across the U.S. and internationally, to discuss issues, conduct research, and develop pertinent case studies that will be useful in addressing the NRC recommendations. Complex scientific issues being discussed include probabilistic methods and accounting for uncertainty and variability in quantitative dose-response; mode of action, background exposures and disease processes, and vulnerable populations in low dose extrapolation; and applying similar quantitative approaches for cancer and non-cancer health assessment.

In particular, ORISE Faculty Fellow Dr. Gary Ginsberg (University of Connecticut) is working with NCEA on developing new methods and models for incorporating information regarding susceptible populations into EPA risk assessments. ORISE Faculty Fellow Dr. David Eastmond is working with NCEA scientists to develop a database on the mutagenic mode of action of certain chemicals of interest to the IRIS program. Drs. Ginsberg and Eastmond have made several seminar presentations to NCEA staff on risk assessment issues.

NCEA has also recruited and hired a Title 42 Division Director to manage NCEA's Research Triangle Park (RTP) Division. NCEA intends to recruit additional Title 42 and/or SL (senior level) scientists to fill critical hiring needs in the organization.

Additionally, NCEA plans to add five ORISE post docs to the IRIS program to work on IRIS assessments. Two scientists have been hired under this program so far and will start in the summer 2010. Interviews for the remaining three positions are ongoing. In addition to the ORISE program, NCEA has also increased capacity in key scientific areas through the American Association for the Advancement of Science (AAAS) and Association of Schools of Public Health (ASPH) Fellowship programs. Several postdocs and fellows have been added to LTG2 as part of the HHRA's NexGen effort. Additionally, a collaborative NexGen effort among other labs and centers has effectively expanded the LTG2 effort. See description of NexGen in response to Recommendation #1.

COORDINATION AND COMMUNICATION

The BOSC stated that communication and coordination activities have been effectively institutionalized within HHRA. These activities are well established and occur vertically and

horizontally within NCEA and with other relevant EPA programs and regional offices. Well-documented systems are in place and have operated for many years to provide a systematic, structured prioritization and communication strategy to assure that EPA program and regional office scientists and managers are effectively involved in setting priorities for assessment development and that HHRA activities such as IRIS and PPRTV assessments reflect the client's needs. The BOSC noted that with the exception of PPRTVs, HHRA products including assessments (such as IRIS and ISAs), methods, guidelines, and reference documents such as the Exposure Factors Handbooks, are all available to the public on the Internet and provide information not available from any other source.

Recommendation 9: PPRTVs far outnumber IRIS assessments and are being developed at four to five times the rate of IRIS assessments. They have been developed specifically to address the site specific needs of EPA's Superfund program. Currently, PPRTVs and their supporting documentation are only available on a Web site restricted to use by EPA staff or to those who obtain special permission from EPA. The BOSC encourages EPA to make the PPRTVs publicly available for use in hazardous waste site risk assessment and promote their use where appropriate.

Original Response: The HHRA Program agrees that PPRTVs are extremely important to the Superfund program and these assessments are important for assessing hazards at waste sites. PPRTVs are available to the states and other partners involved in waste site assessments and they are provided updates on a quarterly basis. PPRTVs are also being made available to other program offices within EPA for screening and prioritization of research needs, e.g. use by Office of Water to prioritize research needs for CCL3 decisions. PPRTVs are also being modified where appropriate to support the development of IRIS assessments and new PPRTVs evaluated for use in IRIS Update Process.

Please note there currently are over 547 chemical assessments on IRIS. PPRTVs have been developed for 381 chemicals.

Original Action/Timeline: PPRTVs are available to the states and other partners involved in waste site assessments and they are provided updates on a quarterly basis. Within EPA PPRTVs are being made available to other program offices for screening and prioritization of research needs.

Updated Response: No change to the ORD action.

Current Progress: PPRTVs are currently available to all EPA staff and by request to states and other partners involved in waste site assessments. Updates are provided on a quarterly basis. NCEA has been proactive about conducting more outreach to EPA's programs and regions, including providing them with information about PPRTVs. As a result, the PPRTV Web site (which is available to any EPA employee) has been shared with several EPA program offices outside of the Superfund program. These programs have indicated this information will help them address screening and prioritization needs as well as the need for toxicity numbers.

At this time, NCEA does not think it is possible to make the PPRTV database publicly available. We have explored the feasibility and think there are potential issues and complicating factors. However, we have planned a follow-up conversation with OSWER to discuss this once again, and we continue to explore the possibility of making the PPRTV database publicly available.

OUTCOMES

The BOSC concluded that outcome measures are extremely well defined for each LTG and that annual measures are well described. The procedures for IRIS and PPRTVs appear to be well considered and to work well, but how decisions are made is not immediately transparent. The BOSC was particularly interested to know whether chemicals that had not reached a high enough priority level to be reviewed in a given year were carried over for consideration in ensuing years, and whether they were accorded a higher priority status by virtue of having been on the list for a period of time. The BOSC also reiterated its recommendation (See Recommendation #4) to consider capturing in the APGs the program's responsiveness to national emergencies and high profile site clean-ups.

Recommendation 10: The HHRA Program needs to consider information on the potential public health concern of various chemicals as it prioritizes them for IRIS or PPRTV review. It appears that some of this information is being provided by the program and regional offices, but it would be of value for the program to make transparent the basis for its prioritization decisions for IRIS and PPRTVs.

