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CHEMICAL RISK ASSESSMENT: WHAT WORKS FOR JOBS AND THE ECONOMY?

HEARING

BEFORE THE

SUBCOMMITTEE ON ENVIRONMENT AND THE ECONOMY

OF THE

COMMITTEE ON ENERGY AND COMMERCE
HOUSE OF REPRESENTATIVES

ONE HUNDRED TWELFTH CONGRESS

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CHEMICAL RISK ASSESSMENT: WHAT WORKS FOR JOBS AND THE ECONOMY?

THURSDAY, OCTOBER 6, 2011

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON ENVIRONMENT AND THE ECONOMY,
COMMITTEE ON ENERGY AND COMMERCE,
Washington, DC.

The subcommittee met, pursuant to call, at 9:07 a.m., in room 2123 of the Rayburn House Office Building, Hon. John Shimkus (chairman of the subcommittee) presiding.

Members present: Representatives Shimkus, Murphy, Pitts, Bass, Harper, Cassidy, Gardner, Barton, Green, Butterfield, Barrow, and DeGette.

Staff present: Caroline Basile, Staff Assistant; Anita Bradley, Senior Policy Advisor to Chairman Emeritus; Jerry Couri, Senior Environmental Policy Advisor, Environment; Dave McCarthy, Chief Counsel, Environment/Economy; Carly McWilliams, Legislative Clerk; Tina Richards, Counsel, Environment/Economy; Chris Sarley, Policy Coordinator, Environment/Economy; Brett Scott, Staff Assistant; Lyn Walker, Coordinator, Admin/Human Resources; Tom Wilbur, Staff Assistant; Alex Yergin, Legislative Clerk; Jacqueline Cohen, Democratic Counsel; and Billie McGrane, Democratic Assistant Clerk.

Mr. SHIMKUS. The hearing will come to order. We want to welcome the first and second panels, and I will start with my first opening statement. And I recognize myself for 5 minutes.

OPENING STATEMENT OF HON. JOHN SHIMKUS, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF ILLINOIS

It has been no secret to anyone following our Committee that we have been taking a very specific look at the regulatory climate in this country where it is imbalanced and unworkable. In doing so, I and others have been clear that while we advocate the maintenance of commonsense environmental and public health protections, we also need to be careful about the impacts of government encroachment and that these efforts not discourage job protection and economic growth. Today's hearing is another step to appreciate these issues.

To understand the final regulatory product and the economic impacts of EPA activities, I think it is important to appreciate the process used by the Agency to get those results. Our hearing will delve into one of the foundational parts of EPA's activities: the work of the Integrated Risk Information System, also known as IRIS.

I have been a strong advocate for high-quality science that is objective and valid. Moreover, I understand that many are concerned about IRIS's activities on specific chemicals. I am not here to defend any particular chemical. This hearing is not about specific chemicals. To truly protect the public from harm and negative economic outcomes, we need an unbiased process informing policymakers about the science, not policymakers informing the science.

IRIS was created over 25 years ago to provide EPA with information to develop policy surrounding human health effects from exposure to chemicals. There is no doubt providing such high-quality science-based assessment is critical to EPA's mission. The question is whether IRIS is in fact fulfilling this goal, or have results begun to develop to support specific policy objectives?

From our subcommittee's perspective, we need to grasp that IRIS is the program making scientific assessments about chemical substances that EPA program offices use to set federal limits for various environmental laws, including the Safe Drinking Water Act and the Solid Waste Disposal Act. In addition, many states rely on IRIS data for their own environmental program purposes.

We are honored today to have a collection of very distinguished witnesses and I appreciate the time and sacrifices they have made to be with us. Among the testimony we will receive is from the administration and their view of IRIS and its role. I look forward to getting an update on EPA's 2009 reforms to IRIS, as well as where things stand with the Chapter 7, the long-term recommendations of the National Academies of Science for IRIS.

In addition, we will have insight on whether IRIS assessments are doing what they should, if states are finding IRIS work reliable, how much we should care about IRIS assessment impacts on jobs and the economy, and is there a better way for EPA to perform these assessments? These recommendations could be helpful as we think about more global issues affecting the EPA.

I hope all members will use this opportunity to understand the process, discuss the integrity of the basic science assessed at EPA, and appreciate how and when policy considerations converge in this process and their impact on jobs and the economy.

And I will now yield back my time and recognize the ranking member, Mr. Green, for 5 minutes.

[The prepared statement of Mr. Shimkus follows:]

Opening Statement of the Honorable John Shimkus
Subcommittee on Environment and the Economy
"Chemical Risk Assessment:
What Works for Jobs and the Economy?"
October 6, 2011

(Remarks Prepared for Delivery)

It has been no secret to anyone following our Committee that we have been taking a very specific look at the regulatory climate in this country where it is imbalanced and unworkable. In doing so, I and others have been clear that while we advocate the maintenance of common sense environmental and public health protections, we also need to be careful about the impacts of government encroachment and that these efforts not discourage job protection and economic growth. Today's hearing is another step to appreciating these issues.

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OPENING STATEMENT OF HON. GENE GREEN, A REPRESENTATIVE IN CONGRESS FROM THE STATE OF TEXAS

Mr. GREEN. Thank you, Mr. Chairman. I thank you for holding this hearing today entitled "Chemical Risk Assessment: What Works for Jobs in the Economy?"

Risk assessment is a critical component in the protection of public health and the environment. Without adequate risk assessment, legislators and regulators cannot make informed and wise decisions about risk management. EPA has the responsibility to manage the Integrated Risk Information System, or IRIS, to inform the public, industry, and policymakers with the strongest and best-available science on a variety of potentially hazardous materials in the most non-political manner.

In 1985, they established IRIS to help the Agency develop consensus opinions within the Agency about the health effects from the chronic exposure to chemicals. Currently, the EPA has assessments of 550 chemicals. These assessments are utilized by the EPA to further their mission and to set standards to protect human health and environment. IRIS assessments can be used in regulations that garner a lot of attention. In recent years, this attention has not been positive.

In 2008, the Energy and Commerce Committee held a hearing in the Oversight and Investigations Subcommittee on IRIS and a GAO report that exposed concerns about the IRIS program. At the hearing, the GAO testified that there was a backlog of 70 chemicals in the IRIS system that needed to be completed but that only four had been completed in 2008. And half the 540 chemicals that were currently in IRIS possibly had outdated risk assessments. On tops of that, there are hundreds of other chemicals that have been referred to the IRIS system but have not even begun the assessment process. I also note that since the hearing in 2008, IRIS has only released assessments on 10 additional chemicals.

In that 2008 hearing, I expressed concern regarding the IRIS assessment of dioxin. If you look at the dioxin section on IRIS webpage, you see a timeline. It appears that IRIS has been assessing dioxin since 1985. I asked questions about this assessment in 2008, and now 3 years later, EPA released a statement that IRIS's assessment on dioxin will be finalized in 2012.

Dioxin is a compound that we know is very dangerous and far too prevalent in and around the district I represent along the Houston Ship Channel. Just outside our district, we have the San Jacinto Waste Pits Superfund site which consisted of submerged waste pits from an old paper mill that were recently discovered to be leaching high levels of dioxin in the San Jacinto River and there into the Galveston Bay. Fish advisories have been extended to larger and larger areas, creating a threat both to the people who fish for food and for the large port fishing industry in the area.

Dioxin status as a toxic compound should not be controversial, so the fact that it has still taken an additional 3 or 4 years for IRIS to complete its risk assessment is very discouraging. If the EPA wants IRIS's assessments to be viewed as legitimately scientific and reliable, they must take steps to streamline their reviewing process to issue assessments in a timely manner so they are not

outdated or make the assessments clearer and easier to understand.

The National Academy of Sciences issued guidance on how to improve IRIS assessments, and I hope the EPA witness can update the committee on the improvements being made in the IRIS program and what they intend to do in the future to correct the problems within the program. We need to restore the public confidence in EPA's risk assessment and chemical regulatory system and the first step must be to ensure the integrity of EPA's scientific information and practices.

I look forward to hearing the testimony of all of our witnesses, but particularly Dr. Honeycutt from TCEQ who is from my home State of Texas and we work with them particularly on that dioxin facility in the San Jacinto area.

And Mr. Chairman, I yield back my time.

Mr. SHIMKUS. The gentleman yields back his time.

Does the gentleman from Mississippi seek time for an opening statement? Gentleman from Louisiana? Having no other members present to seek time, I would like to welcome the first panel.

First of all, let me introduce the entire panel, and then we will go to 5-minute opening statements.

First we have Dr. Paul Anastas, the Assistant Administrator to the Office of Research and Development in the United States Environmental Protection Agency. Sir, welcome. Also, Mr. David Trimble, Director of Natural Resources and Environment for the U.S. Government Accountability Office; and Mr. David C. Dorman, Dean for Research and Graduate Studies at North Carolina State University on behalf of the National Academy of Sciences.

We have two great panels and we again welcome you. And I would like to first turn to Dr. Anastas from the EPA for a 5-minute opening statement. We have got a lot of members. We have got time if you go over. That is not a problem. If it goes too far, then it might be a problem.

So welcome and you are recognized, sir.

STATEMENTS OF PAUL ANASTAS, ASSISTANT ADMINISTRATOR, OFFICE OF RESEARCH AND DEVELOPMENT, ENVIRONMENTAL PROTECTION AGENCY; DAVID C. TRIMBLE, DIRECTOR, NATURAL RESOURCES AND ENVIRONMENT, GOVERNMENT ACCOUNTABILITY OFFICE; AND DAVID C. DORMAN, DEAN FOR RESEARCH AND GRADUATE STUDIES, NORTH CAROLINA UNIVERSITY, ON BEHALF OF THE NATIONAL ACADEMY OF SCIENCES

STATEMENT OF PAUL ANASTAS

Mr. ANASTAS. Good morning, Chairman Shimkus, Ranking Member Greene and other members of the Committee. My name is Paul Anastas and I am the assistant administrator for the Office of Research and Development at the Environmental Protection Agency and the Agency's science advisor. Thank you for the opportunity to be with you here this morning to discuss the Integrated Risk Information System, also known as IRIS.

At the EPA, we firmly believe that the American people deserve the best possible scientific information about the chemicals that

they may encounter in their air, water, and land. When those chemicals may potentially affect their health, their children, and the health of their communities, we have the duty to vigorously study them and share what we know with our citizens.

Every day, expert scientists in EPA's IRIS program work to fulfill that duty providing this information by drawing upon the best science both from the Agency as well as from universities and research institutes around the world. The assessments that we develop as part of the IRIS program are scientific documents, not regulations. This is an important distinction. While the information they contain is useful in our agency decisions, it is also widely used by communities, businesses, environmental groups, and public citizens. For those reasons and more, we recognize the importance of maintaining the highest level of scientific integrity when generating these IRIS assessments. That is why every draft IRIS assessment is made available to the public, to our sister federal agencies, and to the broader scientific community for their review and comment.

The draft assessments we produce undergo one of the most rigorous, independent peer review processes in any scientific field. This peer review process makes our IRIS assessments stronger. The comments that we receive are valued and addressed. This is precisely why we undergo such rigorous review. This is how the scientific process works.

We also recognized that continuous improvement is what science is all about. That is why in May 2009, Administrator Jackson put into place a strengthened and streamlined IRIS process. This new process not only strengthened the scientific integrity of the IRIS program, it also shortened the average time frame for generation of IRIS assessments from 5 years to just 23 months. Since 2009, EPA has completed 20 IRIS assessments, twice as many assessments as were finalized in the previous 4 years combined.

But our efforts to continuously improve didn't stop there. This past July, I announced a plan to further strengthen the IRIS program. Because our assessments are widely used in the decisions of state and local governments, businesses, and American citizens, we have focused on making them clearer, more concise, and ensuring that our methods and scientific assumptions are more transparent to the users. These improvements, which we began aggressively implementing in July, directly address the suggestions from the National Academy of Sciences and other independent experts. The NAS made six major suggestions to improve the generation of IRIS documents, and we are implementing all of those recommendations. Those recommendations and how we are dealing with them are detailed in my written testimony, and I will be happy to expand on those.

We will pursue continuous improvement, but we will proceed in a way that does not slow or prevent our ability to provide the best scientific information to the public. That is what the American people expect and deserve. We recognize that the only reason to deeply understand a problem is to inform and empower its solution. When we look at the information that is being transmitted through our IRIS assessments, information about what makes a chemical hazardous, that information can be used to design the next generation

of chemicals so that they are not hazardous in the first place. We believe this information empowers innovation in the marketplace.

Leading companies understand this potential for innovation and are pursuing it aggressively through the use of green chemistry. Green chemistry is the design of chemical products and processes that reduce or eliminate the use and generation of hazardous substances. By understanding the properties that make a chemical hazardous, scientists and industry and in academia are meeting environmental and economical simultaneously through the principles of green chemistry design.

New life-saving medicines are being developed in ways that produce dramatically less waste through green chemistry. New high-performing materials are being invented to serve their purpose and then degrade harmlessly into the environment through green chemistry design. New products are being introduced into the marketplace that are safe for children and attractive to consumers through green chemistry. All of this progress is being made in sectors ranging from agriculture to energy, transportation to telecommunications, and cosmetics to computing. Companies across the American economy are increasing profits and enhancing competitiveness through green chemistry. That is the power and the potential of green chemistry. And that is why the lessons we learn from toxicology and the IRIS program are important for feeding innovation.

In conclusion, whether it is through IRIS or our other cutting-edge scientific research, EPA is providing critical information to companies, entrepreneurs, and researchers so they can make new discoveries and develop new innovations all while protecting health and the environment. That is the real power of understanding chemical hazard and that is why EPA's IRIS program is so critically important.

We will continue to improve this program using the best science not only to understand the problems of today, but to inform and empower the solutions of tomorrow. It is what is necessary for the environment, for public health, for the economy, and I think we can all agree that it is what the American people deserve.

Thank you for the opportunity to speak here this morning. I will be happy to answer any questions as is appropriate.

[The prepared statement of Mr. Anastas follows:]

WRITTEN TESTIMONY

Paul Anastas, PhD

Assistant Administrator for Research and Development

U.S. Environmental Protection Agency (EPA)

HEARING ON

EPA's Integrated Risk Information System

Before the

U.S. HOUSE OF REPRESENTATIVES

COMMITTEE ON ENERGY AND COMMERCE

SUBCOMMITTEE ON ENVIRONMENT AND ECONOMY

October 6, 2011

Good morning Chairman Shimkus, Ranking Member Greene and other members of the Committee. My name is Paul Anastas. I am the Assistant Administrator for Research and Development (ORD) at the Environmental Protection Agency and the Agency's Science Advisor. It is a pleasure to be here with you this morning to discuss EPA's Integrated Risk Information System (IRIS).

Background and Description of IRIS Program

EPA recognizes the critical role we play in providing timely, high-quality and accessible human health risk information on environmental contaminants that may endanger the health of the American public. Central to this aspect of EPA's mission is the Integrated Risk Information System, commonly called the IRIS program. This program provides health effects information on chemicals to which the public may be exposed from releases to air, water, and land and through the use and disposal of products. IRIS assessments provide a scientific foundation for EPA decisions to protect public health across EPA's programs and regions under an array of environmental laws. These documents provide federal, state, local and other policy makers with the latest scientific information to make decisions about cleanup and other actions to protect

people's health. While they are not complete risk assessments, they provide important information that helps to inform regulations. IRIS assessments provide information on a chemical's potential for causing adverse health effects along with information about the relationship between the dose of the substance and the biological response. When this information is combined with information about exposure, government and private entities frequently use IRIS values to characterize the public health risks of chemical substances. When EPA and others make decisions about chemicals, the scientific information in an IRIS assessment is combined with relevant considerations such as statutory and legal requirements, economic and social factors, risk management options, and public health and cost/benefit information. Therefore, IRIS assessments provide the science to support risk management decisions to protect public health. For instance, the EPA recently released IRIS toxicity values for tricholoroethylene (TCE) will be considered in:

- Establishing cleanup methods at the 761 Superfund sites where TCE has been identified as a contaminant
- Understanding the risk from vapor intrusion as TCE vapors move from contaminated groundwater and soil into the indoor air of overlying buildings
- Revising EPA's Maximum Contaminant Level for TCE as part of the carcinogenic volatile organic compounds group in drinking water, as described in the agency's drinking water strategy
- Developing appropriate regulatory standards limiting the atmospheric emissions of TCE – a hazardous air pollutant under the Clean Air Act

2009 Improvements

After becoming Administrator in early 2009, Administrator Jackson reviewed the IRIS program and asked the Office of Research and Development (ORD) to implement a new IRIS process that would revitalize the program and make it more responsive to the needs of the Agency. The aim of the new process was to ensure the highest level of scientific quality, integrity, transparency, and timeliness.

EPA undertook several actions to implement the new IRIS process in 2009. EPA regularly solicits public comments on the IRIS agenda, and ORD works directly with program

and regional offices to ensure that IRIS assessments meet their needs. To ensure that IRIS assessments are focused on the highest priority needs, EPA expanded the role of the program and regional offices in nominating and prioritizing chemicals for assessment. EPA also has increased efforts to work with other agencies to share data and avoid duplication of effort. These efforts help to increase efficiency and assessment output.

There have been many improvements to the IRIS program as a result of the changes made in 2009. Assessment development time was shortened to 23 months for most assessments, which will speed the availability of IRIS assessments for use by the risk assessment community and public. The IRIS program is now entirely managed by EPA. All of the assessments undergo rigorous, open and independent external peer review that offer multiple opportunities for public review and comment. Additionally, changes in IRIS assessments that occur during the interagency and public process are documented and explained, ensuring a transparent final product.

EPA has created an IRIS logistics team to help streamline the assessment development process. We have developed the Health and Environmental Research Online Database – or HERO – which makes the scientific studies selected and used by the Agency to develop assessments available to the public.

Response to the NAS Report

In April 2011, the National Academy of Sciences (NAS) made suggestions to improve the development of draft IRIS assessments. EPA welcomed those suggestions and is addressing all of them. The Academy recognized that implementing these changes would require a phased-in approach. Although the public will not see the changes for some time, EPA is already implementing many of the NAS recommendations and EPA has a plan for implementing them all.

In their report, the Academy suggested steps that EPA could take "to improve IRIS assessment through the implementation of methods that would better reflect current practices." The Academy report also stated that: "The committee recognizes that the changes suggested

would involve a multiyear process and extensive effort by the staff of the National Center for Environmental Assessment and input and review by the EPA." (see NRC report at page 135)

EPA is working closely with the agency's Science Advisory Board on how to bring to bear its expertise on an ongoing basis to focus on the quality, transparency and scientific rigor of IRIS assessments and guide EPA's response to the NAS recommendations.

A summary of the NAS overall recommendations and EPA's responses to them are described below.[1]

1. **NAS recommended that EPA rigorously edit documents to reduce the text volume and address redundancies and inconsistencies.**

   To respond to this recommendation, EPA is rigorously editing our assessment documents to substantially reduce the volume of text and address redundancies and inconsistencies; building on the existing IRIS guidelines and process to enhance the clarity and transparency of data evaluation and the presentation of findings and conclusions; consolidating related discussions to eliminate redundancies; increasing the use of tables and figures to improve communication of information; and providing reference information on the IRIS website for all studies considered.

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[1] Full text from p. 152 of the final published NAS report.

- To enhance the clarity of the document, the draft IRIS assessment needs rigorous editing to reduce the volume of text substantially and address redundancy and inconsistency. Long descriptions of particular studies, for example, should be replaced with informative evidence tables. When study details are appropriate, they could be provided in appendixes.
- Chapter 1 needs to be expanded to describe more fully the methods of the assessment, including a description of search strategies used to identify studies with the exclusion and inclusion criteria clearly articulated and a better description of the outcomes of the searches (a model for displaying the results of literature searches is provided later in this chapter) and clear descriptions of the weight-of evidence approaches used for the various non-cancer outcomes. The committee emphasizes that it is not recommending the addition of long descriptions of EPA guidelines to the introduction, but rather clear concise statements of criteria used to exclude, include, and advance studies for derivation of the RfCs and unit risk estimates.
- Standardized evidence tables for all health outcomes need to be developed. If there were appropriate tables, long text descriptions of studies could be moved to an appendix or deleted.
- All critical studies need to be thoroughly evaluated with standardized approaches that are clearly formulated and based on the type of research, for example, observational epidemiologic or animal bioassays. The findings of the reviews might be presented in tables to ensure transparency. The present chapter provides general guidance on approaches to reviewing the critical types of evidence.
- The rationales for the selection of the studies that are advanced for consideration in calculating the RfCs and unit risks need to be expanded. All candidate RfCs should be evaluated together with the aid of graphic displays that incorporate selected information on attributes relevant to the database.
- Strengthened, more integrative, and more transparent discussions of weight of evidence are needed. The discussions would benefit from more rigorous and systematic coverage of the various determinants of weight of evidence, such as consistency.

2. **NAS recommended that EPA include a fuller discussion of methods and develop concise statements of the criteria used to exclude, include and advance studies for hazard evaluation and derivation of toxicity values.**

In response to this recommendation, EPA is providing a fuller discussion of the methods used in our assessments, along with concise statements of the criteria used to exclude, include, and focus on the highest quality studies for hazard assessment and for derivation of toxicity values.

3. **NAS recommended standardized evidence tables for all health outcomes.**

EPA is working towards replacing text descriptions of the studies with standardized evidence tables that provide the methods and results of each study for all health outcomes; and including text that will accompany evidence tables to present the criteria used to include or exclude studies.

4. **NAS recommended that EPA provide a clearer articulation of the rationale and criteria for screening studies.**

To accomplish this, EPA is enhancing our sequential approach for progressively focusing on the most pertinent information, including: searching the literature, identifying the pertinent studies, and evaluating study characteristics; evaluating the overall weight of evidence for each health outcome; identifying plausible approaches for developing toxicity values; selecting the most pertinent data and developing toxicity values for each health hazard; and portraying toxicity information graphically.

5. **NAS recommended that EPA use uniform approaches to thoroughly evaluate the strengths and weaknesses of critical studies, summarize findings in tables, and clearly articulate the rationale for the studies used to calculate toxicity values.**

To respond to these two suggestions EPA is streamlining IRIS assessment documents and more fully documenting our approach for assembling and evaluating the range of scientific data. As the NAS report indicated, we have already made similar changes to how we present the scientific evidence on the criteria air pollutants in our Integrated

Science Assessments, and we are confident we can make comparable improvements in how we present our analysis of health study findings for chemicals evaluated in the IRIS program. EPA is also implementing a more uniform approach to our evaluation of the strengths and weaknesses of critical studies to increase the clarity of the rationale for selecting the studies used to calculate toxicity values. Lastly, we are increasing the use of evidence tables that summarize the factual details of pertinent studies for each health hazard and developing standardized language to describe study strengths and limitations.

6. **NAS recommended that EPA provide descriptions to indicate various determinants of weight of evidence to promote understanding of what elements were emphasized in synthesizing the evidence.**

   In response, EPA is augmenting its current analysis of data to indicate which criteria were most influential in evaluating the weight of evidence.

Timeline for Responding to NAS Recommendations

EPA's overarching goal is to continually improve our IRIS assessments, recognizing that these improvements will have a greater impact on our new assessments as opposed to those already in the pipeline. It is important to note that the NAS report viewed the implementation of their recommendations as a multi-year process. For example, the NAS stated 'it is not recommending that EPA delay the revision of the formaldehyde assessment to implement a new approach." To that end, EPA is doing the following:

- ***Assessments that have already been peer-reviewed or released for peer review***: EPA is revising these assessments to address peer review comments, especially those that call for increased transparency of study selection and evidence evaluation. In addition, we are editing the text of these assessments to reduce volume where possible, either by removing redundant text or by moving study descriptions into appendices to enhance readability.

- ***Assessments currently under development but not yet released for peer review***: EPA is revising these assessments to ensure that the rationale for study selection and evidence evaluation is clear. These assessments will also be streamlined and edited to reduce redundancy.

- ***New assessments that have not yet been started***: EPA will comprehensively implement the NAS recommendations, including developing a tighter document structure, using evidence tables to summarize details from pertinent studies, increasing transparency in study selection and evaluation criteria, and placing a greater emphasis on clear analysis and synthesis of available data and clear evaluation of the weight of the evidence for potential health effects.

IRIS assessments are held to the highest Agency standards, including the rigorous independent external peer review for every draft IRIS assessment, as well as internal review by EPA scientists, public review and comment, and opportunities for review by other federal agencies. These standards are among the best in the federal government and the scientific community. In 2008 EPA's Board of Scientific Counselors[2] noted in their reviews of the program that "IRIS assessments are considered to be of the highest quality and reliability" and among "the most heavily peer-reviewed documents produced by scientists anywhere."

Thank you for the invitation to share my thoughts on this important topic. I will gladly answer any questions you have.

[2] Board of Scientific Counselors. 2008. Human Health Risk Assessment Subcommittee Program Review Report.

http://www.epa.gov/osp/bosc/pdf/hhra0804rpt.pdf

Mr. SHIMKUS. Thank you, Dr. Anastas.

And we would now like to recognize Mr. David Trimble. Sir, you are recognized for 5 minutes likewise. Take your time and get through it, and we welcome you here.

STATEMENT OF DAVID C. TRIMBLE

Mr. TRIMBLE. Chairman Shimkus, Ranking Member Green, and members of the subcommittee, I am pleased to be here today to discuss our prior work and recommendations on EPA's Integrated Risk Information System.

As you know, the IRIS database contains EPA's scientific position on the potential human health effects of exposure to more than 550 chemicals in the environment. IRIS assessments are a critical component of the EPA's capacity to support scientifically sound risk management decisions, policies, and regulations.

In March 2008, we reported that the IRIS program was at serious risk of becoming obsolete because the Agency has not been able to complete timely credible chemical assessments or decrease its backlog of 70 ongoing assessments. We found that the time frames for completing assessments were unacceptably long, often taking over a decade. In many cases, assessments became obsolete before they could be finalized and were stuck in an endless loop of assessment and reassessment.

In April of 2008, EPA revised the IRIS process, but the changes made were not responsive to our recommendations. The new process was actually worse than the one it replaced, institutionalizing process that resulted in frequent delays by enabling OMB to determine when an IRIS assessment could move forward. Further, this process effectively excluded the content of OMB's comments to EPA and those from other interested federal agencies from the public record.

Concerned with these programs and the Agency's lack of responsiveness, we added EPA's process for assessing and controlling toxic chemicals to our January 2009 report on government-wide high-risk areas in need of an increased attention by executive agencies and Congress. In May 2009, EPA had made significant changes to the IRIS process. In June of that year, we testified that these changes, if implemented and managed effectively, would be largely responsive to the recommendations we made in our March 2008 report. Let me highlight three of these key changes.

First, the IRIS process would be managed by EPA rather than OMB as the former process was, restoring independence to EPA. Second, it required that all written comments provided by OMB and other federal agencies and draft IRIS assessments be part of the public record, adding transparency and credibility to the process. Third, the procedures consolidated and eliminated steps, streamlining the process.

Notably, the new process eliminated the step under which other federal agencies could have IRIS assessments suspended indefinitely to conduct additional research. As we have reported, we understand that there may be exceptional circumstances under which it may be appropriate to wait for the results of an important ongoing study. However, as a general rule, we believe that the IRIS assessments that are based on the best available science is a stand-

ard that would best support the goal of completing assessments within reasonable time periods and minimizing the need to conduct wasteful rework.

While the May 2009 IRIS process changes reflect a significant improvement that can help EPA restore the integrity and productivity of the IRIS program, EPA still faces significant management challenges as it seeks to completely timely, credible IRIS assessments.

First, EPA must continue to balance the need for using the best available science with completing IRIS assessments in a timely manner. As we have reported, even 1 delay can have a domino effect requiring the process to essentially be repeated to incorporate changing science.

Second, EPA faces long-standing difficulties in completing assessments of chemicals of key concern, those that are both widespread and likely to cause significant health issues. We believe that EPA must continue to focus on the best available science, obtaining credible expert review, and finalizing IRIS assessments.

Third, EPA must be disciplined in keeping the timelines even in the absence of fixed statutory deadlines for completing IRIS assessments.

Lastly, we believe that to produce timely credible IRIS assessments over a sustained period of time, it will be important for EPA to maintain a consistent process going forward.

We are currently reviewing EPA's implementation of its revised 2009 IRIS assessment process and its response to our previous recommendations. As part of this review, we will be examining EPA's response to NAS's recommendations for improvements to the IRIS process. We plan to issue this report later this year.

That concludes the summary of my statement. I will be happy to answer any questions any member of this committee may have.

[The prepared statement of Mr. Trimble follows:]

United States Government Accountability Office

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Testimony

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EPA HEALTH RISK ASSESSMENTS

Oversight and Sustained Management Key to Overcoming Challenges

Statement of David C. Trimble, Director
Natural Resources and Environment

U.S. Government Accountability Office
GAO 90 YEARS 1921-2011
ACCOUNTABILITY * INTEGRITY * RELIABILITY

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Chairman Shimkus, Ranking Member Green, and Members of the Subcommittee:

I am pleased to be here today to discuss our prior work on the Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) program and database. As you know, IRIS is one of the most significant tools that EPA has developed to support its mission to protect people and the environment from harmful chemical exposures. The IRIS database contains EPA's scientific position on the potential human health effects that may result from exposure to more than 550 chemicals in the environment and is a critical component of EPA's capacity to support its mission. IRIS assessments provide the scientific input to risk management decisions, such as whether EPA should establish air and water quality standards to protect the public from exposure to toxic chemicals or set cleanup standards for hazardous waste sites. Consequently, IRIS assessments are a critical component of EPA's capacity to support scientifically sound decisions, policies, and regulations.

EPA created IRIS in 1985 to help the agency develop consensus opinions within the agency about the health effects from chronic exposure to chemicals. Over time, the importance of the program has increased as EPA program offices, state and local environmental programs, and some international regulatory bodies have increasingly relied on IRIS health risk assessment information to support risk-based decision making to protect public health and the environment. As the IRIS database became more widely used and accepted, EPA took steps, beginning in the early 1990s, to improve and maintain the IRIS program and database. Over the years, the agency has implemented a variety of new operational procedures aimed at improving the IRIS program and database—with the most recent change to its IRIS assessment process occurring in May 2009.

Because of the potential for EPA's health risk assessments to lead to regulations that can significantly affect certain industries or federal agencies, IRIS assessments have frequently received considerable attention. For example, in recent months, much attention has been focused on EPA's draft health risk assessment of formaldehyde and the National Academies' review of the draft assessment.[1] In addition to reviewing the draft assessment of formaldehyde,

[1]The National Academies comprises four organizations: the National Academy of Sciences, the National Academy of Engineering, the Institute of Medicine, and the National Research Council.

the National Academies' report also offered some suggestions for improving the preparation and presentation of draft health risk assessments in general. Our work to date has not focused on these aspects of IRIS assessments.

Instead, our body of work on the IRIS program has more broadly evaluated the overall IRIS assessment process and the challenges the program has faced in implementing it. In March 2008, we reported that the IRIS database was at serious risk of becoming obsolete because EPA had not been able to routinely complete timely, credible assessments.[2] After subsequent reports,[3] in January 2009 we added EPA's processes for assessing and controlling toxic chemicals to our list of areas at high risk for waste, fraud, abuse, and mismanagement or in need of broad-based transformation.[4] We are currently undertaking a review of EPA's revised 2009 IRIS assessment process and the agency's progress in implementing it and plan to issue a report later this year.

In this context, my testimony today discusses our past work on (1) the timeliness and credibility of IRIS assessments and (2) EPA's May 2009 IRIS assessment process. We conducted the performance audit work that supports this statement in accordance with generally accepted government auditing standards. Additional information on our scope and methodology is available in each issued product.

Summary

From March through September 2008, we reported on shortcomings in EPA's IRIS process that limited the agency's ability to complete timely and credible IRIS assessments. For example, the

[2]GAO, *Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System*, GAO-08-440 (Washington, D.C.: Mar. 7, 2008).

[3]GAO, *Toxic Chemicals: EPA's New Assessment Process Will Increase Challenges EPA Faces in Evaluating and Regulating Chemicals*, GAO-08-743T (Washington, D.C.: Apr. 29, 2008); *Chemical Assessments: EPA's New Assessment Process Will Further Limit the Productivity and Credibility of Its Integrated Risk Information System*, GAO-08-810T (Washington, D.C.: May 21, 2008); and *EPA Science: New Assessment Process Further Limits the Credibility and Timeliness of EPA's Assessments of Toxic Chemicals*, GAO-08-1168T (Washington, D.C.: Sept. 18, 2008).

[4]GAO, *High-Risk Series: An Update*, GAO-09-271 (Washington, D.C.: January 2009). This high-risk area addresses EPA's implementation of the IRIS program as well as implementation of the Toxic Substances Control Act (TSCA).

Office of Management and Budget (OMB) required and managed interagency reviews of IRIS assessments, and OMB determined when assessments could proceed to the next process step, frequently resulting in delayed IRIS assessments. Such shortcomings contributed to our decision to designate the IRIS program as a high-risk area in January 2009. In June 2009 and July 2011, we testified that EPA's May 2009 IRIS assessment process reforms, if implemented effectively, would represent a significant improvement over the previous IRIS process by restoring EPA control, establishing transparency, and streamlining the process. We are currently undertaking a review of EPA's revised 2009 IRIS assessment process and the agency's progress in implementing it and plan to issue a report later this year.

EPA's Inability to Complete Timely, Credible IRIS Assessments Contributed to the Program's High-Risk Designation

From March through September 2008, we reported on shortcomings in EPA's IRIS process that limited the agency's ability to complete timely and credible IRIS assessments.[5] These shortcomings contributed to our decision to designate the IRIS program as a high-risk area. Specifically, beginning in 2004, OMB began requiring and managing two interagency reviews of IRIS assessments by OMB and other federal agencies with an interest in these assessments, such as the Department of Defense. These reviews contributed to concerns about the timeliness and credibility of IRIS assessments. In particular, EPA was not allowed to move forward with an assessment until OMB determined that EPA had satisfactorily addressed all OMB and other federal agency comments. As a result, IRIS assessments were frequently delayed. In addition, the content of the OMB-required reviews was not publicly available, thus limiting the transparency and the credibility of IRIS assessments. The credibility of the assessments was further limited by the involvement of other federal agencies that could be affected by the assessments if they led to regulatory actions. That is, if EPA issued an IRIS assessment that resulted in a decision to regulate a chemical to protect the public, some of the agencies participating in these reviews, such as the Department of Defense, could face increased cleanup costs and other legal liabilities.

[5]GAO-08-440, GAO-08-743T, GAO-08-810T, and GAO-08-1168T.

In addition, some EPA management decisions to suspend ongoing IRIS assessments to wait for new and ongoing scientific studies to be completed also limited the timeliness of IRIS assessments. In fact, EPA's decisions to await the results of new and ongoing studies before completing some IRIS assessments resulted, in some cases, in delaying them for years. We understand that there may be exceptional circumstances under which it may be appropriate to wait for the results of an important ongoing study, such as a major epidemiological study that will provide new, critical data for an assessment. However, as a general rule, requiring that IRIS assessments be based on the best science available at the time of the assessment is a standard that would best support a goal of completing assessments within reasonable time periods and minimizing the need to conduct significant levels of rework, as we reported in March 2008.

Moreover, in April 2008, EPA revised its IRIS assessment process, but the revised process did not address the issues we raised in our March 2008 report.[6] More specifically, our report contained recommendations for EPA to reevaluate its proposed revisions to the IRIS assessment process and to streamline the process to better ensure that EPA had the ability to develop transparent, credible assessments. However, in April 2008, EPA issued a revised IRIS assessment process that was largely the same as the proposed revisions that we had evaluated and had taken issue with during our review.

As a result of these and other issues, in January 2009 we added transforming EPA's processes for assessing and controlling toxic chemicals to our list of high-risk areas.

EPA's May 2009 IRIS Assessment Process Reforms Appeared to Represent Significant Improvement, but the Viability of the IRIS Program Will Depend on Effective and Sustained Management and Oversight

As we testified before the House Subcommittee on Investigations and Oversight in July 2011,[7] the IRIS assessment process reforms instituted by EPA in May 2009 appeared to represent a

[6]GAO-08-440.

[7]GAO, *EPA Health Risk Assessments: Sustained Management and Oversight Key to Overcoming Challenges*, GAO-11-824T (Washington, D.C.: July 14, 2011).

significant improvement over the previous IRIS process and, if implemented effectively, with sustained management and oversight, could help EPA restore the credibility and increase the timeliness of this important program. The reforms included the following:

- *Restored EPA control.* The new process and the memorandum announcing it indicated that the IRIS assessment process would be entirely managed by EPA, including the interagency science consultations (formerly called interagency reviews). Under EPA's prior process, these two interagency reviews were required and managed by OMB, and OMB determined when assessments could proceed to the next process step. The control restored to EPA under the new process is critical in ensuring that EPA has the ability to develop transparent, credible IRIS chemical assessments that the agency and other IRIS users, such as state and local environmental agencies, need to develop adequate protections for human health and the environment.

- *Established transparency.* The new process addressed a key transparency concern highlighted in our 2008 report and subsequent testimonies. As we recommended, the new process expressly required that all written comments on draft IRIS assessments provided during interagency science consultations by other federal agencies and OMB be part of the public record.

- *Streamlined process.* The new process streamlined the previous one by consolidating and eliminating some steps. Importantly, EPA eliminated the step under which other federal agencies could cause IRIS assessments to be suspended in order to conduct additional research, thus returning to EPA's practice in the 1990s of developing assessments on the basis of the best available science. As noted previously, long delays to await the results of new scientific research do not support a goal of completing assessments within reasonable time periods and minimizing the need to conduct significant levels of rework.

Although EPA's May 2009 IRIS assessment process appeared to represent a significant improvement over the previous IRIS process, we testified in July 2011 that the viability of the IRIS program would depend on effective and sustained management and oversight. We

identified the following factors that collectively could present significant management challenges to EPA's ability to complete timely, credible IRIS assessments.

- Unlike a number of other EPA programs with statutory deadlines for completing various activities, no enforceable deadlines apply to the IRIS program. We believe the absence of statutory deadlines may contribute to EPA's failure to complete timely IRIS assessments. For example, assessment schedules can easily be extended—and frequently are. Chronic delays in completing IRIS assessments have detrimental consequences for EPA's ability to develop timely and scientifically sound decisions, policies, and regulations.

- Because science and methodologies are constantly changing, there will always be a tension between assessing the best available science and waiting for more information. The IRIS program will remain viable only if it continues to use the best science available at the time of its assessments and plans for periodic updates of assessments to identify the need for revisions.

- An overarching factor that affects EPA's ability to complete IRIS assessments in a timely manner is the compounding effect of delays—even one delay can have a domino effect, requiring the process to essentially be repeated to incorporate changing science. For example, delays often require repeating reviews of the scientific literature on a chemical to take into account the time that has passed since the literature review was completed; this, in turn, may require detailed analyses of any new studies found to be relevant.

- Long-standing difficulties in completing assessments of chemicals of key concern—those that are both widespread and likely to cause significant health issues—stem in part from challenges by external parties, including those that may be affected by EPA regulation of chemicals should an assessment lead to such action. Such challenges are to be expected and can be best addressed by EPA's focusing on the best available science, obtaining credible expert review, and completing the assessments.

- IRIS process reforms, such as those issued in May 2009, are not established in regulation or statute and thus can easily be altered. As we have reported, continual changes to the process have presented a challenge to the chemical managers who

undertake the assessments.[8] To produce timely, credible IRIS assessments over a sustained period of time, it will be important for EPA to maintain a stable, consistent process going forward.

In addition to these challenges, in our May 2011 report on EPA's implementation of the Safe Drinking Water Act,[9] we noted that the inability of the IRIS program to provide the Office of Water with new and updated IRIS assessments in a timely manner has impeded effective implementation of EPA's regulatory determinations for drinking water contaminants.[10] When publishing the latest list of chemicals being considered for regulation (contaminant candidate list) in 2009, EPA identified health effects information gaps for 44 of the 104 chemicals on the list. We also note that EPA must address its backlog of demand for IRIS assessments. Moreover, EPA program offices and state and local entities have identified needs for assessments of hundreds of chemicals not yet in IRIS. In addition, as we previously reported, chemicals currently in the IRIS database may potentially need to be updated with new information that would either (1) change an existing risk estimate and/or (2) allow EPA to develop additional risk estimates.

This concludes my prepared statement. I would be happy to respond to any questions that you or other members of the subcommittee may have at this time.

GAO Contact and Staff Acknowledgments

For further information on this statement, please contact David Trimble at (202) 512-3841 or trimbled@gao.gov. Contact points for our Congressional Relations and Public Affairs offices may be found on the last page of this statement. Other staff that made key contributions to this testimony include Diane LoFaro, Assistant Director; Summer Lingard; Antoinette C. Capaccio; Lorraine Ettaro; Robert Grace; Carol Kolarik; and Jamie Meuwissen.

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[8]GAO-09-774T.

[9]*GAO, Safe Drinking Water Act: EPA Should Improve Implementation of Requirements on Whether to Regulate Additional Contaminants*, GAO-11-254 (Washington, D.C.: May 27, 2011).

[10]Under the 1996 amendments to the Safe Drinking Water Act, which remain in effect, EPA is to select for consideration those unregulated contaminants that present the greatest public health concern, evaluate their occurrence and the potential health risks associated with them, and decide whether a regulation is needed for at least five contaminants every 5 years.

Related GAO Products

EPA Health Risk Assessments: Sustained Management and Oversight Key to Overcoming Challenges. GAO-11-824T. Washington, D.C.: July 14, 2011.

Safe Drinking Water Act: EPA Should Improve Implementation of Requirements on Whether to Regulate Additional Contaminants. GAO-11-254. Washington, D.C.: May 27, 2011.

High-Risk Series: An Update. GAO-11-278. Washington, D.C.: February 2011.

EPA Chemical Assessments: Process Reforms Offer the Potential to Address Key Problems. GAO-09-774T. Washington, D.C.: June 11, 2009.

Scientific Integrity: EPA's Efforts to Enhance the Credibility and Transparency of Its Scientific Processes. GAO-09-773T. Washington, D.C.: June 9, 2009.

High-Risk Series: An Update. GAO-09-271. Washington, D.C.: January 2009.

EPA Science: New Assessment Process Further Limits the Credibility and Timeliness of EPA's Assessments of Toxic Chemicals. GAO-08-1168T. Washington, D.C.: September 18, 2008.

Chemical Assessments: EPA's New Assessment Process Will Further Limit the Productivity and Credibility of Its Integrated Risk Information System. GAO-08-810T. Washington, D.C.: May 21, 2008.

Toxic Chemicals: EPA's New Assessment Process Will Increase Challenges EPA Faces in Evaluating and Regulating Chemicals. GAO-08-743T. Washington, D.C.: April 29, 2008.

Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System. GAO-08-440. Washington, D.C.: March 7, 2008.

(361345)

Mr. SHIMKUS. Thank you very much.

Now, I would like to recognize for 5 minutes Dr. David Dorman, who is testifying on behalf of the National Academy of Sciences. Sir, welcome. You have 5 minutes, and take your time on the opening statement.

STATEMENT OF DAVID C. DORMAN

Mr. DORMAN. Thank you. Good morning, Mr. Chairman and members of the subcommittee. My name is David Dorman. I am a professor of toxicology at North Carolina State University and I served on the National Research Council's Committee to Review EPA's Draft IRIS Assessment of Formaldehyde.

The NRC report was developed by 15 scientists drawn by academia, federal laboratories, state government, and other organizations. The scientists that served on the NRC committee were selected by the National Academies and had a wide array of scientific expertise related to this effort. As part of the Academy's process, a draft of the committee's report was subjected to extensive peer review prior to release by the NRC.

It is important to note that the NRC was not asked to conduct an independent assessment of formaldehyde but rather we were charged with examining EPA's identification of potential cancer and non-cancer health effects, the toxicological basis for those health effects, and the way uncertainty factors used to derive the reference concentrations and the quantified cancer unit risk estimates for formaldehyde. The major findings of our NRC committee were as follows:

First, we found that the U.S. EPA was faced with the daunting task of compiling a complex and large toxicological database for formaldehyde. For the most part, the committee agreed that EPA achieved this goal. The EPA's draft assessment for formaldehyde was prepared using the Agency's current format and approach for IRIS documents. Our committee found the EPA's document to be quite cumbersome and was too often lacking in clarity and transparency. We were troubled that previous NRC committees reviewing similar assessments for other chemicals had identified similar deficiencies.

Third, our committee therefore offered a set of suggestions for changes in the IRIS development process that might help EPA improve its approach. In essence, we provided EPA with a roadmap for changes in the development process. The term roadmap was used because the topics that needed to be addressed were set out, but detailed guidance was not provided by the committee since that was seen as beyond our committee's charge.

Thus, the committee provided general guidance for the overall process and some specific guidance on the specific tests and steps of evidence identification, evidence review and evaluation, weight-of-evidence evaluation, selection of studies for derivation and calculation of reference concentrations and unit risk. For each of these steps, there are underlying processes that would need to be examined and reconsidered. The NRC report provides further details on these recommendations.

Finally, the committee recognized that any revision of the approach would involve an extensive effort by EPA staff and others,

and consequently, it did not recommend that EPA delay the revision of the formaldehyde assessment while revisions of the IRIS approach were undertaken. In fact, we provided specific guidance as to the steps needed to revise the existing draft IRIS assessment. Models for conducting IRIS assessments more effectively and efficiently are available, and the committee provided several examples in the present report. Thus, EPA might be able to make changes in its process relatively quickly by selecting and adapting existing approaches as it moves towards a more state-of-art process.

As a member of the committee, I have been pleased to hear that Dr. Anastas and other EPA administrators plan on implementing suggestions found in the NRC formaldehyde report.

In closing, I would like to thank all of you for inviting me here to discuss the NRC's report and I welcome your questions.

[The prepared statement of Mr. Dorman follows:]

REVIEW OF THE ENVIRONMENTAL PROTECTION AGENCY'S DRAFT IRIS ASSESSMENT OF FORMALDEHYDE

Statement of

David C. Dorman, DVM, PhD, DABT, DABVT

Professor of Toxicology
North Carolina State University

and

Member, Committee to Review EPA's Draft IRIS Assessment of Formaldehyde
Board on Environmental Studies and Toxicology
Division on Earth and Life Studies
National Research Council
The National Academies

before the

Subcommittee on Environment and the Economy
Committee on Energy and Commerce
U.S. House of Representatives

October 6, 2011

Good morning, Mr. Chairman and members of the subcommittee. My name is David Dorman. I am a professor of toxicology at North Carolina State University. I served as a member of the Committee to Review EPA's Draft IRIS Assessment of Formaldehyde, a committee of the National Research Council (NRC). The NRC is the operating arm of the National Academy of Sciences and the National Academy of Engineering.

I am pleased to appear before you today to discuss aspects of our committee's report, *Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde*, which was released on April 8, 2011. Our review of the U.S. Environmental Protection Agency (EPA) draft assessment was written by a 15-member committee that had a wide array of scientific expertise, appropriate to the task. We have provided a copy of the report for the Subcommittee, and the Executive Summary is attached.

EPA has been working to update its assessment of formaldehyde for its Integrated Risk Information System (IRIS) for a number of years. The large amount of new research data on formaldehyde since EPA's original assessment in the early 1990s has made the task challenging and lengthy. Given the complex nature of the IRIS assessment and the knowledge that the assessment will be used as the basis of regulatory decisions, the NRC was asked to conduct an independent scientific review of the draft IRIS assessment. Specifically, the committee was asked to answer questions concerning EPA's identification of potential noncancer health effects, the toxicological basis for those health effects, and the basis of the determination of uncertainty factors used to derive the reference concentrations (RfCs). The committee was also asked specifically to comment on the scientific rationale provided for the cancer assessment and the quantified risk estimates derived.

To address its task, the committee reviewed the draft IRIS assessment and key literature, and determined whether EPA's conclusions were supported on the basis of that assessment and the literature reviewed. The committee was not charged or constituted to perform its own assessment and therefore did not

conduct its own literature searches, review all relevant evidence, systematically formulate its own conclusions regarding causality, or recommend values for the RfC and unit risk. Furthermore, given the committee's statement of task, the committee focused on reviewing and critiquing the draft IRIS assessment, and the majority of the committee's report is directed at providing constructive comments and recommendations on improving specifically the draft IRIS assessment of formaldehyde

That said, the committee found that it could not address its charge without considering the methods and structure of the document as a whole, and in responding to its charge questions, the committee found some recurring methodologic problems that cut across components of its charge. Consequently, the committee commented on the general methodology of the assessment in Chapter 2 of the report and offered general suggestions in Chapter 7 with regard to the processes used by EPA to develop IRIS assessments. It did not review the IRIS program itself, but rather focused on "lessons learned" from the formaldehyde assessment.

The general problems identified by the present committee are not unique and have been reported over the last decade by other NRC committees tasked with reviewing EPA IRIS assessments for other chemicals. Problems with clarity and transparency of the methods appear to be a repeating theme over the years, even though some of the documents are very lengthy. In the roughly 1,000-page formaldehyde draft reviewed by the present committee, little beyond a brief (two pages) introductory chapter could be found on the methods for conducting the assessment. In fact, the introductory chapter of formaldehyde is nearly identical to that used in other IRIS assessments. Numerous EPA guidelines are cited, but their role in the preparation of the assessment is not clear. In general, the committee found that the draft was not prepared in a consistent fashion; it lacks clear links to an underlying conceptual framework; and it does not contain sufficient documentation on methods and criteria for identifying evidence from epidemiologic and experimental studies, for critically evaluating individual studies, for assessing the weight of evidence, and for selecting studies for derivation of the RfCs and unit risk estimates. The critical summary sections that

synthesize the evidence are variable and too often brief or not present, and strength of evidence is not characterized with standardized descriptors.

As noted, the committee's review of the EPA draft IRIS assessment of formaldehyde identified both specific and general problems with the document. The persistence of the problems encountered with the IRIS assessment methods and reports concerned the committee, particularly in light of the continued evolution of risk-assessment methods and the growing societal and legislative needs to evaluate many more chemicals in an expedient manner. On the basis of the "lessons learned" from the formaldehyde assessment, the committee offered some suggestions for changes in the IRIS development process that might help EPA improve its approach. The committee recognized that EPA has initiated a plan to revise the overall IRIS process and that it issued a memorandum in 2009 giving a brief description of the steps. However, the focus of the revision as indicated in the 2009 memorandum appears to be on the steps taken after the assessment has been generated (that is, the multiple layers of review). The committee's focus was on the completion of the draft IRIS assessment (that is, the development phase).

The committee offered a several-page roadmap for changes in the development process. The term *roadmap* was used because the topics that need to be addressed are set out, but detailed guidance was not provided because that was seen as beyond the committee's charge. Thus, the committee provided general guidance for the overall process and some more specific guidance on the specific steps of evidence identification, evidence review and evaluation, weight-of-evidence evaluation, selection of studies for derivation of RfCs and unit risk, and calculation of RfCs and unit risks. For each of these steps, there are underlying processes that would need to examined and reconsidered. The report provides further detail.

The committee recognized that any revision of the approach would involve an extensive effort by EPA staff and others and consequently, it did not recommend that EPA delay the revision of the formaldehyde assessment while revisions of the approach are undertaken. In fact, we provided specific guidance as to

the steps needed to revise the existing draft. Models for conducting IRIS assessments more effectively and efficiently are available, and the committee provided several examples in the present report. Thus, EPA might be able to make changes in its process relatively quickly by selecting and adapting existing approaches, as it moves towards a more state-of-art process.

Thank you for the opportunity to testify. I would be happy to answer any questions the subcommittee might have.

Mr. SHIMKUS. Thank you very much. And we will start.

And I will recognize myself for 5 minutes for the first round of questions.

First to Dr. Anastas, you have been clear in the past that IRIS does not perform risk assessments; rather this is done by risk managers in the program office, and I have been trying to handle those differences. EPA's Web site, though, states that IRIS is "a human health assessment program that evaluates quantitative and qualitative risk information on effects that may result from exposure to specific chemical substances found in the environment. If this is true, how can IRIS not be doing "risk assessments" if it has to distill qualitative risk information and quantitative risk information?

Mr. ANASTAS. The elements of a full risk assessment have been outlined in a landmark 1983 NAS report that looks at risk identification and characterization, dose response as well as exposure. What an IRIS assessment is today is looking at the hazard identification and characterization and the dose response. Until that information—which is powerful and actually fundamental to a risk assessment—is combined with the exposure models and the exposures that are expected and anticipated under a regulatory program or some other scenario, that is when it becomes a full risk assessment and is used in risk management. This is the important but only the front-end part of that overall calculus.

Mr. SHIMKUS. Thank you. You did answer this question in your opening statement. I am just going to go through three quick ones. You stated in your opening statement that the IRIS office evaluates peer review recommendations, correct? Is that what you said in your opening statement?

Mr. ANASTAS. Right. When we get any peer review comments, we always review them and address them, yes.

Mr. SHIMKUS. Do you write draft assessments and evaluate public comments?

Mr. ANASTAS. We submit our draft assessments for public comment and the public and the scientific community comments on those drafts.

Mr. SHIMKUS. Does your office decide what to include and exclude and what other changes to be made to its own work based upon those two responses?

Mr. ANASTAS. Through an extensive and iterative process, we receive those comments, address those comments, and transparently show how we have addressed those comments.

Mr. SHIMKUS. Thank you.

Mr. Trimble, what effect does IRIS risk values have on the regulated community or the private marketplace?

Mr. TRIMBLE. Well, as Dr. Anastas has indicated, it forms the basis for many of EPA's regulatory decisions. For example, in drinking water standards, the information in IRIS will be married up with occurrence data whether or not the contaminant has been found in water across the country to inform decisions about whether or not, for example, to regulate a contaminant. So it is the building block for many of EPA's regulatory decisions.

Mr. SHIMKUS. But if the IRIS assessment is not finalized for over a period, then what is that effect?

Mr. TRIMBLE. Then basically everything comes to a screeching halt because the mission teams like the water office or air, they don't have sort of the basic science they need to carry out their mission.

Mr. SHIMKUS. And then the private sector who might be preparing for this are——

Mr. TRIMBLE. Everyone is left hanging.

Mr. SHIMKUS. Thank you. And Dr. Dorman, I have talked about this numerous times in my years here on the committee. What is the value of a risk assessment value that identifies a level below a natural occurring background level?

Mr. DORMAN. So that is a dilemma for a number of chemicals that exist endogenously, and my own opinion—and I think it also was echoed in a report—is that for formaldehyde in particular, those endogenous levels need to inform the assessment as performed by EPA or other agencies. On a personal note, kind of speaking not for the committee, I think that becomes a challenge and I think that oftentimes we don't regulate chemicals, we don't consider the risk assessment in light of that endogenous background.

Mr. SHIMKUS. And endogenous meaning?

Mr. DORMAN. That is what is present normally in the body just from consumption of food or for metabolism. It is basically what your body produces.

Mr. SHIMKUS. So in the numerous years I have been on this committee and dealing with—you know, we have water issues that would have endogenous elements in it, we have ground that has endogenous elements, so I guess for the layman, having a standard that is lower than naturally occurring, cleaning the soil up and then you can't replace it with the same soil. This same soil is still higher than the standard established by this risk assessment, is that correct?

Mr. DORMAN. Correct. That could be the case.

Mr. SHIMKUS. Thank you very much.

Now, I would like to recognize my colleague, Mr. Green, for 5 minutes.

Mr. GREEN. Thank you, Mr. Chairman.

And I guess why IRIS is so important—and I happen to represent the largest petrochemical complex in the country—is that all the chemicals used properly are something that we really benefit from, but that is why IRIS is so important because of those beneficiary uses, but in certain levels. And the best example is formaldehyde and dioxin. We need those but when used properly and that is why IRIS is so important to do.

Mr. Administrator, I mentioned in my opening statement I was concerned with the length of time it has taken IRIS to complete assessment of dioxin due to the presence of dioxin super flight in our district. It is my understanding that IRIS is expected to release a portion of the final dioxin assessment in January of 2012. Is that correct? And can you elaborate very briefly on why this is a two-part assessment? Yes, sir.

Mr. ANASTAS. One of the things that I did try to emphasize is that when we receive comments on an assessment, we take them extremely seriously and we want to fully address all of these com-

ments. We follow the science. The science is what dictates when we can release a final assessment. We submitted the dioxin assessment most recently the received comments on both the cancer portion of the dioxin assessment and the non-cancer portion of the assessment. It is clear that the comments on the non-cancer portion of the assessment are things that can be readily dealt with, addressed, and that we can move quickly ahead.

The complexity of the dioxin cancer portion of the assessment are far more complex and will not be completed on the same time frame as the non-cancer portion of the assessment. And that is based on the science and the complexity of the science and the scientific issues.

Mr. GREEN. This is not the first hearing that our committee has had on IRIS and it is an important program that has been subject to review by the GAO and the National Academy of Sciences Committee for years. It has been targeted because of lengthy delays and because sometimes the politicalization—surprise, surprise—in Washington what should be scientific process. We saw this during the Bush Administration when the OMB took over management of the IRIS program and the pace of the assessments slowed to a crawl. The Government Accountability evaluated the peer review process in 2004 and raised certain concerns.

Mr. Trimble, can you briefly explain the concern GAO had with IRIS review system that was in place from 2004 to 2008? And again I am trying to remember. Obviously, OMB reviews all regulations from agencies, but this is the first time I had seen that OMB would actually control the process between agencies for input. So I appreciate, you know, you answering that.

Mr. TRIMBLE. Briefly, what we found at the time was we had concerns regarding productivity with the IRIS program, which we have talked about. At that time one of the things that we noted in our reports was that OMB had involved itself and taken control of 2 key steps within the process so that reports and IRIS assessments could now move forward without OMB's concurrence. And that was I believe when reports were being sent out for review and when they were being finalized.

So there was one aspect that dealt with productivity and EPA's independent ability to control the process, but the other aspect that we reported on that was troubling was that OMB's involvement and comments were non-transparent so there was a lack of transparency in the public regarding what changes were being made and what those comments were. OMB brought in other federal agencies and also those comments were not transparent being deemed by OMB at the time as deliberative in nature. And so it was those two factors that we reported on at the time.

Mr. GREEN. And again that is a different system than I think we are used to, and there are times that as Members if we lose at the Agency, whether the EPA or somewhere else, we will go to OMB and talk about the economic impacts. And that is what OMB should be doing——

Mr. TRIMBLE. Um-hum.

Mr. GREEN [continuing]. And not getting involved in the actual scientific assessment.

Dr. Dorman, I know you briefly described some of the recommendations that National Science made. Can you talk about particularly with the issue of formaldehyde?

Mr. DORMAN. So I think in the case of formaldehyde, we found largely that we had a number of areas in which we agreed fully with the recommendations or the conclusions that the EPA had in the IRIS document. We did have some areas in which we differed as far as our interpretation of the EPA document in light of the scientific evidence that is available. We did give the Agency some specific recommendations regarding not relying on certain studies. We felt they weren't the best studies available for certain endpoints like sensory irritation and others but hopefully that addresses your concern.

Mr. GREEN. OK, thank you. Thank you, panel.

Mr. SHIMKUS. The gentleman's time has expired.

The chair now recognizes the chairman emeritus, Mr. Barton, for 5 minutes.

Mr. BARTON. Thank you, Chairman Shimkus.

Let me ask Dr. Anastas. Are you career or you a political appointee?

Mr. ANASTAS. I am a political appointee.

Mr. BARTON. OK. And you have been in your position since the Obama Administration took office?

Mr. ANASTAS. Shortly thereafter. Actually, it was January——

Mr. BARTON. OK.

Mr. ANASTAS [continuing]. Of 2010.

Mr. BARTON. Very good. I am going to ask you a little bit different series of question in the hearing because my interest, while I share some of the interest on chemical issues, I am very involved in the air quality issue.

Does your office do any of the studies that relate to ozone?

Mr. ANASTAS. We produce integrated scientific assessments on a wide range of national ambient air quality standards, including ozone.

Mr. BARTON. OK. And mercury?

Mr. ANASTAS. Yes, all of those substances under the program.

Mr. BARTON. And PM2.5?

Mr. ANASTAS. Correct.

Mr. BARTON. OK. Is there any other office within EPA that does studies on those similar to your office?

Mr. ANASTAS. We work closely with our Office of Air and Radiation and while we do the underlying scientific assessments of the kind that we are discussing in IRIS and integrated scientific assessments, the Office of Air and Radiation takes those basic scientific documents into their regulatory process.

Mr. BARTON. When the administrator is looking at tightening the standards on the various criteria of pollutants under the Clean Air Act, who make the decision whether the study to look at the health effects is going to be done internally by your office or externally?

Mr. ANASTAS. The process of generating a scientific assessment on these chemicals would take place internally, relying on a wide range of external studies—universities, research institutes—and those assessments are conducted internally and then put out for peer review.

Mr. BARTON. Would there ever be an instance where your office did not do an internal study, even if the decision was made to do an external study?

Mr. ANASTAS. I am not familiar with a case where it would be conducted completely externally. We rely on a wide range of external studies to inform our assessments, but the assessments that are fed into the regulatory process are constructed internally.

Mr. BARTON. Is it your decision whether to do the external study or the administrator's decision or the deputy administrator's decision or kind of a collective all of the above?

Mr. ANASTAS. The conduct of the studies are dictated by the needs of our regulatory and program offices and they work closely with the Office of Research and Development to identify which studies are necessary to inform their regulatory actions and then we proceed. So that is the process that is used.

Mr. BARTON. I don't necessarily understand that answer, but I don't have but a minute and a half. So can you give me a definition that is generally accepted of what a premature death is?

Mr. ANASTAS. One would look at statistically a life expectancy using epidemiological models and the absence of a particular effect if you are looking at, for instance, a respiratory——

Mr. BARTON. Well, give me a layman's definition. I mean my friends on the Democratic side, when we debate these environmental bills where we are attempting to delay some of the EPA regulation, they trot out these studies, and they are usually 10 to 15 years old, they are usually external, and they all seem to predict 30,000 premature deaths a year, but we have never gotten a definition of what a premature death is.

Mr. ANASTAS. A premature death would be something that shortens the otherwise——

Mr. BARTON. I want to know what the definition is. Is a premature death somebody who has a life expectancy of 80 who dies at 40 because of exposure to ozone, dies at 50, dies at 35? I mean there should be some standard definition. Apparently, there is not. Premature death is in the eyes of the beholder.

Mr. ANASTAS. Their life expectancy would be shortened from what it would otherwise be. So it is not set at a cutoff point of how much shorter. That is——

Mr. BARTON. Could you provide for the record a written answer to what a premature death is?

Mr. ANASTAS. I would be happy to.

Mr. BARTON. Whatever the definition is that your agency uses, I would like to have it in writing.

Mr. ANASTAS. Certainly.

Mr. BARTON. Thank you, sir.

Thank you, Mr. Chairman.

Mr. SHIMKUS. The chair now recognizes the gentleman from Mississippi, Mr. Harper, for 5 minutes.

Mr. HARPER. Thank you, Mr. Chair.

Dr. Anastas, just a question. Who selects who does the peer review? Who is invited to join in that? Is that open? Tell me how that works.

Mr. ANASTAS. Certainly. The peer reviews can be done, for instance, by the National Academy of Sciences. They can be con-

ducted by our Science Advisory Board. They can be conducted by panels of scientific experts. In the case of the National Academies, they are selected certainly by the Academy. The Science Advisory Board assembled ad hoc panels for those reviews, and each of these types of processes is a vetting for balancing different scientific expertise and ensuring that there aren't ethical or conflicts of interest.

Mr. HARPER. When a draft is prepared and done, if there is conflicting opinions by the peer review, how is that dealt with? Does that appear in your draft assessment that there are conflicting reports?

Mr. ANASTAS. The results of conflicting opinions are resolved within the peer review committee themselves. They can represent the different perspectives in their peer review report and we would receive that report.

Mr. HARPER. So is the public ever made aware that there may have been a difference of opinion before that came to you?

Mr. ANASTAS. Thank you. What is a very important point that I should have emphasized is that these peer review panels are publicly held. We receive public comment. The peer reviews are publicly available so actually one of the things that was emphasized by GAO is the necessary transparency, and that is something that is very transparent in this process is the peer review.

Mr. HARPER. When the peer review is being completed, once a final assessment is done, is that final assessment on track to be reevaluated? Is it a perpetual continuous reevaluation? Or something new comes in, is that subject to being changed?

Mr. ANASTAS. There are over 500 assessments on the IRIS database currently, and one of the ongoing processes where we seek public input, we receive input from our various program offices and regional offices is input on what should be in the pipeline for highest priority either due to knowledge of additional scientific information that requires updating or a need to address actions that need to be taken. So that is how we inform how things get updated in what order. As was referenced earlier, this is an ongoing challenge and why it is so important that we have increased the pace of these assessments.

Mr. HARPER. Can you give me the difference between chemistry and green chemistry?

Mr. ANASTAS. Certainly. Chemistry is the study of all matter and material and its transformations and green chemistry is looking at how you manipulate the molecules, how you build them from the atoms up so that they have a reduced ability to cause toxicity to humans or the environment. In the same way that we can design a substance to be green or blue, flexible or brittle, we can design it so that it is either capable of causing harm or far less capable of causing harm.

Mr. HARPER. Well, when I went to college, you could major in biology or chemistry. Do you anticipate that we will see green chemistry majors in our universities?

Mr. ANASTAS. As a matter of fact, there are Ph.D. programs in major universities both in the United States and elsewhere in green chemistry. There are degree programs in everywhere from the U.S., India, China, Australia, and the U.K.

Mr. HARPER. If I have time, I would like to ask Dr. Trimble a question if I may. And I am going to reach a quick peer review committee. This was the NRC formaldehyde committee review just a quote here.

It says, "the committee is concerned about the persistence of problems encountered with IRIS assessments over the years and the draft was not prepared in a consistent fashion. It lacks clear links to an underlying conceptual framework and it does not contain sufficient documentation on methods and criteria for identifying evidence from epidemiologic and experimental studies, for critically evaluating individual studies, for assessing the weight of evidence, and for selecting studies for derivation of the RFCs and unit risk assessments."

Tell me your opinion on that, what that statement was.

Mr. TRIMBLE. This may be better directed to NAS since GAO has not looked or assessed the NAS's study.

Mr. HARPER. Well, certainly defer then.

Mr. DORMAN. Yes, sir. So what we mean by that is that oftentimes when one is trying to put together a database, when you are basically doing literature reviews, before you begin that process, you start to lay out a framework by which you are going to evaluate the literature. And so as you are starting to go looking at literature, you will find, per se, a chemical like formaldehyde there is literally thousands of articles available in the published literature on a chemical where if you search the database using a word like formaldehyde you will find. And so one needs to have a process by which you start to kind of weed that evidence down to a sub-selection of studies and then eventually key studies that you start to use in your assessment, and we just felt that EPA was not transparent in defining that process by which they would both identify what literature you were finding and then either accept or not accept certain studies and bring them forward in their assessment.

Mr. HARPER. I realize I am out of time and if I may, Dr. Trimble, what I was wanting to ask was this: the conclusions in that formaldehyde review committee seemed to indicate that the same problems that were noted by GAO in '06 are still evidence in IRIS and I just want to know if you agree or disagree?

Mr. TRIMBLE. I will probably punt on this. This is going to be part of our ongoing review, which we will be reporting on in the next couple of months looking at how the process has gone since then and part of that review will be looking at the NAS.

Mr. HARPER. That was a very polite way of not——

Mr. TRIMBLE. Yes, I apologize.

Mr. HARPER. Thank you.

Mr. SHIMKUS. The gentleman yields back his time.

The chair now recognizes the gentleman from North Carolina, Mr. Butterfield, for 5 minutes.

Mr. BUTTERFIELD. Let me thank you, Mr. Chairman, for convening this very important hearing today and particularly we thank the witnesses for their testimony.

Mr. Chairman, IRIS, as we all know, is the foundation of our public health and environmental policy and it should be reviewed periodically to ensure it is being carried out at peak performance.

And so the witnesses' testimony today has been very helpful on this subject.

I believe to properly evaluate IRIS's performance, we must have absolute clarity on the function of IRIS. Dr. Anastas, let me start with you. Does IRIS make risk assessments?

Mr. ANASTAS. No, what IRIS does is provide important scientific information that gives insight on the hazards of chemicals and potential health consequences of various chemicals, but in order to have it be a full risk assessment, it needs to have the exposure component. So while this information is fundamental and essential, it is not a full and complete risk assessment.

Mr. BUTTERFIELD. So do you only make hazard assessments or do you do both?

Mr. ANASTAS. The risk assessments are done as part of the regulatory process in our regulatory office.

Mr. BUTTERFIELD. But don't you agree that this is a very important distinction between these two?

Mr. ANASTAS. It is a tremendously important distinction, one that is often confused. Many people do view IRIS members as regulations, as risk assessments, and it is an important distinction that this is looking at just this element of the scientific information.

Mr. BUTTERFIELD. That is very helpful.

Now, does IRIS make EPA regulations? I think we know the answer but I want you to go on the record and say that.

Mr. ANASTAS. Well, we know how important IRIS values are to regulations. They are not regulations and they are not making regulations.

Mr. BUTTERFIELD. So could we say, then, that the primary work of IRIS is to evaluate and integrate existing scientific literature into assessments of potential hazard which are then used by EPA program offices and others to gauge risk and eventually set thresholds for exposure in programs? Is that correct?

Mr. ANASTAS. That is correct.

Mr. BUTTERFIELD. In a little while, Dr. Anastas, we are going to hear from Dr. Honeycutt of the Texas Commission on Environmental Quality. He will claim that the EPA's most recent assessment on formaldehyde calls into question the safety of its hailing. Dr. Honeycutt will state that using EPA's most recent assessment, formaldehyde in your breath that results from normal body functions would be five times higher than the highest level of EPA would call safe. Was the IRIS assessment asserting that this room is now unsafe due to all of the formaldehyde producers currently being breathed at this time? How would you respond to this assertion and what are the implications?

Mr. ANASTAS. Well, the IRIS assessment was not concluding or implying that this room is unsafe because of the air that we exhale. The formaldehyde assessment benefitted greatly from the comments that were supplied by the National Academies and the comments that the National Academies provided are being addressed to strengthen that assessment. But no, the answer is no, the assessment did not imply that we are at risk because of the air that we are breathing in this room.

Mr. BUTTERFIELD. Yes. Thank you very much.

Thank you, Mr. Chairman. I yield back.

Mr. SHIMKUS. I thank my colleague. I would just note, Dr. Anastas, in your response you said "not concluding," brings up my question about are you doing a risk assessment? So that is the part of this whole debate that we are looking into.

The chair now recognizes the gentleman from Pennsylvania, Mr. Pitts, for 5 minutes.

Mr. PITTS. Thank you, Mr. Chairman.

Dr. Anastas, is the source of a study's funding an automatic disqualifier of the contents or quality of the research no matter how well characterized or high quality such a study is?

Mr. ANASTAS. The evaluation of a study is based on the scientific integrity of the study. So the short answer to your question is no. The importance of the rigor of the study, the way that the study is conducted are the important determining factors. With regard to such things as the peer review and peer review panelists, ethical and conflict of interest are considered at that point, for instance, for peer reviewers, but in the conduct of the study, it is the scientific rigor of the study.

Mr. PITTS. Other than industry funded, please tell the committee what other types of funding exist for high-quality scientific work?

Mr. ANASTAS. I think there is extensive funding for high-quality research provided by the Federal Government. There is certainly a wide range of our scientific agencies provide funding to researchers to conduct on a wide range of topics including toxicology, epidemiology, and these are important sources of funding. Whether it is the National Science Foundation, the National Institutes of Health, and of course the Environmental Protection Agency.

Mr. PITTS. Has the EPA ever contracted with the private sector or intentionally obtained scientific research that was paid for by a private interest?

Mr. ANASTAS. I want to make sure that I give you an accurate answer so I don't want to be definitive without checking all of the facts. What I will pledge to do is get back with you with a clear answer on that question.

Mr. PITTS. All right. To what extent does IRIS rely on the scientific pronouncements made by other federal agencies or coordinate with them on their activities like NTP or ATSDR?

Mr. ANASTAS. One of the things that we ensure doing is coordinate what assessments will be done so that we certainly wouldn't want to be duplicative or overlapping or redundant. We coordinate with sister agencies not only which assessments to do to make sure that we are complementary wherever appropriate but also coordinate in our interagency reviews. Interagency reviews are transparent and inclusive and we rely heavily on the scientific expertise on our sister scientific agencies and health agencies, as well as others.

Mr. PITTS. Thank you.

Dr. Dorman, in your opinion, has EPA's IRIS process evolved to reflect improvements in the field of risk assessment?

Mr. DORMAN. So speaking for myself and not as a member of the panel, I think that approaches have been kind of mixed. In some areas, IRIS has been more considerate of modeling efforts and things like that which reflect more state-of-the-art. I think there are other areas in which the IRIS assessment program probably

lags a little bit behind. But I think that IRIS does try to keep up and I think the EPA should be, you know, recognized for trying to keep up with the science as it is evolving.

Mr. PITTS. Are you familiar with other branches of the Federal Government that are engaged in risk assessment, and if so, do those offices employ best practices that could be applied here?

Mr. DORMAN. I serve and do an advisory role on different aspects for the Federal Government, and I think there are some examples of best practices. Speaking on behalf of the committee, we did identify some of those best practices that we thought could serve a template for the Agency as they move forward on looking at revising the IRIS program.

Mr. PITTS. How important is it for the American public that the integrated risk assessment process results in a reasonably correct assessment and what are the practical consequences of an overly precautionary assessment? What are the practical consequences of an assessment that does not identify risk?

Mr. DORMAN. Again, I think as Dr. Anastas pointed out the IRIS program is not doing the risk assessment per se; they are trying to compile the data regarding hazard identification, but I think that is extremely critical for folks. And I think it is not only an issue of an economic issue, but it is also a public health issue where the public doesn't become alarmed over health effects that may or may not be present with a certain chemical. And I think that is another area that, you know, the EPA IRIS documents do try to identify hazard identification and I think it is very critical for the public that it is done in the right way.

Mr. PITTS. Thank you, Mr. Chairman.

Mr. SHIMKUS. The gentleman's time has expired.

The chair recognizes that we have been joined by my colleague from Georgia, which I think he will——

Mr. BARROW. I thank the chairman. I will waive.

Mr. SHIMKUS. He waives. The chair now recognizes the vice chairman of the subcommittee, Mr. Murphy, for 5 minutes.

Mr. MURPHY. Thank you, Mr. Chairman.

Dr. Anastas, the EPA has a draft of the IRIS toxicology report for hexavalent chromium, is that correct?

Mr. ANASTAS. Correct.

Mr. MURPHY. Are you aware that on May 12, 2011, a panel of independent chromium experts had significant concerns with that draft?

Mr. ANASTAS. I am aware of that peer review.

Mr. MURPHY. And is the EPA prepared to incorporate more up-to-date scientific research in that based upon the information that came from the peer review and other input?

Mr. ANASTAS. We are evaluating that peer review. We are evaluating the comments and concerns. While no decisions have been made, it is the practice that I have stated and I appreciate the opportunity to emphasize that we consider and we address the concerns raised in peer review.

Mr. MURPHY. Is there anything you recall in that peer review study that sticks out that says there is something that raises concerns of a particularly salient nature for you?

Mr. ANASTAS. I think that this peer review has raised a number of questions about the science that is currently being conducted and the potential value of that science informing the assessment upon its completion.

Mr. MURPHY. Are you aware also of the NTP study, the doses given to test animals, that something like 5,000 parts per billion but the national drinking water standard for total chromium is 100 parts per million, and drinking water monitoring indicates that hexavalent chromium in drinking water is only about 1 to 4 parts per billion? I mean these seem to be pretty radical differences in terms of information that has come out on hexavalent chromium research versus what is really out there. How do you evaluate that sort of information when you see studies looking at some extremely high levels and then related to what is really out there?

Mr. ANASTAS. It is certainly I will say a traditional methodology when studying the toxicity of a particular chemical that you want to be able to get up to the level where you see a particular toxic effect, and sometimes these levels that are required are fairly high as you mentioned. And then there is the necessary extrapolation. So this is not necessarily unusual for studies of this type.

Mr. MURPHY. But you are also drawing conclusions based upon having toxic levels can give us some misinformation. For example, a person can reach a toxic level of ingestion of H2O, but that doesn't mean we draw conclusions based upon that. And I just want to make sure that we are also looking at these levels. I mean what is the real risk? Because none of us want to misdiagnose and then mistreat the problem.

Mr. ANASTAS. This is the basis of dose response——

Mr. MURPHY. Um-hum.

Mr. ANASTAS. —and getting these dose response curves, the ability to determine at which dose an effect may take place or a no-effect level is the basis of dose response, and so this is something that I know that Dr. Dorman teaches in his classes all the time in North Carolina.

Mr. MURPHY. I also heard our EPA administrator talk about dose response curves and we should look at that.

Now, the Natural Resources Defense Council I believe suggested that chromium alloys pollute our soil and water supplies, but I want to make something clear. Isn't it true that there is no association between the use of chromium alloys in stainless steel in any pollution or illness? Am I correct in that?

Mr. ANASTAS. What we are looking at in the IRIS assessments is the toxicity and the one we are discussing is the toxicity of chromium-6 and different matrices you can expect different considerations, and that is part of the risk assessment/risk management calculation.

Mr. MURPHY. OK. Is that chromium-6 something that is used in stainless steel?

Mr. ANASTAS. I believe chromium-6 is used in stainless steel.

Mr. MURPHY. When it is used in stainless steel, I mean stainless steel is also seen as containers for clean drinking water, surgical equipment, et cetera. Is that an issue that that chromium is actually leaching out of that stainless steel and contaminating those things?

Mr. ANASTAS. Nothing in the IRIS assessment addresses any of those risk scenarios.

Mr. MURPHY. But you can look at things outside of the IRIS assessment? Here is my concern: If we are saying that that is a toxic chemical but it is used in containers which are used to have nontoxic water and sterile equipment, is it correct, then, in saying that that chromium is actually leaching out and causing problems?

Mr. ANASTAS. You are identifying extremely important risk management decisions and exposure factors. Those are exactly the type of questions that are——

Mr. MURPHY. You are not giving me an answer. You are just saying it is important. I need to know——

Mr. ANASTAS. What I am saying is that nothing in this health assessment would address those questions.

Mr. MURPHY. I still don't have an answer but I realize my time is up. Thank you, Mr. Chairman.

Mr. SHIMKUS. Thank you. And at this time I recognize my friend from Colorado, Ms. DeGette, for 5 minutes.

Ms. DEGETTE. Thank you very much, Mr. Chairman.

Dr. Anastas, I want to ask you a couple of things I read in your written testimony. One is about this rider that was attached to the interior EPA appropriations bill this summer that would have delayed all IRIS assessments until the NAS recommendations were adopted and would have required NAS review of additional draft assessments. Does the administration support that policy?

Mr. ANASTAS. What I can say is that the effect of those letters would be significant. I believe that Mr. Trimble did mention the concern I think that we all share of making sure that assessments come out in a timely way. The result of these riders would be significant delay of perhaps as much as a year or 2 years, and an important factor to consider is during that delay, would the assessments that are in development be brought out of date? So the impacts of this would be significant and cascading throughout not only the development of the assessments themselves but the use of these assessments.

Ms. DEGETTE. What types of significant and cascading developments would there be?

Mr. ANASTAS. As was mentioned earlier, these assessments are important as a foundation for different decisions and actions not only in the Agency but by States and municipalities and industry. Would these assessments then be able to inform regulatory decisions or other decisions? The answer of course is no because they would be delayed by these actions.

Ms. DEGETTE. Do you think there would be an effect on public health or the environment by these delays?

Mr. ANASTAS. I certainly believe that our regulatory decisions, the decisions at the state and local level and decisions made by companies and individuals impact human health and the environment, and so yes, if——

Ms. DEGETTE. OK. Your answer is yes.

Mr. ANASTAS. My answer is yes.

Ms. DEGETTE. Thank you. Now, thinking about it from the other side of the issue, the chemical industry and economy in general, if we had uncertainty in these standards, would that potentially also

be harmful to them since they wouldn't know what was coming down the pike?

Mr. ANASTAS. I think the lack of knowledge is always difficult and something to try to avoid, which is why we try to get this information out.

Ms. DEGETTE. Mr. Trimble, GAO has raised concerns about the delays in the IRIS process, and you talked about that earlier and what that would mean for the credibility of assessments. Would suspending all assessments and all actions on past assessments impact the utility and credibility of the program?

Mr. TRIMBLE. I think as Dr. Anastas indicated, the impact would be felt most immediately by the program offices at EPA, as well as the States and others that rely on that to make regulatory decisions.

Ms. DEGETTE. So there would be a lack of certainty?

Mr. TRIMBLE. Yes, certainly there would be a lack of certainty and predictability. Certainly.

Ms. DEGETTE. Now, in your testimony you talk about the compounding effects of delays on assessments and Dr. Anastas referred to that. Can you please explain what you mean by that?

Mr. TRIMBLE. Yes, what we have reported on in the past is that when studies in the past have been suspended or delayed, what happens is that science keeps marching so that when you start to restart that study, a lot of the work has to be redone because there is new scientific literature. We have talked about evolving scientific methods, for example, you know, quantifying risk and things like that. All of those, the state-of-the-art practices change over time, so when you stop and delay, you have to catch up to what is now cutting-edge science to move forward and that causes delays.

Ms. DEGETTE. In your testimony you mention that IRIS processor forms are not established in regulation or statute. Do you have any ideas for this committee about what we can do about that that you would like to share with us?

Mr. TRIMBLE. Well, with that I would politely demur on this.

Ms. DEGETTE. I thought you might.

Mr. TRIMBLE. We have a report that is coming out by the end of this year looking at the implementation of the IRIS programs since the 2009 changes, so we will be reporting on that shortly.

Ms. DEGETTE. Mr. Chairman, we will all look forward to getting a copy of that report. And I yield back.

Mr. SHIMKUS. The gentlelady yields back her time.

I ask unanimous consent for Mr. Murphy to do a unanimous consent request.

Mr. MURPHY. Mr. Chairman, I just ask this letter from the Specialty Steel industry of North America be submitted for the record in which it states, "no hexavalent chromium is present in steel alloys."

Mr. SHIMKUS. That has been shared with the minority? Is there objection? Hearing no objection, so ordered.

[The information follows:]

September 3, 2011

Via Fax to:

The Congressional Steel Caucus

Re: EPA -- Regulation of Exposure to Hexavalent Chromium

Please note the attached letter from the Chairman of SSINA, Dr. Sunil Widge, to EPA Administrator Jackson concerning hexavalent chromium. We believe the letter makes a very reasonable request -- please delay action on proposed regulations for a short period while important and relevant toxicological research on this subject is completed, so the regulatory process can be informed by the best science available.

If you concur that this makes sense, we respectfully request that you make your view known to EPA.

Thank you,

Skip Hartquist and Dana Wood
Counsel to SSINA

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September 1, 2011

The Honorable Lisa Perez Jackson
Administrator
U.S. Environmental Protection Agency
Ariel Rios Federal Building
1200 Pennsylvania Avenue, N.W.
Washington, D.C. 20460

Re: Toxicological Review of Hexavalent Chromium under the Integrated Risk Information System (IRIS) Program

Dear Administrator Jackson:

On behalf of the Specialty Steel Industry of North America (SSINA), the member companies of which employ thousands of highly skilled workers in steel mills and other facilities across the United States and whose customers employ tens of thousands of other workers, we are writing to alert you to the potential impact on our industry of the U.S. Environmental Protection Agency's (EPA's) Toxicological Review of hexavalent chromium under the Integrated Risk Information System (IRIS).

Specialty steels have been used safely for over 100 years and are essential in today's industrialized economy, serving critical national defense needs and applications in aerospace; aircraft; automobiles; appliances; communications, electronic, marine, and power-generating equipment; home utensils and cutlery; construction products; food and chemical processing plant equipment; and medical, health, and sports equipment. The chromium metal that appears in steel alloys is in non-toxic forms. No hexavalent chromium is present in steel alloys; however, during certain production processes (such as welding), hexavalent chromium fumes or dusts may be formed. Worker safety is the industry's top priority and all possible measures are taken to protect worker health, including with respect to potential exposures to hexavalent chromium.

SSINA fully supports and encourages scientifically-based regulation of hexavalent chromium, and has urged EPA to complete the current IRIS assessment after considering all

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Specialty Steel Industry of North America

The Honorable Lisa Perez Jackson
September 1, 2011
Page Two

relevant information, including recently finalized studies that help fill critical data gaps in understanding the carcinogenic mode of action of hexavalent chromium. On May 12, 2011, during a peer review workshop conducted by EPA, a panel of nine scientific experts recommended significant revisions to the current draft IRIS assessment for hexavalent chromium. These scientists urged EPA to incorporate the findings from the significant research program conducted by ToxStrategies. The preliminary results from this research program involving state of the art mode of action and pharmacokinetic information show mounting evidence of a biological threshold for hexavalent chromium toxicity.

EPA staff was aware of this research program when it began in 2009 and has been briefed on the early findings. In fact, program staff has specifically expressed interest in this type of data to inform the agency on whether further regulation is needed and, if so, the basis for such regulation. EPA's original published schedule for issuance of the draft Toxicological Review for hexavalent chromium was Fall 2012, which would have easily enabled EPA staff to incorporate the results of the research studies into the IRIS assessment. However, EPA accelerated the assessment (releasing the draft in the Fall of 2010) and, therefore truncated the process.

The regulatory and potential cost impact of EPA's hexavalent chromium assessment will be far-reaching, including affecting a myriad of downstream users of specialty steel products. Accordingly, it is imperative to ensure that the health effects of hexavalent chromium, particularly at the low levels to which the general public is exposed, are well understood before the Toxicological Review is completed and subsequent regulatory processes are initiated. A delay of a few months to ensure full consideration of the studies noted above is well justified for this ubiquitous substance.

SSINA agrees with the experts on the peer review panel and urges EPA to pause its activity and revert back to the original timeline to allow the scientists' groundbreaking work to be completed and for EPA scientists to review and incorporate the data into EPA's draft Toxicological Review.

We appreciate your attention to this matter and look forward to receiving a favorable reply.

Respectfully submitted,

Dr. Sunil Widge
Chairman, Specialty Steel Industry of North America
Senior Vice President – Strategic Business Development & Governmental Affairs
Carpenter Technology Corporation

Mr. SHIMKUS. The chair now recognizes the gentleman from New Hampshire for 5 minutes, Mr. Bass.

Mr. BASS. Thank you very much, Mr. Chairman.

I want to thank you all for your time and interest in being here today.

Dr. Anastas, OMB guidance defines "highly influential scientific assessment" as "a scientific assessment that could have a potential impact of more than $500 million in any year on either the public or private sector or is a novel, controversial, or precedent setting or has significant interagency interest." Because the estimates support the Agency's regulatory activities, including costly cleanups, are the IRIS assessments routinely recognized as highly influential scientific assessments subject to the information quality and peer review guidelines?

Mr. ANASTAS. I think the important discussion that we have been having has shown that these assessments are scientific inputs into regulatory decisions. They are not regulations; they are not regulatory conclusions. The considerations for economic impact are important and essential and a serious part of the deliberations that the Agency has, but these assessments are not regulations and should not be viewed as such.

Mr. BASS. Well, I guess then in making the determination whether an IRIS assessment is "highly influential," how does the EPA determine whether more than $500 million worth of future impacts are likely?

Mr. ANASTAS. The results of regulatory decisions undertake extensive cost-benefit and regulatory impact analyses. Perhaps the most important point that I could make on this is that while we are, through these assessments, identifying the hazard profile of these substances, in the absence of exposure, there is no risk. If there is no exposure, there is no risk and so there would be no reason for its management. And so while these are important inputs, it would be wrong to assume that because something has a particular hazard profile it is necessarily going to trigger a regulatory action.

Mr. BASS. Is it possible that any IRIS assessment could later be incorporated in a regulation that has impacts of more than $500 million?

Mr. ANASTAS. Yes.

Mr. BASS. OK. All right. I am all set, Mr. Chairman. Thank you.