Original Response: The HHRA Program agrees with the BOSC's recommendation to consider information on the potential public health concern of various chemicals as it prioritizes them for IRIS or PPRTV review and the need for transparency within the program. Criteria for the selection and prioritization of chemicals for new IRIS assessments and reassessments have been established and are available on the IRIS website (www.epa.gov/iris). The IRIS process provides both opportunities for public comment as well as providing available data. Currently NCEA is meeting with the program offices and regions to provide more explicit information on the IRIS process and setting priorities. For the IRIS Update Process a draft process has been developed which includes a detailed selection and prioritization process as well as public notification. The selection of chemicals for development of new PPRTVs or updating assessments is determined by OSWER in consultation with ORD. The selection criteria are based on frequency and extent of contamination at Superfund sites, the availability of toxicity values from other sources and the availability of qualitative and quantitative information.

Original Action/Timeline: NCEA is meeting with the program offices and regions to provide more explicit information on the IRIS process and setting priorities. Progress regarding these efforts will be discussed at the mid-cycle review of the HHRA Program.

Updated Response: NCEA has met extensively with EPA's programs and regions, and recently completed a prioritization exercise using feedback from the programs and regions along with public health information.

Current Progress: NCEA has held extensive meetings with EPA's program and regional offices to discuss the process that is used to prioritize nominated chemicals for assessment through the IRIS program. After several conversations with and feedback from these offices, we have developed a revised process for prioritizing how chemicals will be added to the IRIS agenda. This process includes collecting information about the public health concerns of the nominated chemicals. It also involves more transparency, as well as a "feed-back" loop to the programs and regions. Additionally, NCEA recently conducted an exercise where we asked the programs and regions for input on regulatory and other needs for assessments for chemicals currently on the IRIS agenda for which work has not yet begun. The purpose of this exercise was to help the HHRA Program set priorities for completing currently backlogged assessments.

The HHRA Program will soon issue a FRN requesting nominations for chemicals to be added to the IRIS agenda. This notice will provide more detail than previous notices in an effort to increase transparency about the IRIS program and how decisions are made to add chemicals to the agenda.

NCEA has also developed a list of thousands of chemicals that appear on a variety of priority lists (HAP, CCL3, etc.) and compiled public health information (both exposure and toxicity) about each chemical. This information may be used in the future to help the HHRA Program proactively identify chemicals that may be a concern for public health, which would then be presented to EPA's program and regional offices for input.

NCEA meets regularly with OSWER to set priorities for chemicals to assess under the PPRTV program. NCEA is quite flexible in adding chemicals and reprioritizing when a high priority need is indentified by OSWER. Additionally, as part of NexGen efforts, the HHRA Program is investigating the use of ToxCast and ExpoCast information to help set priorities for adding chemicals to the list for PPRTV development.

The HHRA Program is also looking at options for incorporating public heath information into the program's prioritization process for health assessments using value of information tools. Examples of options that are being considered include consultation with the BOSC workgroup on decision analysis and value of information and other mechanisms.

Additionally, NCEA is currently performing an IRIS human health assessment for six phthalates and developing a cumulative risk assessment for these chemicals as recommended by the NRC in its report *Phthalates and Cumulative Risk: The Tasks Ahead*. It is expected that this cumulative assessment will serve as a framework for extension to other compounds that act by a similar effect. Specifically, the assessment includes the following phthalates: dibutyl phthalate (DBP), di(2-ethylhexyl)phthalate (DEHP), butyl benzyl phthalate (BBP), di-isobutyl phthalate (DIBP), di-isononyl phthalate (DINP), and dipentyl phthalate (DPP). The IRIS Human Health Risk Assessment for Selected Phthalates will include noncancer and cancer qualitative and quantitative human health effects information and estimation of risk where the data are available for each of the phthalates. Several of the phthalates included in this assessment were already on the IRIS agenda. However, after release of the NRC report, the HHRA Program decided to add a few phthalates, as recommended by the NRC, based on their impact on a common health

endpoint. Considering this public health information facilitated the addition of a few new chemicals to the IRIS agenda.

Human Health Risk Assessment Program – BOSC Mid-Cycle Progress Report Summary Table

<table>
<tr><th>Recommendation</th><th>ORD Action</th><th>Timeline for Action</th></tr>
<tr>
<td>Recommendation #1:
NCEA should assess what needs to be done to increase the Program's ability to produce more IRIS and PPRTV assessments per year, not only to meet their own stated objectives but also to satisfy the needs of their clients. This could either be in the form of a recommendation to the Agency for more resources, or the development of a more streamlined process.</td>
<td>Original Response: The HHRA Program is implementing changes addressing development of new IRIS assessments and reassessments, is revising the chemical prioritization and selection process to address client office needs, has initiated development of a process for updating older assessments on IRIS and begun efforts to enhance and streamline the PPRTV process.

Updated Response: No changes to the ORD action.</td>
<td>Original Timeline: The next update of the HHRA MYP will reflect any significant changes in these programs and new metrics agreed upon with OMB. Progress regarding these efforts will also be discussed at the mid-cycle review of the HHRA Program in 2010.

Current Progress: The HHRA program has taken several steps to meet this recommendation. The FY 2010 enacted budget includes additional resources for the IRIS program. Further, the process used to develop IRIS assessments was revised in May 2009 (www.epa.gov/iris/process); the new process allows for more rapid completion of assessments while retaining transparency and opportunity for Agency and Interagency comments, as well as vigorous independent external peer review and public review and comment. The table below illustrates how the new process has greatly improved the ability of the IRIS program to provide high quality human health risk information to EPA's programs and regions in a timely fashion. After the announcement of the new process, the fourth quarter of fiscal year 2009 began. More final assessments were posted on IRIS in that single quarter of one year than in each of the previous three years. Thus, the HHRA's IRIS program has quickly demonstrated progress under the new process and will continue to show significant results in 2010 and beyond.