Mr. SHIMKUS. The gentleman yields back his time.

The chair now recognizes the gentleman from Louisiana, Mr. Cassidy, for 5 minutes.

Mr. CASSIDY. Mr. Anastas, you mention, going back to Mr. Barton's questions, regarding how you define premature. Let us take a person with emphysema. We know that person with emphysema is more likely to have complications from an inhaled toxin, pick ozone, so if the person with emphysema dies at 74 because of a bronchospastic asthmatic event triggered by ozone, is he, compared to the average age someone dies, say 82 for a man, or is he compared to the average age that somebody with emphysema dies?

Mr. ANASTAS. So when we are looking at statistical population distributions, that distribution is going to have various susceptibilities—people who are particularly susceptible——

Mr. CASSIDY. Correct.

Mr. ANASTAS [continuing]. And people who are particularly resilient. So what we are talking about is average lifespan and how different effects would affect a——

Mr. CASSIDY. Correct.

Mr. ANASTAS [continuing]. Population. So I would not draw that conclusion based on an individual because I believe that that would not be a statistically robust approach.

Mr. CASSIDY. Wait, you don't adjust for co-morbidities when determining whether somebody dies prematurely because of exposure to a toxin?

Mr. ANASTAS. No, I am saying that certainly susceptible populations do reside within that overall population——

Mr. CASSIDY. But I think——

Mr. ANASTAS [continuing]. But I am saying that I wouldn't apply it to an individual.

Mr. CASSIDY. I can tell you that that would be counter to what you would do—I am a doctor. That is what you would do in medicine. You would account for co-morbidities knowing that co-morbidities have a huge influence upon the body's reaction to an external event.

Mr. ANASTAS. And I absolutely agree that in dealing with an individual you absolutely need to factor in the individual's susceptibility.

Mr. CASSIDY. But I gather that you are not comparing them——

Mr. ANASTAS. That would be the logical calculation.

Mr. CASSIDY. But I actually think that you actually could find—go to the VA database, for example—find the average lifespan for somebody with a certain level of pulmonary impairment and you would find, yes, for this degree of impairment they die and this degree they die at this age. But I gather that is not necessarily done?

Mr. ANASTAS. I am saying that in many of the epidemiological studies that are relevant to the discussion that we were having about decreased lifespan, that that has not been the basis of those types——

Mr. CASSIDY. OK. I got my answer. And I didn't mean to be rude. I don't mean to be curt. I apologize.

Dr. Dorman, did you participate in the critique of this report, the IRIS report for formaldehyde?

Mr. DORMAN. Yes, sir.

Mr. CASSIDY. Now, I am struck because I just kind of quickly eyeball it. I am quickly eyeballing it so it may come in totally wrong. Join my wife on most occasions.

If the lack of knowledge is a bad thing, misinterpretation of knowledge is even worse. As I look at the summary of your report, you say that "the committee concludes the weight of evidence suggests formaldehyde unlikely to appear in blood as an attack molecule." You go on to say that, you know, kind of absorbed, quickly metabolized, it goes away, unlikely to have a systemic effect. That is kind of the, you know, as I scan what I am getting. So even though this is 1,000 pages—I looked it up—it is 1,043-page report talking about all the things it will do to rat urine and, you know, to human nasal mucosa, really all that strongly suggests there is

pertinent physical effects, and yet your report finds that that may be overstated. Is that a fair statement?

Mr. DORMAN. So I think it is a fair statement that the Academy concluded that the current best evidence indicates that formaldehyde does not reach the systemic circulation in an appreciable way. And so what we did recognize as well, though, is that formaldehyde might have certain health effects that may not require it being delivered systemically. And so, for example, if we have say rhinitis or an irritation in the nose, you might also have headache. Even though that chemical never got to the brain, that would be an example say of a stress that might be associated with that inflammation in the nose.

Where we differed from the conclusions probably related most to the motive action that EPA was considering for the leukemogenic responses that have been associated with formaldehyde exposure where we felt that the weight of evidence didn't strongly support their conclusions.

Mr. CASSIDY. Yes, I am kind of struck that there is 1,043 pages of stuff which documents and if you just read it, you think oh my gosh, isn't this terrible? Then I read your report and when you actually analyze it and put it in context, it isn't quite so frightening. Worrisome, but not quite that 1,043 pages of we have got to regulate. I agree with that.

I also say, as a physician, it seems kind of routine. I am not sure why it has taken you so long to implement these suggestions I put forth because frankly, as a physician, if there is not rigor of methodology being explained, then the paper would never be published in a peer reviewed journal. That seems to be kind of a standard sort of scientific method of presentation.

Mr. ANASTAS. If I could just mention that this is a draft assessment. We put out draft assessments for the purpose of getting this kind of critique so that we improve it for the final assessment. This is what we do. This is why we seek it out.

Mr. CASSIDY. Can I have just a minute more?

Mr. SHIMKUS. Without objection, gentleman is recognized for another minute and a half.

Mr. CASSIDY. OK. Thank you.

Going back to green chemistry, it seems to me as if that would be the basis for a proposal regarding inherently safer technology.

Mr. ANASTAS. Correct.

Mr. CASSIDY. Now, that actually seems you move beyond I think Mr. Butterfield suggested your role as analytic—and I will maybe paraphrase—analytic not prescriptive, but that is a little disingenuous if you are saying listen, we are going to make a value judgment as to whether or not this has a toxic effect and this does not. And frankly, there will be assumptions that credible scientists may disagree with your assumptions, and yet your findings are going to be the basis, I bet you, for regulation promoting inherently safer technology. How would you disagree with that?

Mr. ANASTAS. What I tried to emphasize in my statement was when the information that we generate gives us insights not only that an individual substance may or may not be toxic and in what ways but how it is toxic, that gives us insights into the design——

Mr. CASSIDY. But you are making an assumption of toxicity that again scientists in a peer reviewed journal would disagree with your assumption, but yet your assumptions are going to guide this green chemistry which is going to guide an IST regulation.

Mr. ANASTAS. With all due respect, what I am saying is not on the level of toxicity but the mechanisms by which it has any kind of biological effect. This informs the design of the molecular structures of future chemicals so that we can minimize the possibility, the probability——

Mr. CASSIDY. Give me a specific because right now that sounds very nice, but as I try and think of the particular, it seems you can't divorce yourself from assumptions of the toxicity and we already see credible dispute with your assumptions of toxicity.

Mr. ANASTAS. When I am looking at a molecular structure, I know that whether or not a substance has the ability to even cause any type of toxic effect——

Mr. CASSIDY. But water can drown. Do you see what I am saying? Water has a toxic effect if you put your head underneath it for too long. And so you are right, there has to be a dose effect, and there has to be a certain substrate in which it interacts. How do you account for that?

Mr. ANASTAS. If a substance cannot be inhaled, if a substance cannot be respired, ingested across biological membranes, those are all based on its physical/chemical properties. What chemists do is develop structures to control their physical/chemical properties. You can design a substance to have those physical/chemical properties so as to reduce the probability that it can cause hazardous adverse consequences.

Mr. CASSIDY. I still can't—so formaldehyde——

Mr. SHIMKUS. The gentleman's time has expired.

Mr. CASSIDY. Thank you. I yield back.

Mr. SHIMKUS. There are too many doctors in this room. The IQ has gone up and I can't even understand the English being spoken here sometimes. I ask unanimous consent. My colleague Mr. Green wanted to make a statement before we adjourn this panel.

Mr. GREEN. Mr. Chairman, I know we have votes going to be scheduled and I think we have exhausted our questions of the panel. I want to thank the panel. I know, Doctor, you had to change your plans to be here but when I referred to the dioxin facility in our district—actually in Ted Poe's district—but EPA worked in both administrations, both in '08 and '09, what I consider bureaucratic light speed to get that site on there, and we actually have it encapsulated now. And the next panel we have our Texas Commission on Environmental Quality. They actually are the ones that did the research to trace where all this dioxin would be coming from in the San Jacinto River, so that is a great example. Most people get mad at EPA. Here in Texas, you all don't think we do anything for the environment, but we do. Thank you.

Mr. SHIMKUS. And the chair now also wants to ask unanimous consent that the letter dated October 4 from the American Chemistry Council be submitted for the record. That has been shared with the minority. Without objection, so ordered.

[The information follows:]

CAL DOOLEY
PRESIDENT AND CEO

October 4, 2011

The Honorable John Shimkus
Chairman
House Subcommittee on Environment
and Economy
2125 Rayburn House Office Building
Washington, D.C. 20515

The Honorable Gene Green
Ranking Member
House Subcommittee on Environment
and Economy
2322A Rayburn House Office Building
Washington, D.C. 20515

Dear Chairman Shimkus and Ranking Member Green:

The American Chemistry Council (ACC) welcomes your Subcommittee's hearing on the Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS). ACC and its members have a significant interest in the IRIS program, and we are pleased to provide these comments in advance of your hearing.

In April, 2011, the National Academy of Sciences (NAS) released its review of the draft IRIS assessment for formaldehyde. The report included a number of recommendations to improve the IRIS process, including fundamental changes to the manner in which the IRIS program obtains scientific data, analyzes studies, integrates data using a weight of the evidence approach, conducts causal determinations, and assesses uncertainty. Some of the scientific inadequacies pointed out by the NAS report have persisted for more than a decade. I have attached a summary of the NAS committee's recommendations to IRIS for the Subcommittee's information.

On July 14, 2011, Dr. Paul Anastas, the Assistant Administrator for Research and Development at EPA testified before the Oversight Subcommittee of the Science, Space and Technology Committee. Dr. Anastas acknowledged the NAS review of the IRIS formaldehyde assessment, and indicated that the NAS recommendations would be addressed in a phased-in approach. While ACC welcomed the news that EPA will "fully implement" the NAS recommendations for new assessments, we remain concerned that IRIS assessments currently underway will not benefit from the suite of changes recommended for the program.

IRIS currently lists 49 substances for which it expects to complete assessments between now and the second quarter of 2012, and an additional 14 assessments for which completion dates are yet to be determined.[1] Based on our understanding of Dr. Anastas' July, 2011 statement, however, most if not all of these assessments will not be improved to address the NAS recommendations. For example:

- EPA has indicated that assessments already released for peer review or that have been peer reviewed would be revised to address the peer review comments. Over one-third of the pending and near-term IRIS assessments appear to fall into this category (24 of 63). However, we are not aware that any of

[1] The list of substances is available on EPA's IRIS Track website, at http://cfpub.epa.gov/ncea/iristrac/.

the charge questions posed to the peer reviewers specifically addressed whether the draft IRIS assessments fully comported with the NAS recommendations to improve IRIS.

- EPA also indicated that for assessments under development but not yet released for peer review, the rationale for study selection and evidence evaluation would be examined to ensure they are "clear." Assuming that pending and near-term assessments fall into this category, it appears that EPA is likely to fall woefully short of implementing the complete set of NAS recommendations.

- The NAS review also recommended, among other things, the development of clear guidelines for study selection and a standardized approach to weight-of-the-evidence guidelines. However, the EPA has only committed to providing clarity on what studies and evaluation approaches were used, not to ensure the application of a uniform approach. Equally as important, EPA apparently will not apply the NAS recommendations concerning the calculation of reference doses and unit risks to these assessments, suggesting that the conclusions reached in the assessments will not be complete.

In short, ACC is concerned that an entire generation of IRIS assessments due to be completed in the next 9 to 12 months will suffer from the very same shortcomings that plagued the draft formaldehyde assessment. Flawed assessments create public confusion, unwarranted alarm, unnecessary product de-selection and litigation, all of which can put jobs at risk without sound scientific basis. Moreover, these shortcomings may have significant unwarranted economic impacts, because risk management decisions throughout the federal government, as well as state governments, routinely draw upon the risk numbers contained in IRIS assessments.

ACC believes it is incumbent on the IRIS program to fully implement the NAS recommendations on all pending and near-term assessments. Adopting these changes will improve the reliability of IRIS assessments and their credibility as a basis for future regulation. These changes will also ensure that the IRIS program completes assessments more efficiently and provides answers to the public, public health professionals and industry in a far more timely way.

We commend your Subcommittee's attention to the quality of government assessment programs and the scientific review process. If we can provide any additional information on ACC's view of the IRIS program, please let me know.

Sincerely,

Cal Dooley
President and CEO

Attachment

Mr. SHIMKUS. I too want to thank the first panel and for the second panel we will convene you after votes and they should be calling them any minute. So it really is not productive for us to start. And we will reconvene after votes. So with that, I will recess this hearing.

[Recess.]

Mr. SHIMKUS. We can get through the next panel and also get in between votes on the floor of the House, but I think we have got plenty of time, but we do want to get started.

We want to welcome you. Thank you for your patience. I will do as I did with the first panel I am going to introduce you all across the board, and then we will recognize you individually for your 5-minute opening statements. Because of the time that we have, you know, I won't hold you strictly to the 5 minutes, so take your time. Make sure what you want to present is not rushed.

So on this second panel, we again appreciate you all for being here. We have Dr. Michael Honeycutt, Director of Toxicology Division, Texas Council on Environmental Quality. We also have Dr. Harvey Clewell, the Hamner Institutes for Health Sciences. We have also have Mr. Jerry A. Cook, Technical Director, Chemical Products Corporation. It is good to see a mister and not all doctors. And then finally Dr. Thomas A. Burke, Associate Dean for Public Health Practice and Training, Department of Health Policy and Management at Johns Hopkins Bloomberg School of Public Health.

Gentlemen, thank you for joining us, and I would like to recognize Dr. Honeycutt for 5 minutes for his opening statement.

STATEMENTS OF MICHAEL HONEYCUTT, DIRECTOR OF TOXICOLOGY DIVISION, TEXAS COMMISSION ON ENVIRONMENTAL QUALITY; HARVEY CLEWELL, DIRECTOR, CENTER FOR HUMAN HEALTH ASSESSMENT, THE HAMNER INSTITUTES FOR HEALTH SCIENCES; JERRY A. COOK, TECHNICAL DIRECTOR, CHEMICAL PRODUCTS CORPORATION; AND THOMAS A. BURKE, ASSOCIATE DEAN FOR PUBLIC HEALTH PRACTICE AND TRAINING, DEPARTMENT OF HEALTH POLICY AND MANAGEMENT, THE JOHNS HOPKINS BLOOMBERG SCHOOL OF PUBLIC HEALTH

STATEMENT OF MICHAEL HONEYCUTT

Mr. HONEYCUTT. Good morning, Mr. Chairman and members of the committee. My name is Michael Honeycutt. I am director of the Toxicology Division at the Texas Commission on Environmental Quality. I would like to touch briefly on Texas' perspective on the science that EPA is using or not using for chemical risk assessments in recent years and the implications for regulatory agencies and the public.

I have been a toxicologist and a risk assessor for Texas for over 15 years. In past years, we have had disagreements with EPA, but they have not really been based on science issues so much as on policy issues. An example of this would be that EPA does not want to consider TCEQ rules, which in many cases are more stringent than their cleanup values when addressing a cleanup site in Texas. However, we have always been able to work out our differences amicably.

In recent years, though, EPA chemical risk assessments have become more precautionary in nature instead of relying on scientific data. The heart of the matter is that EPA is moving toward the philosophy that there is no safe level of exposure to a chemical and this is contrary to the cornerstone of the science of toxicology. This change in philosophy results in unrealistically low regulatory levels. And as a result, naturally occurring levels of chemicals may be higher and often cases it is higher than EPA-safe level.

As an example, using EPA's most recent draft assessment of formaldehyde, the formaldehyde in your breath that results from normal body functions would be over five times higher than the highest level that EPA would call safe. Formaldehyde is naturally formed in the air from the breakdown of chemicals released from vegetation, and according to available air data, the only places that would have safe air would be remote locations such as the arctic and South Pacific islands.

In another example, using EPA's most recent draft assessment of arsenic, all fish and shellfish would contain levels of inorganic arsenic that are higher than the highest levels EPA would consider safe. And it is not just fish. Normal dietary food and drinking water consumption would also have arsenic levels substantially higher than EPA-safe level. And we just know that this isn't true. We aren't seeing the health effects that would be predicted or expected in the general population based on EPA's new values.

While we do agree with EPA on being precautious in areas where we don't have good science, we strongly believe that good science should not be ignored and should trump EPA's overuse of precaution. Hexavalent chromium is a good example of this. EPA's recent conclusion that ingesting hex chrome likely causes cancer in humans is based on a study where mice received extremely high levels of hex chrome, and EPA dismissed the human epidemiology and the wealth of other data that contradict this. And in those human studies, there was an occupational study where workers actually had yellow teeth and yellow tongues from ingesting so much arsenic.

And TCEQ isn't the only organization concerned about the science behind EPA's recent assessments. The National Academy of Sciences, many prominent academic researchers, other states and other countries have noted the lack of good science in these assessments.

Because of the lack of scientific defensibility and the implications of EPA's new chemical assessments, Texas has recently decided to develop our own chemical assessments. We have written two state-of-the-science guidance documents and had them externally scientifically peer reviewed by panels of imminent scientists, including scientists from EPA, California EPA, and Canada, and we are in the process of putting our latest document through a second round of public comment.

We had no desire at all to use our limited resources to develop these chemical risk assessments that we have historically been able to rely on EPA for. However, the implications of EPA's new assessments have forced our hand. EPA's new assessments will unnecessarily scare the public and may actually harm public health by diverting public, industry, and government attention and re-

sources away from public health issues that may pose more of a risk.

As an example, EPA currently encourages pregnant women to limit their consumption of fish due to concerns of mercury. However, numerous recent studies show that the health benefit from pregnant women eating fish outweighs the potential risk for mercury. If EPA finalizes their draft arsenic value as it currently stands, then the public, the media, and advocacy groups would perceive fish as being even more unsafe resulting in even more pregnant women avoiding fish and its proven health benefits for them and their infants.

There are also significant implications for remediation programs all across the country. Typical soil and water concentrations of chemicals, even some naturally occurring, would be considered unsafe. In other words, there is no safe place to live. How can you cling to below-background levels if background levels are unsafe? All replacement soils that we would use to fill in a backyard would also contain these unsafe background levels. So where are we going to put this so-called contaminated soil that we would have to dig up from somebody's yard?

Your constituents will not stand for having soil and water that is deemed unsafe by EPA's new risk assessments even if it is naturally occurring and we can't do anything about it. So these are just some of the issues that we will have to face if EPA stays on their course, and I thank you for this opportunity to testify.

[The prepared statement of Mr. Honeycutt follows:]

Comments by Michael Honeycutt, Ph.D., with the Texas Commission on Environmental Quality Regarding the Use of Science in, and Implications of, EPA's Chemical Risk Assessments

On behalf of the Texas Commission on Environmental Quality (TCEQ), I would like to touch briefly on Texas' perspective on the science that EPA is using, or not using, for chemical risk assessments in recent years and the implications for regulatory agencies and the public.

In years past, we have had disagreements with EPA, but they have not been on science issues so much as on science policy issues. An example would be that EPA does not want to consider TCEQ rules, which are more stringent in many cases, when addressing a cleanup site in Texas. However, we have always been able to work out our differences amicably.

But in recent years, EPA chemical risk assessments have become more precautionary in nature *in lieu* of relying on scientific data. The heart of the matter is that EPA is moving toward the philosophy that there is no safe level of exposure to a chemical, which is contrary to the cornerstone of the science of toxicology. This change in philosophy results in unrealistically low levels that they consider safe. As a result, naturally occurring levels of chemicals will be higher than EPA's safe level.

For example, using EPA's most recent assessment of formaldehyde, the formaldehyde in your breath that results from normal body functions would be over 5 times higher than the highest level that EPA would call safe. Formaldehyde is naturally formed in the air from the breakdown of chemicals released from vegetation. According to available air data, the only places that would have safe air would be remote locations such as the arctic or South Pacific islands. Using EPA's most recent assessment of arsenic and available data from recent fish studies, all fish and shellfish would contain levels that are higher than the highest levels EPA would consider safe. You may have heard of the recent Dr. Oz controversy about arsenic in apple juice where he mistakenly assumed all types of arsenic in the juice were the most toxic form. We accounted for the most toxic form of arsenic in fish and shellfish in looking at the food safety implications of EPA's new draft arsenic assessment. Fish is not the only issue, normal dietary food and drinking water consumption would also be substantially higher than EPA's safe level. We know this is not true. We are not seeing the health effects that would be expected in the general population because these values are not based on good science.

While we agree with EPA on being precautious in areas where we do not have good science, we strongly believe that good science should not be ignored and should trump EPA's overuse of precaution. Formaldehyde is again a good example of this. EPA's recent conclusion that formaldehyde causes leukemia in humans is based on one study that did not show effects at occupational levels, much less

environmental levels. However, a wealth of solid scientific data show that formaldehyde cannot cause cancer outside of the respiratory tract, but EPA dismissed these data.

TCEQ is not the only organization concerned about the science behind EPA's recent risk assessments. The National Academy of Sciences, many prominent academic researchers, other states, and other countries have noted the lack of good science in these assessments. For that reason, states like Texas are conducting more of their own chemical risk assessments.

Because of the lack of scientific defensibility and the implications of EPA's new chemical assessments, we decided to develop our own chemical assessments. We have written two state-of-the-science based guidance documents, had them externally scientific peer reviewed by panels of eminent scientists including scientists with EPA, California EPA, and Canada, and are in the process of putting our latest document through another round of public comment.

We had no desire to use our limited resources to develop chemical risk assessments that we have historically been able to rely on EPA for. However, the implications of EPA's newer assessments have forced our hand. EPA's new assessments will unnecessarily scare the public and may actually harm public health by diverting public, industry, and government attention and resources away from public health issues that may pose more of a risk. For example, EPA currently encourages pregnant women to limit their consumption of fish due to concerns from mercury. However, numerous recent studies show that the health benefit from pregnant women eating fish outweighs potential risks from mercury. If EPA finalizes their draft arsenic value as it currently stands, then the public, the media, and advocacy groups would perceive fish as unsafe, resulting in even more pregnant women avoiding fish and its proven health benefits for them and their infants.

There are also significant implications for remediation programs all across the country. Typical soil and water concentrations of chemicals, some even naturally occurring, would be considered unsafe. In other words, there is no safe place to live. How can you clean to below background levels if background levels are unsafe? All replacement soils that we would use to fill in a backyard would also contain these unsafe background levels. Where are we going to put all of this so-called contaminated soil? Your constituents will not stand for having soil and water that is deemed unsafe by EPA's new risk assessments; even if it is naturally occurring and we cannot do anything about it.

These are just some of the issues that you and I will have to address if EPA stays on their course of not using good science. Attached are the technical comments (excluding appendices) that TCEQ has submitted to EPA recently which outline in more detail the numerous scientific shortcomings of recent EPA chemical risk assessments.

Supplemental Information for Comments by Michael Honeycutt, Ph.D., with the Texas Commission on Environmental Quality Regarding the Use of Science in, and Implications of, EPA's Chemical Risk Assessments

Attachment A – TCEQ Comments on EPA Formaldehyde Assessment

Texas Commission on Environmental Quality
Comments Regarding the U.S. Environmental Protection Agency
Draft Toxicological Review of Formaldehyde in Support of
Summary Information on the Integrated Risk Information System (IRIS)
Notice of Public Comment Period and Listening Session
75 FR 30825, June 2, 2010
Docket ID No. EPA-HQ-ORD-2010-0396

On June 2, 2010, the U.S. Environmental Protection Agency (EPA) published a Federal Register notice (Federal Register/Vol. 75, No. 105/Wednesday, June 2, 2010/Notices) of a 90-day public comment period (ending August 31, 2010) for the, "Draft Toxicological Review of Formaldehyde in Support of Summary Information on the Integrated Risk Information System (IRIS)," hereafter referred to as the draft IRIS review (EPA/635/R-10/002A). The draft IRIS review provides draft inhalation unit risk factors (URFs) for nasopharyngeal cancer, leukemia, Hodgkin lymphoma, and a combined URF for formaldehyde. It also provides a draft inhalation reference concentration (RfC), although EPA has not historically calculated an RfC for formaldehyde. The Texas Commission on Environmental Quality (TCEQ) has developed comments on the draft IRIS review to the extent practicable in the time allotted by EPA, focusing on the draft URFs, and provides the following limited comments for EPA consideration.

General Comment:

The assessment of the carcinogenic (and non-carcinogenic) potential of formaldehyde has great implications both in a regulatory context and in the public's perception of risk. Given their important role in the protection of public health, EPA regulatory risk assessors have a duty to perform the most scientifically-defensible assessments possible while giving careful and due consideration to comments and recommendations from other regulatory agencies, the public, external experts, stakeholders, etc. Although regulatory risk assessors have a penchant for erring on the side of health-protectiveness and conservative defaults, if erring on the side of conservatism significantly overestimates risk or hazard and is not fully justified, then harm to public health may result from diverting public, industry, and government attention and resources away from chemicals which may represent more of a public health risk at environmental levels. Therefore, TCEQ encourages EPA to give full, thoughtful, and careful consideration and evaluation to comments and recommendations from TCEQ, other regulatory agencies, the public, and external experts.

90-Day Comment Period:

The 90-day comment period is insufficient for regulatory agencies and others to provide thorough and meaningful comments based on an in-depth review and analysis of the draft IRIS review. There is great complexity associated with multiple issues relevant to the assessment of formaldehyde inhalation risk and hazard. The draft IRIS review alone is 1,043 pages, and there are hundreds of pages (at a bare minimum) of other documents and studies relevant to the assessment of formaldehyde risk and hazard due to inhalation exposure. Given the complexity and volume of relevant materials, it is impracticable for EPA to expect detailed specific comments from external experts given the short period allowed for a critical review of the draft IRIS review and procedures employed by EPA. The 90-day comment period only allows a very cursory review of the draft IRIS review at best, leads to a less-than-desirable level of

transparency and peer review, and undermines confidence in the process. Consequently, TCEQ is only able to provide preliminary comments based on a cursory review. If EPA seeks detailed and meaningful public input and technical comments, at a minimum EPA should extend the comment period at least 90 days past the August 31 deadline to allow stakeholders to perform a more detailed review of the volumes of relevant information and to comment on problematic issues associated with the draft IRIS review.

Toxicology-Based Comments:

Key Study for Hodgkin Lymphoma and Leukemia Unit Risk Factors

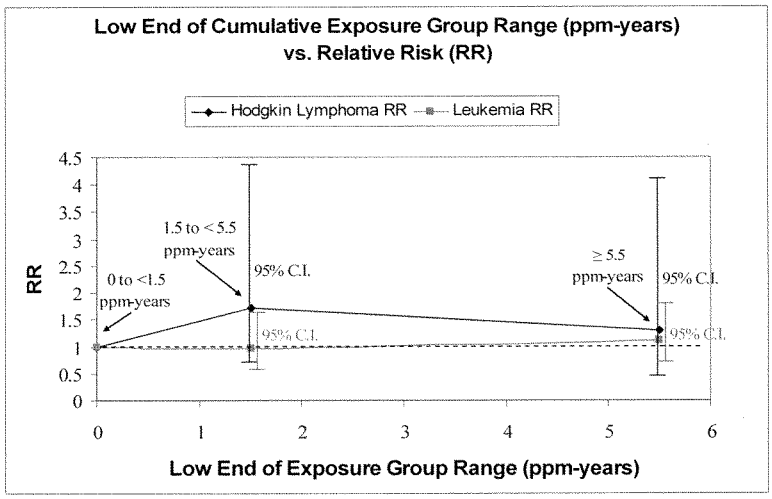
EPA utilizes the Beane Freeman et al. (2009) study to calculate draft URFs for Hodgkin lymphoma and leukemia. While there were statistically significant trends for Hodgkin lymphoma and leukemia with peak exposure, there were no statistically significant trends for any lymphohematopoietic malignancy with cumulative exposure. EPA indicates (p. 5-91) that it is not clear how to extrapolate risk estimates based on peak exposure estimates to meaningful estimates of lifetime extra risk of cancer from environmental exposures, and that the average exposure metric is also problematic because it suggests that duration of exposure is not important. Because EPA could not derive URFs for Hodgkin lymphoma and leukemia based on the dose metric for which there was a significant association (peak exposure), EPA used a dose metric for which there was no significant association (cumulative exposure) despite the fact that dose-response data for this dose metric are inadequate. EPA calculated draft URFs based on cumulative exposure despite that: (1) there were no statistically significant trends for Hodgkin lymphoma and leukemia with cumulative exposure; (2) regardless of statistical significance considerations, there is no apparent dose-response relationship between cumulative exposure and risk to provide adequate data for URF development; (3) if there is a causal relationship, study results indicate that peak exposure (as opposed to cumulative) is the most significant determinant of risk; and (4) if there is a causal relationship, study results suggest that duration of exposure, which is inherently part of the cumulative exposure dose metric, is not important (per EPA, p. 5-91).

Dose-Response Data

A primary reason that EPA used the cumulative exposure metric in order to be able to derive URFs is that, "the elevations in risk with that metric were consistent with significant elevations observed with the peak exposure (for Hodgkin lymphoma and leukemia)." However, this is not the case. While the relative risks (RR) for Hodgkin lymphoma and leukemia may show a monotonic dose-response relationship with peak exposure, the RRs do not appear to show a dose-response relationship for the cumulative exposure dose metric used by EPA. For example, for Hodgkin lymphoma the RR for the highest cumulative dose group (RR of 1.30) is actually lower than that for the medium dose group (RR of 1.71). For leukemia, the RRs for the highest and medium cumulative dose groups are essentially equal to 1 (RRs of 1.11 and 0.96, respectively), consistent with no elevated risk. The RRs for Hodgkin lymphoma and leukemia based on cumulative exposure (RRs of 0.96-1.71) are not consistent with a strong relationship and all RR confidence intervals easily include 1 (i.e., the lower end of the RR confidence intervals range from 0.40 to 0.70), consistent with the possibility of no elevated risk. Additionally, the Beane Freeman et al. (2009) study is not informative regarding what the RR might be for environmental exposures, which would fall into the cumulative exposure category used as the referent group (0-1.5 ppm-years), and the intermittent peak exposures associated with elevated RRs for workers (> 2 ppm) are significantly higher than environmentally-relevant levels. EPA does not attempt to provide a robust

justification for use of the cumulative exposure metric, and given the results of the Beane Freeman et al. (2009) study, TCEQ does not believe a robust justification is possible (i.e., use of the cumulative exposure metric is not scientifically defensible).

In addition, the cancer guidelines (EPA 2005a) recommend use of enough dose groups to provide an indication of the shape of the dose-response curve, as characterization of the shape of the dose-response curve is important in providing relevant dose-response data for assessing human risk. A relatively broad exposure range should make it relatively easy to discern the shape of any underlying dose-response curve in a well-conducted study. However, it is clear based on examination of the figure below that the data from Beane Freeman et al. (2009) provide too few dose groups and do not provide a monotonic dose-response curve, much less provide an indication of any reasonable shape of any underlying dose-response curve. As an example, for Hodgkin lymphoma the RR for the highest cumulative dose group (RR of 1.30) is actually lower than that for the medium dose group (RR of 1.71). These data are nonsensical from a dose-response perspective and clearly inadequate for derivation of a URF. For leukemia, again, the RRs for the highest and medium cumulative dose groups are essentially equal to 1 (RRs of 1.11 and 0.96, respectively) and do not provide an indication of a dose-response shape or increased risk relevant to environmental exposure for that matter. The ability to fit a line through data points does not necessarily mean that the underlying data adequately define the shape of the dose-response curve, including the critical low dose region. Based on the above considerations, the underlying data modeled by EPA clearly do not provide a basis for dose-response assessment. Dose-response is the cornerstone of toxicology, but the data modeled by EPA do not provide a solid foundation upon which to build these URFs.



In summary, EPA decided to use the cumulative exposure dose metric to calculate draft URFs despite the lack of statistically significant trends, despite not having the necessary dose-response data to do so in a scientifically-defensible manner, despite information suggesting that peak exposure (as opposed to

cumulative) is the most significant determinant of any risk, and despite information suggesting that duration of exposure (inherently part of the cumulative exposure dose metric) is not important (per EPA). To restate EPA's sentence (p. 5-91) in a slightly different but equally valid manner, it is not clear how to extrapolate risk apparently associated with peak exposures to *meaningful* estimates of lifetime extra risk of cancer due to cumulative or average environmental exposure. As data indicate that risk (if any) is most closely related to peak exposure, not cumulative or average exposure, the scientific validity and predictive value of risk estimates (e.g., URFs) calculated based on a cumulative exposure dose metric for which there is no apparent dose-response relationship is highly questionable. These significant issues are in addition to arguments concerning the lack of biological plausibility.

Leukemia and Hodgkin Lymphoma Contribution to the Combined URF

Leukemia URF

The URF for leukemia is by far the highest of the three combined by EPA (nasopharyngeal, Hodgkin lymphoma, leukemia) for the draft URF, contributing 60% of the risk for the combined draft URF. However, the draft URF for leukemia is likely the least scientifically defensible. As indicated above, for leukemia the RRs for the highest and medium cumulative exposure dose groups are essentially equal to 1, with RRs of 1.11 and 0.96, respectively. Obviously, the RR confidence intervals for the highest (0.70-1.74) and medium (0.60-1.56) cumulative exposure dose groups include 1. These RRs and confidence intervals for cumulative exposure are consistent with no elevated risk and there is no significant dose-response for leukemia with cumulative exposure, yet leukemia is the combined URF risk driver. Additionally, there is no dose-response based on average concentration; the RRs for the medium (RR of 1.13) and high (RR of 1.10) exposure groups show no dose-response and are essentially equal to 1 with confidence intervals containing 1 (i.e., the lower end of the RR confidence intervals range from 0.68 to 0.71). Even for peak exposure for which there was a trend, only the highest exposure group (≥ 4 ppm) has a RR greater than 1 (RR of 1.42), and the confidence interval for that group includes 1 (0.92-2.18). The RR for the medium peak exposure group, comprised of workers exposed to much higher than environmentally-relevant concentrations (2 to < 4 ppm), was 0.98 and consistent with no elevated risk.

In summary, the draft combined URF is driven by the URF for leukemia, for which the only RR greater than 1 in the derivation is the RR of 1.11 for the highest cumulative exposure group (≥ 4 ppm). This RR and the associated confidence interval containing 1 (0.70-1.74) are consistent with no excess risk yet will likely drive unachievable outdoor and indoor regulatory air levels (see relevant comment sections below). The URF for leukemia based on cumulative exposure is not scientifically defensible based on RRs essentially equal to 1 and the lack of a statistically significant or apparent dose-response (there are also biological plausibility issues). Based on Beane Freeman et al. (2009) study results, if any association exists between formaldehyde exposure and leukemia it may be with intermittent peak exposures levels greater than 4 ppm, an exposure scenario for which EPA acknowledges (p. 5-91) that no meaningful URF applicable to environmental concentrations can be calculated.

Hodgkin Lymphoma URF

The URF based on Hodgkin lymphoma contributes 23% of the risk for the combined draft URF. Several of the reasons why the URF for leukemia based on cumulative exposure is not scientifically defensible also apply to the URF for Hodgkin lymphoma. There is a lack of a statistically significant trend and lack

of a monotonic dose-response relationship between Hodgkin lymphoma and cumulative exposure. The RR for the highest cumulative dose group (RR of 1.30) is actually lower than that for the medium dose group (RR of 1.71) and neither indicates a strong relationship. The RR confidence intervals include 1 (i.e., the lower end of the RR confidence intervals range from 0.40 to 0.66) consistent with the possibility of no excess risk, yet this URF will be a significant driver in likely unachievable outdoor and indoor regulatory air levels (see relevant comment sections below). In addition to no significant or apparent dose-response relationship with cumulative exposure, there is none between Hodgkin lymphoma and average exposure. If any association exists between formaldehyde exposure and Hodgkin lymphoma, it may be with intermittent peak exposures levels, an exposure scenario for which EPA acknowledges (p. 5-91) that no meaningful URF applicable to environmental concentrations can be calculated.

Conclusions Regarding the Leukemia and Hodgkin Lymphoma URFs

In summary, the draft URFs for leukemia and Hodgkin lymphoma based on cumulative exposure are not scientifically defensible (e.g., lack of dose-response). If a relationship does exist, it appears to be with peak exposure, and EPA indicates that it is not clear how to extrapolate risk estimates based on the peak exposure estimates to meaningful estimates of lifetime extra risk of cancer from environmental exposures. However, in effect this is exactly what EPA did, extrapolating apparently peak-associated risk to lifetime extra cancer risk by using a dose metric (cumulative exposure) for which there is no dose-response, resulting in URFs of highly questionable meaning. Clearly, EPA should redact these draft URFs. Alternatively, EPA should provide a robust justification for the need to derive URFs for leukemia and Hodgkin lymphoma in the absence of a dose-response for cumulative exposure and scientific defensibility.

Formaldehyde Exposure, Leukemia, and Lymphohematopoietic Cancers

Findings regarding associations between formaldehyde and leukemia are inconsistent across studies, and whether formaldehyde is capable of causing lymphohematopoietic malignancies is not scientifically established and is of great scientific debate and controversy. TCEQ disagrees with EPA (p. 4-535) that human epidemiological evidence is sufficient to conclude a causal association between formaldehyde exposure, leukemia, and lymphohematopoietic cancers as a group considering the inconsistency of the associations, the weakness of the associations as demonstrated by the RRs and confidence intervals discussed above for the principal study used by EPA, and biological implausibility considerations. As additional examples, for the cohorts summarized by EPA (pp. 4-493 to 4-495), no standardized mortality ratios (SMRs) for lymphohematopoietic cancers are greater than 3, with only 1 of 18 greater than 2, indicating a very weak association if any. In fact, 5 of 18 SMRs are less than 1 and 67% of the SMR confidence intervals include 1, consistent with a lack of association. For leukemia, only 3 of the 21 SMRs exceed 2, with 5 being less than 1, overall consistent with a lack of association. Additionally, in 100% of the cases where leukemia SMR confidence intervals are given they include 1. EPA should weigh the human epidemiological evidence more carefully before deciding to calculate URFs based on the Beane Freeman et al. (2009) study where the association was with peak exposure and not the cumulative exposure dose metric used by EPA (a separate issue).

Implications of Lu et al. (2010) for EPA URF Development

A well-conducted study by Lu et al. (2010) has very recently been able to clearly differentiate between endogenous and exogenous formaldehyde-induced DNA adducts and DNA-DNA cross-links, allowing the quantitative examination of formaldehyde-induced adducts and cross-links in a multitude of tissues following inhalation exposure. This study shows that even in rats exposed to much higher concentrations (10,000 ppb) than environmental exposures of humans, exogenous formaldehyde-induced adducts and cross-links only occur in the rat nasal mucosa (the clear target site of rat carcinogenesis) and not at sites remote to the portal of entry. In other words, this study clearly shows that exogenous formaldehyde-induced genotoxic effects at sites remote to the portal of entry are implausible. Additionally and directly relevant to the hypothesis by EPA and others that hematopoietic stem cells/early progenitor cells in the circulation or residing in the nasal passages may be exposed in the nose and travel to the bone marrow to be transformed into leukemia cells (e.g., pp. 4-529 to 4-535), Lu et al. (2010) used a very sensitive method (the method could detect levels ≈ 30 times less than the number of adducts from endogenous formaldehyde) to show that neither white blood cells nor bone marrow contained exogenous formaldehyde-induced DNA adducts (or cross-links). The EPA draft IRIS review gives no serious evaluation of the significant implications of these study results for the scientific defensibility of deriving URFs for Hodgkin lymphoma and leukemia. The significant implications of this recent research are inconsistent with deriving URFs for Hodgkin lymphoma and leukemia and were simply ignored in the draft IRIS review document.

Regression Coefficient for Nasopharyngeal Cancer

EPA utilizes a regression coefficient (β) based on nasopharyngeal cancer *mortality* to calculate the URF for nasopharyngeal cancer *incidence* (pp. 5-83 to 5-84). However, the survival rate for nasopharyngeal cancer is significant (≈ 50%), and no robust justification is provided for the assumption or expectation that nasopharyngeal cancer mortality and incidence share the same dose-response relationship and therefore use of a β based on mortality is justified for incidence.

Application of Age-Dependent Adjustment Factors

EPA indicates that: (1) there is an adequate weight of evidence to consider formaldehyde-induced mutations relevant to human carcinogenic risk (p. 6-24); (2) that formaldehyde carcinogenicity can be attributed, at least in part, to a mutagenic mode of action (MOA) (p. 6-25); and (3) therefore, age-dependent adjustment factors (ADAFs) should be applied in accordance with EPA guidance (EPA 2005b) (p. 5-104). However, EPA provides no discussion concerning the scientific defensibility of applying ADAFs derived from data for mutagenic carcinogens to a chemical like formaldehyde with a mixed MOA for which EPA has only determined that mutagenicity plays a part.

Implementation-Based Comments:

Implications of the URF for Ambient and Indoor Air

TCEQ notes that the 1 in 100,000 excess risk air concentration of 0.08 ppb based on the draft URF is not met anywhere in the world, indoors or outdoors (or in our own breath). This includes remote locations such as Alert, Nunavut, Canada, located in the arctic only 500 miles from the north pole (average of 0.4 ppb), and the remote South Pacific island of Eniwetok Atoll (average of 0.4 ppb) (IARC 2006). The

average reported for Alert, Nunavut is based on data collected during polar night, a time during which contributions from photochemical oxidation of hydrocarbons would be negligible.

TCEQ risk-based air monitoring comparison values are set at an excess risk level of 1 in 100,000. Using the draft URF and a 1 in 100,000 air concentration (0.08 ppb) would mean that formaldehyde levels at the arctic's Alert, Nunavut and the South Pacific's remote Eniwetok Atoll island would need to be reduced by a factor of at least 5 times. Even the 1 in 10,000 excess risk air concentration of 0.8 ppb based on the draft URF is almost not met anywhere in the world, with a few exceptions such as remote locations like Alert, Nunavut and Eniwetok Atoll (averages of 0.4 ppb) (IARC 2006). As levels of formaldehyde in indoor air are often significantly higher than levels outdoors, indoor air concentrations would be expected to significantly exceed (i.e., at least by an order of magnitude) even the 1 in 10,000 excess risk air concentration (IARC 2006). Use of the draft URF would imply that air neither indoors nor outdoors (or even your own breath, see below) is safe from a regulatory perspective.

Implications of the URF for Endogenously-Produced Formaldehyde

Formaldehyde is produced endogenously in the human body. TCEQ notes that the air concentration corresponding to the upper end of the EPA acceptable risk range (1 in 10,000 excess cancer risk) using the draft URF is 0.8 ppb (p. 5-143). However, even this highest regulatory-acceptable air concentration is over 5 times lower than the median normal human breath level (4.3 ppb) reported in 344 healthy men and women (positive alveolar gradient, negligible room air concentrations reported in Moser et al. 2005), and is 50 times lower than the reported 97.5th percentile normal formaldehyde breath level (40 ppb). At face value, use of this draft URF and data imply that formaldehyde breath levels resulting from normal endogenous production would clearly represent an unacceptable level of risk from a regulatory perspective (e.g., risk of 5.4E-04 to 5.0E-03 using EPA's draft URF and the median and 97.5th percentile normal breath levels). Using the lower end of the acceptable risk level (1 in 1,000,000), the corresponding air concentration is 0.008 ppb, which is 537 times lower than the median reported breath level and 5,000 times lower than the 97.5th percentile normal formaldehyde breath level (positive alveolar gradient, negligible room air concentrations reported in Moser et al. 2005). Regulating formaldehyde at concentrations anywhere from 5-5,000 times lower than normal breath concentrations presumably resulting from normal endogenous production simply makes no sense as it offers insignificant risk reduction compared to the risk which would result from normal breath levels due to endogenous production (assuming there is in fact risk at these levels).

References

Beane-Freeman, LE; Blair, A; Lubin, JH; et al. (2009) Mortality from lymphohematopoietic malignancies among workers in formaldehyde industries: the National Cancer Institute cohort. J Natl Cancer Inst 101:751–761.

International Agency for Research on Cancer (IARC). 2006. IARC monographs on the evaluation of carcinogenic risk of chemicals to humans. Vol. 88: Formaldehyde, 2-butoxyethanol, and 1-tert-butoxypropan-2-ol. World Health Organization, Lyon, France.