<table>
<tr><th>IRIS</th><th colspan="2">Draft Assessments Start Interagency Review/Consultation</th><th>Draft Assessments Start Independent External Peer Review</th><th rowspan="11">Second Interagency Review/Discussion</th><th>Final Assessments Posted on IRIS</th></tr>
<tr><td>FY2006</td><td colspan="2">11</td><td>1</td><td>2</td></tr>
<tr><td>FY2007</td><td colspan="2">16</td><td>12</td><td>2</td></tr>
<tr><td>FY2008</td><td colspan="2">5</td><td>12</td><td>5</td></tr>
<tr><td rowspan="3">FY2009</td><td>1st qtr.</td><td>3</td><td>0</td><td>0</td></tr>
<tr><td>2nd qtr.</td><td>4</td><td>1</td><td>1</td></tr>
<tr><td>3rd qtr.</td><td>2</td><td>2</td><td>0</td></tr>
<tr><td>May 21, 2009 New IRIS Process</td><td>4th qtr.</td><td>1</td><td>7</td><td>6</td></tr>
<tr><td>FY 2009 Total</td><td colspan="2">10</td><td>10</td><td>7</td></tr>
<tr><td>FY2010 (Qu. 1-3)</td><td colspan="2">5</td><td>7</td><td>3</td></tr>
<tr><td>FY2010 Projected</td><td colspan="3"></td><td>15</td></tr>
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		Additionally, we have developed an IRIS Logistics Team to coordinate all aspects of administrative support for the IRIS program. The development of this team has created efficiencies by centralizing logistical activities and relieving scientific staff of administrative burdens. This is a matrix managed team that includes project officers of contracts for IRIS document development, technical editing, and peer review; the NCEA Webmaster; the IRIS coordinator, who maintains the public tracking system for IRIS assessments, organizes listening sessions, and works with the chemical manager to develop project schedules; members of the NCEA Technical Information Staff, who develop and coordinate FRNs and clearance for documents; the interagency point of contact, who handles all correspondence with interagency reviewers; and the NCEA communications director, who coordinates all communications dealing with IRIS draft and final assessments. Administrative support staff schedule, organize and administer IRIS-related meetings and briefings and coordinate with the SAB and NAS when these bodies conduct peer reviews of IRIS assessments. NCEA has met extensively with EPA's Program and Regional offices to better understand their assessment needs. Additionally, NCEA is working with Cal/EPA's OEHHA and ATSDR under separate MOUs. It is anticipated that these efforts will eventually increase efficiency and assessment output. NCEA has also begun a program to update older IRIS assessments. Additional details on this program are described in our progress under Recommendation #2. We have taken steps to facilitate more efficient production of PPRTV assessments by: (1) developing a PPRTV review team within NCEA; (2) streamlining the information included in a PPRTV assessment to focus on pertinent data and decision-making sections; (3) educating EPA contractors about expectations for PPRTV assessment documents; and (4) batching assessment development and internal and external reviews. This has proven to be a successful effort. In FY 2009, NCEA produced 69 new PPRTV assessments. These 69 PPRTV assessments included a total of 140 new individual toxicity values (e.g., RfD, RfC, Oral Cancer Slope Factor, etc.) that were added to the PPRTV database. NCEA has also negotiated new program metrics with OMB. Specifically, NCEA's newly negotiated performance metric indicates the HHRA program will complete health hazard and dose response assessments of high priority chemicals as interagency science consultation drafts or external peer review drafts with a program-defined value of 50 points applied to a 3-year rolling average. Additionally, the HHRA program will post on the IRIS Web page completed health hazard assessments of high priority chemicals for public dissemination with a program defined value of 20 points applied to a 3 year rolling average. To account for differences in the level of complexity of assessments, the HHRA program has also negotiated with OMB a tiering system that provides three different levels of complexity and associated points for reaching milestones for assessments. Tier 1 assessments are standard assessments that are expected to require a typical level of effort from NCEA scientists and be limited in controversy and the complexity of the