Moser B, Bodrogi F, Eibl G, et al. 2005. Mass spectrometric profile of exhaled breath-field study by PTR-MS. Respir Physiol Neurobiol 145:295-300.

U.S. Environmental Protection Agency (EPA). 2005a. Guidelines for Carcinogen Risk Assessment. Risk Assessment Forum. Washington, DC: EPA/630/P-03/001B.

U.S. Environmental Protection Agency (EPA). 2005b. Supplemental Guidance for Assessing Susceptibility from Early-Life Exposure to Carcinogens. Washington, DC: EPA/630/R-03/003F.

Attachment B – TCEQ Comments on EPA Arsenic Assessment

Texas Commission on Environmental Quality
Comments Regarding the United States Environmental Protection Agency
Draft Toxicological Review of Inorganic Arsenic: In Support of the Summary Information on the Integrated Risk Information System (IRIS)
Notice of Public Comment Period
75 FR 7477, February 19, 2010
Docket ID No. EPA–HQ–ORD–2010–0123

The Texas Commission on Environmental Quality (TCEQ) provides the following comments on the United States Environmental Protection Agency (USEPA) announcement of the public comment period regarding its *Draft Toxicological Review of Inorganic Arsenic: In Support of the Summary Information on the Integrated Risk Information System (IRIS).*

On February 19, 2010, the USEPA published a Federal Register notice of a 60-day public comment period (ending April 20, 2010) for the *Draft Toxicological Review of Inorganic Arsenic: In Support of the Summary Information on the Integrated Risk Information System (IRIS)* (Federal Register/Vol. 75, No. 33/Friday, February 19, 2010/Notices). USEPA will only guarantee that comments submitted by March 26, 2010, will be provided to the Scientific Advisory Board in time for their meeting to consider the final draft EPA document. This final draft USEPA document (EPA/635/R-10/001) derives an oral slope factor (SFo) for arsenic to ultimately be published on IRIS. To the extent practicable in the time allotted by USEPA, Toxicology Division staff of the TCEQ have developed comments for USEPA consideration.

60-Day Public Comment Period

The 60-day comment period is insufficient for regulatory agencies and others to provide meaningful comments based on an in-depth review and analysis of the derivation of the final draft SFo. There is great complexity associated with multiple issues relevant to the assessment of arsenic risk due to oral exposure. The final draft document alone is 575 pages, with the Science Advisory Board (SAB) comments on three USEPA documents relevant to USEPA's final draft arsenic assessment being almost another 100 pages, and hundreds of pages (at a bare minimum) of other documents (e.g., National Research Council 1991 and 2001 reviews) and studies relevant to the assessment of risk due to oral arsenic exposure. Given the complexity and volume of relevant materials, it is impracticable for USEPA to expect detailed specific comments from external experts given the short period allowed for a critical review of the document and procedures employed by USEPA. To exacerbate the short review time problem, the 5-day Society of Toxicology 49th Annual Meeting (March 7-11) and the 3-day Alliance for Risk Assessment dose-response conference (*Beyond Science and Decisions: From Issue Identification to Dose-Response Assessment*, March 16-18) fall within the review period, and TCEQ staff and many other external expert peer reviewers will be in attendance. The 60-day comment period only allows a cursory review of the document at best, leads to a less-than-desirable level of peer review and transparency, and undermines confidence in the final draft SFo value. Consequently, TCEQ is only able to provide preliminary comments on the final draft SFo value, barely scratching the surface of the document. The comment deadline should be extended at least 60 days past the current April 20th deadline to allow for a detailed review of the hundreds of pages of documents (at a bare minimum) and complex issues relevant to derivation of the final draft SFo for arsenic.

Arsenic SFo

The final draft SFo of 25.7 per mg/kg-day represents a 17-fold increase over the SFo currently on IRIS (1.5 per mg/kg-day). This is a significant change in the estimated carcinogenic potency of arsenic. Arsenic already has a relatively high SFo and such a large change would have far reaching regulatory implications. Thus, the final draft SFo deserves greater scrutiny than allowed by the 60-day public comment period. In addition to TCEQ's concerns, we understand both external groups and internal USEPA staff have expressed serious concerns about the final draft SFo. Brief discussions of four areas of TCEQ concern relevant to the toxicological basis for the derivation of the final draft SFo are provided below. This discussion is followed by comments on some practical implications that highlight the importance of EPA developing a scientifically-defensible SFo for arsenic.

Toxicological Concerns with the Final Draft Arsenic SFo

Water Intake and Non-water Arsenic Intake

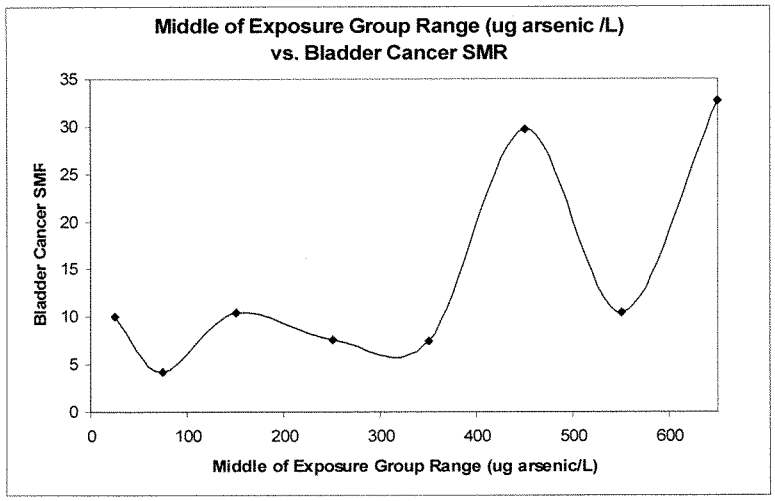
The final draft USEPA document acknowledges that there is significant uncertainty associated with water intake (e.g., see page 117 "few precise data," "limited information"; page 120 "drinking water exposure information is not available for individual study subjects") and non-water arsenic intake (e.g., see page 118 "relatively little data," "considerable confusion about" how to include this; page 123 "data supporting this value are scarce") for the exposed Taiwanese populations. Data on variations in arsenic drinking water levels with time are also lacking. TCEQ believes it unreasonable to exclude arsenic intake from water used for cooking rice and produce (e.g., rice and yams are staples) from dietary intake for exposed populations for the primary analysis as indirect water intake estimates are around 1 L/day (page 124), significantly underestimating dose. Additionally, there are no drinking water arsenic data for the reference populations, and TCEQ has serious concerns about the reasonableness of assuming zero arsenic drinking water intake for reference populations. TCEQ also has significant concerns about assuming the same non-water arsenic intake (10 μg/day) for both the reference and exposed populations given that USEPA acknowledges that exposed populations may be exposed to 15-211 μg/day (50 μg/day average) from food (page 123). The examination of such issues in a sensitivity analysis does not alleviate USEPA's duty to derive the most accurate SFo possible in the primary analysis by incorporation of the most informed estimates possible for factors known to be critical for derivation of a reasonably predictive SFo (e.g., population-specific factors influencing total dose such as indirect water and food intake).

USEPA appears to lack data sufficient to establish the extent to which total arsenic exposure (i.e., dose) differed for the exposed and "nonexposed" populations, making derivation of a reasonably accurate SFo problematic. Accurate water intake and non-water arsenic intake data are critical in deriving defensible dose estimates and a scientifically-defensible carcinogenic assessment, but are lacking. The admitted absence of accurate dose estimates due to lack of good water intake and non-water arsenic intake data precludes the conduction/derivation of an accurate dose-response assessment and SFo.

Dose-Response Data

USEPA used lung and bladder mortality data from Morales et al. (2000) for the dose-response assessment for the final draft SFo. Morales et al. (2000) uses these mortality data to calculate standardized mortality ratios (SMRs) and notes, "Although the computed SMRs display a large amount of noise, there appear to

be higher SMRs at high exposure levels compared to exposures in the lower range, especially for bladder and lung cancer." To say that there is "noise" in the SMRs over the eight exposure categories is an understatement. Dose-response is the cornerstone of toxicology, but the lung and bladder mortality data (SMRs) from Morales et al. (2000) provide a poor basis for dose-response assessment as a dose-response is not apparent and not monotonic. Breaking the data down into the form of age-specific person-years at risk and cancer deaths does not improve the basis for dose-response assessment; it only obscures the lack of a good dose-response which is readily apparent from examination of the SMRs. For example, for lung cancer, SMRs greater than 3 were essentially only obtained for drinking water levels greater than 400 µg/L, which does not indicate a particularly strong dose-response. Even at 500-600 µg/L, the SMR was only 3.32. For bladder cancer, the dose-response data from Morales et al. (2000) and used by USEPA do a poor job of characterizing the shape of the dose-response curve, as can be seen from the figure below (line added for emphasis).



The cancer guidelines (USEPA 2005) recommend use of enough dose groups to provide an indication of the shape of the dose-response curve, as characterization of the shape of the dose-response curve is important in providing relevant dose-response data for assessing human risk. A relatively large exposure range should make it relatively easy to discern the shape of any underlying dose-response curve in a well-conducted study. However, despite the eight exposure groups in Morales et al. (2000), the figure above illustrates that the shape of the dose-response curve for bladder cancer, which had the highest SMRs by far, has not been adequately defined by the dose-response data selected by USEPA for derivation of the SFo. As an example, the SMR for the 0-50 µg/L exposure group (plotted at 25 µg/L) is higher than that for the 300-400 µg/L exposure group (plotted at 350 µg/L), and similar to that for the 500-600 µg/L exposure group (plotted at 550 µg/L). The ability to fit a line through data points does not necessarily mean that the underlying data adequately define the shape of the dose-response curve, including the

critical low dose region. Based on the above considerations, the underlying data modeled by USEPA provide a poor basis for dose-response assessment.

Biological Effects of Ionizing Radiations (BEIR) IV Model

Appendix E to the final draft USEPA document indicates that a modified BEIR IV model was used, which takes as inputs the dose-response "b" coefficient, background cancer incidence data, and age-specific mortality data, to estimate bladder and lung cancer incidence for the US population. A modification by Gail et al. (1999) was used to obtain estimates of incidence within multi-year age strata, which itself would have associated uncertainty. The short time allotted for review is inadequate for a full examination of the appropriateness of the modified BEIR IV methodology used by USEPA (and a plethora of other potential issues). However, generally, the BEIR IV methodology for calculating excess risk is mathematically correct only when the specified response is mortality and mortality rates are used, not when the specified response is mortality and incidence rates are used, or when the specified response is incidence and incidence rates are used with BEIR IV equations which have not been appropriately derived for incidence. The beta or "b" value used by USEPA for *incidence* calculations at a given dose is based on *mortality* (pages 127, E-1), which is inappropriate. Additionally, BEIR IV equations are for mortality and may not be used for incidence without modification (i.e., derivation of appropriate BEIR IV equations specifically for incidence). This potential error is demonstrated in Appendix 1 to these comments. Although time did not allow for a more detailed review, USEPA does not indicate that any specific alterations were made to BEIR IV equations to account for incidence as the response. Therefore, TCEQ believes that USEPA may have used inappropriate BEIR IV methodology.

Some Practical Implications of Final Draft Arsenic SFo

USEPA's Soil Screening Levels

The current USEPA regional screening level (RSL) for inorganic arsenic in residential soil is 0.39 mg/kg. The US Geological Survey reports the mean for arsenic in soil is 7.2 mg/kg (ATSDR 2007), and TCEQ uses a median background arsenic concentration for Texas soils of 5.9 mg/kg. Thus, the current residential soil RSL is already 18 times less than typical background soil arsenic concentrations. Adoption of the final draft SFo would reduce the current USEPA residential soil RSL by a factor of 17 to approximately 0.02 mg/kg at a conservative target excess risk level of 1 in 1,000,000. Even a residential soil RSL of 2 mg/kg corresponding to the upper end of the USEPA acceptable risk range (1 in 10,000) using the final draft SFo would be below typical background concentrations, making achievement of acceptable risk as defined by USEPA practically impossible at remediation sites. More importantly, this analysis would imply that typical naturally-occurring levels of arsenic in residential soil are unsafe for human contact.

In regard to individual excess lifetime cancer risk (IELCR), USEPA states on their website (http://www.epa.gov/oust/rbdm/sctrlsgw.htm)), "The IELCR represents the incremental (over background) probability of an exposed individual's getting cancer (i.e., a risk occurring in excess of or above and beyond other risks for cancer such as diet, smoking, heredity). Cleanup standards calculated on the basis of excess risk limits correspond to *allowable levels in excess of the background concentrations of the chemicals of concern normally present in the source media*" (emphasis added). Since regulatory agencies are concerned with regulating excess risk (i.e., risk over natural background), the risk due to

naturally-occurring background soil arsenic levels should be excluded from comparisons to the USEPA acceptable risk range. In effect, this is typically accomplished by USEPA acknowledging that although above the RSL or proposed remediation goal (PRG), soil arsenic levels at a remediation site are within background so no action is necessary in regard to arsenic. In a more strict sense, however, since per USEPA regulatory agencies calculate cleanup values based on excess risk over background, the soil RSL/PRG could be added to a representative background concentration to derive a comparison value which represents a regulatory acceptable level of excess risk (i.e., risk over background).

Implications for Food and Drinking Water Safety: Typical Dietary Exposure, Rice Consumption, Drinking Water, and Fish/Shellfish Consumption as Examples

A scientifically-defensible and realistic dose-response assessment for inorganic arsenic is critical given the grave implications of the final draft SFo for the US food and water supply. The examples below illustrate how estimates of risk due to dietary exposure to inorganic arsenic using the final draft SFo may have dire consequences on the perceived safety of US food and drinking water.

Typical Dietary Exposure

Using the final draft SFo for inorganic arsenic results in excess cancer risk estimates from dietary exposure exceeding the USEPA acceptable risk range (1 in 1,000,000 to 1 in 10,000). ATSDR (2007) reports the mean average US adult intake of inorganic arsenic is around 10.22 µg/day (range of 0.93-104.89 µg/day) based on a study (MacIntosh et al. 1997) which utilized residue data collected for the Food & Drug Administration Total Diet Study. Using the final draft SFo, excess calculated cancer risk would range from about 3.4 in 10,000 to 3.9 in 100, with an average calculated risk of about 3.8 in 1,000 due to dietary exposure. Even the calculated risk associated with the lower end of dietary inorganic arsenic exposure (3.4 in 10,000) would exceed the upper end of the USEPA acceptable risk range (1 in 10,000), and the calculated risk associated with the high end of dietary exposure would be 390 times the upper end of acceptable risk. Such analyses would imply that the US diet results in arsenic risk that is considered unsafe from a regulatory perspective.

Rice Consumption

In regard to eating rice specifically, the average excess risk for US adult (70 kg) rice eaters would be calculated at around 1.7 in 1,000 based on an average intake of 61.2 g dry rice/day (around 1 cup cooked) based on National Health & Nutrition Examination Survey data (Batres-Marquez and Jensen 2005) with 0.276 µg total arsenic/g US white rice and 27% of the total arsenic as inorganic arsenic (Williams et al. 2005). Even using a US adult average for rice intake that includes non-rice eaters (11.4 g dry rice/day) would still result in an excess risk of 3.1 in 10,000 for white rice, which exceeds the upper end (1 in 10,000) of USEPA's risk management range. Risk estimates would be higher for US brown rice than white rice due to a higher average percentage of total arsenic being inorganic (51%) (Williams et al. 2005), with average excess risk for US adult rice eaters being around 2.6 in 1,000 (26 times higher than the upper end of USEPA's risk management range). Such analyses would imply that rice and other food items (e.g., fish/shellfish) are unsafe for human. Consequently, there may be a potential for unwarranted advisories or warning labels on certain foods.

Drinking Water

Another implication of the draft final SFo is that the water used to prepare the rice (see example above) is itself by this calculation unsafe for human consumption. Drinking water in the US generally contains an average of 2 μg/L of arsenic (ATSDR 2007). Based on final draft SFo estimates, USEPA indicates that drinking water concentrations corresponding to 1 in 10,000 combined cancer risks for males and females are 0.21 and 0.14 μg/L, respectively. The implication is that on average all across the US, people's drinking water contains arsenic levels that exceed the upper end of the USEPA acceptable risk range (1 in 10,000) by approximately 10-14 times. In other words, on average, the level of arsenic in the nation's drinking water supply is unsafe.

For bladder cancer alone, the incidence risk calculated by USEPA based on final draft values for males/females is 3.1E-04 per μg/L. Therefore, based on 2 μg/L as an average drinking water concentration, the estimated bladder cancer risk for the US population would be 6.2 per 10,000 or 62 per 100,000. However, the actual occurrence of bladder cancer in the US is about 23 cases per 100,000 (males/females combined). It would take 3 times the actual bladder cancer incidence for US males/females combined to even make possible the 62 cases per 100,000 estimated due to arsenic exposure from drinking water alone. Thus, the incidence risk calculated by USEPA final draft values for bladder cancer appears to be inaccurate and overly conservative. Proceeding with this SFo will unnecessarily alarm the public by giving a greater perception of harm and risk than is actually taking place.

Fish/Shellfish Consumption

Shellfish and other marine foods contain the highest arsenic concentrations and are the largest dietary source of arsenic. Based on an FDA Total Diet Study, ATSDR (2007) reports that concentrations in canned tuna, fish sticks, haddock, and boiled shrimp were 0.609-1.470, 0.380-2.792, 0.510-10.430, and 0.290-2.681 mg/kg dry weight, respectively. The foods with the highest mean arsenic levels were haddock, canned tuna, fish sticks, shrimp, and fish sandwiches, with arsenic concentrations ranging from 0.568-5.33 mg/kg dry weight. Most recent studies show an arsenic concentration range of 0.82-37 mg/kg dry weight for fish (e.g., flounder, cod, sole, tuna), mussels, clams, oysters, shrimp, and blue crab, including fish, blue crabs, shrimp, mussels, and oysters from Texas (0.82-9.67 mg/kg) (see Galveston Bay/Gulf of Mexico results in Table 6-4 of ATSDR 2007).

The general consensus in the literature is that approximately 10% of the arsenic in the edible parts of marine fish and shellfish is inorganic arsenic (ATSDR 2007). A 10% adjustment to these reported arsenic levels in fish yields an inorganic arsenic concentration range of 0.029-3.7 mg inorganic arsenic/kg dry weight. Using the final draft SFo, a saltwater fish ingestion rate of 15 g/day (only two fish meals per month approximately), and an adult body weight (70 kg), the fish tissue concentration corresponding to the upper end of the USEPA acceptable risk range (1 in 10,000) is 0.017 mg inorganic arsenic/kg dry weight. The range of estimated inorganic arsenic levels in all these fish/seafood items (0.029-3.7 mg inorganic arsenic/kg) exceeds the fish tissue concentration calculated at the upper end of acceptable excess risk (1 in 10,000) using the final draft SFo. Regarding Texas specifically, the range of estimated inorganic arsenic levels in Galveston Bay/Gulf of Mexico seafood (0.082-0.967 mg/kg dry weight based on Table 6-4 in ATSDR 2007) is 5-57 times higher than the fish tissue concentration (0.017 mg/kg) calculated at the upper end of acceptable excess risk using the final draft SFo. These analyses would

imply that fish/shellfish in the US diet are unsafe for human consumption from a regulatory perspective. In turn, a determination of unacceptable risk due to arsenic in fish tissue would likely cause more waterbodies to be listed as impaired unnecessarily. As a result, there could be future inappropriate regulatory actions and unneeded expenditure of resources to investigate and try to reduce arsenic. There could also be negative public health consequences from such impairments, because fish consumption and the associated health benefits would decrease due to the false perception that arsenic is making fish unsafe to eat.

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Attachment C – TCEQ Comments on EPA Hexavalent Chromium Assessment

Texas Commission on Environmental Quality
Comments Regarding the U.S. Environmental Protection Agency
Draft Toxicological Review of Hexavalent Chromium in Support of
Summary Information on the Integrated Risk Information System (IRIS)
Notice of Public Comment Period and Listening Session
75 FR 60454, September 30, 2010
Docket ID No. EPA-HQ-ORD-2010-0540

On September 30, 2010, the U.S. Environmental Protection Agency (EPA) published a Federal Register notice (Federal Register/Vol. 75, No. 189/Thursday, September 30, 2010/Notices) of a 60-day public comment period (ending November 29, 2010) for the, "Draft Toxicological Review of Hexavalent Chromium in Support of Summary Information on the Integrated Risk Information System (IRIS)," hereafter referred to as the draft assessment (EPA/635/R-10/004A). On November 10, EPA extended the comment deadline 30 days to December 29, 2010 (Federal Register/Vol. 75, No. 217/Wednesday, November 10, 2010/Notices). The draft IRIS assessment provides a draft oral slope factor (SFo of 0.5 per mg/kg-day) based on small intestine tumors in male mice in the National Toxicology Program (NTP 2008) drinking water study. The Texas Commission on Environmental Quality (TCEQ) has developed comments on the draft assessment to the extent practicable in the time allotted by EPA, focusing on the draft SFo, and provides the following comments for EPA consideration.

General Comments:

The assessment of the carcinogenic potential of hexavalent chromium (CrVI) has great implications in a regulatory context. Given their important role in the protection of public health, EPA regulatory risk assessors have a duty to perform the most scientifically-defensible assessments possible while giving careful and due consideration to comments and recommendations from other regulatory agencies, the public, external experts, stakeholders, etc. Although regulatory risk assessors have a penchant for erring on the side of health-protectiveness and conservative defaults, if erring on the side of conservatism significantly overestimates risk or hazard and is not fully justified, then harm to public health may result from diverting public, industry, and government attention and resources away from chemicals that may represent more of a public health risk at environmental levels. Therefore, TCEQ encourages EPA to give full, thoughtful, and careful consideration and evaluation to comments and recommendations from TCEQ, other regulatory agencies, the public, and external experts.

TCEQ is concerned that recent draft EPA assessments (e.g., dioxin, arsenic, formaldehyde) along with the draft CrVI assessment seem to demonstrate a pattern where the EPA timeline is sufficient for a less-than-desirable level of initial EPA analysis but insufficient: (1) for the public to be able to provide fully detailed comments on the many shortcomings of the draft assessments; (2) for EPA to seriously and meaningfully evaluate the scientific merit of public comments; (3) for EPA to conduct the additional analyses required to fully respond to public comments and appropriately revise the draft assessment based on the scientific merit of comments; and (4) for EPA to conduct the fully credible, balanced, and transparent assessment the public deserves where the effects of the significant uncertainties associated with certain key decisions and procedures are fully examined qualitatively and quantitatively. Such shortcomings undermine the confidence of States and other parties who often rely on EPA toxicity factors

and over time, will tend to marginalize EPA in terms of a reliable source for scientifically objective, defensible, and predictive toxicity factors. This may be one reason States are progressively deriving more toxicity factors as opposed to relying on EPA assessments, which often rely heavily on a penchant for default procedures representing a seemingly nonobjective and insurmountable hurdle for alternative analyses strongly supported by data (e.g., nonlinear dioxin carcinogenicity assessment, cytotoxicity-induced regenerative cell proliferation carcinogenic mode-of-action (MOA) for formaldehyde-induced respiratory tract cancer).

90-Day Comment Period:

The 90-day comment period is insufficient for regulatory agencies and others to provide the most thorough and meaningful comments possible based on an in-depth review and analysis of the draft IRIS assessment. There is great complexity associated with multiple issues relevant to the assessment of CrVI risk and hazard. The draft IRIS assessment alone is 300 pages, and there are hundreds of pages (at a bare minimum) of other documents and studies relevant to the assessment of CrVI risk and hazard. Given the complexity and volume of relevant materials, it is impracticable for EPA to expect detailed specific comments from external experts given the short period allowed for a critical review of the draft assessment and more specifically, the procedures, calculations, and supporting arguments employed by EPA therein. Given that external experts cannot devote all their time to review and comment, the 90-day comment period only allows a superficial review of the draft assessment at best, leads to a less-than-desirable level of transparency and peer review, and undermines confidence in the process. Consequently, TCEQ is only able to provide comments based on a cursory review. If EPA seeks more detailed and meaningful public input and technical comments, at a minimum EPA should extend the comment period at least 30 days past the December 29 deadline to allow stakeholders to: (1) perform a more detailed review of the volumes of relevant information; (2) more fully examine statistical procedures and the rationale and scientific support for key EPA decisions and analyses; and (3) provide more detailed specific comments on all problematic issues associated with the draft IRIS assessment.

Toxicology-Based Comments:

Biological Plausibility of a Mutagenic Carcinogenic MOA and Exceedance of the Mouse Gastrointestinal (GI) Tract Reductive Capacity

EPA's conclusion that mutagenicity (and consequently carcinogenicity) can occur at doses within GI reductive capacity relied on an entirely speculative mouse reductive capacity, flawed arguments, and is not scientifically sound. When discussing data supportive of the hypothesized mutagenic MOA for CrVI (and default linear, low-dose extrapolation by corollary), EPA admits that overwhelming the GI reductive capacity of the mouse is a plausible explanation for CrVI-induced genotoxicity following sufficiently high mouse oral exposure. By corollary, overwhelming the mouse's GI reductive capacity is a plausible explanation for CrVI-induced carcinogenicity in the NTP (2008) drinking water study. However, EPA wholly rejects this "plausible explanation" (p. 207) since, "there are inconsistencies."

Firstly, all studies are rarely (if ever) 100% consistent, and lack of 100% consistency does not preclude sound conclusions based on best scientific judgment and consideration of all relevant data in a weight of evidence approach. For example, there are inconsistencies with CrVI being genotoxic *in vivo* and *in vitro*

since not all results are positive (see Tables 4-23 and 4-21 of draft assessment), but this certainly does not (and should not) preclude EPA from concluding that CrVI is genotoxic (see Section 4.7.3.4).

Secondly, as evidence that exceedance of the mouse GI reductive capacity is not required for genotoxicity and carcinogenicity, EPA indicates that: (1) the average rate of CrVI exposure at even the highest dose in the NTP (2008) study was within the "estimated" reductive capacity of the mouse GI tract; (2) Devi et al. (2001) found positive genotoxicity results in leukocytes at doses > 10-fold lower than those used in the NTP study and within the "estimated" reductive capacity of the mouse; and (3) Stout et al. (2009) did not find an upward inflection (threshold) point in nonlinear data (tissue concentration and/or mouse small intestine neoplasm data) as evidence of where dose may have saturated reductive capacity. However, regarding (1) above, *the "estimated" mouse GI reductive capacity is entirely speculative* (scaling from humans to mice with body weight ($BW^{3/4}$)). In fact, EPA elsewhere (p. 211) states, "data are not available for the reductive capacity of the mouse." Regarding (2), the Devi et al. (2001) study was an oral gavage study while the speculative GI reductive capacity was calculated on an hourly basis. Thus, *a direct comparison of the speculative hourly mouse reductive capacity and the bolus doses in the Devi et al. gavage study is not appropriate*. Additionally, the positive results for leukocytes examined in Devi et al. (2001) are of questionable relevance for the carcinogenic MOA compared to the entirely relevant negative genotoxicity findings in the cancer target tissues examined in De Flora et al. (2008). *The DNA damage demonstrated by Devi et al. (2001) in mouse leukocytes does not result in cancer-causing mutations in that tissue, much less demonstrate how CrVI causes cancer in actual target tissues where De Flora et al. (2008) did not find DNA damage,* even at drinking water concentrations 50 and 200 times the federal maximum contaminant level (MCL) (i.e., "brightly yellow" levels). Regarding (3) above, Stout et al. (2009) also relied upon the speculative mouse GI reductive capacity to conclude that the absence of an upward inflection point in nonlinear data did not support a threshold. However, as the "estimated" mouse reductive capacity is entirely speculative, no scientifically sound conclusions can be made by Stout et al. (2009) or EPA based on it. *It is more plausible that all doses exceeded actual mouse GI reductive capacity (see TCEQ comments below).* Therefore, all data used by Stout et al. are from points on the dose-response curve higher than the inflection point, making the observance of an inflection point impossible. *Contrary to the draft assessment, EPA cannot make sound scientific conclusions concerning the relationship between GI reductive capacity and the potential for genotoxicity and/or carcinogenicity in the absence of actual mouse GI reductive capacity data or similarly informative data.*

Overwhelming the reductive capacities of the mouse and rat GI tracts remains a plausible explanation for the carcinogenicity observed in NTP (2008). There are data which are informative concerning whether or not mouse GI reductive capacity was exceeded at the NTP (2008) study doses. More specifically, NTP (2007) provides evidence of CrVI absorption in mice at around 10 mg/L and higher in drinking water (see blood results in Table G1), but not at lower doses. This evidence strongly suggests that GI reductive capacity was exceeded by all mouse doses (14.3-267 mg/L) in the NTP (2008) study. In regard to rat reductive capacity and the oral carcinogenicity observed in NTP (2008), NTP (2007) (see blood results in Table G1) and Sutherland et al. (2000) provide evidence of CrVI absorption in rats at around 10 mg/L and higher in drinking water, but not at lower doses. Similar to the mouse, these rat results strongly suggest that reductive capacity was exceeded by all rat doses (14.3-516 mg/L) in the NTP (2008) study. *Thus, for both mice and rats, EPA had data strongly suggesting that NTP (2008) doses exceeded GI reductive capacity.* Had the NTP (2008) doses associated with 14.3-516 mg/L truly been within actual GI reductive capacity, CrVI would have been effectively reduced to CrIII and significant absorption into the

bloodstream would not have occurred in NTP (2007) at water levels around ≥ 10 mg/L. Instead of relying on these actual data, EPA relied on a speculative mouse reductive capacity estimate to make a key decision and conclude that mutagenicity (and consequently carcinogenicity) can occur at doses within the GI reductive capacity. *For EPA to admit that overwhelming the reductive capacity of the mouse GI tract was likely responsible for the carcinogenicity observed in NTP (2008) would inconveniently put EPA off the linear, low-dose extrapolation pathway with issues EPA is ill-prepared to address quantitatively within this carcinogenic assessment* (e.g., doses at which the mouse and human GI reductive capacities are exceeded (thresholds for carcinogenicity), human relevance of the mouse tumors given exceedance of the mouse GI reductive capacity and given truly environmentally relevant lifetime human doses), *especially given the lack of data necessary to address some of these issues* (e.g., lack of species-specific GI reductive capacity data).

The above comments highlight serious shortcomings in EPA's story about exceedance of the mouse GI reductive capacity not remaining a plausible explanation for CrVI-induced genotoxicity and subsequent carcinogenicity. EPA's discussion fails to adequately support their conclusions concerning study doses not exceeding mouse GI reductive capacity. *TCEQ notes that for EPA to acknowledge this explanation would be contrary to their use of default linear, low-dose extrapolation (i.e., no biological threshold for CrVI mutagenicity based on stomach/GI reductive capacity) and call into question the human relevance of the mouse tumors observed.*

Human Relevance of the Mouse Tumors

The small intestine neoplasms in mice (and oral cancers in rats) observed in NTP (2008) are of questionable relevance to humans. Reasons include: (1) mouse GI reductive capacity may have certainly been exceeded (e.g., there are no actual mouse GI reductive capacity data, blood data from NTP (2007) suggest that NTP (2008) doses exceeded GI reductive capacity); (2) epidemiological worker data are not supportive; and (3) the NTP (2008) study doses are not relevant to the truly low, typical environmental doses. The issue in (1) was discussed in TCEQ comments above.

Regarding (2), *epidemiological worker data do not support elevated GI cancer risk.* A meta-analysis of thirty-two CrVI worker studies (Gatto et al. 2010) showed no significant increase in GI tract cancers (although a much smaller highly-exposed subgroup had slightly elevated esophageal cancer). Additionally, none of the studies reported statistically elevated oral cavity or small intestine risk. For example, the meta-analysis included GI tract cancer data obtained from the study authors of Luippold et al. (2003) and Gibb et al. (2000), which did not show excess cancers of the GI tract (e.g., stomach, oral). This information is relevant since workers can be exposed to air concentrations sufficiently high that ingestion is significant. For example, 48% and 39% of the chromate workers in Public Health Service (PHS 1953) had yellow tongues and teeth, respectively. Yellow tongues and teeth were not attributable to smoking and yellow tongue scrapings contained chromium (see pp. 76-77 and Figures 10 and 11 of PHS 1953). While this discoloration was due to the ingestion of relatively high oral doses of CrVI by these workers, no excess GI cancers were found in PHS (1953) or in Luippold et al. (2003) or Gibb et al. (2000), which evaluated some of the same workers. Regarding a comparison between worker and NTP (2008) study doses, Gatto et al. (2010) estimated a daily worker oral dose of 0.004 mg/kg-day, which could vary by an order of magnitude in either direction depending on cohort-specific air concentrations and particulate size/solubility. The doses that produced small intestine cancers in mice (and oral cancers

in rats) in NTP (2008) are orders of magnitude higher than this estimated occupational oral dose (whether +/- an order of magnitude). The difference in GI cancer outcome between NTP (2008) and Gatto et al. (2010) and these other worker studies could be that although workers were exposed to estimated oral doses significantly higher than typical environmentally relevant doses, exposure was within the GI reductive capacity of the workers as opposed to the laboratory mice/rats in NTP (2008) exposed to significantly higher doses beyond their GI reductive capacity. *The bottom line is that even in occupational workers exposed to sufficiently high air levels of CrVI as to produce (via ingestion) yellow tongues and teeth in 39-48% of the workers, PHS (1953) looked for but did not find excess GI cancers or any cancer excesses outside the respiratory tract (see p. 56 of PHS 1953), and these study results are supported by other studies as well (e.g., Gatto et al. 2010, Luippold et al. 2003, Gibb et al. 2000).*

In regard to (3), *the NTP (2008) study drinking water doses are not relevant to humans.* For example, the mouse doses (0.38-8.7 mg/kg-day) are 130-3000 times higher than the human adult dose ((0.1 mg/L x 2 L/day)/70 kg = 0.0029 mg/kg-day) at the federal MCL. CrVI drinking water concentration data from Midland, Texas, have been used recently to suggest that the NTP (2008) doses are relevant to human exposures since the lowest cancer-producing dose from the NTP study scaled to humans using $BW^{3/4}$ (0.166 mg/kg-day) is comparable to the estimated human dose at the maximum detected concentration (5.41 mg/L) in Midland (0.155 mg/kg-day) (Collins et al. 2010). However, this comparison is erroneous for several reasons. The NTP (2008) study is a lifetime exposure study where laboratory animals were exposed to a constant concentration in drinking water. By contrast, based on community input to TCEQ, some people in the affected area in Midland were already drinking bottled water due to generally poor water quality (e.g., high total dissolved solids). Additionally, others stopped drinking the water as CrVI concentrations began to rise and the water began to turn yellow around ≥ 1 ppm, which was indicated in the source (TDSHS 2009) cited by Collins et al. (2010) but which the authors for some reason failed to mention. Consequently, public exposure was for far less than a lifetime. Also, although exposure concentrations changed over time, they were significantly lower than the maximum concentration assumed by Collins et al. (2010). Thus, this comparison by Collins et al. (2010) is based on erroneous assumptions in a failed attempt to demonstrate the human relevance of the NTP study doses. Although there is significant uncertainty in how water concentrations changed over time, a more reasonable worst-case scenario might be: 0.7 mg CrVI/L (average) x 2 L/day x 5 years/70 years = 0.0014 mg/kg-day, which is over 110 times less than the lifetime average mouse dose cited by Collins et al. (2010). *The doses on NTP (2008) are hundreds or thousands of times higher than typical environmentally relevant doses. Therefore, for this and other reasons discussed, study results and the draft SFo are of questionable utility and predictive ability for use in risk assessment.*

Disparate EPA Scientific Standards

EPA appears to hold a higher standard for the scientific defensibility of data that do not support a default or pre-determined EPA assessment pathway. For example, in discussing the hypothesized mutagenic carcinogenic MOA, EPA did not consider the De Flora et al. (2008) drinking water study data to be informative about genotoxicity in the cancer target tissues because it was only for 9 months, although it is still a chronic study and genotoxicity/mutagenicity would be expected early in the carcinogenic process if a CrVI produces cancer though a mutagenic MOA. These data would lend weight against a mutagenic MOA and subsequent linear, low-dose extrapolation. Conversely, EPA judged comparisons of entirely speculative estimates of mouse GI reductive capacity to various study doses (e.g., Devi et al. 2001, Stout

et al. 2009) as sufficient to conclude that genotoxicity/mutagenicity can occur at doses within GI reductive capacity, which is needed to justify the absence of a threshold and to assert use of linear, low-dose extrapolation. EPA's selection of relevant study data reflects a bias, where data supporting EPA's default linear, low-dose extrapolation are considered sufficiently conclusive and any data not supporting that approach are dismissed.

In addition to the comments above pertaining to an example of apparent disparate standards applied to data within the CrVI assessment, *there appears to be inconsistency across assessments regarding the data deemed by EPA to be sufficient to support the direction of an assessment.* For example, using EPA's apparent standard of "inconsistency" as applied to data concerning exceedance of GI reductive capacity in the current assessment as sufficient to discount a certain hypothesis as unsupportable (i.e., existence of a biological threshold for CrVI mutagenicity/carcinogenicity based on GI reductive capacity), it is abundantly clear that EPA should have never derived a unit risk factor (URF) for Hodgkin lymphoma and leukemia for formaldehyde in the 2010 draft assessment. Only a minority of epidemiological data support a link, the hypothesized MOA is highly speculative and biologically implausible (e.g., Lu et al. 2010), EPA indicates that there is no way to derive a meaningful URF for environmental exposure where risk is determined by environmentally irrelevant peak exposures, there is no dose-response relationship between cumulative exposure and risk that might have produced a meaningful URF, and yet EPA derived a formaldehyde URF for non-Hodgkins lymphoma and leukemia not only in the midst of inconsistency but of scientific indefensibility. *Disparate standards are even applied by EPA to the same data depending upon whether they support default assessment procedures.* For example, in the 2010 draft dioxin reanalysis, EPA judged AhR-mediated MOA data to sufficiently support the biological plausibility of dioxin being a known human carcinogen, but judged the same MOA data as insufficient to justify the corollary nonlinear carcinogenic assessment. *Overall, this appears to lend support to the existence of a double standard where a high standard is applied to data contrary to a pre-determined path* (e.g., EPA's treatment of De Flora et al. 2008 in the CrVI genotoxicity discussion), *requiring only the interjection of some level of ever-present uncertainty for rejection, while a lower standard is used to judge data that justify the default or desired path* (e.g., EPA's treatment of Devi et al. 2001 and Stout et al. 2009 in the discussion of CrVI GI reductive capacity, EPA's hypothesized MOA and derivation of formaldehyde URFs for Hodgkin lymphoma and leukemia, EPA's treatment of the formaldehyde BBDR model).

In effect, the unequal treatment of data results in "cherry-picking" data, an unbalanced and biased approach towards risk assessment, and undermines user and public confidence. *The same standard should be applied to data regardless of whether or not they support a EPA default procedure or preferred assessment pathway (e.g., linear, low-dose extrapolation based on an assumption of no threshold).*

Bioavailability

Serious issues exist regarding the predictiveness of the draft SFo given likely differences between the bioavailability in mice (and rats) at the doses used in NTP (2008) and in humans at typical environmentally relevant doses. In regard to the bioavailability of CrVI, TCEQ notes that the human study cited by EPA where as high as 10% of CrVI was absorbed (Kuykendall et al. 1996) involved a bolus dose 25 times higher than the dose associated with consuming 2 liters of drinking water all at once at the current MCL. The limited human bioavailability at the high bolus dose used raises serious questions about the bioavailability at much lower, environmentally relevant doses (e.g., lower, non-bolus doses).

Additionally, the rodent data cited by EPA are of little relevance for proving bioavailability in humans at environmentally relevant doses as the rodent doses cited (p. 210) were very high on a body weight basis and human GI reductive capacity is expected to be different. Humans and mice are likely to differ in GI reductive capacity (a likely important determinant of risk) due to several factors such as varying stomach pH, fluid production rates, food content, and emptying and Cr reduction rates. For example, the human fasted stomach pH is around 2-3 times less than that of the mouse and rat (McConnell et al. 2008, Ruby et al. 1996), which would be expected to be associated with a greater human CrVI reductive capacity. *The differences between the bioavailability in mice (and rats) at the doses used in NTP (2008) and in humans at typical environmentally relevant doses would have to be quantitatively accounted for to derive a scientifically defensible and predictive SFo for regulatory decision making.* This is especially critical considering that the NTP (2008) doses likely exceeded the mouse (and rat) GI reductive capacity (see TCEQ comments above).

Genotoxicity versus Mutagenicity

EPA appears to inappropriately automatically equate and discuss genotoxicity data as direct evidence of mutagenicity. While evidence of genotoxicity certainly has bearing on potential mutagenicity and is important supportive information under EPA guidelines (EPA 1986, 2007), it is not direct evidence of the generation of mutations as seemingly characterized by EPA in the draft CrVI assessment. EPA guidelines on mutagenicity risk assessment (EPA 1986) concern *heritable* mutagenic changes, and not all carcinogenic chemicals that are capable of interacting with DNA will have a mutagenic MOA for cancer (EPA 2007). EPA discusses no positive *in vivo* data for mutagencity in cancer target tissues in oral animal studies, only genotoxicity data (e.g., DNA-protein crosslinks, DNA strand breaks) in non-target tissues of unknown relevance to the tumors observed in NTP (2008) which EPA inappropriately automatically equates and discusses as direct evidence of mutagenicity (see first paragraph p. 204). This *in vivo* genotoxicity discussed by EPA does not result in cancer-causing mutations in those tissues (e.g., liver, leukocytes), much less explain how CrVI causes cancer in actual target tissues for which existing genotoxicity data (De Flora et al. 2008) are negative.

Interspecies Scaling

The interspecies scaling used by EPA should be fully justified. The draft SFo was calculated using $BW^{3/4}$ scaling from mice to humans (p. 229). The tumors observed in mice (small intestine tumors) were portal-of-entry (POE) and not systemic in nature. EPA (2005) is unclear as to whether the data which support this adjustment include POE tumor data. *EPA should fully justify use of $BW^{3/4}$ scaling for this purpose or conduct no such adjustment, especially given that humans and mice are likely to differ in GI reductive capacity (see TCEQ comments above).*

Imminent Generation of Data Critical to the Carcinogenic MOA Analysis

TCEQ strongly urges EPA to postpone finalizing the draft CrVI assessment as the generation of new data critical to understanding the carcinogenic MOA is imminent. Unlike the typical situation where regulatory agencies are asked to delay an assessment for years pending results of a study which might be informative, study data are currently being generated that are directly relevant and critical to a scientifically defensible carcinogenic MOA analysis by EPA. The overall goal of the CrVI MOA Research Program is to understand the contribution of different potential carcinogenic MOAs for CrVI

(e.g., genotoxicity, cytotoxicity, inflammation, oxidative stress) across a broad range of doses in order to provide both statistical and biological understanding of potential thresholds for CrVI carcinogenicity. The contributions of various MOAs over a range of doses will be determined by a combination of genome-wide microarray analyses in intact animals, high data content imaging of activation of key DNA-damage pathways, and consideration of dose dependencies in dosimetry. These data may elucidate the shape of the rodent dose-response curve and the human relevance of these responses prior to development of the final SFo. Detailed information may be found at http://www.tera.org/Peer/Chromium/Chromium.htm. All technical manuscripts are expected to be completed no later than the end of the 2nd quarter, 2011, before the final assessment is due in the 3rd quarter (http://cfpub.epa.gov/ncea/iristrac/index.cfm?fuseaction=viewChemical.showChemical&sw_id=1107). *The data to be generated by the*

CrVI MOA Research Program will address many important MOA data gaps (see the Appendix) and are of paramount importance to a scientifically rigorous CrVI carcinogenic assessment. These data may help explain such issues as why the mutagenic MOA hypothesized in the draft assessment (even at exposures below the GI reductive capacity) would predict GI tumors in highly orally-exposed workers (PHS 1953) and in multiple tissues in the NTP (2008) study but in fact such tumors did not occur. Additionally, they may explain more convincingly than the draft assessment (Section 4.7.3.3) why intestinal tumors only occurred in animals with prolonged hyperplasia, or may support an alternative carcinogenic MOA as much more plausible (e.g., Thompson et al. 2010). *TCEQ strongly encourages EPA to utilize these data to inform the carcinogenic MOA analysis and revise the draft assessment as justified (even if the EPA timeline is pushed farther out) as opposed to viewing these important data as an inconvenient late development in the assessment process and simply interjecting some level of uncertainty and proceeding down the previously prescribed path.*

Implication-Based Comments:

While significant implications themselves do not speak to the scientific defensibility of the draft SFo for CrVI, they emphasize the critical importance of deriving the most scientifically defensible, biologically relevant, and predictive toxicity factors possible.

Health-Protective Environmental Media Levels

Because the draft SFo for CRVI is relatively high, there are important implications for the calculation of health-protective environmental media levels such as EPA surface soil preliminary remediation goals (PRGs) and the MCL. Soil PRGs for CrVI may decrease by a factor of 10 or more even without the use of age-dependent adjustment factors (ADAFs). Soil PRGs will be at the low end of the range of background chromium soil levels (US mean of 37 mg/kg, ATSDR 2008), with a residential PRG of 0.29 mg/kg and a commercial/industrial PRG of 5.6 mg/kg. *Soil CrVI PRGs within background chromium levels will require costly remediation site-specific soil studies to differentiate between CrVI and other forms (e.g., CrIII) at all sites where it is a chemical of potential concern (COPC).*

The draft SFo also has significant implications for the federal drinking water MCL. *Using the EPA acceptable risk range (1E-06 to 1E-04) and draft SFo, the MCL would need to be from 0.07 to 7 ppb (without use of ADAFs) for adequate protection of public health. Compared to the current MCL of 100 ppb, this represents approximately a 14-1,400 fold decrease.* With typical US drinking water supplies containing total chromium levels within a range of 0.2 to 35 ppb (most supplies < 5 ppb, ATSDR 2008), a

new MCL for total chromium of 0.07-7 ppb conservatively based on the draft SFo could be exceeded on a wide basis depending upon the target risk level used. If a CrVI-specific MCL is promulgated, water suppliers would have to begin analyzing for chromium using a method that can speciate forms and one sensitive enough to detect chromium at concentrations much lower than now required to demonstrate compliance with the current MCL. Available analytical methods do not appear to be capable of detecting CrVI at the lower end of the potential new MCL range (ATSDR 2008). *A new MCL may be problematic for many public drinking water supplies.* For example, a recent California drinking water survey showed that 14% of drinking water sources had concentrations of ≥ 10 ppb CrVI (ATSDR 2008), which is above the potential new MCL range of 0.07-7 ppb based on the EPA acceptable risk range and the draft CrVI SFo. Additionally, based on a review of treatment removal technologies, process-efficient and cost-effective methods for CrVI removal from drinking water supply sources appear to be lacking (Sharma et al. 2008).

Closing Remarks:

TCEQ acknowledges the significant agency effort and resources required to produce draft toxicological assessments, review public comments, and make scientifically justified revisions and additions. The public deserves regulatory agencies to be able to make good risk management decisions using realistic risk estimates based on the most scientifically defensible and predictive toxicity factors possible, not based on toxicity factors of uncertain predictive ability that are just conservative by default. Consequently, for this and other draft assessments, TCEQ urges EPA to give thoughtful scientific and common-sense consideration to these and other comments and the weight of scientific evidence which supports or contradicts key decisions and procedures employed in the draft EPA assessment. Agreement with the ultimate final SFo value necessarily implies agreement with its ability to reasonably predict risk at commonly encountered, environmentally relevant doses, and agreement with the unavoidable conclusions about public health that will naturally follow from risk estimates based on the SFo. Additionally, TCEQ encourages EPA to postpone finalizing the draft assessment as necessary since the generation of new data which will address important MOA data gaps is imminent through the CrVI MOA Research Program. Appropriate consideration and incorporation of these data would result in a more scientifically rigorous CrVI carcinogenic assessment.

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Attachment D – TCEQ Comments on EPA Dioxin Interim Preliminary Remediation Goals

Texas Commission on Environmental Quality
Comments Regarding the U.S. Environmental Protection Agency
Draft Recommended Interim Preliminary Remediation Goals for Dioxin
in Soil at CERCLA and RCRA Sites
Notice of Availability and Announcement of Public Comment Period
75 FR 0984, January 7, 2010
Docket ID No. EPA-HQ-SFUND-2009-0907

The Texas Commission on Environmental Quality (TCEQ) provides the following comments on the U.S. Environmental Protection Agency (EPA) announcement of the public comment period regarding its proposal to adopt interim preliminary remediation goals (PRGs) applicable to dioxin (2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD)) and other dioxin-like compounds in soils at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA / Federal Superfund) and Resource Conservation and Recovery Act (RCRA / Federal Hazardous Waste) corrective action sites.

EPA proposes to substantially reduce the PRGs for dioxin in residential soils from the present value of 1 part per billion (ppb) TCDD toxicity equivalents (TEQ) to .072 ppb TCDD TEQ. For dioxin in soils at commercial/industrial sites, EPA proposes to reduce the PRG from a level within the concentration range from 5 to 20 ppb TCDD TEQ to .950 ppb TCDD TEQ. EPA expects to finalize these revised PRGs in June 2010 and that they will remain in effect in the interim until it issues the final reassessment of dioxin toxicity which it plans to accomplish by the end of 2010. EPA intends to then issue updated PRGs based on its final dioxin reassessment and to reevaluate cleanup decisions that were based on these 2010 interim PRGs in order to ensure that those cleanups remain protective of human health.

Toxicology-Based Comments:

The TCEQ provides the following comments which question the rationale for issuing revised PRGs for dioxins in soils until such time as scientifically defensible toxicity values are available upon completion of the dioxin reassessment.

- The complexity of the analysis of dioxin toxicity, the unknown outcome of the final dioxin reassessment, and the potential for significant implications associated with the interim PRGs, all indicate that EPA should allow a longer comment period for stakeholders to prepare comments. The allotted 50 days to prepare comments does not provide for an appropriate level of peer review and undermines confidence in the interim PRG values. At a minimum, EPA should extend the comment period at least 60 days past the February 26 deadline to allow stakeholders to perform a more detailed review of the volumes of relevant information and to comment on problematic issues associated with the interim PRG calculations.

- The draft interim PRG document states that the proposed interim PRGs are informed by the best available science at this time.[1] The document negates this claim when it also states "there is uncertainty associated with these draft recommended interim PRGs because they do not take into account peer review comments on the new science that was reviewed by the National Academy

[1] Page 2, www.epa.gov/superfund/policy/remedy/pdfs/Interim_Soil_Dioxin_PRG_Guidance_12-30-09.pdf

of Sciences (NAS), and new science that was released since the NAS review."[2] This contradiction calls into question the transparency of the PRG development process. The proposed interim PRGs are not based on the best available science at this time. Specifically, the carcinogenic oral slope factor (SFo) (EPA, 1985) and the non-carcinogenic chronic minimum risk level (MRL) (ATSDR, 1998) toxicity factors used in the PRG calculations are 25 and 12 years old, respectively. Also, the proposed interim PRGs do not take into account the National Toxicology Program (NTP) animal studies (NTP, 2004 and 2006) released after the 2003 draft reassessment. The final dioxin reassessment will provide a better basis for revised PRGs provided the recommendations from the NAS are appropriately incorporated into the final analysis (e.g., incorporation of nonlinear and probabilistic approaches, quantitative characterization of uncertainty and variability in risk, transparency in selection of key data, and assessing dose-response model goodness of fit). The TCEQ concludes that there is sufficient uncertainty regarding dioxin toxicity that EPA should not issue revised dioxin PRGs until all stakeholders have had an opportunity to help determine the best science available at this time.

- EPA did not include the 2007 California EPA SFo[3] used for the draft drinking water public health goal (CalEPA, 2007) when discussing the available SFo values for use in PRG calculations. The CalEPA's 2007 SFo is based on a 2004 NTP study (NTP, 2004) and is the only SFo available that is informed by the latest science. The CalEPA and others consider that study to be a superior basis for SFo calculations, due to its careful design and conduct and the improved survival rate, as compared to the 1978 Kociba study (Kociba RJ, Keyes DG, Beyer JE, et al., 1978) adopted by EPA for its 1985 SFo[4] and used in the interim PRG calculation. The CalEPA's 2007 SFo is six times less conservative than the EPA's 1985 SFo and is based on the latest and perhaps best animal study conducted to date for carcinogenic risk assessment.

- The monkey study (Schantz SL, Ferguson SA, Bowman RE., 1992) data which serve as the basis of the 1998 non-cancer toxicity factor[5] (ATSDR, 1998) used by EPA for the interim PRG calculations were excluded from the quantitative assessments of tolerable daily intakes by several international agencies.[6] Substantial amounts of non-TCDD compounds (e.g., polychlorinated dibenzo-p-dioxins, polychlorinated dibenzo-p-furans, and dioxin-like polychlorinated biphenyls (PCBs)) were found to be contributing to the TCDD TEQ concentrations for several of the TCDD-exposed monkeys and other non-exposed monkeys (Alward LL, Lakind JS, Hays SM., 2008). Use of the daily dose of TCDD from this study to derive the chronic MRL is problematic, since that value likely underestimates the TCDD TEQ concentration that was present at the time of the observed effects.

- EPA should develop a reasonable estimate of relative bioavailability (less than 1) of soil dioxin from available studies and then use that value in the PRG calculations. EPA assumes the dioxin bioavailability from soil is the same as the dioxin bioavailability in the toxicological studies used as the basis for the toxicity factors, i.e., the SFo and chronic MRL.[7] EPA's use of a relative bioavailability of 1 in the interim PRG calculations[8] demonstrates this assumption, which is

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[2] Page 4, www.epa.gov/superfund/policy/remedy/pdfs/Interim_Soil_Dioxin_PRG_Guidance_12-30-09.pdf
[3] 26,000 per mg/kg-day
[4] 156,000 per mg/kg-day
[5] ATSDR's chronic MRL
[6] Joint Expert Committee on Food Additives (JECFA) of the World Health Organization (WHO) and Food and Agricultural Organization (FAO), European Commission Scientific Committee on Foods (ECSCF), and United Kingdom Committee on Toxicity (UKCOT).
[7] Page 11, www.epa.gov/superfund/policy/remedy/pdfs/Interim_Soil_Dioxin_PRG_Guidance_12-30-09.pdf
[8] Pages 23-24, www.epa.gov/superfund/policy/remedy/pdfs/ Interim_Soil_Dioxin_PRG_Guidance_12-30-09.pdf

questionable since animals in toxicological studies are typically dosed with more bioavailable forms of chemicals than those occurring in soil.

- The draft interim PRG document[9] also mentions that EPA is requesting comments on the utility of alternative PRGs at a 1E-06 excess cancer risk level. The above comments also apply to these alternative PRGs with the additional concern that setting PRGs within or below background concentrations is not feasible from a compliance perspective. Such an approach could result in costly studies to determine site-specific background concentrations whenever TCDD or other dioxin-like compounds are present at a site.

Implementation-Based Comments:

The TCEQ provides the following implementation-based comments which conclude that

EPA should not issue revised PRGs for dioxin and dioxin-like compounds in soils until such time as it completes the final reassessment of dioxin toxicity. However, if EPA decides to issue the interim PRGs, then it should, previously or concurrently, release additional guidance that more specifically discusses how the interim PRGs are to be applied to active and closed dioxin sites. Also, EPA should clarify in such guidance that it does not intend to use revised PRGs, prior to its completion of the final dioxin reassessment and issuance of associated PRGs, to conclude that any site that has been appropriately evaluated and/or remediated in response to its 1998 dioxin PRGs requires additional response to be protective of human health.

- EPA is not being consistent with its own logic presented in the 1998 Office of Solid Waste and Emergency Response (OSWER) memorandum which memorializes the dioxin cleanup levels historically used by EPA at CERCLA and RCRA cleanup sites. That memorandum states, "The Office of Solid Waste and Emergency Response does not believe it is prudent to establish new, and possibly varying, precedents for Superfund or RCRA dioxin levels just prior to the release of this reassessment report." (EPA, 1998). The TCEQ concurs with EPA's previously stated view that it should not release interim PRGs just prior to the release of the final dioxin reassessment.

- EPA states that it intends to issue interim PRGs for dioxin this June and that it expects to complete the dioxin reassessment by the end of 2010. If this is the case, then the TCEQ questions the purpose and utility of EPA issuing interim PRGs when those PRGs are likely to change, after being reassessed, in only six or seven months. On the other hand, when EPA stated its expectation to complete the dioxin reassessment by the end of 2010, it also stated that completion by that date was "subject to further consideration of the science and the scope and complexity of the revisions that will need to be made."[10] EPA has been working since 2004 to incorporate the comments provided by the NAS with regard to its last version of the dioxin reassessment issued in 2003. When EPA issues its proposed final dioxin reassessment, it should expect comments regarding whether it has appropriately addressed the concerns expressed by the NAS in 2004 and whether new research regarding dioxin toxicity has been appropriately incorporated into the reassessment. So it seems reasonable to expect that EPA will need more time, and perhaps significantly more time, beyond the end of 2010 to complete the dioxin reassessment. In this circumstance, the TCEQ objects to the issuance of interim PRGs for dioxin in soils that are not based on the best science currently available and that could remain in effect for an unknown

[9] Page 13, www.epa.gov/superfund/policy/remedy/pdfs/ Interim_Soil_Dioxin_PRG_Guidance_12-30-09.pdf
[10] Page 1, www.epa.gov/superfund/policy/remedy/pdfs/ Interim_Soil_Dioxin_PRG_Guidance_12-30-09.pdf

number of years. Both of these possible circumstances support the conclusion that EPA should wait until the final dioxin reassessment is completed before it issues revised PRGs for dioxins.

- The discussion that EPA provides on implementation issues in the public review draft of the recommended interim PRGs for dioxins in soils does not provide sufficient detail for stakeholders to be able to evaluate how EPA intends to use the revised PRGs. Additional detail is needed which describes how EPA intends its regions to reevaluate CERCLA and RCRA corrective action sites that have been evaluated and/or remediated in the intervening period between its issuance of the interim PRGs and the final PRGs that are to be consistent with the final dioxin reassessment. Also, the document does not discuss whether EPA intends to use the interim PRGs when it reevaluates CERCLA and RCRA corrective action sites that have been evaluated and/or remediated using its 1998 PRGs.[11] However, EPA does mention that its regions should "consider" this public review draft document on the recommended interim PRGs when performing five-year-reviews of CERCLA sites containing dioxin or dioxin-like compounds to determine whether the original remedy stated in the Record of Decision remains protective. EPA should release additional guidance no later than the issuance of any interim PRGs that more specifically discusses how the interim PRGs are to be applied to active and closed dioxin sites. This guidance should specifically address how PCB sites that have only Arochlor data, and for which TCDD TEQs cannot be calculated, are to be handled. Also, EPA should clarify in this guidance that it does not intend to use the interim PRGs, prior to its completion of the final dioxin reassessment, to conclude that any site that has been appropriately evaluated and/or remediated in response to its 1998 dioxin PRGs requires additional response to be protective of human health.

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[11] Pages 2, 14-16, www.epa.gov/superfund/policy/remedy/pdfs/ Interim_Soil_Dioxin_PRG_Guidance_12-30-09.pdf

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Attachment E – TCEQ Comments on EPA Dioxin Reanalysis

Texas Commission on Environmental Quality
Comments Regarding the U.S. Environmental Protection Agency
Draft EPA's Reanalysis of Key Issues Related to
Dioxin Toxicity and Response to NAS Comments
Notice of Public Comment Period
75 FR 28610, May 21, 2010
Docket ID No. EPA-HQ-ORD-2010-0395

On May 21, 2010, the U.S. Environmental Protection Agency (EPA) published a Federal Register notice (Federal Register/Vol. 75, No. 98/Friday, May 21, 2010/Notices) of a 90-day public comment period (ending August 19, 2010) for the, "Draft EPA's Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments," hereafter referred to as the draft reanalysis (EPA/600/R-10/038A). EPA will only guarantee that comments submitted by July 7, 2010, will be provided to the Scientific Advisory Board (SAB) in time for their panel meeting for independent external peer review of the draft reanalysis. The draft reanalysis: (1) details EPA's technical response to the key comments and recommendations included in the 2006 National Academy of Sciences (NAS) report, "Health Risks from Dioxin and Related Compounds: Evaluation of the EPA Reassessment," with a focus on dose-response issues; (2) classifies 2,3,7,8-tetrachlorodibenzo-p-dioxin (TCDD or dioxin) as carcinogenic to humans; (3) provides an oral slope factor for TCDD; and (4) provides an oral reference dose (RfD) for TCDD, although EPA has not historically calculated an RfD. The Texas Commission on Environmental Quality (TCEQ) has developed comments on the draft reanalysis to the extent practicable in the time allotted by EPA and provides the following limited comments for EPA consideration.

General Comment:

The assessment of the carcinogenic and non-carcinogenic potential of TCDD has great implications both in a regulatory context and in the public's perception of risk. Given their important role in the protection of public health, EPA regulatory risk assessors have a duty to perform the most scientifically defensible assessments possible while giving careful and due consideration to comments and recommendations from other regulatory agencies, the public, external experts such as NAS, stakeholders, etc. Although regulatory risk assessors have a penchant for erring on the side of health-protectiveness and conservative defaults, if erring on the side of conservatism significantly overestimates risk or hazard and is not fully justified, then harm to public health may result from diverting public, industry, and government attention and resources away from chemicals that may represent more of a public health risk at environmental levels. Therefore, TCEQ encourages EPA to give full, thoughtful, and careful consideration and evaluation to comments and recommendations from TCEQ, other regulatory agencies, the public, and external experts such as NAS despite the artificial imposition of a December 31, 2010, deadline for release of the final TCDD reassessment.

90-Day Comment Period:

The 90-day comment period is insufficient for regulatory agencies and others to provide thorough and meaningful comments based on an in-depth review and analysis of the draft reanalysis. There is great complexity associated with multiple issues relevant to the assessment of TCDD risk and hazard due to oral exposure. The draft reanalysis alone is 1,850 pages, with the SAB comments relevant to EPA's draft

reanalysis being another 268 pages, and hundreds of pages of other documents (e.g., EPA draft for NAS review, EPA response to NAS review document) and studies relevant to the assessment of TCDD risk and hazard due to oral exposure. Given the complexity and volume of relevant materials, it is impracticable for EPA to expect detailed specific comments from external experts given the short period allowed for a critical review of the draft reanalysis and procedures employed by EPA. The 90-day comment period only allows a very cursory review of the draft reanalysis at best, leads to a less-than-desirable level of transparency and peer review, and undermines confidence in the process. Consequently, TCEQ is only able to provide preliminary comments based on a cursory review of the draft reanalysis.

If EPA seeks detailed and meaningful public input and technical comments, at a minimum EPA should: (1) extend the comment period at least 90 days past the August 19 deadline to allow stakeholders to perform a more detailed review of the volumes of relevant information and to comment on problematic issues associated with the draft reanalysis; (2) reschedule the SAB panel meeting to 90 days past the original dates of July 13-15; and (3) similarly extend the July 7 deadline for submitting comments for SAB consideration prior to the panel meeting.

Toxicology-Based Comments:

The complexity of the dose-response analyses of dioxin toxicity (cancer and non-cancer) and the potential for significant implications associated with the SFo (1E+06 per mg/kg/day) and RfD (7E-10 mg/kg-day) provided in the draft reanalysis indicate that EPA should allow a longer comment period for stakeholders to prepare more detailed comments. The allotted 90 days to prepare comments (August 19, 2010 deadline): (1) does not provide for an appropriate level of technical peer review for a draft 1,850-page document which represents years of work (e.g., dose-response analyses); (2) undermines confidence in the analyses and cited SFo and RfD values; and (3) calls into question the transparency of the TCDD toxicity factor development process as a thorough scientific review during this time frame is essentially unfeasible. Requiring comments be submitted by July 7, 2010, to be considered by SAB prior to the SAB panel meeting exacerbates the already significantly inadequate review time. Consistent with the inadequate review time allotted by EPA, extremely limited general toxicology-based comments are provided below.

Extrapolation Approach for the Carcinogenic Assessment

EPA has chosen to use a linear, low-dose extrapolation method for cancer effects as opposed to a nonlinear extrapolation method as recommended by NAS. EPA should adopt a nonlinear approach per the NAS committee, who unanimously agreed that the current weight of scientific evidence on the carcinogenicity of TCDD is adequate to justify the use of nonlinear extrapolation methods. TCEQ concurs with the NAS that scientific evidence (e.g., mode of action, tumor dose-response data) is adequate to favor the use of a nonlinear model that would include a threshold response over the use of the default linear assumption. This determination is based on several lines of evidence, including: (1) available data suggest that TCDD (and other dioxins and dioxin-like compounds) are not directly genotoxic, and there is general consensus in the scientific community that nongenotoxic carcinogens exhibit nonlinear dose-response relationships and thresholds (doses below which the expected response would be zero) are likely to be present; (2) there is widespread agreement in the scientific community that all or nearly all the adverse effects of TCDD (and other dioxins and dioxin-like compounds) depend on a receptor-mediated mechanism, acting through a mechanism involving the Ah receptor, and Ah receptor

activation is a phenomenon that would be likely to cause the dose-response relationship to be sublinear at low doses (indeed, EPA has determined in previous evaluations of receptor-mediated carcinogens (e.g., numerous pesticides) that a nonlinear, low-dose model that may accommodate a threshold is appropriate); and (3) there is evidence of nonlinearity in various dose-response relationships for TCDD-induced tumors. In regard to (3) above, evidence of substantial hepatoxicity and a sublinear dose-response relationship in tumor-bearing female rats suggests that linear low-dose extrapolation is inappropriate. Additionally, for two types of epithelial tumors (keratinizing epithelioma of the lung and squamous cell tumors of the oral mucosal epithelium) the shape of the dose-response relationship suggests that they may be nonlinear. Also, the recent National Toxicology Program bioassay data (NTP 2004) are more consistent with a sublinear response that approaches zero at low doses rather than a linear dose response. Such evidence supports a nonlinear, low-dose extrapolation method as more justified and appropriate than the linear, low-dose extrapolation method used by EPA. However, contrary to the NAS and this evidence, EPA concludes that there is insufficient evidence to support a nonlinear approach. EPA should adopt a nonlinear approach per the NAS recommendation as the weight of scientific evidence supports it.

Additionally, EPA chose to use a 95% upper confidence limit (95%UCL) over the statistical best estimate of the regression coefficient. If EPA elects not to follow the NAS recommendation for a nonlinear approach, TCEQ suggests use of a SFo based on the best estimate of the regression coefficient as opposed to the 95%UCL. Based on Table 5-4 of the draft reanalysis, a SFo of around 5E+05 per mg/kg/day is preferred over use of the 95%UCL SFo as it is based on the statistical best estimate of the regression coefficient. This human study-based SFo is very similar to and supported by the SFo based on the well-conducted NTP (2006) rat study (Table ES-2), the most comprehensive evaluation of TCDD chronic rodent toxicity to date. Based on a very cursory review of the 1,850-page draft document, it does not appear to address, much less justify, use of a 95%UCL over the statistical best estimate of the regression coefficient.

Intrahuman Uncertainty Factor

EPA should give further consideration to justifying the reduction of the intrahuman uncertainty factor (UF_H) from 3 to 1 as the critical effects observed in the co-principal studies used to derive the RfD were found in sensitive subpopulations (children, neonates). There is historical precedent for EPA using a UF_H of 1 when the RfD is based on data in sensitive subpopulations such as infants and children (e.g., nitrate, nitrite, fluorine/soluble fluoride). Using a UF_H of 3 as in the draft reanalysis results in an RfD that may be interpreted by the public to mean that based on average U.S. dietary intake (ATSDR 1998), which exceeds the draft RfD, TCDD-induced health effects such as increased thyroid stimulating hormone in neonates are likely occurring in the general population on a widespread basis.

Implementation-Based Comments:

Again, EPA must consider providing adequate review time for a critical examination of the bases of the SFo and RfD because these values have significant consequences for issues such as food safety, the federal drinking water maximum contaminant level (MCL) and surface water quality standards, and preliminary remediation goals (PRGs) applicable to dioxin (and other dioxin-like compounds) in soils at Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA/Federal Superfund) and Resource Conservation and Recovery Act (RCRA/Federal Hazardous Waste) corrective

action sites. Consistent with the inadequate review time allotted by EPA, extremely limited general implementation-based comments are provided below.

Food Safety

TCEQ questions the risk assessment utility of an RfD value that is within or below the range of reported average dietary intake. The average intake from meat and eggs alone exceeds the RfD (ATSDR 1998). This draft RfD inevitably would raise public concerns about the safety of the U.S. food supply, especially given that the public frequently interprets the exceedance of a regulatory value as equivalent to an expectation of the occurrence of adverse health effects. A margin of exposure approach appears more appropriate than an RfD to evaluate the potential for non-cancer effects. The SFo provided in the draft reassessment also raises concerns about food safety given that risk from average dietary intake is above the acceptable excess risk range (1E-06 to 1E-04) established by EPA. Analyses such as these, using the RfD and SFo from the draft reanalysis, would imply that the U.S. diet results in TCDD hazard and risk that are considered unsafe and unacceptable from a regulatory perspective. Use of unjustifiably conservative toxicity factors for a chemical (or class of chemicals) may unnecessarily alarm the public and result in at least two negative responses: diluting the message of any future government risk warnings or diverting focus, funding, and resources from chemicals which realistically represent more of a public health hazard.

Surface Soil PRGs

The SFo given in the draft reanalysis (1E+06 per mg/kg/day) is 6.4 times higher than that used for the interim preliminary PRGs (1.56E+05 per mg/kg/day; EPA 2009), so revised cancer-based PRGs could be a factor of 6.4 times lower. The new RfD (7E-10 mg/kg-day) is 30% lower than that used for the interim preliminary PRGs (1E-9 mg/kg-day; EPA 2009), so revised non-cancer-based PRGs could decrease by 30%. Although the interim preliminary PRGs were ultimately based on non-cancer PRGs (EPA 2009), the greater conservativeness of the SFo given in the draft reanalysis may cause cancer-based PRGs to be the critical final PRGs. If protective at the 1E-05 excess risk level (similar to the interim preliminary PRGs in EPA 2009), the residential and commercial/industrial worker surface soil PRGs could be over 150 times lower than the current PRGs (1 ppb for residential; 5 ppb for commercial/industrial (lower end of the range); EPA 1998), with the final residential PRG possibly being within the range of rural background concentrations (EPA 2009). EPA should reconsider finalizing a SFo which may result in setting a final residential PRG within background concentrations because such a PRG would not be feasible from a compliance perspective and could result in costly studies to determine site-specific background concentrations.

In regard to individual excess lifetime cancer risk (IELCR), EPA states on their website (http://www.epa.gov/oust/rbdm/sctrlsgw.htm), "The IELCR represents the incremental (over background) probability of an exposed individual's getting cancer (i.e., a risk occurring in excess of or above and beyond other risks for cancer such as diet, smoking, heredity). Cleanup standards calculated on the basis of excess risk limits correspond to allowable levels *in excess of the background concentrations of the chemicals of concern normally present in the source media*" (emphasis added). Since regulatory agencies are concerned with regulating *excess risk* (i.e., risk over natural background), technically, the risk due to naturally-occurring background soil levels should be excluded from comparisons to the EPA acceptable risk range. In other words, as EPA and other regulatory agencies are concerned with regulating excess

risk over background, background TCDD levels (dioxin/furan TEQ) should be excluded from comparison to the TCDD PRG. Only levels *in excess of background concentrations* should be compared to TCDD PRGs since per EPA, "cleanup standards calculated on the basis of excess risk limits correspond to allowable levels *in excess of the background concentrations.*" Alternatively but based on the same considerations and with the same effect, the applicable soil PRG could be added to a representative background concentration for a site to derive a comparison value that represents a regulatory acceptable level of excess risk (i.e., risk over background). Since EPA is concerned with regulating excess risk over background, EPA should simply acknowledge that no action is necessary when TCDD levels (dioxin/furan TEQ) are within background at a remediation site, even if levels are above the applicable PRG.

Federal Drinking Water MCL and Surface Water Quality Standards

The SFo given in the draft reanalysis also has implications for the federal MCL for TCDD. Using the current SFo (1.56E+05 per mg/kg/day), risk associated with drinking water ingestion at the MCL is at the high end of the risk range deemed acceptable by EPA (≈ 1E-04). Use of the draft reanalysis SFo would result in the MCL being associated with a risk (≈ 9E-04) significantly higher than the upper end of the EPA acceptable risk range. The new RfD also has significant implications for the MCL. As the relative source contribution factor in the MCL calculation would likely be no greater than 1% (i.e., over 99% of exposure comes primarily from food), for a hazard quotient of 1 the current MCL would likely have to be reduced by over a factor of 100. Derivation of the most scientifically-defensible SFo and RfD values possible is also imperative due to the potentially significant impacts on surface water quality standards.

Recommendation:

Again, if EPA seeks thorough, detailed, and meaningful input and technical comments from the public and external experts on the EPA analyses conducted, at a minimum EPA should: (1) extend the comment period at least 90 days past the August 19 deadline to allow stakeholders to perform a more detailed review of the volumes of relevant information and to comment on problematic issues associated with the draft reanalysis; (2) reschedule the SAB panel meeting to 90 days past the original dates of July 13-15; and (3) similarly extend the July 7 deadline for submitting comments for SAB consideration prior to the panel meeting. If EPA chooses not to provide additional time, EPA should carefully consider the broader consequences of finalizing the draft SFo and RfD values currently proposed, which could result in additional burdensome and costly regulation without meaningful protection of public health.

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National Toxicology Program (NTP). 2004. Toxicology and Carcinogenesis Studies of 2,3,7,8-Tetrachlorodibenzo-p-dioxin (TCDD) (CAS No. 1746-01-6) in Female Harlan Sprague-Dawley Rats (Gavage Study). NIH Publication No. 044455. NTP TR 521. National Toxicology Program, Public Health Service, National Institutes of Health, Research Triangle Park, NC.

National Toxicology Program (NTP). 2006. NTP technical report on the toxicology and carcinogenesis studies of 2,3,7,8-tetrachlorodibenzo-p39 dioxin (TCDD) in female harlan Sprague-Dawley rats. National Toxicology Program. RTP, NC. 06-4468. 197605

Mr. SHIMKUS. Thank you for your testimony.

And now I would like to recognize Dr. Harvey Clewell. Sir, you have 5 minutes. And we are getting you fresh water. And you are recognized.

STATEMENT OF HARVEY CLEWELL

Mr. CLEWELL. Thank you, Mr. Chairman. Good morning, Mr. Chairman, members of the subcommittee. My name is Harvey Clewell. I am the director for the Center for Human Health Assessment at the Hamner Institutes for Health Sciences in Research Triangle Park, North Carolina.

In my position at the Hamner, as well as in my previous consulting positions, I have performed risk assessment research and consulting for a large number of government and industry clients, including the EPA. I am here today to present my professional opinions. I am not representing the Hamner or any other organization.

I am very familiar with EPA risk assessment practices. Over the last 30 years, I have assisted EPA on risk assessments for a number of compounds including methylene chloride, cadmium, styrene, vinyl chloride, trichloroethylene, chloroform, and perchlorate. I have served on the EPA's FIFRA Scientific Advisory Panel and the recent EPA Science Advisory Board on IRIS assessments for dioxin. I have also served as a peer reviewer for a number of recent EPA guidelines, including those for cancer risk assessment and risk characterization.

I consider EPA to be a leader in advancing risk assessment methods and have been favorably impressed by a number of recent IRIS assessments for which I was a peer reviewer, including those for one for dioxane and acrylamide. Nevertheless, I am concerned that the lack of objectivity and transparency in some recent IRIS assessments will impair the ability of decision-makers to make informed risk management decisions.

I am particularly concerned that in some recent IRIS assessments, such as those for inorganic arsenic, formaldehyde and dioxin, only a single cancer risk assessment approach has been presented: a low-dose-linear default that assumes these chemicals are carcinogenic at any concentration. However, there is strong evidence for each of these chemicals that the true dose-response is nonlinear, and that the default greatly overestimates the actual risk at current human exposure levels.

This IRIS practice of presenting only a single approach disregards the recommendation in the OMB memorandum entitled, "Updated Principles for Risk Analysis," to provide a characterization of the dispersion of risk estimates associated with different models, assumptions, and decisions. The OMB principles provide valuable guidance for assuring that risk assessments adequately inform decision-makers faced with complex risk management options. Following the OMB recommendations should be a key objective of all IRIS assessments.

The failure to objectively describe the evidence for alternative risk assessment approaches and to provide risk estimates other than the default has been a major deficiency in the IRIS risk assessment process. Even in the case of IRIS cancer assessments

where alternative low-dose extrapolation options are discussed, there has been a clear bias towards presenting evidence that supports the selection of the default linear approach, even in cases where there is strong support for a nonlinear approach in the scientific community. Decision-makers would be better informed by a balanced and objective discussion of both alternatives and the presentation of analyses based on both alternative approaches in the risk characterization section of the assessment.

As a justification for presenting only the default low-dose-linear risk assessment approach, the IRIS assessments have cited uncertainty in the evidence for alternative approaches. However, EPA guidance states that in the face of uncertainty, multiple approaches can be presented. The EPA's 2005 Guidelines for Carcinogen Risk Assessment state that "Nonlinear extrapolation having a significant biological support may be presented in addition to a linear approach when the available data and a weight of evidence evaluation support a nonlinear approach, but the data are not strong enough to ascertain the mode of action applying the Agency's mode of action framework. If more than one approach, e.g. both a nonlinear and linear approach are supported by the data, they should be used and presented to the decision-maker."

In a number of cases, NAS and the EPA Science Advisory Board peer reviews have requested that the IRIS assessment be modified to objectively present multiple risk assessment options but the Agency has not complied. I believe that the repeated refusal of the EPA to implement recommendations from the NAS and SAB peer reviews to objectively present alternative risk assessment options has greatly delayed the completion of the IRIS assessments for a number of important chemicals, in some cases for more than a decade.

In addition to being inconsistent with agency guidance, presentation of only a conservative default approach when there is a viable alternative provides the decision-maker with an inaccurate characterization of risk that compromises his ability to make informed risk management decisions.

In my opinion, IRIS assessments currently do not provide an objective and transparent characterization of the potential risks associated with chemical exposure. The inadequacy of the risk characterization in IRIS assessments, coupled with the sole use of conservative default approaches, hampers the ability of decision-makers to make informed risk management decisions and gives the public an inaccurate impression of their potential risks from chemical exposure. I believe that this deficiency could to a large extent be addressed by assuring that IRIS assessments adhere to the risk assessment principles elaborated in the OMB memorandum in the information quality principles.

Thank you.

[The prepared statement of Mr. Clewell follows:]

Testimony to the
Committee on Energy and Commerce
Subcommittee on Environment and the Economy
October 6, 2011

"Chemical Risk Assessment: What Works for Jobs and the Economy"

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Introduction: Good morning, my name is Harvey Clewell, and I'm Director of the Center for Human Health Assessment at the Hamner Institutes for Health Sciences in Research Triangle Park, North Carolina. The Hamner, which was previously known as the Chemical Industry Institute of Toxicology, has now become an independent research institute with a diverse funding portfolio. I have more than thirty five years of experience in environmental quality research, toxicology research, chemical risk assessment, and hazardous materials management. I played a major role in the first uses of physiologically based pharmacokinetic modeling in cancer and non-cancer risk assessments by EPA, ATSDR, OSHA, and FDA, for such chemicals as methylene chloride, trichloroethylene, vinyl chloride, and retinoic acid. I received a Masters Degree in Chemistry from Washington University, St. Louis, MO, and a PhD in Toxicology from the University of Utrecht, the Netherlands. I served for 20 years as an officer in the U.S. Air Force; my positions included Deputy Director of the Air Force Toxic Hazards Research Unit, Director of Hazardous Materials Safety for the Air Force Aeronautical Systems Center, and consultant to the Air Force Surgeon General on Chemical Risk Assessment. After retiring from the Air Force I worked as a consultant in risk assessment at ICF and later Environ, before coming to The Hamner. In 2007 I received the Society of Toxicology's Arnold J. Lehman award for major contributions to chemical safety and risk assessment.

In my position at the Hamner, as well as in my previous consulting positions, I have performed research and consulting for a large number of government and industry clients, including the EPA. I am here today at the request of the Committee to present my professional opinions. I am not representing The Hamner or any other organization.

I am very familiar with EPA risk assessment practices. Over the last 30 years I have assisted EPA on risk assessments for a number of compounds, including methylene chloride, cadmium, styrene, vinyl chloride, trichloroethylene, chloroform, and perchlorate. I have served on the EPA's FIFRA Scientific Advisory Panel and the recent EPA SAB on the IRIS assessment for dioxin. I have also served as a peer reviewer for a number of recent EPA guidelines, including those for cancer risk assessment and risk characterization. I consider EPA to be a leader in advancing risk assessment methods and have been favorably impressed by a number of recent IRIS assessments for which I was a peer reviewer, including those for dioxane and acrylamide. Nevertheless, I am concerned that the lack of objectivity and transparency in some recent IRIS assessments will impair the ability of decisionmakers to make informed risk management decisions.

Comments on IRIS risk assessment practice: I am particularly concerned that in some recent IRIS assessments, such as the assessments for inorganic arsenic, formaldehyde and dioxin, only a single cancer risk assessment approach has been presented: a low-dose-linear default that assumes these chemicals are carcinogenic at any concentration. However, there is strong evidence for each of these chemicals that the true dose-response is nonlinear, and that the default greatly overestimates the actual risk at current human exposure levels. This IRIS practice of presenting only a single approach disregards the recommendation in OMB memorandum M-07-24, "Updated Principles for Risk Analysis" (Sep 19, 2007), to provide a characterization of the dispersion of risk estimates associated with different models, assumptions, and decisions. The OMB principles provide valuable guidance for assuring that risk assessments adequately inform decisionmakers faced with complex risk management options. Following the OMB recommendations should be a key objective of all IRIS assessments. The failure to objectively describe the evidence for alternative risk assessment approaches and to provide risk estimates other than the default has been a major deficiency in the IRIS risk assessment process. Even in the case of IRIS cancer assessments where alternative low-dose extrapolation options are discussed, there has been a clear bias towards presenting evidence that supports the selection of the default linear approach, even in cases where there is strong support for a nonlinear approach in the scientific community. Decisionmakers would be better informed by a balanced and objective discussion of both alternatives and the presentation of analyses based on both alternative approaches in the risk characterization section of the assessment.

As a justification for presenting only the default low-dose-linear risk assessment approach, the IRIS assessments have cited uncertainty in the evidence for alternative approaches. However, EPA guidance states that in the face of uncertainty, multiple approaches can be presented (Guidelines for Carcinogen Risk Assessment, EPA/630/P-03/001B, March 2005, p.3-23/24):

"Nonlinear extrapolation having a significant biological support may be presented in addition to a linear approach when the available data and a weight of evidence evaluation support a nonlinear approach, but the data are not strong enough to ascertain the mode of action applying the Agency's mode of action framework."

"In the absence of data supporting a biologically based model for extrapolation outside of the observed range, the choice of approach is based on the view of mode of action of the agent arrived at in the hazard assessment. If more than one approach (e.g., both a nonlinear and linear approach) are supported by the data, they should be used and presented to the decisionmaker."

In a number of cases, NAS and EPA SAB peer reviews have requested that the IRIS assessment be modified to objectively present multiple risk assessment options, but the agency has not complied. I believe that the repeated refusal of the EPA to implement recommendations from NAS and SAB peer reviews to objectively present alternative risk assessment options has greatly delayed the completion of the IRIS assessments for a number of important chemicals, in some cases for more than a decade. In addition to being inconsistent with agency guidance, presentation of only a conservative default approach when there is a viable alternative provides the decisionmaker with an inaccurate characterization of risk that compromises his ability to make informed risk management decisions.

In my opinion, IRIS assessments currently do not provide an objective and transparent characterization of the potential risks associated with chemical exposure. The inadequacy of the risk characterization in IRIS assessments, coupled with the sole use of conservative default approaches, hampers the ability of decisionmakers to make informed risk management decisions and gives the public an inaccurate impression of their potential risks from chemical exposure. I believe that this deficiency could to a large extent be addressed by assuring that IRIS assessments adhere to the risk assessment principles elaborated in OMB memorandum M-07-24.

Mr. SHIMKUS. Thank you. Now, I would like to recognize Mr. Cook for 5 minutes, sir.

STATEMENT OF JERRY A. COOK

Mr. COOK. My name is Jerry Cook. I am the technical director of Chemical Products Corporation, a small 78-year-old Georgia corporation which employs about 200 people in Cartersville, Georgia, which is in the metropolitan Atlanta area, on the fringe I guess you would say. We are the last U.S. producer of barium chemicals and I have been dealing with barium toxicology and regulation for more than 28 years. I joined Chemical Products in late October 1982 as technical director.

The IRIS database is supposed to determine sound science concerning the toxicology of chemicals to guide EPA's regulatory activities as we have heard today. If IRIS functioned properly, that could be used as a basis for sane regulation of various chemicals in the environment. Unfortunately, in the case of the IRIS barium file, I have found that the IRIS chemical managers and their superiors were not nearly as interested in sound science as they were in bureaucratic expediency. They simply did not want to hear sound science if it caused them to have to reevaluate the positions that they had previously taken.

A brief history of barium regulation is as follows: in 1975 in the statement of basis and purpose for the national interim primary drinking water regulations, under barium, EPA stated, "No study appears to have been made of the amounts of barium that may be tolerated in drinking water or of effects from prolonged feeding of barium salts from which an acceptable water guideline may be set." They arbitrarily chose a value at that time based on the hypothesis that perhaps barium in drinking water could cause a small but significant increase in blood pressure and that that would be a danger to those already suffering from high blood pressure. That was a hypothetical effect that they derived from the fact that acute toxicity from barium salt ingestion does include heart effects including hypertension for the period of time until the barium is cleared from the body.

The barium chemicals manufactured by Chemical Products Corporation are used in the ceramics industry to manufacture bricks and tiles, in the manufacture of luminous paints for highway signage and airport striping, and in heat treating of high-strength steel and the manufacture of catalysts. Many of our customers are small and medium-sized U.S. companies which are literally fighting for survival. Our customers tell us that the costs associated with retroregulation of barium are a substantial burden on them.

In our efforts to change the retroregulation of barium, the IRIS determination of what was considered a safe level was cited as the reason why the retroregulations were not going to change. So that is how IRIS functions. IRIS is the basis upon which regulatory decisions are made. If the science in IRIS is bad, the regulatory decisions are going to be bad.

The CEO of Summitville Tile, one of our customers, asked me to convey the following message to the members of this committee. "The overregulation of American industry is making it increasingly more difficult for American manufacturers to compete in today's

global economy. Summitville Tiles is a case in point. It is a 100-year-old manufacturer of quarry tile and brick products based in Eastern Ohio. In recent years, it has had to close 2 tile manufacturing facilities and 16 distribution centers, laying off over 450 employees. Summitville Tile is today one of the last American tile companies to remain in business. In fact, it is the only remaining charter member of the tile industry's National Trade Association, the Tile Council of North America. With foreign imports now comprising approximately 80 percent of the U.S. domestic tile market, the last thing that the tile industry needs is more regulations. What is needed more than anything else is regulatory relief."

I think that sums up the feeling of many of the small and medium-sized manufacturers in this country today. As a small or medium-sized company, they are really not equipped to deal with unnecessary regulatory burdens, and I think that that is exactly how I would characterize the regulation of barium because when a sound scientific study became available in 1994, when the NTP published a lifetime study of the effect of barium on rats and mice, IRIS greatly resisted acknowledging that study because it did not find the effect that was listed in IRIS. It did not find increased blood pressure. It instead found at much higher levels that barium would have an effect on the kidneys but the levels to find that effect were orders of magnitude higher than the level that was promulgated in IRIS.