		science as well as the level of effort required for the assessment. Tier 1 assessments are assigned a point value of "1" for each major negotiated milestone met. Tier 2 assessments are more extensive in that they require more FTE effort, have a greater level of controversy or visibility, and are more scientifically complex than Tier 1. Tier 2 assessments are assigned a point value of "2" for each major negotiated milestone met. Tier 3 assessments are the most complex. They require an exceptional level of FTE support, are highly controversial and/or visible, and are exceptional in the complexity of the science involved in the assessment. Tier 3 assessments are assigned a point value of "5" for each major negotiated milestone met. Additionally, the HHRA program has begun a pilot project on advancing the next generation of risk assessment (NexGen) that will explore the feasibility of using advances in molecular and systems biology for developing health assessments. It is anticipated this pilot project will help pave the way for using high throughput data to develop rapid health assessments. This is a collaborative effort across ORD and with NIEHS, NHGRI, and Cal/EPA.
Recommendation #2: Mechanisms should be considered for retaining IRIS assessments older than 10 years that have not been updated, rather than allowing these assessments to expire and be removed from the IRIS database and Web site. One option is to simply annotate them as such.	**Original Response:** Implementation of the IRIS update process is underway. **Updated Response:** No changes to the ORD action.	**Original Timeline:** Progress regarding these efforts will be discussed at the mid-cycle review of the HHRA Program in 2010. **Current Progress:** NCEA has decided that IRIS assessments older than 10 years will not be removed from the IRIS database. Additionally, a process for updating old IRIS chemical assessments has been developed and is nearing the implementation stages. The HHRA program issued a FRN in October 2009 announcing the establishment of this IRIS Update Project. Additionally, the HHRA program has developed a two-tiered peer review process consisting of a Federal Standing Science Committee followed by a Standing External Review Panel of the SAB under FACA. The SAB issued a FRN in March 2009 requesting the nomination of experts to serve on this committee. Committee members have since been identified and the panel has been established. The intent of the IRIS Update project is to re-visit all dose-response assessment values (RfDs, RfCs, Oral Cancer Slope Factors, and Inhalation Cancer Unit Risks) in IRIS with a posting date more than 10-years old. The values under current assessment by the standard IRIS process (on IRIS Track) and the values for pesticides not in active use are eliminated from the list of IRIS values greater than 10-years old. Then the remaining values are prioritized for being updated. This prioritization takes into consideration several factors, including frequency of occurrence in NPL waste sites, occurrence as hazardous air pollutants used in residual risk assessments, the presence of chemicals on the CCL, and other intra- and inter-agency interests. From this list, smaller batches of assessments (~10) are selected for literature searches by a contractor. After the literature search, the path for development of a revised dose-response assessment value is based on whether new data exists or not and whether new values are proposed or not (binning).
Recommendation #3: The HHRA Program should	**Original Response:** The HHRA Program has	**Original Timeline:** Further efforts will be presented at the mid-cycle review of the HHRA Program in 2010.

continue to develop ties with NCCT, and should provide formal input to that Program on the aspects of its research that will be of value to HHRA.	initiated and will continue to seek opportunities to further collaborations with NCCT and to share data and information. In addition, NCEA is continuing to build and strengthen expertise in the area of computational toxicology. **Updated Response:** No change to the ORD action.	**Current Progress:** NCEA has taken several steps to further develop ties between NCEA and NCCT. For example, NCEA scientists participated in the NCCT ToxCast meeting in May 2009. NCEA facilitated that participation by organizing a half-day seminar prior to the meeting to provide an overview of ToxCast and computational toxicology tools in preparation for that meeting. Additionally, NCEA has developed a pilot project, which involves NCCT, to focus on the next generation (NexGen) of risk assessment. This is driven by 1) new scientific advances, particularly in understanding the gene environment; 2) challenges to current risk assessment practices as articulated by the NRC in their 2009 report Science and Decisions: Advancing Risk Assessment; and 3) the European Union's REACH legislation that will require new testing and assessment of tens to hundreds of thousands of chemicals in commerce. In developing this program, the HHRA program has worked with NCCT, as well as ORD's other labs and centers and EPA's program and regional offices. NexGen assessments will be developed at three levels of complexity to be responsive to the risk context. Category 1 would use reliable high and medium throughput assays and structure-activity analyses to conduct a screening assessment and rank chemicals for further analysis. Depending on the priority established in Category 1, the risk context and the available data, two levels of additional analyses could be conducted: assessments prepared for data poor chemicals based upon a relatively narrow context of use and relying on standard practices (Category 2, e.g., PPRTV-like); or a broader, more complex assessment relying on state-of-the-science practices (Category 3). The HHRA program has provided information on chemicals of key concern to the NCCT program for inclusion in the ToxCast Program. Included are those chemicals currently on the IRIS agenda or under assessment in the PPRTV program. Additionally, NCEA has developed a list of thousands of chemicals that appear on a variety of priority lists (HAP, CCL3, etc.) and compiled public health information (both exposure and toxicity) about each chemical. This information was also provided to the NCCT program. All of these chemicals will be added to Phase 2 of the NCCT's ToxCast program, per NCEA's suggestion. NCEA is also actively involved in an effort to expand the ToxRef database to include developmental neurotoxicity data. In collaboration with NCCT, NCEA has provided funding for data entry, and NCEA scientists are serving as advisors in developing the database structure and in assuring accurate interpretation of the data for entry. NCCT and NCEA share postdocs through the Cross-ORD Postdoctoral fellowship program. Dr. Holly Mortensen works with both NCCT and NCEA. At NCCT, she has developed a toxicity pathway database that will be used to assess ToxCast assay results. This approach is in line with NAS' Toxicity Testing in the 21st Century's long range vision of moving toward a toxicity