Let me tell you a little bit about barium if I may. Barium is an alkaline earth metal, one of the group which includes magnesium and calcium. It is not carcinogenic and barium is rapidly eliminated from the body. In cases of acute barium ingestion, the effects are usually gone within a week. Barium is widely dispersed in the natural environment in the mineral barite, barium sulfate, which is insoluble in water and acids. Because it is insoluble, barium sulfate is not toxic. This is the chemical administered as an x-ray contrast medium for gastrointestinal x-rays. The infamous barium meal, I have never had one, but I understand it is not particularly tasty. It doesn't matter which end you put it in, it works for gastrointestinal x-rays.

If a large amount of soluble barium is ingested or inhaled, it is toxic because it temporarily interferes with the body's cellular potassium transport. EPA's IRIS database deals with chronic toxicity, which is a different situation. It is smaller amounts of a chemical consumed daily for many years over a lifetime. There is no known instance of any chronic toxic effect in a human due to barium and no animal studies were available as I read to you when EPA began regulating barium in the mid-1970s.

Mr. SHIMKUS. Mr. Cook, I did tell folks they could go over 5. You are almost at 3 minutes over that so if you can kind of——

Mr. COOK. Yes, sir. I appreciate it very much. I think you have gotten the gist of my situation.

Mr. SHIMKUS. We have and we will follow up with questions.

Mr. COOK. Thank you.

[The prepared statement of Mr. Cook follows:]

Testimony

of

Jerry A. Cook, Technical Director
Chemical Products Corporation

before the

U.S. House Committee on Energy and Commerce
Subcommittee on Environment and the Economy

October 6, 2011

Summary

Chemical Products Corporation, the last remaining manufacturer of barium carbonate and barium chloride in the U.S., has suffered a continuing decline in the market for its barium products. We believe that this decline is due, in part, to the over-regulation of barium by EPA under RCRA which has posed a continuing hardship on our industrial customers.

EPA's Integrated Risk Information System (IRIS) should function as an up-to-date repository of chemical toxicology assessments to be relied upon as the scientific basis for regulatory decision-making throughout EPA. We found IRIS to be unresponsive to new studies showing that barium was significantly less toxic than previously assumed. It took 11 years, and actions resulting from submission of Requests for Correction and Reconsideration after OMB instituted the "Information Quality Act", to achieve an IRIS barium file assessment that reflected sound science. In July 2005 the IRIS barium file was finally revised to recognize the 1994 National Toxicology Program Technical Report 432 as the principal study defining chronic barium toxicology and identifying a higher No Observed Adverse Level.

The RCRA regulatory level for barium is still the same arbitrary value set in the 1970's when no toxicological studies existed to provide a scientific basis for regulation.

EPA should make every effort to correct the structural deficiencies in IRIS and utilize up-to-date sound science to identify and remove regulatory burdens from U.S. industry which do not benefit human health or the environment.

Testimony

My name is Jerry Allen Cook. I am the Technical Director of Chemical Products Corporation (CPC), a 78 year old Georgia corporation which employs approximately 200 people in Cartersville, Georgia. My company is the last U.S. producer of barium chemicals and I have been dealing with barium toxicology and regulation for more than 28 years. EPA maintains a chemical toxicology database called IRIS – the Integrated Risk Information System. EPA's IRIS database is supposed to determine sound science concerning the toxicology of chemicals to guide EPA's regulatory activities. If IRIS functioned properly, EPA could identify unnecessary regulations offering no benefit to human health and the environment and remove these burdens from U.S. industries. Unfortunately, in the case of the IRIS barium file, I have found IRIS chemical managers, and their superiors, to be much more interested in bureaucratic expediency than in sound science; this has resulted in over-regulation of barium by EPA. An overview of EPA regulation of barium and a history of EPA's IRIS barium file is attached as an appendix.

The barium chemicals manufactured by Chemical Products Corporation are used in the ceramics industry to manufacture bricks and tiles, in the manufacture of luminescent paints for highway signage and airport striping, in heat-treating high-strength steel, and in the manufacture of catalysts. Many of our customers are small and medium-sized U.S. companies which are literally fighting for survival. Our customers tell us that the costs associated with RCRA regulation of barium are a substantial burden on them.

The CEO of Summitville Tiles, Inc., one of our customers, asked me to convey the following message to the members of this committee, "The over-regulation of American industry is making it increasingly more difficult for American manufacturers to compete in today's global economy. Summitville Tiles is a case in point: A 100 year old manufacturer of quarry tile and brick products based in eastern Ohio, in recent years it has had to close two tile manufacturing facilities and sixteen distribution centers, laying off over 450 employees. Summitville Tile is today one of the last American tile companies to remain in business. In fact, it is the only remaining charter member of the tile industry's national trade association, The Tile Council of North America. With foreign imports now comprising approximately 80% of the U.S. domestic tile market, the last thing that the tile industry needs is more regulations. What is needed more than anything else is regulatory relief."

Concern on the part of Chemical Products Corporation's existing and potential customers that the miscellaneous waste they generate in the course of their everyday manufacturing activities could exceed the existing, unnecessarily strict RCRA regulatory limit for soluble barium has led many of these companies to reduce or eliminate the use of CPC's barium products.

Barium is an alkaline earth metal, one of the group which includes magnesium and calcium. It is not carcinogenic and barium is rapidly eliminated from the body. Barium is widely dispersed in the natural environment in the mineral barite (barium sulfate) which is insoluble in water and acids. Because it is insolubile, barium sulfate is not toxic; this

is the chemical administered as an X-ray contrast medium for gastro-intestinal X-rays (the infamous "barium meal").

If a large amount of soluble barium is ingested or inhaled, it is toxic because it temporarily interferes with the body's cellular potassium transport. EPA's IRIS database deals with chronic toxicity – smaller amounts of a chemical consumed daily for many years. There is no known instance of any chronic toxic effect in a human due to barium and no animal studies were available when EPA began regulating barium in the mid-1970's, so EPA arbitrarily set a drinking water standard and a RCRA hazardous waste regulatory limit.

When EPA's IRIS database first put its barium file on-line in 1987, EPA had funded limited chronic barium toxicity studies. The IRIS chemical manager for barium appeared to be placing inordinate weight only the single study that tended to justify the arbitrary regulatory levels set by EPA in the mid-1970's instead of seeking a sound scientific basis which could have eased EPA's regulation of barium – a study conducted through EPA's own Health Effects Research Laboratory found barium to be much less toxic than the study emphasized in the IRIS assessment. IRIS adopted a very low level of barium intake as its recognized safe exposure level.

In 1994 the National Toxicology Program published a study of soluble barium toxicity – NTP Technical Report 432. This 2-year study is still the definitive scientific study for assessment of barium chronic toxicity.

The IRIS toxicological evaluation of barium should have been a

straightforward exercise after the publication of the NTP technical report. Instead, EPA's IRIS staff failed to adopt sound science when the IRIS barium file was revised in 1998. I examined the peer review record of this 1998 revision – available only in a Reading Room in Cincinnati - and found that the peer review had not been conducted according to EPA required procedures. Ineffective accountability and oversight mechanisms had resulted in EPA's IRIS database failing to fulfill its purpose.

Finally, after 11 years had elapsed, and only as a result of OMB implementation of the "Information Quality Act", the IRIS barium file was revised in July 2005 to recognize the 1994 NTP study as the principal study from which to derive a critical effect for barium.

For most of the period that Chemical Products Corporation was struggling to achieve revision of the IRIS barium file to reflect sound science, the IRIS assessment program was completely under the control of EPA. Then, for several years, interagency reviews of draft IRIS file revisions were required and managed by OMB. Since 2009, the IRIS assessments and revisions are, once again, entirely managed by EPA. Unless EPA is able to establish and maintain much better oversight mechanisms than it previously employed, this change is unlikely to correct the deficiencies we encountered when seeking to correct the 1998 IRIS barium file revision.

Unfortunately, EPA has not adjusted the RCRA regulatory level for barium upward to relieve some of the burden on U.S. industry even though an upward revision is appropriate based on the information now available in the IRIS database.

APPENDIX

Overview of Barium Regulation and history of the IRIS barium file

EPA established a drinking water Maximum Contaminant Level (MCL) for barium in 1975. In "Statement of Basis and Purpose for the National Interim Primary Drinking Water Regulations", December 1975, under "barium", EPA stated, "No study appears to have been made of the amounts of barium that may be tolerated in drinking water or of effects from prolonged feeding of barium salts from which an acceptable water guideline may be set." Arbitrarily, a Maximum Contaminant Level (MCL) of 1 ppm of barium was promulgated at that time in the absence of scientific data. The RCRA regulatory limit for barium was set at 100 times this drinking water standard; this RCRA regulatory level remains in effect. CPC believes that this regulatory level for barium in solid waste is far below a level which would be protective of human health and the environment. Our efforts to make the Oral Reference Dose for soluble barium in IRIS reflect sound science are motivated by our desire to eventually achieve an increase in the RCRA regulatory limit for soluble barium.

Between 1980 and 1985 EPA funded three sub-chronic exposure studies of barium; two of these found no hypertensive effect, but one study (Perry), administering substantially lower doses than the other two studies, reported a small but significant increase in blood pressure in rats exposed to 100 ppm barium for only 4 weeks. In 1985 a study by McCauley in EPA's Health Effects Research Laboratory concluded, "There were no significant trends toward hypertension in any of the rats given as much as 1000 ppm Ba for 16 weeks." This refers to the highest dose tested by McCauley; it is 10 times higher than

the dose reported by Perry to cause hypertension in rats after only 4 weeks exposure.

When the IRIS barium file was brought on-line in 1987, the safe oral intake level for barium that was established roughly corresponded to the drinking water Maximum Contaminant Level established by EPA in 1975 and the critical effect from chronic barium ingestion was stated to be hypertension. Perry's reported blood pressure increase in rats exposed to relatively low levels of barium was cited as the basis for this IRIS determination – other studies which did not find hypertensive effects in rats exposed to much higher levels of soluble barium for longer periods of time were essentially ignored.

In 1989 EPA proposed raising the drinking water standard (Maximum Contaminant Level Goal or MCLG) for barium to 5 ppm from 1 ppm (54 Federal Register, page 22062, May 22, 1989); the drinking water standard was eventually raised only to 2 ppm barium in 1991.

In 1994 NTP issued "Technical Report on the Toxicology and Carcinogenesis Studies of Barium Chloride Dihydrate (CAS no. 10326279) in F344/N rats and B6C3F1 mice (drinking water studies)" (NTP TR 432, NIH pub. no. 943163. NTIS pub PB94214178, 1994). It reported finding no blood pressure increase in rats after administration of up to 4000 ppm barium chloride dihydrate for 13 weeks in the drinking water; this is 40 times the dose reported by Perry to cause hypertension in rats after only 4 weeks exposure. None of the physiological effects of hypertension were found after 2 years exposure to elevated levels of soluble barium in the drinking water. This NTP

report states at page 52, ".... an association between barium and cardiovascular effects in the present studies does not seem to be likely....".

CPC submitted information letters to the IRIS Information Submission Desk dated July 11, 1994; October 13, 1994; June 16, 1995; and January 3, 1996 bringing 6 recently published papers concerning barium toxicology, in addition to NTP Technical Report 432, to the attention of IRIS. We repeatedly urged IRIS to place a high priority on basing its oral reference dose for barium on credible science - stated in the February 25, 1993 Federal Register at page 11491 to be EPA's goal for IRIS.

On June 28, 1996, CPC submitted a petition to EPA seeking to have the barium compounds category deleted from EPCRA Section 313 Toxic Release Inventory reporting requirements. In that petition CPC, citing the 1994 NTP technical report on barium chloride which had not been considered in IRIS, asked that the effects of chronic barium ingestion be evaluated as part of the consideration of CPC's petition. EPA's Office of Pollution Prevention and Toxics (OPPT) performed a toxicological assessment and the conclusions of OPPT's toxicological assessment were published in the Federal Register on January 3, 1997 (62 FR 366-372). This OPPT toxicological assessment identified kidney effects as the critical effect for chronic ingestion of soluble barium and identified a No Observed Adverse Effect Level (NOAEL) and a Lowest Observed Adverse Effect Level (LOAEL) based on NTP Technical Report 432 (making it the principal study for OPPT's assessment).

EPA published a revised IRIS toxicological assessment for barium in

1998 through its newly-implemented IRIS Pilot Program. This 1998 IRIS assessment continued to identify cardiovascular effects (hypertension) as the critical effect for chronic barium ingestion as had earlier IRIS assessments. It contained no mention of the toxicological evaluation conducted by OPPT reported in 62 FR 366-372 (January 3, 1997). There was no explanation of how a radically different interpretation of the same data could be justified. The No Observed Adverse Effect Level (NOAEL) adopted in the IRIS barium file was 0.21 mg/kg/day, whereas OPPT had adopted the NOAEL values from the NTP Technical Report 432 - 70 mg/kg/day in rats and 165 mg/kg/day in mice (cardiovascular effects were not detected in the NTP studies at dose rates far above those reputed to cause hypertension in IRIS).

To present our concerns regarding deficiencies in the 1998 revision of the IRIS barium file, a colleague and I met with Dr. William H. Farland, Director of the National Center for Environmental Assessment, on July 7, 1998. Dr. Farland indicated that minor editorial revisions could be made. During our meeting we expressed our belief that even with significant editorial changes, the March 30, 1998 IRIS barium file revision would be seriously flawed because it incorrectly evaluated and weighted the scientific evidence to arrive at an incorrect and untenable Oral Reference Dose for barium.

I visited the IRIS reading room in Cincinnati in early 1999 to review the barium file revision dossier. I found that the peer review of this revision had not been conducted according to required EPA procedures. We informed Assistant Administrator Norine Noonan and Deputy Administrator Peter D.

Robertson, as well as GAO, by letter of the serious deficiencies in the peer review conducted on this work product. In a May 25, 1999 letter to Mr. Peter F. Guerrero, Director of Environmental Protection Issues at GAO, I described the serious deficiencies I found in the Peer Review Record for the IRIS barium file revision and further stated, "CPC is submitting the above information to you to demonstrate the veracity of the statement in your 1996 report, GAO/RCED-96-236 Peer Review at EPA, on page 6, 'Although we agree that the issues EPA and others have raised may warrant further consideration, we believe that EPA's uneven implementation is primarily due to (1) confusion among agency staff and management about what peer review is, what and when and how it should be conducted and (2) ineffective accountability and oversight mechanisms to ensure that all products are properly peer reviewed by program and regional offices.' Ineffective accountability and oversight mechanisms may extend to the highest levels within EPA. We ask that the information contained in this letter and its attachments be included in GAO's continuing evaluation of EPA's peer review practices; we consider this information to be particularly worrying in view of the fact that the Office of Research and Development, of which IRIS is a part, is entrusted with the responsibility of determining whether peer reviews throughout EPA are conducted according to EPA policies."

Uncorrected deficiencies in the IRIS barium file prompted CPC to submit a Request for Correction under the "Information Quality Act" on October 29, 2002 seeking revisions in the IRIS barium file to make it consistent with the OPPT toxicological evaluation published in the January 3, 1997 Federal

Register – the principal study should be NTP Technical Report 432 and the critical effect should be kidney effects. CPC's Request for Correction was denied in a letter from EPA dated January 30, 2003 on the grounds that our request ""offers an alternative assessment of the relevant science but fails to demonstrate that EPA's assessment is not consistent with EPA guidelines regarding objectivity and reproducibility."

A Request for Reconsideration under the "Information Quality Act" was submitted on March 14, 2003 based on the premise that our request was a matter of scientific objectivity, not simply "an alternative assessment." I met with EPA Assistant Administrator Paul Gilman later in 2003. Based partly on EPA's characterization of a 1995 University of Michigan study which CPC had submitted to IRIS as "new information" a review of the IRIS barium file was initiated. The University of Michigan study, which was available to IRIS staff long before the 1998 barium file revision, found that barium acted to prevent sodium-induced hypertension [Schnermann, J (1995) Effects of barium ions on tubuloglomerular feedback. Am. J. Physiol. 268 (Renal Fluid Electrolyte Physiol. 37): F960-F966].

Finally, on July 11, 2005, a revised IRIS barium file reflecting the conclusions presented in the 1997 OPPT toxicological assessment – NTP Technical Report 432 is recognized as the principal study and nephropathy (kidney effects) are recognized as the critical effect – was put on-line. From 1997 until 2005 there were two divergent toxicological assessments of barium within EPA. In 2005 the straightforward assessment of a very small number of

scientific studies completed by OPPT in only a few months was finally recognized in IRIS after an untold number of man-hours of effort over a period of 8 1/2 years.

The RCRA regulatory level for barium has not been revised to reflect the higher Oral Reference Dose now contained in the IRIS barium file.

Mr. SHIMKUS. Thank you.

The chair now recognizes Dr. Burke for 5 minutes.

STATEMENT OF THOMAS A. BURKE

Mr. BURKE. Thank you, Mr. Chairman. I appreciate this opportunity. I am Tom Burke and I am the associate dean and a professor at the Johns Hopkins School of Public Health, I also direct the Johns Hopkins Risk Sciences and Public Policy Institute, I served as a member of the Board on Environmental Sciences and Toxicology at the National Academy, I am a member of the EPA Science Advisory Board, and I chaired the National Academy report Science and Decisions, which really took a hard look at risk assessment practices at the EPA.

Perhaps most relevant to today's hearing, though, is I have served as a state official. I was the director of the Toxics Program, the director of Science and Research at the New Jersey DEP, and the deputy health commissioner in charge of environmental issues in that State. So I worked closely with 4 governors on very challenging issues, responding to public health emergencies, which ranged from water contamination to contamination of our beaches to food contamination to the cleanup of hazardous waste sites.

So as a frontline health official, I can tell you that risk assessment is really important. We need information when things bang in the night. And it is an essential tool for protecting the public's health. IRIS has been a part of that. So I would like to address 3 points today.

One is risk assessment itself as an important tool. Second is the IRIS program, and the third I would like to say a little bit about, Science and Decisions and the National Academy recommendations to change the way we approach risk assessment.

So first, as I mentioned, risk assessment is really important to public health officials and it is used by not just EPA but public health agencies around the world. I have helped most of our national agencies from DOD to USDA to use risk assessment. And as a state official, I have worked with other state officials in doing this. And EPA is recognized as providing most of us with the gold standards for evaluating hazards. Part of this is a tremendous use of the IRIS documents, but unfortunately, there are inherent uncertainties.

And as you heard from the panel, there are lots of things about toxicology and epidemiology that are uncertain and they provide the basis for risk assessment. So for instance, does cancer in laboratory animals necessarily mean that exposure will cause cancer in humans? Or more appropriate perhaps in some of the debates about IRIS, if you have 2 conflicting studies, one says you see a health hazard and the other doesn't, which one does EPA go with and how do you make that decision? Well, there have been lots of arguments about this. There is lots of uncertainty that has led to a very polarized confrontation, as you might imagine. So I am no stranger to this phenomenon called dueling risk assessments. An agency will present their risk assessment and their approach to a problem and there is the opposite approach. And we have this situation where EPA is being called way to precautionary and indus-

try's risk assessments aren't listened to because they are seen as not being protective of public health.

So the challenge before us is this process itself, how to be more transparent, meet the needs of decision-makers, and break the log jam we now have. Now, the IRIS program, as you heard today, has a very unenviable task of synthesizing a lot of scientific information, and it appears to be the program everyone loves to hate. So they provide these very comprehensive overviews of health effects and they weigh the scientific evidence, and it is very important in determining if we have hazards. Not surprisingly, this is controversial. They are the starting point for many of the Agency's most difficult decisions. They provide insight into the magnitude of risk but they don't tell us how to manage risks.

I am very familiar with the challenges of IRIS and I actually think the NAS report on formaldehyde provides a sound roadmap for them to improve that.

Now, I would like to finish with a few words about risk assessment. We have blurred the line today I think between risk assessment and the IRIS hazard assessments. Risk assessment is about decisions and should start with, as Science and Decision lays out, the problem formulation making sure we ask the right questions, including the assessment that looks at the various options for control.

And finally, with risk management decision justification, very important to this committee, is this decision justified, particularly in light of costs? So I think just to kind of sum up, the framework that Science and Decisions offers perhaps can help us improve the application of IRIS and risk assessment and risk management and consider the very important considerations of economics and jobs.

So finally, can risk assessments work for jobs and the economy? Well, in my experience as a state official in New Jersey, a clean environment is definitely good for business, just ask the resort owners of the Jersey Shore or the businesses along the redeveloped Brownfields and the Hudson River shoreline. Getting better solutions for environmental problems goes well beyond IRIS and should focus on advancing risk assessment to better inform our public policies.

Thank you for the opportunity to speak to you today.

[The prepared statement of Mr. Burke follows:]

Testimony of Thomas A. Burke, PhD, MPH
Professor and Associate Dean for Public Health Practice
Johns Hopkins Bloomberg School of Public Health
Director of the John Hopkins Risk Sciences and Public Policy Institute

U.S. House of Representatives
Committee on Energy and Commerce
Subcommittee on Environment and the Economy

Hearing on Chemical Risk Assessment

October 6, 2011

Thank you for the opportunity to address the Subcommittee on Environment and the Economy at today's hearing on Chemical Risk Assessment. I am Dr. Thomas Burke, Professor and Associate Dean at the Johns Hopkins Bloomberg School of Public Health. I am also Director of Johns Hopkins Risk Science and Public Policy Institute. I have served as a member of the National Academy of Sciences Board on Environmental Science and Toxicology, and am a Member of the EPA Science Advisory Board. I also served as Chair of the National Academy of Sciences Committee on Improving Risk Analysis Approaches Used by the U.S. EPA. Perhaps most relevant to today's topic, I served as Director of Science and Research at the New Jersey Department of Environmental Protection, and as Deputy Commissioner of Health for the State. In those positions I worked closely with four governors, responding to public health emergencies and advising them on difficult environmental health risks including drinking water contamination, food safety, pollution at the beaches, and the clean-up of hazardous waste sites. As a front line health official I can tell you that risk assessment is an essential tool for protecting the public's health with applications that go far beyond the regulatory mandates of EPA.

I would like to address three points today:

1. Risk assessment is an essential tool that informs public health policy decisions far beyond the regulatory mandates of EPA
2. The EPA IRIS program plays a critical role in providing the scientific assessment of hazards, yet there is an important distinction between the IRIS assessment process and the ultimate risk management decision.

3. The National Academy of Science report "Science and Decisions" provides a framework for improving the risk assessment process and addressing the needs of decision makers.

Risk Assessment – An Essential Tool

The principle tool for integrating science into environmental health policies is risk assessment. This stepwise tool provides a framework to define public health problems, identify hazards, and characterize to probability of adverse impacts. Risk assessments are used by EPA and public health and environmental agencies around the world to guide policy decisions, standard setting, and regulations. Throughout the world the EPA is recognized as a leader in developing guidelines for evaluating hazards, assessing population exposures, and characterizing public-health risks. These tools are used by public health professionals to guide their work in assuring health and safety in our communities.

Unfortunately, there are inherent uncertainties in toxicology and epidemiology studies that provide the scientific basis for risk assessments. Does cancer in a laboratory animal mean that exposure will cause cancer in humans? If two studies give conflicting results for an adverse health effect which do you choose? These are vexing questions and the ongoing arguments led polarized confrontation and an erosion of the credibility of the process. I am no stranger to the phenomenon I call "dueling risk assessments" – is it just a coincidence that the agency risk assessment are accused of being overly precautionary, while industry risk assessments are accused of not protective of public health?

The challenge before us is to improve the process of risk assessment, supporting improved scientific analysis and a more inclusive transparent process to meet the needs of decision-makers, break the log jam, and develop workable solutions to environmental health problems.

The EPA IRIS process

The EPA IRIS program is charged with the unenviable task of synthesizing enormous amounts of scientific information to evaluate hazards. The IRIS program does not actually conduct risk assessments, but its toxicological assessments are the building blocks for the risk assessment process. The program does not conduct original research, but works to synthesize the scientific literature to present a comprehensive overview of the acute and chronic health hazards associated with chemicals. The process also includes weighing the scientific evidence that a chemical may cause adverse impacts such as developmental and reproductive effects or cancer. The documents provide a tremendous resource to the scientific community, business and industry, academia, and public health and environmental agencies. Not surprisingly, they are also controversial. They are also the starting point for many of the agency's most difficult and far-reaching decisions about environmental pollutants. They provide insights on the magnitude of risks---but they do not tell us what level of risk is "acceptable". Nor do they tell us how to manage or reduce risks.

Some have said that IRIS documents are the most extensively reviewed scientific reports ever written. While this is difficult to determine, it is clear that each document goes

through an exhaustive process of review, comment, and revision. As a participant in several reviews I am familiar with both the documents and the process. I have also heard the frustrations of stakeholders toward public comment periods and am familiar with the recommendations of several reports from the NAS. Many of these criticisms have been about the process rather than the science, and the format and clarity of the documents rather than their scientific conclusions. Indeed many of the public criticisms address the implications for the costs of risk management rather than scientific content of the IRIS assessments. I agree the IRIS process needs to be continually improved, and the Agency has taken important steps forward. The recommendations of the NAS *Review of EPA's Draft IRIS Assessment of Formaldehyde* provide a sound roadmap for the future.

The National Academy of Science report "Science and Decisions"

The NAS report *Science and Decisions* (NAS 2009) provides a stepwise framework for improving decision making. A diagram of the framework is included in my written testimony. The highlights of the framework are

- Problem Formulation – asking the right questions including stakeholder input, what are we trying to solve and what are the options?
- Planning and Assessment – what are the risks of the proposed options, what is the level of uncertainty? Does it address risk management options and is it peer reviewed?
- Risk Management – What is the decision and its justification, in light of the costs and uncertainties of each option?

This framework has the potential to change the way risk assessment is conducted and improve the application of science in risk management decisions. It provides for enhanced stakeholder involvement, improved consideration of the economic impacts, and an evaluation of the effectiveness of our risk management policies.

Can risk assessment work for jobs and the economy? In my experience in as a state official in New Jersey, a clean environment is definitely good for business. Just ask the resort owners at the Jersey Shore, or the businesses along the redeveloped Hudson River shoreline. Reaching better solutions for environmental problems goes well beyond IRIS and should focus upon advancing risk assessment to better inform our policy decisions.

Thank you for this opportunity to speak with you today on this important environmental health challenge.

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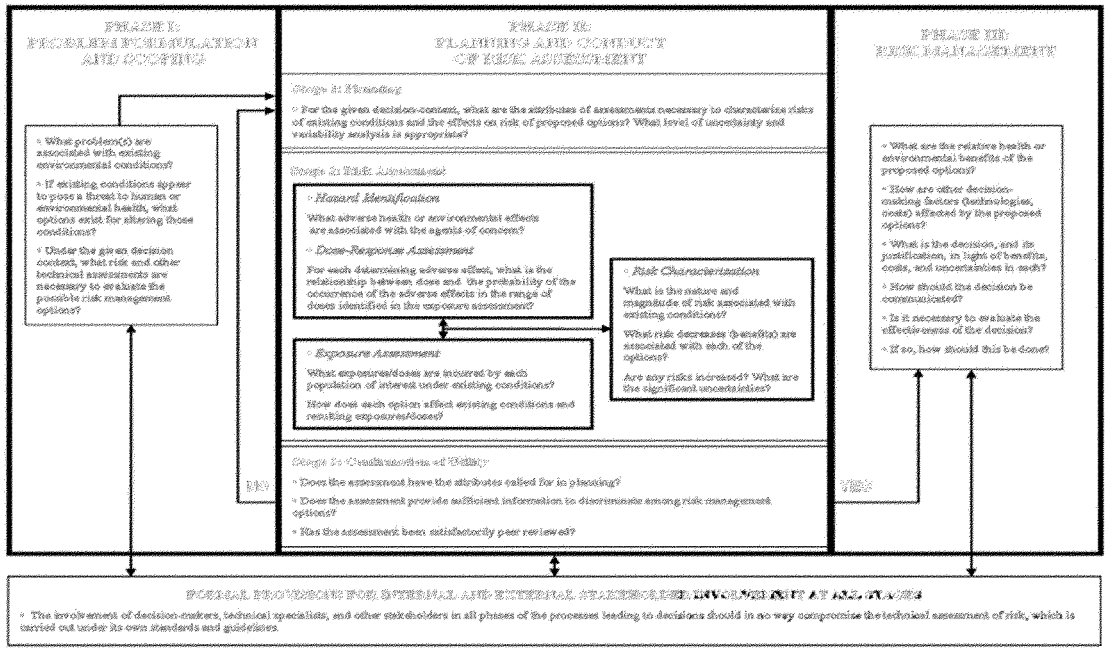

Science and Decisions (NAS 2009) framework for risk-based decision making

Mr. SHIMKUS. Thank you, Dr. Burke.

And now I would like to recognize myself for 5 minutes for opening questions in this panel. I will start with Mr. Cook because a lot of our focus here in this Congress has been on the effects of regulations on jobs and the economy. We do want to make sure that that is balanced, but we also, especially in the environment that we are in, we know that excessive regulations really are creating a burden.

You have highlighted some of those burdens in your opening statement. If the chemicals you produce are not available, what substitutes would be made?

Mr. COOK. In some cases, there would be substitutes available. In other cases, I am not sure there would be. In the case of the airport striping and signage, our barium carbonate is formulated by 2 manufacturers in the United States into very tiny barium glass beads. Barium gives that glass a very high refractive index, so when light shines on a paint containing these glass beads, it glows. I think that is a major safety consideration for airports and certainly it helps visibility of highway signs and probably has a safety impact there, too. I am not sure what material other than lead—lead glass also has a high refractive index.

Mr. SHIMKUS. Barium would probably be better than lead.

Mr. COOK. Given as I say there really is no chronic effect to barium until you get to very, very high levels that are just not found anywhere in nature.

Mr. SHIMKUS. And let us just talk through this. Also, you opening statement mentioned if we are not certain that the IRIS analysis is based upon credible sound science, what effect does that have on you?

Mr. COOK. Well, for the past almost 29 years now, I have been trying to effect a change in the regulatory limit. And as I said, that regulatory limit was established back in the '70s when there was no data. Unfortunately, when IRIS came along in 1987, by that point, EPA had funded two studies. One found a slight but—they claimed—significant blood pressure increase at low levels of barium in drinking water. The study in EPA's own health effects research lab, giving the rats 10 times as much barium for a longer period of time found no blood pressure increase. EPA chose to go with this study that found the blood pressure increase and said aha, here it is, once again, over-precautionary. It was not a particularly good study. They recognized that and yet they set their limits on that.

Mr. SHIMKUS. And there is terminology, abundance of caution, at the different levels as the regulation moves forward, and I think you are highlighting that.

Mr. COOK. Yes.

Mr. SHIMKUS. Dr. Honeycutt, in your written testimony, you are pretty blunt. You say, "because of the lack of scientific defensibility and the implications of EPA's new chemical assessments, we decided to develop our own chemical assessments." Can you describe the scientific defensibility that you refer to? Because I hear Mr. Cook talk about barium and I am not sure anyone in essence disagrees with that analysis, but can you talk about what you are referring to here?

Mr. HONEYCUTT. Sure. There is no doubt that EPA comes up with safe levels. I mean there is no doubt about that. The question is can you have a higher level that is still just as safe? And that is where you have to get away from default procedures and actually look at how a chemical work in the body. How does it work in the rat versus how does it work in the human and then at what levels are they exposed to? Because chemicals will exhibit different levels of toxicity depending on the dose. A good example is Tylenol. Twenty tablets will kill you, two tablets will cure your headache, a half a tablet or a quarter of a tablet won't do anything to you that is an adverse effect. So you have to look at those differences in dose.

Mr. SHIMKUS. In your opinion, is the IRIS program receptive to suggestions for program improvements to address this example you just gave?

Mr. HONEYCUTT. Well, they actually have guidance on some of the things that we are talking about. The problem is their inconsistency in using their own guidance. They talk the talk but when it comes to doing the assessment, they just revert back to their old precautionary selves.

Mr. SHIMKUS. Thank you. My time has expired. And depending upon how many people show up, we may go around a second time. I know there is more I want to address.

So I would like to recognize Mr. Green for 5 minutes.

Mr. GREEN. Thank you, Mr. Chairman.

Both Houses of Congress seem to be interested in addressing the IRIS recommendations whether it is strengthening IRIS or suspending it. And our colleagues in the Senate sent a letter to one of our first panelists calling for suspension of IRIS assessments until the NAS recommendations can be incorporated. On the first panel, we heard from Dr. Anastas and the NAS on why such a suspension is not necessary and wouldn't protect public health. Now, with this panel, we are fortunate to have an expert on risk assessment who was quoted in that Senate letter.

Dr. Burke, you are quoted as saying, "A sleeping giant is the EPA sciences on the rocks and if you fail you become irrelevant." Would you explain that statement?

Mr. BURKE. Sure, and thanks for asking that question. So that statement was made at a meeting of the EPA Science Advisory Board where we presented with the ORD vision for how science will be conducted in the future. And knowing the incredible pressures and having been on those frontlines, applying science to society's problems, I issued that as a warning statement. Obviously, there is lots of criticism; then the credibility of science is really important.

So why is EPA in a crisis? Well, because of the incessant attacks on their credibility not because they are not trying to put together the best science and not because they don't have a good Science Advisory Board that provides them, but I think it is important to put that into context. EPA is under siege. The very mission of protection of our environment is being questioned, sometimes with good cause because of the economic considerations. But I think there is a crisis. There is a crisis in credibility and that roadmap of improving IRIS will be a very important step toward addressing that crisis.

Mr. GREEN. OK. And you are familiar with the rider that I mentioned and do you think that rider would strengthen the IRIS program?

Mr. BURKE. Unfortunately, I think it would be a disservice to public health agencies throughout the country and even perhaps the world and it would bring things to a halt in a way that would not serve us well.

Mr. GREEN. OK. It seems there is a difference of opinion among our panel members on IRIS assessments and what they should be. Dr. Honeycutt suggested in his testimony the IRIS assessment provides EPA's judgment in how much a chemical can be in fish or apple juice for it to be considered safe, but these evaluations require assessing that exposure, something IRIS does not do. Dr. Burke, can you clarify the distinction between assessing the hazard and assessing the risk?

Mr. BURKE. Yes, so understanding the hazard it is like knowing. So this is anthrax over here and this is bad stuff, can cause a real problem and it can cause problem at different levels. So it allows us to understand what the risks might be to people who are exposed. That is very different than the problem-oriented process of risk assessment that says we have a facility here that has a problem and potentially emitting things into the environment. How do we evaluate what is acceptable in terms of a response to manage that risk. So the risk assessment is site-specific; it is population-specific, very different than just identifying the hazard and evaluating the epidemiology and toxicology.

Mr. GREEN. So there is a difference between the risk assessment and what risk is acceptable?

Mr. BURKE. Yes. And the hazard assessment will never tell you what risk is acceptable. That is a societal issue. It can consider social issues. There are lots of things that we don't regulate to very low levels because they are naturally occurring, and it is a policy question, not a science question except ability of risk. But understanding a hazard, that is all about good science.

Mr. GREEN. Well, here we understand asbestos is a toxic substance but you can go out in some places and dig up asbestos since it is a rock. And we know we can't prohibit it because you can be exposed by just digging it up. Although asbestos for decades was used very substantially to retard fire risks, so an assessment of the danger and also what could be acceptable if you encapsulate it and do lots of things you can deal with that.

Dr. Honeycutt, I want to thank you for appearing before the committee, and you have heard, I have worked with TCEQ over the years and TCEQ actually alerted our office because for years we have had a heightened dioxin level in upper Galveston Bay and the Houston Ship Channel and most of my industries are getting blamed for it. And there was some concern because we couldn't quantify it until TCEQ did. Can you tell us what efforts TCEQ has taken in regard to dioxin just as a substance? Like I joke I want dioxin, I want white shirts, but I also know that I don't want to drink it. So if you can tell us what TCEQ in Texas has done with it.

Mr. HONEYCUTT. Yes, sir. Thank you. I am very familiar with the San Jacinto pit site. We have developed our own policy-based num-

ber that we have used over the years for dioxin, and as I mentioned in my testimony, we are developing our own procedures for coming up with these toxicity values that has been through a peer review and that is out for public comment right now. So once that is finalized, we are going to run dioxin through a process and see what our number looks like. So we are actively looking at that. I can't tell you right now where the number will come, whether ours is more or less or higher or lower than EPA's but we are going to be actively involved in that.

Mr. GREEN. OK. Is there going to be any conflict between when EPA is coming out in 2012 or will the TCEQ's be earlier than, you know, a year from now?

Mr. HONEYCUTT. It won't be earlier than a year from now definitely.

Mr. GREEN. OK. It would be good to have two different assessments because, one, that is how you get what we can do with the risk and also I know I am over time but I appreciate your testimony that having spent 20 years in the Texas legislature and getting mad at EPA on a regular basis, we also recognize, as you said in your testimony, we sit down and can work things out but sometimes we have to lower the decibel level to get there.

So thank you, Mr. Chairman.

Mr. SHIMKUS. The gentleman yields back his time.

The chair recognizes the gentleman from Louisiana, Mr. Cassidy, for 5 minutes.

Mr. CASSIDY. Thank you. I am an erstwhile academic so I will speak to Dr. Clewell and Dr. Burke because clearly as I gather IRIS is supposed to be here to use science to inform policy. The concern, though, is that policy is manipulating process in science to achieve an advocacy as opposed to achieving truth, truth being the highest calling of science. Fair statement? And that is, if you will, the question before us.

Now, Dr. Clewell, when I read yours that there is clear bias towards presenting evidence that supports the selection of a default linear approach even when there is support for a nonlinear approach in the scientific community, if I was co-writing a paper with a medical student and she brought something to me that had only one explanation even though I knew that there was an alternative explanation which she does not address, I would give her a mulligan. I would say you are a medical student; you need to learn to do better. Bring it back discussing the alternative explanation and use this as a teaching moment. When EPA is using it to drive public policy, my blood pressure goes up. I must have just taken a boatload of barium because, you know, why in the world are we making decisions that affect an incredible number of jobs on something which doesn't have a plausible alternative explanation. So you have made your point.

Let me ask Dr. Burke whether or not you disagree with the point Dr. Clewell made but by the way is a similar point to what NAS made that the neurobiological effects of the formaldehyde could be attributed to other things, which the thousand-page document did not discuss. So Dr. Burke?

Mr. BURKE. I don't think we fundamentally disagree that EPA should present as comprehensive a picture as possible with the al-

ternatives. I think we probably disagree in the fundamental mission of EPA and there in my testimony——

Mr. CASSIDY. Can I stop you for a second?

Mr. BURKE. Yes.

Mr. CASSIDY. Because I am actually talking about not EPA but IRIS.

Mr. BURKE. OK.

Mr. CASSIDY. IRIS and a thousand-page document presumably presenting a comprehensive discussion——

Mr. BURKE. Right.

Mr. CASSIDY [continuing]. Did not present a plausible alternative explanation that NAS came up with.

Mr. BURKE. Right.

Mr. CASSIDY. Now, this is not, you know, industry. This is NAS.

Mr. BURKE. Right.

Mr. CASSIDY. And so you open a thousand-page document, IRIS did not discuss it. It has to beg the question have they moved beyond advocating science for truth to selective presentation of science to pursue policy?

Mr. BURKE. OK. Well, again, not being part of the IRIS program and not being part of that review, I know that the standard default that not just EPA but public health officials use, again, throughout the world particularly for carcinogens is the linear default, that we are not quite sure because genetic damage can happen at very low levels, just how low that straight line might go. However——

Mr. CASSIDY. Now, that I have to say surprises me because we know that a 20-pack a year history of cigarette smoking is strongly related to a risk of something less is a threshold effect. Indeed, Dr. Anastas spoke about how—I have it written down here someplace and of course I have lost it—that they look for a dose-related effect.

Mr. BURKE. Yes.

Mr. CASSIDY. So that would be a nonlinear effect. I am not sure why we are still mired in something conceived of 3 decades ago as defining how we should approach a problem in this year.

Mr. BURKE. Well, I think it is the strength of evidence, and when we are looking at hormonal effects and we are looking at neurological effects on the unborn, the fundamental question is, a very important one, shouldn't we present the whole picture about what the alternatives may be. But that may not change the public health decision that where there is uncertainty we have to make decisions.

Mr. CASSIDY. But my concern is apparently they are not presenting the whole picture which in effect skews the——

Mr. BURKE. That is where I think we agree.

Mr. CASSIDY. Excuse the assumption. Dr. Clewell, I am kind of speaking for you. Could you speak for yourself?

Mr. CLEWELL. Thank you, sir. I am particularly troubled because I worked closely with William Farland when they were developing the cancer guidelines trying to change from the old way of doing things with just a default. And the cancer guidelines was important because it was the first time that priority was given to a chemical-specific decision that did not rely on the default and a justification was required that there was insufficient data to support using a default. But in recent years there has been use of 1968 guidelines. It is a default. They don't demonstrate a balanced presentation of

the different alternatives that are being discussed in the scientific community. They paint a picture of evidence supporting the default.

Mr. CASSIDY. That is either suggesting incompetence or it is suggesting the pursuit of a political agenda.

Mr. CLEWELL. Absolutely not incompetence. They are very competent people. I believe that they are public health professionals who are very concerned about public health and want to make sure they are conservative. And in trying to make sure that the protection is provided, they may not provide complete descriptions of alternative approaches that would generate a lower-risk estimate.

Mr. CASSIDY. That is a patronizing approach to the use of truth in science. And I as a person who is sitting on here trying to make an informed decision am offended that they assume I don't have the intellectual firepower to figure it out. And that is a disservice to the American people.

Mr. CLEWELL. Actually, the Office of Water has the same problem. They are pretty much hamstrung by the arsenic risk assessment and decisions they would like to make like saying you don't have to clean up the entire western country of arsenic in soil and river water are difficult to make when there is only a linear risk estimate.

Mr. CASSIDY. I agree with Dr. Burke that there is indeed a threat to IRIS's reputation and I think we are seeing it in terms of an uncovering of how they present facts. I yield back.

Mr. SHIMKUS. The gentleman yields back his time.

For the sake of getting my colleagues angry at me, I would like to go to a second round. I think the panel is well informed. We are learning a lot. The risk will be members may come back which might hold you a little bit longer, but I would like to go a second round if that is oK with our guests and my colleagues here. If no objection, then so ordered. We will go to a second round, 5 minutes each. And I may not take my whole 5 minutes, but with that, I will recognize myself.

And this is just a great debate. My concern is an overabundance of caution at IRIS and an overabundance of caution at EPA with the policymakers could create job loss, economic dislocation, and movement of production overseas. So we have got to get the science right and I don't question the public health officials' intent to protect human health. I do agree that this debate on dosage and what is really harmful is very, very important.

So with that, Dr. Burke, I want to address just one question on the delay because the question is what would you deem more harmful to human health and the economy? A 1- or 2-year delay in an assessment that would ensure the scientific robustness of the result or an assessment based on poor processes that is pushed through with questionable science?

Mr. BURKE. I think we owe it to the American public, I think we owe it to the scientific community to use the data appropriately and to synthesize the scientific information to inform decisions. However, having been in emergency situations where the data wasn't perfect, for instance, the trailers in Louisiana where the data on formaldehyde weren't perfect, I worked with the CDC to try and make sure we didn't have acute exposures. So sometimes

in public health we have imperfect information. However, I agree with you, Mr. Chairman, that it would be better to do it right than to destroy the credibility of the process.

Mr. SHIMKUS. And that is this whole debate from the Senate, from what we did on the rider to say let the National Academy of Sciences' report be, you know, followed before we continue to move forward just so we get it right. But the great thing about a lot of things we do on this committee and on our health subcommittee is that people in this arena are public servants and want to do things right. But again we wanted to raise that issue.

To Dr. Honeycutt, I raised this in maybe my opening statement or the first round. We have talked about it before and we just mentioned it with the water and arsenic in the Southwest. I remember it well because one of my colleagues, Heather Wilson, always talked about that, arsenic levels in drinking water although it was naturally occurring. So with that, this question: In your opinion are there broader economic consequences associated with publishing an IRIS value that is lower than background levels, and if so, what impact do you feel it has on the jobs in the economy?

Mr. HONEYCUTT. Oh, absolutely there is an impact. Two real quick examples, one is mercury. EPA is actually, they are outliers from the rest of the world and what is a safe level of mercury in fish. All other regulatory agencies have higher safe levels. And they came home to Texas just a few weeks ago.

Mr. SHIMKUS. Let me interrupt. Is that true in the European standards?

Mr. HONEYCUTT. Yes, the World Health Organization has a higher safe level for mercury in fish than EPA does.

Mr. SHIMKUS. That is funny. I never hear my colleagues mention that when we debate that issue.

Mr. HONEYCUTT. But Lumina Energy laid off 500 people just a couple of weeks ago. So it does have direct or indirect—it depends on how you look at it—economic consequences.

And another example is the arsenic that you are talking about. In Texas, there are a lot of really small locally owned utilities that won't be able to meet this, so they are going to close down. And so people then will have to drill their own water wells and that is a real public health concern because that water won't be tested or monitored and they are going to be at their own risk that the public water systems won't be able to provide that level of safety.

Mr. SHIMKUS. And let me just finish with this. Mr. Cook talked about barium quite a bit in his analysis and his response. His statements on barium and the health risk—and I kind of assumed everyone sort of agreed with that analysis—can you go on record saying you agree with Mr. Cook on his analysis on barium?

Mr. HONEYCUTT. Yes, sir. Barium in the grand scheme of things is not a very toxic chemical at all.

Mr. SHIMKUS. Dr. Clewell?

Mr. CLEWELL. Yes, I agree.

Mr. SHIMKUS. Dr. Burke?

Mr. BURKE. I really don't know the issue. I will have to——

Mr. SHIMKUS. That is fine. That is fine. And that is why I wanted to clarify because I did make an assumption. I didn't want to do that.

So I am going to yield back 18 seconds and ask my colleague, Mr. Green, to be recognized for 5 minutes.

Mr. GREEN. Thank you, Mr. Chairman.

Dr. Burke, in listening to my colleague from Louisiana, Dr. Cassidy, and I think your comments sound like it blurs the line between the mission of IRIS, which is to assess the risk and not the issue of regulations, which is the management of that risk, which is EPA's job. I guess there may be some concern that by the assessment from IRIS, it may raise the level of concern but, you know, like we have heard from Dr. Honeycutt, you know, IRIS is supposed to give the assessment but the risk is an EPA decision and not necessarily what may come out of the study.

For example, the water, you know, obviously water we need for our lives, but if you take it from a fire hose, you are going to drown. And so there is a reasonable amount that you can have that is necessary but it is, you know, too much of anything is bad.

And Dr. Burke, naturally occurring levels of chemicals, they are not always safe. A good example of arsenic in water, I can tell you in West Texas and all over the West there are waterholes or water that people should not drink and know they shouldn't drink because of whatever the chemical is in there that are naturally occurring. So just because they are naturally occurring doesn't mean it is safe. You just have to have a certain level of it I guess to keep it. And is that something we are continually confused, the difference between assessment and risk?

Mr. BURKE. Well, it is a very important point. We can't possible clean up the Earth's crust, nor can we regulate volcanoes for spewing mercury. And we have these naturally occurring materials and we have to balance that in the decision-making. On the other hand, what we know about arsenic comes from actually naturally occurring contaminated wells in other parts of the world where people drank very high amounts and had acute effects as well as cancer effects. And so it comes down to being reasonable about how we approach regulation with the right information on the public health effects to help us make those decisions.

Mr. GREEN. OK. You know, I have announced where I come from. I have the biggest petrochemical complex in the world in our district—in the country, second largest in the world, and so I guess my focus is on the relationship. Dr. Burke, as a former state regulator and you have seen the risk assessment and effective risk management, what effect can it have on the jobs? Every product we make in the Houston Ship Channel, it wouldn't be made if somebody didn't need it. I mean industries don't do that. They don't make any money on it. So someone needs it but it depends on how you make it and how that product is used, whether it be in gasoline or some other additive or something else.

But is there a direct correlation between effective risk management and the impact on jobs and the economy, which is I think what the whole subcommittee was getting at?

Mr. BURKE. I think that is a very important point in major regulatory decisions. I am not an economist. I can only speak from experience, and clearly there are regulations that have added cost to industry and therefore may impact jobs and may impact the general public as well. But as we recommended in Science and Deci-

sions, that should be part of the deal in conducting the assessment to make sure you are making the right risk management choice.

That doesn't change what happens in the epidemiologic studies or in the mice, but we can take that data and if it is properly presented make good decisions. So in my experience again, New Jersey, very industrialized, lots of heavy industry, lots of refineries, pollution was much worse for jobs and unsafe workplaces were much worse for jobs than environmental regulations. However, I completely understand that analyzing the impacts on the economy on jobs should be part of the decision process.

Mr. GREEN. Thank you, Mr. Chairman. And following your lead, I will yield back my 46 seconds.

Mr. SHIMKUS. I thank my friend.

The chair now recognizes the gentleman from Louisiana, Mr. Cassidy, for 5 minutes.

Mr. CASSIDY. Again, I am learning a heck of a lot in this meeting, so thank you all for all being here. I am struck how sometimes processes used to manipulate the response to the findings. Now, Dr. Honeycutt, I am impressed that you all—I haven't read about a regression coefficient since I have been here, you know, been practicing whatever, and you all did an analysis—now, that is a 1,043-page document which is stultifying, redundant, and sometimes irrelevant, and yet you had to do all 1,043 pages. Now, it makes me think that it would be incredibly time-intensive, resource-intensive to really do an adequate review. If you have a statistician doing a regression coefficient on nasopharyngeal cancer mortality to criticize or critique the method by which they determined incidents, you got some money tied up in staff working on this project. Fair statement?

Mr. HONEYCUTT. Yes, sir, it is.

Mr. CASSIDY. Now, if it is 1,000 pages do they give you 120 days or—do you see what I am saying?

Mr. HONEYCUTT. Yes, sir. No, you get the same amount of time. And the deal with IRIS is you don't get to give input on the front end; you give input on the back ends after EPA has already—the train has left the station and they are recalcitrant to change their mind. So that is what you are left with.

Mr. CASSIDY. I see everybody nodding their head yes. Now, that is disturbing because again if we have a premise which I think you all agree with is that sometimes they are not given the complete picture but at the same time it takes an incredibly intensive process in order to uncover how that is not complete, then you are going to have policy decisions made upon something which may, some cynics would say, deliberately made onerous upon which to review. Again, it goes back to is science deriving policy or is science being presented in such a way as to serve as advocacy for a policy end?

Now, we heard in the first panel and NAS and others criticize the fact that OMB was allowed to at times review the EPA documents in order to say, oK, wait a second, time out, let us look at this. But Dr. Burke, I had a sense from you that in this whole analysis needs to be some sort of cost-benefit return on investment, what is the true sort of economic cost? Here we have people losing their jobs for something which is nominally and maybe even spe-

ciously toxic. Now I am thinking maybe OMB needs to be involved. I mean maybe there needs to be a delay if once the train has left the station you have so little time to review something which is so complex to review.

Dr. Clewell, what would be your comments on that?

Mr. CLEWELL. I am not what sure what would be the level of oversight, but I do believe that OMB plays an important role in verifying that the agencies are doing the best job to make the process reviewable, and so I would be in favor of there being a better dialogue between OMB and EPA so that that could be accomplished.

Mr. CASSIDY. And in fairness, I think the critique is that they should be more transparent in their questions, but I think there was also a criticism as regards sending EPA back to repeat an analysis. What I have learned today is that maybe EPA does need to be sent back to be more inclusive in their analysis. I am feeling more sympathy for OMB right now. So let us see if there is anything else in this.

Now, who is a chemist? Anybody up there a chemist? The idea that Dr. Anastas said that with green chemistry they know the actual effect of every chemical compound is going to have upon skin, respiratory system, digestive system, et cetera seems to me like the epitome of intellectual kind of hubris.

Mr. CLEWELL. It might have been somewhat hyperbolic. I think he is trying to indicate that there is an ability—and drug companies use it all the time—to try to estimate activity from structural properties and that is trying to be harnessed. They are trying to harness that in order to develop safer compounds.

Mr. CASSIDY. There is also the presumption, though, that you can make everything inert, and I am not sure you can make life inert.

Mr. CLEWELL. I am fairly confident you cannot.

Mr. CASSIDY. Yes, so I agree with that.

Let me finish up. I will also yield back by saying to Mr. Cook, Mr. Cook, you are the only guy in this whole room that creates jobs, so on behalf of the American people, thank you for creating jobs, and I am very sorry for the impediments put in front of you by the Federal Government. We sincerely wish we could be creating a lot more jobs.

Thank you. I yield back.

Mr. SHIMKUS. The gentleman yields back. At this time, the chair now recognizes Mr. Harper from Mississippi for 5 minutes.

Mr. HARPER. Thank you, Mr. Chairman. And thank you, witnesses, for being here today and giving your insight into what is continuing to be a very important issue for us.

And I will start if I may with you, Dr. Honeycutt, if I could just with some follow up questions on what you had earlier.

And I have to ask what types of evidence are necessary to establish a causal relationship between exposure to a substance and some health effect or health risk. What are you looking for?

Mr. HONEYCUTT. Yes, that is a very good question and it is well known. It is called the Hill criteria for causation. It is well documented. What you need to do is show that a chemical can cause the effect that you are looking at and it can cause it at the concentrations you are looking at and that it is reproducible. It hap-

pens over and over again, not just one time in one study, and that the effect happens after the exposure. Sometimes we regulate chemicals on if the effect happens before the exposure.

Mr. HARPER. Um-hum.

Mr. HONEYCUTT. And that it is not just a background occurrence, the health effect that you are looking at, that if there is an increased incidence of cancer in this community that it is indeed increased, it is well above background, not just a tiny bit above background.

Mr. HARPER. Are you always able to figure those problems out? It is a search I am sure many times.

Mr. HONEYCUTT. Sometimes it happens very easily and sometimes it is harder. The health effects of ozone are based on a 1 to 4 percent increase in premature mortality, whatever that is, and how do you quantitate that? It is very, very difficult. And in studies the EPA use, you can't quantitate that.

Mr. HARPER. And is it true that substances at a high level which may create that risk, they may be safe, perhaps even necessary at a low level. Would that be certainly true to say?

Mr. HONEYCUTT. Absolutely. Every vitamin you take, most of the minerals in your food that you eat, some of them are essential nutrients that if you get too much of them, they will kill you.

Mr. HARPER. If I could, Dr. Cook, I wanted to ask you——

Mr. COOK. Mr. Cook.

Mr. HARPER. Mr. Cook, I am sorry. That just shows you the respect that we have for your being here today.

Earlier today we had on the first panel—I believe you were in the room when they were here—Mr. Trimble from GAO testified on panel one that the EPA should take the IRIS program back in-house to avoid meddling from OMB or other departments or agencies. Based upon your experience, do you think that is a wise move?

Mr. COOK. If it had not been for OMB's implementation of the Information Quality Act in 2002, I do not believe we ever would have seen IRIS recognize the true chronic effect from barium. Four years after the 1994 NTP study, the definitive study was published on barium chronic toxicity, the revised IRIS assessment in 1998 still argued and ignored the sound scientific evidence that there was no blood pressure effect from small low levels of barium, if it had not been for OMB's intervention, I don't think we ever would have gotten any response from EPA to make the change that was finally put into effect in IRIS in 2005.

Mr. HARPER. Thank you. Also, Mr. Cook, another question I have is, you know, some concerns about IRIS relate to cleanup levels that must be attained under our federal environmental laws. Do you have any experience where IRIS's uncertainty or inappropriate values caused a hazardous waste cleanup to either stall or be delayed or the costs rise substantially?

Mr. COOK. We are still in the throes of determining financial responsibility for a superfund cleanup that is still ongoing in North Carolina. Ward Transformer Company operated just near the Raleigh, North Carolina, Airport rebuilding transformers from 1963 until they finally went out of business I think in 2004. They were designated as a superfund site, the plant site there I think in about

1979. Some of the potentially responsible parties negotiated a settlement with EPA to clean up the actual plant site. The contamination is all PCBs from transformer oil. And they were given a choice at the time that they came to a settlement with EPA of either cleaning up to a 25-parts-per-million standard or a 1-part-per-million standard. The consultant that was working with them reported in the document that I obtained from Region 4 EPA that the choice to clean up to a very stringent 1–PPM standard was made primarily because of a fear that EPA would come back later and require a further cleanup because the safe level had not been clearly defined in IRIS and they were not sure what might come down the pike.

Mr. HARPER. So an abundance of caution made them do that at a much greater cost than probably what was necessary.

Mr. COOK. Yes. I think they even ended up spending about 2–1/2 times what they thought they were going to spend to clean up to a 1–PPM standard.

Mr. HARPER. I thank each of you and I yield back.

Mr. SHIMKUS. I thank my colleagues for joining and for you, thank you for putting up with 2 rounds of questions from us. We really appreciate it. And you can tell from the questions by my colleagues that they were sincere in trying to work through this process.

I want to put on the record that the record will be open for 10 days. You all may see some additional written question as the first panel might from us. If you could answer those questions in writing and send them back within that period of time or as soon as possible, we would greatly appreciate that. We do appreciate your time and I adjourn the hearing.

[Whereupon, at 12:49 p.m., the subcommittee was adjourned.]

[Material submitted for inclusion in the record follows:]

Opening Statement of the Honorable Joe Barton
Chairman Emeritus, Committee on Energy and Commerce
Subcommittee on Environment and the Economy
"Chemical Risk Assessment: What Works for Jobs and the Economy?"
October 06, 2011

Thank you, Mr. Chairman for holding this hearing today on "Chemical Risk Assessment: What Works for Jobs and the Economy". I look forward to the testimony of our witnesses today. I hope we can get a better understanding of the framework of the United States Environmental Protection Agency (EPA's) Integrated Risk Information System (IRIS) as it stands today. I have deep concerns as to the ENTIRE agency's ability to remain objective and stick to the science as they are expected to do.

Since IRIS is the program that makes scientific assessments about chemical substances that the EPA program offices use to set federal limits for various environmental laws, it is imperative that they use accurate data. The conclusions made are transferred downstream to the state agencies and traditionally the states will set standards based on the information flow from IRIS. The Safe Drinking Water Act and the Superfund have been formulated around the 'science' of the respective chemicals evaluated by IRIS.

Since the program was formed it has gone through a number of changes, particularly in regards to the process which the assessments are reviewed. The hope was that the changes made in the process would help the program finalize their assessments without any influence from the White House, the industry or the regulated agencies.

In 2009, GAO placed the program on its 'High Risk Series' because the EPA was unable to complete timely, credible chemical assessments or decrease its backlog of ongoing assessments. The EPA has made some changes based on the GAO's recommendations regarding outside review, but they have been much slower on the recommendations made by the National Academy of Sciences (NAS). The draft assessments sent to NAS for review have been poorly received and heavily criticized by the NAS and not correcting those flaws hurts the program's credibility.

The changes made by the EPA in 2009 were to provide for an expedited streamlined process by which a transparent objective review would be given. To date, that's not happening. There is still a backlog of over 70 assessments and the EPA is still allowing the White House to provide input. The problem we are facing is that the EPA has been consistently coming out with data that is producing assessments that are not scientifically credible.

We can use formaldehyde as a perfect example. Even where the scientific data is available the EPA will often not consider including it in their assessment. The EPA concluded that formaldehyde causes leukemia in humans. This was based on a single study. Scientific data has shown that formaldehyde cannot cause cancer outside of the respiratory tract, but the EPA has not changed their position.

Why would the EPA not utilize the guidelines and concepts that in part, already exist within their OWN decision making framework? The NAS has given solid recommendations to go forth. Why has the EPA not adopted these solid policies?

It is important, very important, to consider the safety of the population, but that goes both ways. If you are over cautious and create an unnecessary panic where it should not exist you can do irreparable harm by these actions as well.

Hopefully today we can have a better understanding of how the EPA prepares their assessments and how they come to their conclusions. This has been difficult to assess in the past by this committee. In other hearings related to the 'science' this committee and others have requested the scientific documentation on the methods and criteria utilized for their rulings. We have had proven data from reliable sources available showing much different results than that the EPA provided within their criteria for their rule. This ability to provide sufficient documentation on their methods and criteria by which they base their claims does not seem to exist.

By creating over burdensome regulations our regulatory agency fails the public in many respects. From what I see, there is an important balance that has not been achieved because of seriously flawed basic operational guidelines.

"The chief danger in life is that you may take too many precautions." ~ Alfred Adler. (Renowned Austrian Medical Doctor and psychotherapist.) With that I thank you again for your testimony today, and I yield back.

Committee on Energy and Commerce
Subcommittee on Environment and Economy
"Chemical Risk Assessment: What Works for Jobs and the Economy?"
Thursday, October 6, 2011

First, I would like to thank each of the witnesses for speaking with us today to examine the EPA's chemical risk assessment program, IRIS.

As many of you know, Southern California faces serious air and water quality issues. According to a recent study, Riverside County – where my district is located - has above average levels of Hexavalent chromium, also known as chromium-6.

What does this mean for my constituents? To answer this basic, but vital question, we need a comprehensive assessment of the chemical's impact on human health. This is where IRIS comes in.

I have heard from constituents that are both concerned about contaminated drinking water – and those who are concerned about the implications and burden of creating new regulations. Regardless, one thing is clear: regulatory decisions and chemical assessments must be based on sound science assessments.

Moreover, it's imperative that we find regulatory balance. I understand the human health stakes that we are dealing with today – particularly for sensitive populations such as children, pregnant women, and the elderly. At the same time, the overregulation of industry is making it increasingly more difficult for American companies to compete and create jobs.

IRIS's profiles of individual chemicals are a cornerstone for a host of activity from government regulation decisions and safety approaches by industry. Therefore, I would just like to emphasize the importance of these assessments – and that they must be done accurately. I appreciate the input from our witnesses, and I remain hopeful that steps can be taken to ensure that the IRIS process is efficient and scientifically credible.

THE COMMITTEE ON ENERGY AND COMMERCE

INTERNAL MEMORANDUM

October 4, 2011

MEMORANDUM

To: Members, Subcommittee on Environment and the Economy

From: Committee Staff

Subject: Hearing on Environmental Regulation and its Impact on the Economy

The Subcommittee on Environment and the Economy will be holding an oversight hearing entitled: "Chemical Risk Assessment: What Works for Jobs and the Economy?" on Thursday, October 6, 2011, at 9:00 a.m. in 2123 Rayburn House Office Building.

The purpose of the hearing is to explore U.S. Environmental Protection Agency's (EPA) chemical risk assessment program, the Integrated Risk Information System (IRIS), and the relationship between that program and EPA's regulatory requirements, specifically whether IRIS is producing high quality science-based risk assessments that are suitable for regulatory objectives, or policy judgments that could harm businesses and the public. Witnesses will be by invitation only.

Background

EPA created IRIS in 1985 to help the agency develop positions within the EPA about human health effects from chronic exposure to chemicals. The IRIS database contains EPA's positions on the potential human health effects that may result from exposure to more than 540 chemicals in the environment and is a critical component of EPA's capacity to support its mission.[1]

The IRIS assessment program and its database are maintained by the EPA's National Center for Environmental Assessment (NCEA) within the Office of Research and Development (ORD).[2] IRIS evaluates information on effects that may result from human exposure to environmental contaminants. Through this program, IRIS issues these assessments to support the Agency's regulatory and other program activities. Scientific values issued by IRIS have been used to set cleanup levels for the Comprehensive Environmental Response, Compensation, and Liability Act (CERCLA) and to develop hazard assessments for the Solid Waste Disposal Act,

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[1]Testimony of David Trimble, Director of Natural Resources and Environment, U.S. Government Accountability Office (GAO), July 24, 2011.
[2]http://www.epa.gov/iris/help_ques.htm#whatiris

reference doses for drinking water contaminant levels under the Safe Drinking Water Act, and air quality standards under the Clean Air Act.

State and local environmental programs and some international regulatory bodies have also relied on IRIS health assessment information to support decision making for laws and regulations to protect public health and the environment.[3]

More recently, EPA program offices are no longer required to concur with IRIS assessments and internal EPA comments are still not transparent. The quality of assessments being produced also continues to be an issue. Since 2005, five assessments have been referred to the National Academies of Science (NAS) for evaluation. All of the NAS reviews have severely criticized EPA's assessments, and offered numerous recommendations, which EPA has yet to fully implement.[4]

Although, IRIS operates without explicit congressional authorization, EPA's policies and programs affect virtually all segments of the economy, society, and government. IRIS assessments have regulatory and non-regulatory implications that are complex and controversial.

IRIS, What Is It?

EPA states that IRIS is a human health assessment program that evaluates quantitative and qualitative risk information on effects that may result from exposure to specific chemical substances found in the environment.[5] The IRIS database contains information that can be used to support the first two steps (hazard identification and dose-response evaluation) of the risk assessment process. When supported by available data, IRIS provides oral reference doses (RfDs) and inhalation reference concentrations (RfCs) for chronic non-cancer health effects, and oral slope factors and inhalation unit risks for carcinogenic effects. Combined with specific exposure information, government and private entities use IRIS to help characterize public health risks of chemical substances in a site-specific situation.

More specifically, the RfDs and RfCs provide quantitative information for use in risk assessments for health effects known or assumed to be produced through a nonlinear (also known as a "threshold") mode of action. The RfD (expressed in units of mg of substance/kg body weight-day) is defined as an estimate (with uncertainty spanning perhaps an order of magnitude) of a daily exposure to the human population (including sensitive subgroups) that is likely to be without an appreciable risk of deleterious effects during a lifetime.[6] IRIS also uses a cancer weight-of-evidence (WOE) descriptor to describe a substance's potential to cause cancer in humans and the conditions under which the carcinogenic effects may be expressed. This judgment is independent of consideration of the agent's carcinogenic potency.

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[3]Trimble, op. cit., page 2.
[4][http://science.house.gov/sites/republicans.science.house.gov/files/documents/hearings/071411_charter.pdf\
[5]http://www.epa.gov/ncea/iris/help_ques.htm
[6]http://www.epa.gov/ncea/iris/help_ques.htm

IRIS Substance Listings and the Process

EPA develops a list of substances for IRIS assessment development on an annual basis. The IRIS program submits queries to EPA Program Offices and Regions and the public for nominations for new assessments or updates of assessments currently on IRIS. Substances are selected based on one or more of the following factors: (1) potential public health impact; (2) EPA statutory, regulatory, or program-specific implementation needs; (3) availability of new scientific information or methodology that might significantly change the current IRIS information; (4) interest to other governmental agencies or the public; and, (5) availability of other scientific assessment documents that could serve as a basis for an IRIS assessment. The decision to assess any given chemical substance depends on available Agency resources. Availability of risk assessment guidance, guidelines, and science policy decisions may also have an impact on the timing of EPA's decision to assess a chemical substance.[7]

EPA's process for developing IRIS assessments consists of: (1) a Federal Register announcement of EPA's IRIS agenda and call for scientific information from the public on the selected substances; (2) a search of the current scientific literature, a Federal Register announcement that the literature search is available on the IRIS internet site, and a call to submit additional scientific information on the substance; (3) development of a draft Toxicological Review or other assessment document; (4) internal peer consultation; (5) internal Agency Review; (6) Science Consultation with other Federal agencies and White House offices; (7) external peer review and public comment; (8) final internal Agency Review, Interagency Science Discussion and ORD management approval; and (9) posting on the IRIS database.[8]

Risk Assessment vs. Risk Management

Risk assessment is the use of the factual base to define the health effects of exposure of individuals or populations to hazardous materials and situations. In the NAS 1983 report, "Risk Assessment in the Federal Government: Managing the Process," the National Research Council (NRC) panel identified four components of a complete risk assessment: hazard identification; dose-response evaluation; exposure assessment; and risk characterization. Risk management is the process of weighing policy alternatives and selecting the most appropriate regulatory action, integrating the results of risk assessment with engineering data and with social, economic, and political concerns to reach a decision.[9]

Some stakeholders believe the line between actual science, risk assessment, and risk management is blurred at IRIS. Controversy regarding IRIS has flared when certain stakeholders have argued that IRIS work actually reflects more policy, through its default assumptions, than IRIS is supposed to undertake. Of note, EPA's 2004 "Examination of EPA Risk Assessment Principles and Practices" states: "science policy positions and choices are by necessity utilized during the risk assessment process."[10]

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[7] Ibid.
[8] Ibid.
[9] http://www.nap.edu/openbook.php?isbn=0309033497
[10] http://www.epa.gov/osainter/pdfs/ratf-final.pdf

The 2009 Bipartisan Policy Center's Science for Policy Project report recommended "that when federal agencies are developing regulatory policies, they explicitly differentiate, to the extent possible, between questions that involve scientific judgments and questions that involve judgments about economics, ethics and other matters of policy." It further stated: "The first impulse of those concerned with regulatory policy should not be to claim "the science made me do it" or to dismiss or discount scientific results, but rather to publicly discuss the policies and values that legitimately affect how science gets applied in decision making."[11]

EPA's 2009 Reforms to IRIS

Amid concerns about the integrity of EPA science, EPA announced the following changes to IRIS:

EPA control. The new IRIS process would be entirely managed by EPA, including the interagency science consultations (formerly called interagency reviews). Under EPA's prior process, these two interagency reviews were required and managed by the Office of Management and Budget (OMB), and OMB determined when assessments could proceed to the next process step.

Transparency. The new process requires that all written comments on draft IRIS assessments provided during interagency science consultations by other federal agencies and OMB be part of the public record.

Streamlined process. The new process streamlines the previous one by consolidating and eliminating some steps. Specifically, EPA would eliminate the step under which other federal agencies could cause IRIS assessments to be suspended in order to conduct additional research.

National Academies of Science (NAS) Long-Term IRIS Recommendations

In April 2011, in a study commissioned by EPA, the NAS's Board on Environmental Studies and Toxicology published *EPA's Draft IRIS Assessment of Formaldehyde.* Chapter 7 of that report states: "The persistence of limitations of the IRIS assessment methods and reports is of concern, particularly in light of the continued evolution of risk-assessment methods and the growing societal and legislative pressure to evaluate many more chemicals in an expedient manner."[12] NAS made the following recommendations to provide long-term solutions to the IRIS program[13]:

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[11] http://www.bipartisanpolicy.org/sites/default/files/BPC%20Science%20Report%20fnl.pdf
[12] http://www.nap.edu/openbook.php?record_id=13142&page=152
[13] http://science.house.gov/sites/republicans.science.house.gov/files/documents/hearings/071411_charter.pdf

General Guidance for the Overall Process

- Elaborate an overall, documented, and quality-controlled process for IRIS assessments.
- Ensure standardization of review and evaluation approaches among contributors and teams of contributors; for example, include standard approaches for reviews of various types of studies to ensure uniformity.
- Assess disciplinary structure of teams needed to conduct the assessments.

Evidence Identification: Literature Collection and Collation Phase

- Select outcomes on the basis of available evidence and understanding of mode of action.
- Establish standard protocols for evidence identification.
- Develop a template for description of the search approach.
- Use a database, such as the Health and Environmental Research Online (HERO) database, to capture study information and relevant quantitative data.

Evidence Evaluation: Hazard Identification and Dose-Response Modeling

- Standardize the presentation of reviewed studies in tabular or graphic form to capture the key dimensions of study characteristics, weight of evidence, and utility as a basis for deriving reference values and unit risks.
- Develop templates for evidence tables, forest plots, or other displays.
- Establish protocols for review of major types of studies, such as epidemiologic and bioassay.

Weight-of-Evidence Evaluation: Synthesis of Evidence for Hazard Identification

- Review use of existing weight-of-evidence guidelines.
- Standardize approach to using weight-of-evidence guidelines. Conduct agency workshops on approaches to implementing weight-of-evidence guidelines.
- Develop uniform language to describe strength of evidence on non-cancer effects.
- Expand and harmonize the approach for characterizing uncertainty and variability.
- To the extent possible, unify consideration of outcomes around common modes of action rather than considering multiple outcomes separately.

Selection of Studies for Derivation of Reference Values and Unit Risks

- Establish clear guidelines for study selection.
- Balance strengths and weaknesses.
- Weigh human vs. experimental evidence.
- Determine whether combining estimates among studies is warranted.

Calculation of Reference Values and Unit Risks

- Describe and justify assumptions and models used. This step includes review of dosimetry models and the implications of the models for uncertainty factors; determination of appropriate points of departure (such as benchmark dose, no-observed-adverse-effect level, and lowest observed-adverse-effect level), and assessment of the analyses that underlie the points of departure.

- Provide explanation of the risk-estimation modeling processes (for example, a statistical or biologic model fit to the data) that are used to develop a unit risk estimate.
- Assess the sensitivity of derived estimates to model assumptions and end points selected. This step should include appropriate tabular and graphic displays to illustrate the range of the estimates and the effect of uncertainty factors on the estimates.
- Provide adequate documentation for conclusions and estimation of reference values and unit risks.

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If you have any questions concerning this hearing, please contact Jerry Couri or Heidi King at extension 5-2927.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

FEB 2 4 2012

OFFICE OF
RESEARCH AND DEVELOPMENT

The Honorable John Shimkus
Chairman, Committee on Energy and Commerce
Subcommittee on Environment and the Economy
U.S. House of Representatives
Washington, DC 20515

Dear Mr. Chairman:

Thank you for your October 28, 2011, letter transmitting the questions for the record from the Committee members relating to the October 6, 2011, hearing entitled, *Chemical Risk Assessment: What Works for Jobs and the Economy?* The agency's responses to those questions are enclosed.

Again, thank you for your letter. If you have further questions, please contact me or your staff may contact Laura Gomez in the EPA's Office of Congressional Affairs and Intergovernmental Relations at 202-564-5736.

Sincerely,

Paul T. Anastas

Paul T. Anastas
Assistant Administrator

Enclosure

The Honorable John Shimkus

1. **How many IRIS assessments do you consider as "assessments currently under development but not yet released for peer review?"**

   a. **Please provide a list of these IRIS assessments and a schedule indicating when each of these assessments is to be released for public comment and independent scientific peer review.**

   There are 32 IRIS assessments that are considered to be currently under development but not yet released for peer review. These chemicals, along with a tentative estimate of when they will be released for public comment and expert peer review, are:

Chemical	Estimated Release
Acetaldehyde	FY2013
Ammonia	FY2012
Benzo[a]pyrene	FY2012
Beryllium	FY2013
Butanol, t-	FY2012
Butyl benzyl phthalate (BBP)	FY2012
Cadmium	FY2013
Chloroethane	FY2013
Chloroform	FY2013
Cobalt	FY2013
Copper	FY2013
Dibutyl phthalate (DBP)	FY2012
Di(2-ethylhexyl) adipate (DEHA)	FY2013
Di(2-ethylhexyl) phthalate (DEHP)	FY2012
Diethyl phthalate	FY2013
Diisobutyl phthalate (DIBP)	FY2012
Diisononyl phthalate (DINP)	FY2012
Dipentyl phthalate (DIPP)	FY2012
Ethyl Tertiary Butyl Ether (ETBE)	FY2013
Hexabromocyclododecane	FY2012
Hexachlorobutadiene	FY2013
Hexahydro-1,3,5-trinitro-1,3,5-triazine (RDX)	FY2012
Methyl Tertiary Butyl Ether (MTBE)	FY2013
Naphthalene	FY2014
Nickel	FY2013
Phthalates (cumulative)	FY2012
Polychlorinated biphenyls (noncancer) (PCBs)	FY2012
Trimethylbenzene, 1,2,4-	FY2012
Trimethylbenzene, 1,3,5-	FY2012
Uranium	FY2013
Vinyl acetate	FY2013

b. **Please indicate for each of these assessments whether it will include the full implementation of all improvements in the scientific practices the NAS panel described in Chapter 7 of the formaldehyde report in the section of Chapter 7 entitled "Reframing the Development of the IRIS Assessment" as elements the committee "considers critical for the development of a scientifically sound IRIS assessment".**

The Agency agrees with and is implementing all of the NAS recommendations in a phased-in approach. The EPA is revising these assessments to address the NAS recommendations in a manner that is consistent with the NAS' "Roadmap for Revision" in Chapter 7 of the formaldehyde review report. Specifically, the NAS stated that "the committee recognizes that the changes suggested would involve a multiyear process and extensive effort by the staff of the National Center for Environmental Assessment and input and review by the EPA Science Advisory Board and others."

c. **For those assessments that will not include the improvements, please explain your rationale for excluding in such assessments the scientific improvements deemed "critical" by the NAS panel.**

Using a phased-in approach, all IRIS assessments are being revised to implement the NAS recommendations consistent with the NAS' "Roadmap for Revision." The NAS viewed the full implementation of their recommendations as a multi-year process. The Agency is aggressively implementing the NAS recommendations related to the development of draft assessments.

2. **How many IRIS assessments do you consider to be "assessments that have already been peer-reviewed or released for peer review?"**

a. **Please provide a list of these IRIS assessments that have been peer-reviewed or released for peer review and schedule indicating when each of these assessments is to be released as a final.**

There are currently 20 IRIS assessments that have already been peer-reviewed or released for peer review.

Fourteen of these assessments have already completed peer review. These chemicals, along with a tentative estimate of when they will be completed, are:

Chemical	Estimated Final Release Date
Arsenic, inorganic (cancer)*	TBD
Chromium VI (oral)*	TBD
Dichlorobenzene, 1,2-*	FY2012
Dichlorobenzene, 1,3-*	FY2012
Dichlorobenzene, 1,4-*	FY2012
Ethylene oxide (cancer)*	FY2012
Formaldehyde*	FY2013
Halogenated platinum salts*	FY2012

Methanol (noncancer)*	FY2013
Polycyclic aromatic hydrocarbon (PAH) mixtures*	FY2013
Tetrachlorodibenzo-p-dioxin, 2,3,7,8- (dioxin), noncancer*	FY2012
Tetrachlorodibenzo-p-dioxin, 2,3,7,8- (dioxin), cancer*	FY2013
Tetrachloroethylene*	FY2012
Tetrahydrofuran*	FY2012

Six of these assessments have been released for peer review, but they have not completed peer review (the EPA has not received the final peer review report). These chemicals, along with a tentative estimate of when they will be completed, are:

Chemical	Estimated Final Release Date
Acrylonitrile	FY2013
Biphenyl	FY2013
Butanol, n-	FY2012
Dioxane, 1,4- (inhalation)	FY2012
Libby amphibole asbestos	FY2013
Vanadium pentoxide	FY2013

In the IRIS program, science guides completion of assessments. Thus, the estimated final release date depends on the complexity of the final peer review comments.

b. **Please note, for each assessment, whether the assessment includes the full implementation of all of the improvements in the scientific practices the NAS panel described in Chapter 7 of the formaldehyde report in the section of Chapter 7 entitled "Reframing the Development of the IRIS Assessment" as elements the committee "considers critical for the development of a scientifically sound IRIS assessment".**

In accordance with the EPA's plan for implementing the NAS recommendations, the EPA is revising these assessments to address peer review comments, with particular attention to those that call for increased transparency and clarity of study selection and evidence evaluation. In addition, the EPA is editing the text of these assessments to reduce volume where possible, either by removing redundant text or by moving study descriptions into appendices to enhance readability. For example, the recently posted final IRIS assessments for hexachloroethane, urea, and trichloroacetic acid were edited to reduce text volume and improve transparency, streamlined to remove redundancies, and made greater use of tables.

c. **For those assessment that will not include all of the improvements, please explain your rationale for excluding in such assessments the scientific improvements deemed "critical" by the NAS panel.**

Using a phased-in approach, all IRIS assessments are being revised to implement the NAS recommendations consistent with the NAS' "Roadmap for Revision." The NAS viewed full implementation of their recommendations as a multi-year process. The Agency is aggressively implementing the NAS recommendations related to the development of draft assessments.

3. **Has EPA initiated a review of existing weight-of-evidence guidelines? With public/stakeholder engagement? If so, please describe Agency actions. If not, why not?**

   The Agency will hold a public workshop on this topic in 2012. The public and stakeholders will have an opportunity to participate in this public workshop. The Agency is in the early planning stages; details about the workshop will be forthcoming. The EPA's peer-reviewed risk assessments and guidelines provide criteria for evaluating studies, and the IRIS program follows these criteria in developing health assessments. The Agency is currently evaluating guidelines for weight of evidence approaches that other agencies use to evaluate studies.

4. **In the now more than six months since the NAS issued its report, has EPA taken any steps to conduct agency workshops on approaches to implementing weight-of-evidence frameworks? If so, please describe Agency actions. If not, why not, and when will this action be initiated by EPA?**

   See previous response.

5. **The OMB's "Updated Principles for Risk Analysis" require EPA to provide "the expected risk or central estimate of risk for the specific populations [affected]" (http://www.whitehouse.gov/sites/default/files/omb/assets/regulatory_matters_pdf/m07-24.pdf). Please indicate which IRIS assessments (both draft and final) have provided a central estimate of risk, and which have not.**

   The OMB's 2007 memorandum "Updated Principles for Risk Analysis" encourages agencies, to the extent practicable, to present the expected risk or central estimate of risk for the specific populations affected, along with the appropriate upper-bound or lower-bound estimate of risk, in documents made available to the public in support of a regulation. IRIS health assessments are scientific documents that provide information on the first two steps, hazard identification and dose-response assessment, of the four-step process for estimating risk from chemicals found in the environment and, as such inform population risk estimates (which require both dose response and exposure information) and ultimately risk management and policy making decisions that are made by the EPA's program offices and regions.

   To provide risk assessors and risk managers with the capability to develop broad risk characterizations that can inform a range of policy options to reduce risk, IRIS assessments include detailed information on the range of adverse effects associated with exposure to a particular chemical substance if these data are available. In addition, dose-response modeling, if conducted, includes presentation in the assessment of central estimates of dose (BMDs) and lower bounds on dose (BMDLs) that elicit critical noncancer effects. For cancer effects, both central and upper bound estimates of potency, based on the results of dose-response modeling (if conducted), are presented in IRIS assessments. These estimates based on noncancer and cancer effects can then be used to fully characterize noncancer hazard and cancer risk, respectively, in a population when combined with specific exposure information from that population.

6. **The OMB "Updated Principles for Risk Analysis" also requires EPA to provide "the range of scientific and/or technical opinions regarding the likelihood of plausible alternate judgments and the direction and magnitude of any resulting changes that might arise in the analysis due to changes in key judgments. Every effort should be made to perform a quantitative evaluation of reasonable alternative assumptions."**

   a. **Over the last ten years, please list IRIS assessments (draft or final) that have been issued evaluating a cancer endpoint.**

   Since 2000, the IRIS program has evaluated 38 chemicals (external review draft or final) that evaluated a cancer endpoint. The majority of these chemicals have been characterized as having one of the three following cancer descriptors: human carcinogen, likely to be carcinogenic to humans and suggestive evidence of carcinogenic potential. For three of these chemicals, i.e., chloroform, EGBE, perchlorate, the EPA characterization was described as "not likely to be carcinogenic to humans". For these three compounds the descriptor was used for doses that are at or below the levels which were expected to lead to non cancer effects.

Chemical	Extrapolation Method
Acrylamide	Linear (mutagenic mode of action)
Acrylonitrile (draft)	Linear (mutagenic mode of action)
Arsenic (draft)	Linear
Benzene	Linear
Biphenyl (draft)	Both non-linear (threshold) and linear
Bromate	Linear
1,3-Butadiene	Linear
Carbon tetrachloride	Linear (non-linear/threshold presented as alternative)
Chlordecone (Kepone)	Linear
Chloroform (oral)	Non-linear (threshold)
Chloroprene	Linear (mutagenic mode of action)
Chromium VI (oral) (draft)	Linear (mutagenic mode of action)
2,2',3,3',4,4',5,5',6,6'-Decabromodiphenyl ether	Linear
1,2-Dibromoethane	Linear
Dichloroacetic acid	Linear
1,4-Dichlorobenzene (draft)	Linear
Dichloromethane	Linear (mutagenic mode of action)
1,3-Dichloropropene	Linear
1,4-Dioxane	Linear
Ethylene glycol monobutyl ether (EGBE)	Non-linear (threshold)
Ethylene oxide (draft)	Linear (mutagenic mode of action)
Formaldehyde (draft)	Linear (mutagenic mode of action)
Hexachloroethane	Linear
Libby Amphibole asbestos (draft)	Linear
Naphthalene (draft)	Linear
Nitrobenzene	Linear

Pentachlorophenol	Linear
Perchlorate (ClO4) and Perchlorate Salts	Non-linear (threshold)
Quinoline	Linear
2,3,7,8-Tetrachlorodibenzo-p-dioxin (draft)	Linear (non-linear analyses presented as possible alternative approaches)
1,1,2,2-Tetrachloroethane	Linear
Tetrachloroethylene (draft)	Linear
Tetrahydrofuran (draft)	Linear
Trichloroacetic acid	Linear
Trichloroethylene	Linear (mutagenic mode of action)
1,2,3-Trichloropropane	Linear (mutagenic mode of action)
Vanadium pentoxide (draft)	Linear
Vinyl chloride	Linear

b. Please indicate whether each assessment utilized a linear low dose method for determining potential cancer risks.

Please see table above. Additional explanation is provided below.

The method used for extrapolating to low doses is dependent on the available data to inform the shape of the dose-response curve. In accordance with the EPA's *Guidelines for Carcinogen Risk Assessment* (U.S. EPA, 2005), the approach for extrapolation below the observed data considers the understanding of the agent's mode of action at each tumor site. For the majority of the assessments where a linear low dose approach has been taken, little or no information was available to inform the mode of action. Consistent with the guidelines, "In the absence of sufficiently, scientifically justifiable mode of action information, the EPA generally takes public health-protective, default positions regarding the interpretation of toxicologic and epidemiologic data: animal tumor findings are judged to be relevant to humans, and cancer risks are assumed to conform with low dose linearity." For those assessments (25 out of 38) with little or no information to inform the mode of action, a linear low dose approach has been used.

A linear low dose method is also recommended by the EPA's *Guidelines for Carcinogen Risk Assessment* when the available mode of action data indicate that the dose-response curve is expected to be linear at low doses. One common instance in which this applies is for chemicals that are DNA-reactive and have direct mutagenic activity. The Agency has characterized the mode of carcinogenic action as mutagenic for nine chemicals and has, therefore, utilized a linear low dose approach in estimating cancer risk in these instances.

The Agency concluded that the mode of action data supported a threshold, non-linear approach for estimating cancer risks in three final IRIS health assessments (perchlorate, chloroform and EGBE) and one external peer review draft assessment (biphenyl), i.e., four out of 38 assessments.

c. **Also note whether each IRIS assessments (draft or final) included discussion of a non-linear, threshold mode of action as a plausible alternative, and whether each included a quantitative assessment of the potential cancer risk associated with the alternative, non-linear threshold model.**

The Agency evaluates the available data for each chemical that it assesses in the IRIS program to determine whether there are data to inform the mode of action. As stated in the EPA's *Guidelines for Carcinogen Risk Assessment,* "where alternative approaches have significant biological support, and no scientific consensus favors a single approach, an assessment may present results using alternative approaches."

Accordingly, the EPA has included qualitative discussions of the available mode of action data and how the data might inform the cancer quantitation in all assessments that have been developed since 2005. For several assessments where the data were sufficient to support a plausible non-linear mode of action, a threshold analysis was included as an alternative to the linear low dose approach. These assessments include carbon tetrachloride (final) and dioxin (external peer review draft).

d. **If quantitative assessments of the plausible, non-linear threshold mode of actions were not included, please indicate the rationale.**

As stated above, the majority of the carcinogenic chemicals that have been evaluated have little or no data available to inform the mode of action and the dose-response at low doses. If the EPA determines that the carcinogenicity of a chemical is supported by a plausible, non-linear threshold mode of action, then that determination would be reflected in a quantitative manner in the assessment.

7. **Please explain the EPA's decision to issue the dioxin assessment in two separate and distinct sections – non-cancer and cancer – to be issued many months apart. Please explain whether EPA intends to simultaneously issue a clear statement that the cancer evaluation in the 2003 dioxin reassessment is not finalized and the quantitative assessments contained therein should not be used for risk assessment or risk-management decision-making.**

In August 2011, the EPA announced that is would split the 2010 draft "Reanalysis of Key Issues Related to Dioxin Toxicity and Response to NAS Comments" (Reanalysis) into two parts – noncancer and cancer (http://yosemite.epa.gov/opa/admpress.nsf/1e5ab1124055f3b28525781f0042ed40/dae0812e5b4ef50e852578fb0057355b!OpenDocument). Based on the clear direction that the SAB and NAS gave the EPA to develop a more robust non-linear model for cancer, the EPA decided to complete the noncancer portion of the Reanalysis by the end of January 2012. The Agency will then address the SAB comments related to the cancer health assessment, including the uncertainty analysis, and complete that portion of the Reanalysis as expeditiously as possible.