		pathway perturbation based risk assessment approach. At NCEA, she is working on the use of genomics to inform intraspecies differences in response to toxic agents. She is currently co-authoring a manuscript on the use of 'omics data to inform susceptibility. On several occasions, the Center Directors for NCCT and NCEA have done joint presentations on the future of toxicology and risk assessment, including a briefing for the Senate Appropriations Committee staff on June 9, 2009. Other events where the importance of the two centers working together was presented include: The NAS' May 2009 symposium on toxicity-pathway-based risk assessment (http://dels-old.nas.edu/best/risk_analysis/symposium.shtml) and the BOSC's Computational Toxicology Subcommittee in September 2009. NCEA and NCCT are collaborating through the RAF to provide training for scientists in the ORD on the application of computational methods in risk assessment, training for risk assessors on computational tools that are available for application in risk assessment (hazard and dose response), and training for decision makers on the implications of these new technologies. Finally, several NCEA scientists have joined NCCT on detail assignments to the NCCT fellowship program. This relationship has been beneficial to both NCEA and NCCT and has led to additional collaborations between the two Centers and also between NCEA and other labs within ORD. This work will develop assessment applications for high throughput and high content data, methods and models. It will feed into and complement ORD's new integrated transdisciplinary research program on *Safe Products for a Sustainable World.*
Recommendation #4: The Subcommittee considers the responsiveness of the staff members to national emergencies and the HHRA Program's contributions to particularly difficult cleanup sites as being of such high value that this should somehow be captured in the APGs.	**Original Response:** The HHRA Program has started to better track these activities and the resources expended both internally and across ORD. The program will also work more closely with EPA's Office of Emergency Management to be better prepared to respond to such events. **Updated Response:** No change to the ORD action.	**Original Timeline:** The next update of the HHRA MYP will include a section or description relating to these response efforts. **Current Progress:** NCEA is tracking these emergency support activities and is holding discussions internally about how this should be described in the next version of the HHRA MYP. While it is impossible to predict the number and type of emergency response activities that may arise, we expect this tracking will give us a better idea of what level of commitment we could reasonably expect in the future for this type of support. Over the past calendar year, NCEA has assisted with several high-profile support activities. In the summer of 2009, NCEA scientists provided extensive support to the Agency as it dealt with characterizing the risk of PCBs in caulk in schools and other buildings. HHRA scientists developed a PCB exposure estimation tool and developed advisory limits for indoor school air concentrations. NCEA also provided support in 2009 to Region 5 and OSWER, completing an evaluation of the UMDES. This evaluation provided perspective on how the UMDES results could inform Agency decision-making concerning dioxin in soils in Region 5. NCEA also provided rapid support to Region 7 as they dealt with an emergency situation involving hexavalent chromium. NCEA coordinated a conference call and presentation to provide

		information to Region 7 about the health effects of hexavalent chromium. As a result of this request, NCEA convened a meeting with other EPA programs and regions with an interest in hexavalent chromium to discuss accelerating an IRIS assessment for the chemical. Because of these meetings, NCEA has rapidly developed a draft health assessment document for hexavalent chromium that meets the identified needs of the programs and regions; that assessment is moving through the IRIS process at an accelerated rate. NCEA has maintained a consistent level of support and visibility to EPA's programs and regions. Through high profile, timely, and high quality support as identified above, as well as through established programs like the Superfund Technical Support Center and the PPRTVs, NCEA has become the "go to" organization for high quality and rapid scientific support. NCEA has enhanced this visibility by conducting outreach to EPA's regional offices through 1-2 day regional visits. These visits typically consist of both informal discussions and formal presentations on a variety of topics. The goals of the meeting are to inform the regions of NCEA's products and capabilities, better understand regional issues and concerns, and strengthen ties at the management and staff levels. So far, NCEA has visited regions 2, 3, 6, 8, and 9 with very successful results. Additional visits are being planned. Finally, NCEA is currently helping the Agency respond to the Gulf oil spill emergency by providing information on the potential toxicity of constituents in crude oil and the dispersants used in cleaning up the spill.
Recommendation #5: The Subcommittee recommends that, in addition to the goals of 16 new IRIS and 50 new or revised PPRTV assessments per year, goals be established for increasing the number of IRIS assessments. The Subcommittee recognizes that it may not be possible to do more, given current staffing and budgetary limitations.	**Original Response:** Given current limitations, the HHRA Program has begun a number of efforts to streamline and increase the number of assessments produced per year such as: 1) the development of an IRIS Update Process; 2) significant modifications to the PPRTV development process; 3) the modification of PPRTVs with sufficient data for entry into the IRIS process and 4) PPRTV assessments are being evaluated for use in IRIS Update Process	**Original Timeline:** Ongoing. Progress regarding these efforts will be discussed at the mid-cycle review of the HHRA Program in 2010. **Current Progress:** The HHRA program has taken several steps to meet this recommendation. The FY 2010 enacted budget includes additional resources for the IRIS program. Further, the process used to develop IRIS assessments was revised in May 2009; the new process will allow for more rapid completion of assessments while retaining transparency and opportunity for Agency and Interagency comments, as well as vigorous independent external peer review and public review and comment. The table provided in the response to Recommendation #1 illustrates how the new process has greatly improved the ability of EPA's IRIS program to provide high quality human health risk information to EPA's programs and regions in a timely fashion. After the announcement of the new process, the fourth quarter of fiscal year 2009 began. More final assessments were posted on IRIS in that single quarter of one year than in each of the previous three years. Thus, HHRA's IRIS program has quickly demonstrated progress under the new process, and will continue to show significant results in 2010 and beyond. Additionally, we have developed an IRIS Logistics team that coordinates all IRIS-related administrative support. Additional details are provided in the response to Recommendation #1.

	Consultations are also ongoing with OMB on new measures and metrics for the program. **Updated Response :** No change to the ORD action.	We have met extensively with EPA's Program and Regional offices to better understand their assessment needs. Additionally, we are working with Cal/EPA and ATSDR under Memoranda of Understanding; we expect these efforts to eventually increase our efficiency and assessment output. We have also begun a program to update older IRIS assessments. Additional details on this program are described in our progress under Recommendation #2. We have taken steps to facilitate more efficient production of PPRTV assessments by: (1) developing a PPRTV review team within NCEA; (2) streamlining the information included in a PPRTV assessment to focus on pertinent data and decision-making sections; (3) educating EPA contractors about expectations for PPRTV assessment documents; and (4) batching assessment development and internal and external reviews. This has proven to be a successful effort. In FY 2009, NCEA produced 69 new PPRTV assessments. These 69 PPRTV assessments included a total of 140 new individual toxicity values (e.g., RfD, RfD, Oral Cancer Slope Factor, etc.) that were added to the PPRTV database. NCEA has also negotiated new program metrics with OMB. Specifically, NCEA's newly negotiated performance metric indicates the HHRA program will complete health hazard and dose response assessments of high priority chemicals as interagency science consultation drafts or external peer review drafts with a program-defined value of 50 points applied to a 3-year rolling average. Additionally, the HHRA program will post on the IRIS Web page completed health hazard assessments of high priority chemicals for public dissemination with a program defined value of 20 points applied to a 3 year rolling average. To account for differences in the level of complexity of assessments, the HHRA program has also negotiated with OMB a tiering system that provides three different levels of complexity and associated points for reaching milestones for assessments. Tier 1 assessments are standard assessments that are expected to require a typical level of effort from NCEA scientists and be limited in controversy and the complexity of the science required for the assessment. Tier 1 assessments are assigned a point value of "1" for each major negotiated milestone met. Tier 2 assessments are more extensive in that they require more FTE effort, have a greater level of controversy or visibility, and are scientifically more complex than Tier 1. Tier 2 assessments are assigned a point value of "2" for each major negotiated milestone met. Tier 3 assessments are the most complex. They require an exceptional level of FTE support, are highly controversial and/or visible, and are exceptional in the complexity of the science involved in the assessment. Tier 3 assessments are assigned a point value of "5" for each major negotiated milestone met. The figures provided in the report text illustrate the HHRA Program's progress in meeting these program metrics.
Recommendation #6: The Subcommittee recommends	**Original Response:** HHRA management is	**Original Timeline:** Progress regarding these efforts will be discussed at the mid-cycle review of the HHRA Program in 2010.

that well-developed PPRTVs be considered as a source of prioritization in the development of full IRIS documents	routinely evaluating new and renewed PPRTVs for potential development of new IRIS assessments or updating existing IRIS assessments. Thus far PPRTVs for vanadium pentoxide and cobalt have been selected for modification into IRIS assessments. **Updated Response:** In late 2008, the Program made a decision to focus resources on ongoing assessments that were at or beyond the Agency review step of the assessment development process in order to accelerate the agenda. The specific examples chosen from the PPRTV program were in the earlier stages of assessment. The feasibility of using PPRTVs for development of IRIS assessments continues to be explored.	**Current Progress:** NCEA has looked at the possibility of using the PPRTVs for cobalt and vanadium pentoxide as sources for IRIS assessments. In 2008, NCEA decided to focus assessment efforts on those chemicals on the IRIS agenda that were further along in the assessment process. Those chemicals at the earlier stages of work, or for which work had not yet begun, were temporarily put on hold so staff could focus their efforts on completing those assessments that were further along in the process. Cobalt and vanadium pentoxide were in this group, called "Table 2", in the earlier stages of assessment. To better understand the Agency's needs, NCEA has proactively sought advice from EPA's Program Offices and Regions in an effort to identify the highest priority assessment needs across the Agency for chemicals currently on the IRIS agenda. Those highest priority needs will be addressed through the IRIS program. Where needs have been identified as a lower priority, NCEA has consulted with the Programs and Regions to determine if a PPRTV would meet the identified need. This would allow the assessment to be completed in a more rapid timeframe and free up capability within the IRIS program for the highest priority needs. This exercise also helped us to set priorities for those chemicals on "Table 2" so as staff time becomes available as chemical assessments are completed, we can focus efforts on the highest priority chemicals first.
Recommendation #7: In order to maintain the high level of quality that is evident in the HHRA work products, the Subcommittee strongly recommends that steps be taken to ensure the transparency of decisions made in the process of performing IRIS and PPRTV assessments and ISA	**Original Response:** The HHRA program is developing and implementing a new IRIS development process which includes extensive intra- and interagency and public involvement, revised approaches to chemical prioritization and accountability, and a new	**Original Timeline:** An update on the development of IRIS assessments, PPRTVs, and ISAs will be provided at the mid-cycle review in 2010. **Current Progress:** In May 2009, the Administrator of the EPA announced a new IRIS process that is more streamlined yet retains a strong commitment to transparency through multiple opportunities for intra and inter-Agency review, external peer review, and public comment. Additionally, in March 2010, EPA announced the availability of the Health and Environmental Research Online (HERO) database, which was praised by EPA as "a milestone in transparency" and a part of EPA's "open government directive to conduct business with transparency, participation, and collaboration." The publicly accessible HERO database provides an easy way to review the scientific literature behind NCEA's science assessments.

assessments	Update Process. ISAs are being developed as part of the new NAAQS process which includes extensive collaboration and consultation between ORD and OAR and public involvement throughout the entire review. **Updated Response:** NCEA has also developed and is using the Health and Environmental Research Online (HERO) system, which houses the scientific literature used to develop ISA, IRIS and PPRTV assessments. Additionally, several steps have been taken to further increase transparency and communication.	www.epa.gov/hero The database includes more than 300,000 scientific articles including the authors, titles, dates, and abstracts. In addition, through a simple keyword search, anyone can see information from the articles that were used to develop specific risk assessments. HERO includes peer-reviewed literature used by EPA to develop its ISAs that support the NAAQS review. It also includes references and data from IRIS, a database that supports critical agency policymaking for chemical regulation, and from PPRTVs. At the time of the BOSC review, EPA was in the process of implementing revisions to the NAAQS review process, and NCEA was developing ISAs for reviews of the NAAQS for nitrogen oxides and sulfur oxides. In the past three years, NCEA has completed the initial set of ISAs for oxides of nitrogen and sulfur (NOx- health effects, SOx – health effects, and ecological effects of NOx and SOx) along with ISAs for PM and CO, meeting several court-ordered deadlines along the way. In the process, NCEA has restructured the ISA to place a concise summary and integrative synthesis of the key findings at the beginning of the assessment, focusing on the key policy-relevant findings with figures that present the findings from across health studies relevant to pollutant concentrations to better inform decision-makers. NCEA has developed a causality framework that has been used in all five ISAs, and provides transparency and consistency in the process of drawing conclusions and causal judgments. CASAC panels have lauded the implementation of the causal framework, the process for developing the ISA and the structure of the ISA; positive comments have been received during the peer reviews of draft ISAs for both PM and CO. Also, in the recent draft dioxin report entitled, *EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments (*http://www.epa.gov/dioxin), there is lengthy discussion and accompanying schematics detailing the delineated study selection process for the identification of appropriate studies for TCDD dose-response analysis. In addition, in February 2009, to assist NCEA in responding to the NAS, NCEA convened a scientific workshop to identify and address issues related to the dose-response assessment of TCDD and to ensure that EPA's response to the NAS focused on the key issues and reflected the most meaningful science. This workshop was open to the public and included scientific experts from academia, industry, non-profit organizations, and government. These experts discussed potential approaches to TCDD dose-response assessment and considerations for EPA's response to NAS. As a result, the process used by EPA to determine key scientific approaches and decisions in the development of the recent draft dioxin report can be held up as a model for transparency and public participation. NCEA has also been providing listening sessions for the public and stakeholders for chemicals on the IRIS agenda. Additionally, for high profile chemicals like formaldehyde, dioxin, and arsenic, NCEA has provided briefings for other Agencies and stakeholders at key points in the assessment

		process. Finally, NCEA has taken steps to standardize assessment practices within the Center. Standard Operating Procedures for developing IRIS assessment documents have been written, and NCEA has started to convene regular science policy discussion meetings with staff to make sure science policy practices are consistent across assessments.
Recommendation #8: The HRRA Program should consider using available resources to recruit one or two additional senior scientists, especially into the LTG 2 Program where efforts are underway to integrate emerging technologies into the risk assessment processes.	**Original Response:** Recently, HHRA program recruited a senior scientist from NHEERL Dr. Linda Birnbaum. In addition, ORD has obtained authority to hire experts and senior scientists under Title 42. The HHRA Program has initiated one recruitment action under this program and will announce an additional recruitment in 2009. **Updated Response:** Dr. Birnbaum has taken a new job. She is now the Director of NIEHS.	**Original Timeline:** Ongoing. **Current Progress:** For the last three years NCEA has had the benefit of input from two senior statisticians who participate in the ORISE fellows program. Dr. Kenny Crump has been a leading investigator in the field of dose response modeling over the past 30 years. His participation in the ORISE fellows program has allowed him to contribute to important science issues faced by EPA in the area of quantitative risk assessment. In particular he has delved deeply into issues regarding application of biologically based dose response models for risk assessment needs. This effort has sharpened our understanding of the strengths and limitations of such models in advancing understanding of chemical risks. Dr. Crump is currently working on the quantitative application of genomics and other high-throughput data in chemical risk assessment. Dr. Bimal Sinha, Professor of Statistics with University of Maryland Baltimore County, has worked with NCEA to advance statistical methods for several areas of quantitative risk assessment. These areas have included application of more robust statistical procedures in modeling data from pharmacokinetic studies, extension of methods for incorporating experimental error estimates in benchmark dose modeling, and analysis of exposure statistics data. The HHRA program has used the ORISE program to bring on board a few senior scientists to help address some of the complex scientific issues discussed in the 2009 National Research Council (NRC) Report, *Science and Decisions: Advancing Risk Assessment*. Additionally, scientists from the HHRA program are actively engaged with scientists in academia, state governments, and industry, both across the U.S. and internationally, to discuss issues, conduct research, and develop pertinent case studies that will be useful in addressing the NRC recommendations. Complex scientific issues being discussed include probabilistic methods and accounting for uncertainty and variability in quantitative dose-response; mode of action, background exposures and disease processes, and vulnerable populations in low dose extrapolation; and applying similar quantitative approaches for cancer and non-cancer health assessment. In particular, ORISE's Faculty Fellow Dr. Gary Ginsberg (University of Connecticut) is working with NCEA on developing new methods and models for incorporating information regarding susceptible populations into EPA risk assessments. ORISE Faculty Fellow Dr. David Eastmond is working with NCEA scientists to develop a database on the mutagenic mode of action of certain chemicals of interest to the IRIS Program. Drs. Ginsberg and Eastmond have made several seminar presentations to NCEA staff on risk assessment issues. Additionally, Dr. Brian

		Patchkowski was recently hired as an ORISE post-doctoral fellow in NCEA. NCEA has also recruited and hired a Title 42 Division Director to manage NCEA's RTP Division. NCEA intends to recruit additional Title 42 and/or SL (senior level) scientists to fill critical hiring needs in the organization. Additionally, NCEA plans to add five ORISE post docs to the IRIS program to work on IRIS assessments. Two scientists have been hired under this program so far and will start in the summer 2010. Interviews for the remaining three positions are ongoing. Several postdocs and fellows have been added to LTG2 as part of the HHRA's NexGen effort. Additionally, a collaborative NexGen effort among other labs and centers has effectively expanded the LTG2 effort. See description of NexGen in response to Recommendation #1.
Recommendation #9: PPRTVs have been developed specifically to address the site specific needs of EPA's Superfund Program. Currently, PPRTVs and their supporting documentation are only available on a Web site restricted to use by EPA staff or to those who obtain special permission from EPA. The Subcommittee encourages EPA to make the PPRTVs publicly available for use in hazardous waste site risk assessment and promote their use where appropriate.	**Original Response:** PPRTVs are available to the states and other partners involved in waste site assessments. Updates are provided on a quarterly basis. Within EPA, PPRTVs are being made available to other program offices for screening and prioritization of research needs. **Updated Response:** No change to ORD action.	**Original Timeline:** Further efforts will be discussed at the mid-cycle review of the HHRA Program in 2010. **Current Progress:** PPRTVs are currently available to all EPA staff. NCEA has been doing more outreach to EPA's Programs and Regions, including providing them with information about PPRTVs. As a result, the PPRTV Web site (which is available to any EPA employee) has been shared with several EPA program offices outside of the Superfund Program. These programs have indicated this information will help them address screening and prioritization needs as well as the need for toxicity numbers. At this time, NCEA does not think it is possible to make the PPRTV database publicly available. We have explored the feasibility and think there are potential issues and complicating factors. However, we have planned a follow-up conversation with OSWER to discuss this once again, and we continue to explore the possibility of making the PPRTV database publicly available. PPRTVs are currently available to all EPA staff and by request to states and other partners involved in waste site assessments. Updates are provided on a quarterly basis.
Recommendation #10: The HHRA Program needs to consider information on the potential public health concern of various chemicals as it prioritizes them for IRIS or PPRTV review. It appears that some of this information is being provided by the program and regional offices,	**Original Response:** NCEA is meeting with the program offices and regions to provide more explicit information on the IRIS process and setting priorities. **Updated Response:** NCEA has met extensively with	**Original Timeline:** Progress regarding these efforts will be discussed at the mid-cycle review of the HHRA Program in Fall 2009. **Current Progress:** NCEA has held extensive meetings with EPA's Program and Regional offices to discuss the process that is used to prioritize nominated chemicals for assessment through the IRIS program. After extensive conversation and feedback from these offices, we have developed a revised process for prioritizing how chemicals will be added to the IRIS agenda. This process includes collecting information about the public health concerns of the nominated chemicals. It also involves more transparency, as well as a "feed-back" loop to the programs and regions. Additionally, NCEA recently conducted an exercise where we asked the Programs and

but it would be of value for the Program to make transparent the basis for its prioritization decisions for IRIS and PPRTVs.	EPA's programs and regions, and recently completed a prioritization exercise using feedback from the programs and regions along with public health information.	Regions for input on regulatory and other needs for assessments for chemicals currently on the IRIS agenda for which work has not yet begun. The purpose of this exercise was to help the HHRA program set priorities for completing currently backlogged assessments. The HHRA program will soon issue a FRN requesting nominations for chemicals to be added to the IRIS agenda. This notice will provide more detail than previous notices in an effort to increase transparency about the IRIS program and how decisions are made to add chemicals to the agenda. NCEA has also developed a list of thousands of chemicals that appear on a variety of priority lists (HAP, CCL3, etc.) and compiled public health information (both exposure and toxicity) about each chemical. This information may be used in the future to help the HHRA program proactively identify chemicals that may be a concern for public health, which would then be presented to EPA's Program and Regional Offices for input. NCEA meets regularly with OSWER to set priorities for chemicals to assess under the PPRTV program. NCEA is quite flexible in adding chemicals and reprioritizing when a high priority need is indentified by OSWER. Additionally, as part of NexGen efforts, the HHRA program is investigating the use of ToxCast and ExpoCast information to help set priorities for adding chemicals to the list for PPRTV development. The HHRA program is also looking at options for incorporating public heath information into the program's prioritization process for health assessments using value of information tools. Examples of options that are being considered include consultation with the BOSC workgroup on decision analysis and value of information and other mechanisms. Additionally, NCEA is currently performing an IRIS human health assessment for six phthalates and developing a cumulative risk assessment for these chemicals as recommended by the NRC in its report *Phthalates and Cumulative Risk: The Tasks Ahead.* It is expected that this cumulative assessment will serve as a framework for extension to other compounds that act by a similar effect. Specifically, the assessment includes the following phthalates: dibutyl phthalate (DBP), di(2-ethylhexyl)phthalate (DEHP), butyl benzyl phthalate (BBP), di-isobutyl phthalate (DIBP), di-isononyl phthalate (DINP), and dipentyl phthalate (DPP). The IRIS Human Health Risk Assessment for Selected Phthalates will include noncancer and cancer qualitative and quantitative human health effects information and estimation of risk where the data are available for each of the phthalates. Several of the phthalates included in this assessment were already on the IRIS agenda. However, after release of the NRC report, the HHRA program decided to add a few phthalates, as recommended by the NRC, based on their impact on a common health endpoint. Considering this public health information facilitated the addition of a few new chemicals to the IRIS agenda.