Yes, the EPA intends to make it clear that the cancer evaluation in the draft 2003 dioxin reassessment is not final and the information should not be used for risk assessment or risk

management decision-making. The Agency has updated information on its website to clarify this: http://cfpub.epa.gov/ncea/cfm/recordisplay.cfm?deid=209690. Additionally, upon release of the final Reanalysis, Volume 1 (noncancer), the EPA will reiterate this message and clearly communicate that Volume 1 (noncancer) and Volume 2 (cancer), when complete, will supersede the 2003 draft dioxin reassessment and that the quantitative assessments contained in the 2003 reassessment should not be used for risk assessment or risk management decision-making.

8. **EPA has stated that one of the roles of the IRIS program is to meet the needs of the regulatory program offices. The Safe Drinking Water Act (SDWA) requires EPA, through the Office of Water, to base drinking water standards on "the best available, peer-reviewed science and supporting studies conducted in accordance with sound and objective scientific practices." 42 U.S.C. §300g-1(b)(3)(A)(i). If EPA does not include the findings from the MOA and PK research into its revised IRIS Toxicological Review for Hexavalent Chromium, please explain how the assessment will supplemented by additional studies to meet the statutory requirements of the SDWA.**

Rigorous, independent peer review is a cornerstone of the IRIS process. The Agency is seriously considering the recommendations of the peer review panel and the public comments on the draft IRIS assessment of hexavalent chromium, including those related to ongoing research, in its decision regarding next steps for the assessment.

The Honorable Joe Barton

1. **How do you establish your priorities? (In other words, what chemicals do you study first and foremost) Do you have a criteria set forth in a policy format?**

   In establishing priorities and setting its agenda, the IRIS program first issues a Federal Register Notice inviting voluntary public nominations for chemical substances not already included on the IRIS agenda. It also invites the public to comment on assessments on the current IRIS agenda. To nominate a substance, the public is asked to complete a standard form identifying their name, title and affiliation, and the chemical substance they are nominating. At the same time, the IRIS program also invites nominations from the EPA's Program and Regional Offices, as well as other federal agencies, requesting this same information. In setting priorities for the IRIS program, several factors are considered, including: 1) the potential public health impacts for the chemical; 2) the chemical-specific EPA mandate or program need (e.g., statutory, regulatory, or court-ordered deadline); 3) priorities for stakeholders outside of the EPA (e.g., states, tribes, local governments, environmental organizations, industries, or other IRIS users); 4) the availability of other assessments of the substance; 5) the availability of significant new scientific data or risk assessment methodology for chemicals that are nominated for which there is an existing IRIS assessment; 6) other relevant factors that would make the substance a priority for an IRIS assessment (e.g., widespread exposure, expected toxicity, or potentially susceptible populations). These criteria are published in the Federal Register Notice when the EPA invites nominations for chemicals to be added to the IRIS agenda. This occurred most recently in December 2010.

2. **What analytical systems do you utilize to determine the potential risks to a population? Do you have a standardized system?**

   The IRIS program serves the EPA's Program and Regional Offices by providing health effects information on chemicals of common concern. IRIS assessments provide a scientific foundation for the EPA's decisions to protect public health across most of the EPA's programs under an array of environmental laws.

   Consistent with the 1983 National Research Council report, "Risk Assessment in the Federal Government: Managing the Process," the EPA uses an established risk assessment process to determine the potential risks to a population. The risk assessment paradigm consists of four steps: Step 1: Hazard Identification; Step 2: Dose-Response Assessment; Step 3: Exposure Assessment; and Step 4: Risk Characterization. Scientists in the IRIS program develop Hazard Assessments (Step 1) and Dose-Response Assessments (Step 2) for chemicals of environmental concern. The Agency's Program and Regional Offices use this information to develop full risk assessments by including information on exposure (Step 3) and characterizing risk (Step 4) for specific situations. They then consider the full risk assessments with other factors, including cost and technical feasibility, to develop policies.

3. **What external agencies do you gain your knowledge base from on exposures to chemicals? AMA/ACS/NAS etc?**

   IRIS assessments include information on hazard and dose response. In some cases, background information on exposure may be included in an IRIS assessment relying on existing scientific databases such as the National Health and Nutrition Examination Survey (NHANES) database, as well as the existing peer reviewed literature.

4. **Please explain a step by step process by which you go about evaluation of a particular chemical.**

   The Agency follows a seven step process (http://www.epa.gov/iris/process.htm) to develop IRIS health assessments for chemicals. The Agency first conducts a comprehensive literature search and then announces a request for information to supplement the results of its search. The Agency then develops the draft IRIS assessment (Step 1). In doing so, relevant studies are identified, and the most informative are selected for further evaluation. The completed draft IRIS assessment is sent to internal Agency review (Step 2) and then science consultation with other Federal agencies and White House Offices (Step 3). The draft assessment is revised based on review comments and then released for independent public review, expert peer review and comment (Step 4). The release of the document, the public comment period, a public listening session, and the date of the peer review meeting are announced in a Federal Register Notice. The Agency holds a public listening session and peer review meeting. The EPA then revises the assessment to address the peer review and public comments and prepares a response to comments (Step 5). The draft final assessment is then sent once again to the internal Agency reviewers (Step 6A). The draft final assessment and the EPA's response to peer review and public comments then undergo interagency review with other Federal agencies and White House Offices (Step 6B). The completed IRIS assessment is then posted to the IRIS database (Step 7).

The Honorable Bill Cassidy

1. **Dr. Anastas, this is a follow up to confirm something you stated in response to a question: Many EPA recommendations are concerned with effects of a specific substance on a specific population. An example is the increase in mortality caused by ozone on patients with underlying bronchospatic pulmonary disease or an increase in deaths due to myocardial infarction. But in your testimony you stated that when EPA or IRIS calculates such death effect or rates, EPA does not compare those who die with a cohort with similar underlying co-morbidities. Rather, those who die are compared with the general population. Is my understanding of your testimony correct?**

   The health effects evidence that the EPA relies upon in calculating the risk of all-cause accidental mortality, or cause-specific mortality, varies in design and study population. Epidemiological studies conduct analyses utilizing the general population (e.g., time-series studies), as well as focusing on specific groups of individuals that may develop the health effect over the study period (e.g., prospective cohort study). Cohorts may represent the general population, or may be limited to populations with specific attributes, e.g. preexisting diseases. A study conducted among the general population will include some individuals with underlying risk factors. In contrast, other studies limit their population to only individuals with underlying risk factors or those that develop the outcome of interest (e.g., case-crossover study). Therefore, the EPA does not *a priori* determine the comparison of risk within a study population. The Agency always applies results from epidemiological studies to populations that closely match the populations in the studies. The study design is the determining factor in Agency analyses of risk within a general population or specific at-risk populations.

United States Government Accountability Office
Washington, DC 20548

Monday, November 14, 2011

The Honorable John Shimkus
Chairman
Subcommittee on Environment and the Economy
Committee on Energy and Commerce
House of Representatives

Attention: Alex Yergin

Enclosed is our response to the questions submitted for the record by you regarding our October 6, 2011 testimony entitled *EPA Health Risk Assessments: Oversight and Sustained Management Key to Overcoming Challenges* (GAO-12-148T). If you should have any questions, please contact me on 202-512-3841 or TrimbleD@gao.gov or my Assistant Director, Diane LoFaro, on 404-679-1986 or LoFaroD@gao.gov.

Sincerely yours,

David C. Trimble
Director, Natural Resources and Environment

Enclosure

The Honorable John Shimkus

1. What kinds of regulations might use a value such as that produced by the IRIS program?

IRIS assessments provide the foundation for several types of environmental risk management decisions, such as whether EPA should establish air and water quality standards to protect the public from exposure to toxic chemicals or set cleanup standards for hazardous waste sites. In addition, state and local environmental programs, as well as some international regulatory bodies, rely on IRIS health effects information in managing their environmental protection programs.[1]

1 a. In your experience, do the costs of cleanup vary with the IRIS value? Do they vary a lot?

We have not conducted work in this area. However, it is important to note that IRIS assessments are not regulations. Rather, the toxicity assessments in the IRIS database fulfill the first two critical steps of the risk assessment process—providing hazard identification and dose-response assessment. As such, an IRIS assessment for a given contaminant is just one of numerous factors that ultimately determine the nature and extent, and therefore the cost, of a hazardous waste site cleanup.

2. How many substances are listed in the IRIS program? Have some of those substances been in the program for a long time? How long?

The IRIS database contains EPA's scientific position on the potential human health effects that may result from exposure to more than 550 chemicals in the environment. In 2008, we reported that EPA data from 2001 through 2003 indicated that 287 of the chemicals in the IRIS database may potentially need to be updated.[2] Specifically, EPA reviewed the scientific literature on the 460 chemicals in the database at that time to identify assessments that may need to be updated in light of new studies or information that could potentially change the risk estimates currently in the IRIS assessments. In addition, while conducting these literature reviews, EPA identified new studies or information that would enable the agency to develop additional risk estimates. EPA's "screening level review" found new information that could potentially (1) change an existing risk estimate for 169 chemicals and/or (2) allow EPA to develop additional risk estimates for 210 chemicals. Although EPA identified these chemicals as candidates for reassessment, as of fiscal year 2007, the agency had initiated reassessments of only a few of these chemicals. In

[1]GAO, *Chemical Assessments: Low Productivity and New Interagency Review Process Limit the Usefulness and Credibility of EPA's Integrated Risk Information System*, GAO-08-440 (Washington, D.C.: Mar. 7, 2008).

[2]GAO-08-440.

addition, as of December 2007, most of the 70 ongoing IRIS assessments had been in progress for over 5 years. We have not done the work to update this information, however, from May 2009 through September 30, 2011 EPA completed 20 IRIS assessments, and therefore it is unlikely that the situation has significantly improved.

3. In your opinion, is there a way to cost-effectively improve IRIS so that it helps promote jobs and domestic economic growth as well as protect public health?

As we reported in 2008, the toxicity assessments in the IRIS database fulfill the first two critical steps of the risk assessment process—providing hazard identification and dose-response assessment.[3] Decisions on whether, and if so how, to regulate a chemical are made after an IRIS assessment is completed and may involve other factors such as such as economic information on the costs and benefits of mitigating a risk. The degree to which EPA takes into account factors other than public health in making these risk management decisions is determined by the relevant program legislation. We have not conducted the work necessary express an opinion. Our recommendations to EPA were to develop timely chemical risk information the agency needs to effectively conduct its mission and better ensure the development of transparent, credible chemical assessments.

4. Are federal dollars being spent in the most efficient and effective way by IRIS? How about between the program offices and IRIS on basic science?

We have not conducted the work necessary to answer this question.

[3]GAO-08-440.

Dr. Michael Honeycutt (TCEQ) Responses to Questions from The Honorable John Shimkus

1. *You testified "EPA's new assessments will unnecessarily scare the public and may actually harm public health by diverting public, industry, and government attention and resources away from public health issues that pose more of a risk." Can you share with us more examples of industry and government action based on these values that have diverted resources?*

A perfect example is mercury. In their recent proposal to reduce emissions, specifically mercury, from power plants, EPA themselves determined that the rule will not have an effect on mercury levels in fish in America's watersheds. This rule will cost utilities, states, and the public (through higher energy costs) millions of dollars with little or no public health benefit. EPA continues to overstate the health risks of lower IQ and heart disease from mercury, while ignoring the very-well demonstrated health benefits of eating seafood. EPA used a study known as the Faroe Islands study to set their safe level for mercury, where the mothers ate whale meat and blubber contaminated with PCBs in addition to eating fish containing mercury. The Faroe Island infants ingested 600 times EPA's safe dose of PCBs in breast milk in addition to ingesting mercury. The effects EPA attributed to mercury could more justifiably be attributed to PCBs. A similar study in the Seychelle Islands that did not include PCB exposures was essentially negative. EPA ignores the fact that Japanese eat 10 times more fish than Americans do and have higher levels of mercury in their blood, but have lower rates of coronary heart disease and high scores on their IQ tests. Methyl mercury is a toxic chemical, but the scientific data overwhelmingly do not support EPA's position on the health risk of mercury. In fact, EPA may have the most conservative safe level for mercury in the world. The FDA, the ATSDR, the World Health Organization, and Canada have all set a higher safe level for mercury. Further, EPA still uses decade-old data when they say that 6% of the women in the US have unsafe levels of mercury in their blood. Newer data shows this isn't the case. Plus, the levels they say are "unsafe" are well below the levels shown to cause health effects. There are no widespread mercury health effects issues in the United States. In fact, unwarranted concerns about mercury may be causing women to avoid eating fish, which itself could lead to adverse health effects.

2. *You testified that EPA is moving toward a philosophy that there is no safe level of exposure to a chemical. And that includes naturally occurring chemicals? What does that mean, in practical terms?*

The philosophy that there is no safe level of exposure to a chemical means that any dose of a chemical, no matter how small, causes an adverse effect. This philosophy has typically been applied to carcinogens like arsenic, a naturally occurring chemical that can be found in soil and water. In practical terms, this means that an individual would have an increased risk of developing cancer

even if he/she were only exposed to a very low dose of arsenic. Based on EPA's most recent IRIS assessment of arsenic and available data from recent fish studies, all fish and shellfish would contain levels of arsenic that are higher than the highest levels EPA would consider safe. Normal dietary food and drinking water consumption would also contain levels of arsenic that would be substantially higher than the highest levels EPA would consider safe. We know these levels of arsenic are not unsafe because we are not seeing the increased cancer rates (and other health effects) in the general population that would occur if EPA's levels were realistic.

3. *What do you see as the key problems in EPA's IRIS assessments? Why are they important? Are these problems found in other science and health based agencies of the Federal government?*

Some key issues in EPA's IRIS assessments include: 1) they often don't follow their own guidance; 2) they ask for input from outside experts late in the process (after their minds are made up); 3 they allow very short time periods for public comment (e.g. 30 or 60 days to review a thousand page document is typical); 4) they tend to not finalize assessments when the science doesn't back up their position (e.g., the dioxin assessment has been draft for over two decades); 5) they are getting away from science-based assessments and going more towards precautionary policy-based assessments (e.g. when science demonstrates that a chemical is not as toxic as they think it should be, they ignore the science in favor of a policy decision); and 6) they don't do common-sense ground-truthing of their values (e.g., their unsafe levels for essential elements like copper are lower than what is recommended by the FDA).

Consistency, transparency, and the highest scientific integrity are paramount in regulatory decisions. If EPA consistently utilizes good science in their decisions, including in the IRIS program, then the motivation exists to develop good science. When EPA ignores good science which demonstrates that a chemical is not as toxic as they think it is, it creates an atmosphere of distrust, not to mention litigation. Developing "chicken little" toxicity values for chemicals - values that are below background levels or that (like copper) deem FDA recommendations as being unsafe – make the public either jaded or unnecessarily scared.

The TCEQ works more closely with and is more familiar with EPA policies and procedures, so I can't offer an opinion on other federal agencies.

4. *In your opinion, are there broader economic consequences associated with publishing an IRIS value that is lower than background levels? Will it impacts jobs and the economy?*

Yes. Such a risk assessment may have unintended consequences. Not only is it impossible to cleanup below background levels, costs in the daily lives of the public would be driven up from industry being forced to switch to alternatives (if available). While IRIS merely develops toxicity values, they have far reaching implications as they are used by regulatory agencies to make regulatory decisions. When a regulatory decision is made using a toxicity value that is extremely conservative, impacts are felt across the board. Not only does a company have to modify their process to accommodate use of a different chemical, which is expensive in itself, the cost is then transferred onto the public.

For example, IRIS toxicity factors are used to develop federal maximum contaminant level (MCLs) standards. States are required to use these standards to regulate levels of chemicals in public drinking water supply systems. The current arsenic MCL of 10 ppb is set at an "unacceptable" excess cancer risk level, according to the current IRIS toxicity values. However, arsenic is a naturally occurring constituent in soil and water and can naturally be present in water at levels above the MCL of 10 ppb, as is the case in different parts of the US, such as West Texas. As a result, public water systems may have to institute costly measures to treat the water in order to comply with federal regulations or pay costly fines for violating regulations. Costs are then passed on to the consumer. Also, many rural water systems serving relatively few customers over a large geographic area may be forced out of business due to the increased costs. This would require homeowners to drill their own private wells, which would likely not be regularly tested and treated like public water supplies.

5. *What is the value of a risk assessment value that identifies a level below background level?*

Achievement of acceptable risk, as defined by the EPA IRIS toxicity values, would be practically impossible at not only remediation sites, but also at residential homes as the toxicity value would imply that typical naturally-occurring levels of a chemical were unsafe for human contact. Such assessments are unnecessarily alarming to the public and only cause more harm than good (e.g., can cause stress in the public, are unnecessarily expensive, etc.). When an agency, which is looked to for development of the toxicity values used in risk assessments, begins routinely developing extremely conservative values that are below background, confidence in values that agency develops, and the agency itself, is diminished. Agency resources would then be focused on responding to the public or remediating sites to chemical levels that are overly conservative instead of being focused on real environmental risks and dangers. Limited federal and state resources should be focused where the greatest health benefit can be obtained.

6. *Is it standard practice for a risk assessment to produce a range of values, such as a high-end and low-end estimate of risk? Why is that important?*

It is typically not standard practice to develop a range of values for a chemical risk assessment. The one exception on the IRIS database is benzene, which does have a range of values. It is important to provide risk managers and policy makers adequate information to make informed decisions. Sufficient information would include limitations and confidence in the data used to develop the risk values, concentrations known to produce health effects, and the likelihood of exposure to the chemical.

7. *Is it true that a substance can be associated with risk at high levels, but be safe and even necessary for health at low levels? Can you share any examples? (Over-the-counter analgesics, or food supplements, for example?) Does this imply that risks assessed at high levels are not necessarily the same risks at lower levels?*

Yes, vitamins and essential nutrients can be associated with adverse health effects at high levels, but are necessary for health at lower levels. Examples include Vitamin A, iron, and selenium. High doses

of Vitamin A can cause liver toxicity and birth defects, high doses of selenium can affect the brain, and high doses of iron can cause liver toxicity and metabolic acidosis. Low doses of these substances are essential for life. This means that there is a risk of adverse health effects if not enough exposure occurs and a risk of adverse health effects if too much exposure occurs. For this reason, the effects of a chemical are not proportional, i.e., an effect at a higher dose cannot be assumed to indicate that a lower dose would have the same adverse effect.

8. *Recently, a toxicologist Dr. Peter Valberg testified before the Energy and Power subcommittee that "The dose makes the poison". What does that mean, in assessing risk?*

The phrase, "the dose makes the poison," is attributed to the 'father' of toxicology, Paracelsus (1493-1541). What he described was the dose-response concept and it is one of the fundamental ideas in assessing risk, in that, typically at higher doses the severity of an adverse effect increases. Even though some things are described as nontoxic, essentially everything, even naturally occurring chemicals, can be toxic at a high enough dose (e.g., water, caffeine, aspirin, sugar). For example, even water is toxic at a high enough dose. Water intoxication can cause disturbances in electrolyte balance, resulting in a rapid decrease in serum sodium concentration and eventual death.

Health-based standards are often based on maximum acceptable concentrations of a chemical, assuming that exposure to below that standard or threshold would be safe. However, as a precaution some chemicals for regulatory purposes are considered not to have a threshold (for example, some cancer-causing chemicals) and thus, risk assessment involves ensuring the dose-response of a chemical is properly characterized.

9. *Is having something peer reviewed a sign of quality work?*

Most often, yes, if the peer review process is conducted properly. Scientific work is self-monitored through peer review which provides an initial stamp of validity to other scientists and the public. Peer review should involve the thorough examination of a study or manuscript by other knowledgeable scientists in the field who can provide a critical analysis and review. Typically, most scientists will not consider a study valid unless it has been through a peer review process. Without it, results would be considered preliminary. The peer review process is not perfect. As much as possible, peers reviewing the work should have the appropriate expertise and not have conflicting interests. Ideally, peer reviewers and their comments should be publicly identified, though their comments do not necessarily have to be directly attributable to them. Also, the scientist doing the original work should make responses to the peer reviewer's comments public. Peer reviewers are not infallible and thus, may make mistakes or miss important deficits. However, a scientist knowing their study will be vetted through peer review, by itself, may make the study more rigorous than it would otherwise be without that process. In general, the process works by improving scientific work.

10. *Does IRIS exaggerate risk? Why should we care?*

Yes, IRIS exaggerates risk. All regulatory toxicity values exaggerate risk to some extent. Regulators (including me) have a penchant to err on the side of conservatism (health-protectiveness) when extrapolating potential health effects from animal studies or clinical/worker human studies to the general population. Developing toxicity values is a branched, multi-step process. At each intermediate step, if no scientific data is available, one can use policy-derived default values that are intentionally overly-conservative. At the end of the process, the various branches are multiplied (which compounds the conservatism) together to derive the toxicity factor. The problem with IRIS is that EPA tends to ignore scientific data that demonstrates the policy-derived default values are not appropriate. When this happens, the IRIS values are not just conservative they are not scientifically based.

A good example is EPA's most recent IRIS assessment for formaldehyde. Ample scientific data exist that clearly demonstrates that when living organisms inhale formaldehyde, it does not enter the blood stream and circulate to other parts of the body. It stays in the respiratory tract. However, EPA ignored this data and chose instead to rely on a single epidemiology study[1] that *did not* show a statistically significant association between formaldehyde and Hodgkin lymphoma and leukemia, but they used it anyhow. In order for formaldehyde to cause these diseases, it would have to enter the blood stream, but it clearly does not based on studies that examine whether or not inhaled formaldehyde is absorbed from the lungs and transferred throughout the body. As a result of assuming formaldehyde can cause Hodgkin lymphoma and leukemia, along with the compounded conservatism of the process, EPA's proposed formaldehyde toxicity value would mean that the formaldehyde in human breath that results from normal body functions would be over 5 times higher than the highest level that EPA would call safe.

This assessment will unnecessarily scare the general public. Formaldehyde is naturally formed in the air from the breakdown of chemicals released from vegetation. According to available air data, the only places that would have safe air would be remote locations such as the arctic or South Pacific islands.

11. *How useful do you find IRIS values when they are set to levels below background or lower than naturally occurring background levels? Can you please speak to the issues that have challenged your state in this area?*

IRIS values set to levels below background or lower than naturally occurring background levels are typically not useful. If a toxicity value derivation process comes up with such a value, it should be carefully examined to see how much confidence can be placed in the value; to put the value in context with levels where adverse effects are known to occur.

[1] Epidemiology studies are designed to show a correlational rather than causal relationship between exposure and effect. Epidemiology studies are useful in hazard identification, and if accompanied by accurate exposure data, may be useful in the dose-response assessment for a toxicant. Use of epidemiological studies may be limited by confounding factors (e.g., predisposing lifestyle factors, preexisting health problems), reliability of the exposure data, and lack of a causal relationship between exposure and effect.

Since these new toxicity values (formaldehyde, arsenic, hexavalent chromium, etc.) are draft, Texas has not yet felt an impact. However, because these draft values are overly conservative, we are anticipating the need to develop our own toxicity values for these chemicals to use in our soil remediation program. Unfortunately, should Texas develop more scientifically rigorous values that are higher than EPA's value, the public might not think we are being health-protective. Further, developing state values where the EPA has already created toxicity values is a diversion of resources that could be focused elsewhere.

Dr. Michael Honeycutt (TCEQ) Responses to Questions from The Honorable Joe Barton

1. *How do you establish your priorities? (In other words, what chemicals do you study first and fore-most) Do you have a criteria set forth in a policy format?*

Chemicals are studied in order to develop toxicity factors and screening levels used in TCEQ air monitoring, air permitting, and remediation programs. Chemicals are prioritized based on a number of factors including whether they have been detected in ambient air monitoring, whether TCEQ frequently issues permits for them, whether they have been detected in soil and/or water sampling associated with remediation activities, and if the public has expressed concerns about them. These criteria are specified in the TCEQ Toxicology Division's DRAFT 2011 "Guidelines to Develop Inhalation and Oral Cancer and Non-Cancer Toxicity Factors." (http://www.tceq.texas.gov/toxicology/esl/guidelines/about.html)

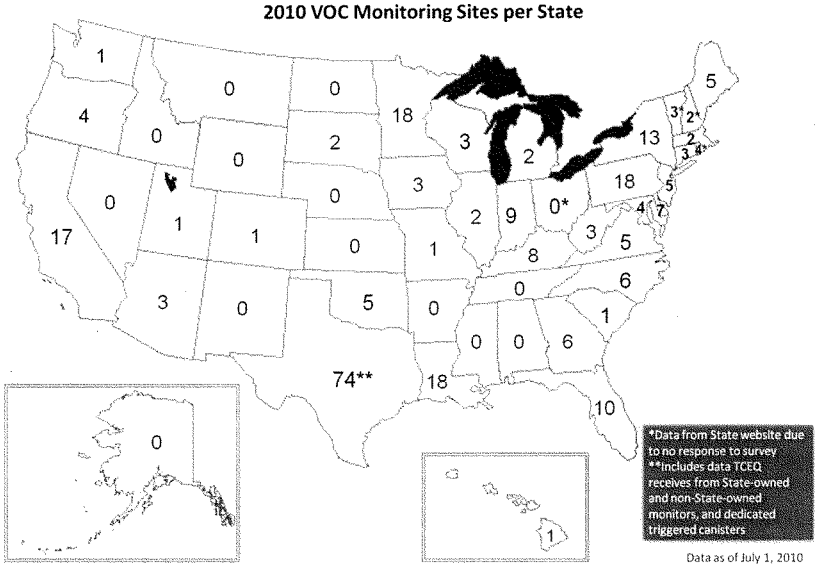
2. *What analytical systems do you utilize to determine the potential risks to a population? Do you have a standardized system?*

The state of Texas currently conducts routine ambient monitoring of air and water, which is analyzed using EPA-approved methodologies. Soil is sampled and analyzed as needed (e.g., remediation sites, complaints from citizens, field investigations) also using EPA-approved methodologies and typically evaluated using the Texas Risk Reduction Program (TRRP) Protective Concentration Levels (PCLs), which are cleanup levels set to protect public health from a long-term direct exposure perspective.

There are federal standards for drinking water and state standards set (as approved by EPA) for surface water quality. The TCEQ Office of Water has several water programs and routinely evaluates the waters of the state for compliance with water quality standards.

For ambient air, federal standards exist for six criteria pollutants. For all other chemicals emitted in the state of Texas, we have developed screening levels. The TCEQ routinely monitors ambient air via stationary monitoring, mobile monitoring and field investigations. The TCEQ has the most extensive ambient air toxics monitoring network in the country, monitoring for more than 120 chemicals across the state (see figure below). The TCEQ monitors for compliance with criteria air pollutants and routinely evaluates air toxics data across the state. If a potential issue with ambient air is identified, the chemical and area are highlighted on the Agency's Air Pollutant Watch List (referred to as the APWL). This list serves as a tool for the Agency to focus resources on correcting potential issues.

2010 VOC Monitoring Sites per State



3. *What external agencies do you gain your knowledge base from on exposures to chemicals? AMA/ACS/NAS etc?*

The TCEQ refers to numerous sources for toxicity and exposure information on chemicals. Initially, because of time and resource constraints, published toxicity values and/or data developed by another federal or state agency are evaluated. When a toxicity factor or guideline level is identified in the scientific literature or in a database, it is reviewed to determine whether the approach used to develop the factor is similar to the procedures used by the TCEQ to develop its toxicity factors. If so, the TCEQ may adopt the published toxicity factor or guideline level, with preference given to values that have undergone an external peer review and public involvement process. However, because more recent information may be available, the TCEQ also evaluates peer-reviewed scientific studies available after the published date of the toxicity factor or guideline level to ensure the latest data are considered. Specific external agencies the TCEQ frequently cite include the Agency for Toxic Substances and Disease Registry (ATSDR), EPA, California EPA, National Advisory Committee for Acute Exposure Guideline Levels for Hazardous Substances, DOE, OSHA, ACGIH, CDC, WHO, and other international organizations.

4. *Please explain a step by step process by which you go about evaluation of a particular chemical.*

TCEQ has developed a state-of-the-science, peer-reviewed process for developing toxicity values for chemicals. When a chemical undergoes this evaluation a development support document (DSD) is

created. The DSD provides a summary of information on the development process and the key toxicity information upon which the toxicity values are based. The first step in this process is to conduct an exhaustive review of the available scientific literature and solicit information from interested parties. Once the literature review is completed, there are two main types of toxicity values developed; acute (short-term) and chronic (long-term), which protect against short- and long-term exposures, respectively.

For development of an acute toxicity value, the first step is to determine if there is enough acute toxicity data available to develop a toxicity value. If there isn't sufficient data available, a default or generic health-based toxicity value will be developed using conservative procedures as specified in the TCEQ Toxicology Division's DRAFT 2011 "Guidelines to Develop Inhalation and Oral Cancer and Non-Cancer Toxicity Factors." Otherwise, the next step involves analyzing the collected literature to determine how the chemical produces toxic effects in the body (i.e., mode of action (MOA)). Once the MOA is determined, an acute toxicity value is developed. After developing an acute health-based toxicity value, welfare-based (i.e., odor and vegetation) toxicity values are developed (if necessary).

For development of a chronic toxicity value, the next step involves determining if enough chronic data is available to develop a cancer-based and/or a non-cancer based chronic toxicity value. If there isn't sufficient data available, a generic health-based toxicity value may be developed. Otherwise, the chronic literature is then evaluated to determine the chronic MOA (if different from the acute MOA). As with the acute toxicity values, once the MOA is determined a chronic carcinogenic toxicity value is developed (if appropriate). If data is available to support a non-carcinogenic MOA, the next step is to develop a chronic non-carcinogenic toxicity value. After developing the chronic health-based toxicity value(s), a welfare-based (i.e., vegetation) toxicity value is developed (if necessary).

Once toxicity factors are initially developed, they go through a rigorous internal review for scientific consensus within the TCEQ Toxicology Division. After that, the toxicity factors are considered proposed, high profile chemicals may undergo a peer-review at this point and all DSDs undergo a 90-day public review and comment period. For data-rich or controversial substances, additional time may be allowed for the review and comment period. After the review and comment period ends, the comments are addressed and resolved, the document undergoes another round of internal review for consensus and the document is then finalized with responses to the received comments.

November 12, 2011

John Shimkus
Chairman
Subcommittee on Environment and the Economy

Please find below my responses to the additional questions I received following the hearing entitled "Chemical Risk Assessment: What Works for Jobs and the Economy?"

I appreciate the opportunity to participate in the hearing.

Harvey Clewell, PhD, DABT
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The Hamner Institutes for Health Sciences
6 Davis Drive / PO Box 12137
Research Triangle Park NC 27709

The Honorable John Shimkus

1. **You testified that "the inadequacy of the risk characterization in IRIS assessments, coupled with the sole use of conservative default approaches, hampers the ability of decision-makers to make informed risk management decisions and gives the public an inaccurate impression of their potential risks from chemical exposure." Are there examples where the public or decision-makers have received an inaccurate impression of their potential risk?**

Response: There have been a number of recent cases where IRIS risk assessments have hampered the ability of decision makers to make informed risk management decisions and have given the public an inaccurate impression of their potential risks from exposure to the chemical. I will briefly describe examples for arsenic, formaldehyde, and dioxin, all of which have a potential for major impact both economically and in terms of raising public concerns.

a. Arsenic: The current IRIS cancer risk estimate for inorganic arsenic ingestion was based on increased skin cancer in a population in Taiwan chronically exposed to extremely high concentrations of arsenic in drinking water, well above levels present in U.S. drinking water. Only the default linear risk assessment approach was performed, despite strong scientific evidence of a nonlinear mode of action for the carcinogenicity of arsenic. In making the decision to provide only a default linear risk assessment approach, the EPA ignored the recommendations of its own Expert Panel on Arsenic Carcinogenicity (Eastern Research Group, 1997). The Expert Panel agreed that, "for each of the modes of action regarded as plausible, the dose-response would either show a threshold or would be nonlinear (Eastern Research Group, 1997, p. 31)". A revised IRIS assessment is currently under review that continues to rely solely on a linear default approach; the revised risk estimates are more than 10-fold greater than the previous values. As a result of the continued provision by IRIS of only a linear approach, the EPA Office of Water has no option other than to use linear risk estimates in determining the Maximum Contaminant Level (MCL) for inorganic arsenic in drinking water. These highly conservative linear risk estimates result in a very low MCL, entailing significant costs to many local communities in the United States (USEPA, 2001d). The current Ambient Water Quality Criterion (AWQC) for arsenic (0.000018 mg/L) was based on the current IRIS linear estimate of a water concentration associated with a risk of one in a million for cancer from water consumption of 2L/day. This concentration is below the natural concentration of arsenic in some Western rivers. Use of the newly proposed IRIS value would reduce the AWQC even further, pootentially bringing much of the Western U.S. into non-compliance.

b. Formaldehyde: The IRIS assessment for formaldehyde that was recently reviewed by the National Academy of Science (NAS) relies solely on default linear cancer risk estimates derived from studies associating occupational exposures to formaldehyde with increased cancer. The NAS review criticized the EPA for failing to conduct

alternative risk approaches and for neglecting to consider the fact that formaldehyde is a natural component of the body. In fact, formaldehyde has been measured in exhaled air at concentrations as high as 40 parts per billion (ppb); the use of the new EPA linear risk estimates would associate this normal exhaled concentration with a cancer risk of over 1 per thousand. To the contrary, there is strong scientific evidence that the carcinogenicity of inhaled formaldehyde is limited to exposures at concentrations associated with severe irritation, above 100 ppb. As a result, in 2006, the German government concluded that a guideline value of 100 ppb, based on irritation, was protective against cancer as well. The EPA Office of Air, however, using the IRIS risk estimate, would have to conclude that formaldehyde in the air even in rural environments (around 1 ppb) is associated with an unacceptable cancer risk.

c. Dioxin: The EPA has been working on a dioxin risk assessment for well over a decade, but has faced repeated delays due to their unwillingness to present a nonlinear risk assessment approaches in their IRIS assessment as requested by the NAS. The consequences of the sole use of a linear-based model are significant. For example, the EPA in 1993, using the linear model, set the acceptable daily intake of dioxin at 0.006 picograms (pg) per kilogram per day. In contrast, the Canadian Health and Welfare Department, using a threshold model, set the acceptable daily intake at 10 pg/kg/day.

2. **Some politicians like to argue that the "science made them do it" when they support expensive or unpopular policies. Do you consider the "science" to be the policy forcing mechanism if compound conservative assumptions are imbedded in the work? Do you think it not only is more accurate, but also more transparent for policy considerations to be labeled explicitly as such and not obliquely rolled into a characterization of the science?**

   Response: I believe that the documentation of a risk assessment should clearly distinguish between those decisions and calculations that are based on science and those that are based on policy. When conservative assumptions are applied, the impact of those assumptions on the risk estimates should be characterized by comparison with alternative options consistent with the best science. This approach would be more consistent with the recommendation of OMB memorandum M-07-24, "Updated Principles for Risk Analysis" (Sep 19, 2007), to provide a characterization of the dispersion of risk estimates associated with different models, assumptions, and decisions. .

3. **Do you believe that basic science should build policy defaults into it or should policy considerations, like adding levels of uncertainty?**

   Response: I believe that policy defaults are necessary to cover situations where the science is inadequate to develop a more appropriate approach, but the use of defaults should require justification. This same philosophy is embedded in the EPA's 2005 Guidelines for Carcinogen Risk Assessment, which defines a default as the "no-information" option, the use

of which must be justified by the agency on the basis of the lack of sufficient information on a specific chemical to support a more preferred, chemical-specific approach. This definition stands in contrast to past practice, in which the default position was treated as the preferred approach, and justification was required for departing from it on the basis of chemical-specific information.

a. Do you agree that the IRIS program's risk assessment practices systematically exaggerate actual risks and thereby seriously compromise the value of risk assessments as inputs to regulations and regulatory impact analyses?

Response: I believe that the practice in IRIS of presenting only a conservative default approach when there are viable, more scientifically sound alternatives provides the regulatory decisionmaker with an inaccurate characterization of risk that compromises his ability to make informed risk management decisions.

b. Is this a new problem new or has it been a historic one?

Response: IRIS risk assessments have always been intentionally conservative in order to assure the protection of public health. To compensate for perceived uncertainties in the process, default approaches were developed that made heavy use of health-conservative assumptions and/or uncertainty factors. Historically, EPA approaches for quantitative chemical risk assessment relied almost exclusively on default approaches; however, in the 1990s, when Dr. William Farland was Director of the EPA's National Center for Environmental Assessment, it was recognized that a number of chemical-specific factors, such as kinetics and mechanism of toxicity, that were ignored by the default approaches, could greatly impact the relative risks for different chemicals. As a result, a number of key risk assessment guidelines were written, intended to foster more accurate, chemical-specific, risk assessment approaches. This period culminated in the publication of the 2005 Guidelines for Carcinogen Risk Assessment. Unfortunately, recent IRIS risk assessments have not fulfilled the promise of these guidelines and there appears to have been a return to default-based, highly-conservative risk assessment practices.

References:

Eastern Research Group. 1997. Report on the expert panel on arsenic carcinogenicity: review and workshop. Prepared by Eastern Research Group, Lexington, MA, for the National Center for Environmental Assessment, Washington, DC, under EPA contract no. 68-C6-0041.

US Environmental Protection Agency. (2001). National Primary Drinking Water Regulations: Arsenic and Clarifications to Compliance and New Source Contaminants Monitoring. Final Rule. 40 CFR Parts 141 and 142, Fed. Reg. 66(14):6976-7066.

U.S. Environmental Protection Agency. (2006). Guidelines for Carcinogen Risk Assessment. EPA/630/P-03/001F. Risk Assessment Forum, USEPA, Washington, DC.

The Honorable John Shimkus

Mr. Cook, you testified that the regulatory level for barium is an arbitrary value, set in a time when there were no toxicology studies. Is it your opinion that there are other substances that are regulated using evaluations based on outdated or incomplete science?

Yes, I am of the strong opinion that a substantial number of other substances are also being regulated based upon bad science. In fulfilling Chemical Products Corporation's product stewardship obligations, I have found over-regulation based on bad science for both of the materials I have investigated. Not only have I encountered a resolute disregard for sound science at IRIS and failure by EPA to relax regulatory levels for barium consistent with sound science, but I have also encountered egregious scientific misconduct at the National Toxicology Program to support bad science concerning another of our products, Anthraquinone. I believe that it is beyond the realm of possibility that only the two substances I have evaluated are being over-regulated to the detriment of U.S. manufacturers.

Anthraquinone, another of Chemical Products Corporation's products, is a useful and benign industrial chemical. In the early-1990s, NTP obtained an Anthraquinone sample for animal testing which was contaminated with a potent mutagen. NTP did not become aware of this contamination until years after animal testing had been completed. Anthraquinone is not a mutagen; this fact was only acknowledged by NTP as a result of a Request for Correction and a subsequent Request for Reconsideration I submitted in 2003 under the Information Quality Act. In December 2004, highly significant false information was presented to peer reviewers to finally gain approval of the conclusions advocated by NTP staff. In 2006, NTP staff fabricated a document to support NTP's rejection

of my Request for Correction of the final Technical Report 494.

Anthraquinone has been an important raw material for the production of textile dyes for more than a century; more recently it has also found a use in the U.S. paper industry as a catalyst to increase pulp yields and thereby decrease energy usage and paper production costs. Anthraquinone has not been manufactured in the U.S. since the early 1980's; Chemical Products Corporation purchases imported Anthraquinone as a dry powder and formulates it into a stable slurry that our paper industry customers can easily store and pump into their papermaking processes.

NTP incorrectly declared that Anthraquinone was a mutagen, based upon its own positive mutagenicity assay of a single contaminated sample, when it published the results of its animal studies in 1999. Even though several earlier published studies had reported that Anthraquinone is not mutagenic, NTP chose to dismiss those studies without investigating the issue. NTP reported in 1999 that it had found clear evidence that Anthraquinone caused cancer in rats and mice.

When NTP's startling assertions were published for public review and comment in early 1999, I investigated further and found that a specific potent mutagenic contaminant had been identified in some Anthraquinone samples. This information was contained in the International Uniform Chemical Information Database and also in EPA's TSCA file for Anthraquinone. The identified mutagenic contaminant came from an obsolete manufacturing process which is no longer practiced anywhere in the world. I obtained a sample of NTP's test material and had it analyzed in late 1999; I found this same potent mutagen in NTP's test material. NTP had unwittingly obtained contaminated test material produced by an obsolete, dirty manufacturing process; no commercial Anthraquinone anywhere in the world has been contaminated with this

potent mutagen for nearly two decades. I immediately informed NTP of my findings. NTP took no action to correct its technical report for more than three years after it was informed that it had tested a contaminated Anthraquinone material.

When the Information Quality Act came into effect in late 2002, I immediately submitted a Request for Correction which was promptly denied by NTP. I then submitted a Request for Reconsideration in 2003; it was adjudicated by the Deputy Director of the National Institute of Environmental Health Sciences. He concluded that the mutagenic contamination in the Anthraquinone sample tested by NTP made it impossible to be certain what had caused the cancers in the test animals; he withdrew NTP's 1999 Technical Report 494 on Anthraquinone in September 2003.

In 2004 NTP staff issued a revised technical report which acknowledged that Anthraquinone is not a mutagen and that a mutagenic contaminant had been found in the material that NTP had fed to rats and mice. However, NTP still insisted that its test results proved that Anthraquinone was solely responsible for the cancers found in rats and mice. The revised technical report was peer reviewed first in February 2004 and then reopened for additional peer review in December of 2004.

In December 2004, NTP's present Associate Director orchestrated the removal of the restrictions placed in Technical Report 494 by the February 2004 peer review panel. "New" highly significant false information was presented to the peer review panel in December without the requisite prior publication for public review and comment. This false information was incorporated into the final technical report along with the same conclusions that had been in the 1999 technical report – those conclusions allowed NTP staff to proceed with publication of a paper characterizing Anthraquinone as a carcinogen in March 2005.

NTP Technical Report 494 on Anthraquinone was published in September 2005. California's Proposition 65 statute requires that any chemical identified as a carcinogen in a NTP technical report be added to the Proposition 65 list under the "Authoritative Bodies Mechanism". Thus, U.S. papermakers have been faced with the dilemma of weighing the energy and cost savings achieved by using Anthraquinone in their pulping process against the risk that their myriad paper products entering California might be challenged under the Proposition 65 regulation. We feel certain that sales of our Anthraquinone product have been adversely impacted by the bad science contained in NTP Technical Report 494.

Multiple Freedom of Information Act requests and a Freedom of Information Act appeal have permitted me to compile documentary evidence demonstrating that the new information presented to the December 2004 peer review panel and incorporated into the published NTP Technical Report 494 is false.

By May 2006 I had determined that Technical Report 494 was fatally flawed; I submitted a Request for Correction under the Information Quality Act seeking its withdrawal. My Request was denied by NTP. I then submitted a Request for Reconsideration at the end of 2006; my submission included additional documents demonstrating conclusively that Technical Report 494 contains highly significant false information. My submission was adjudicated by the Director of the Office of Science Policy at the National Institute of Environmental Health Sciences. After an 18 month delay, my Request for Reconsideration was denied on September 22, 2008; the documentation I submitted had been ignored.

I turned to the Office of Research Integrity for help and discovered that ORI does not concern itself with evidence of scientific misconduct at NTP. Director John E. Dahlberg of the Division of Investigative Oversight stated in a letter to me dated January 16, 2009, "I also note that ORI does

not have authority to conduct the investigation you request. Our role is limited by departmental policy to conducting oversight review of investigations conducted by the institutions where the alleged misconduct took place." Thus, as long as NTP does not enforce scientific integrity by investigating alleged misconduct by its staff, ORI will not concern itself with scientific misconduct at NTP. NIEHS and NTP Director Linda S. Birnbaum has refused to investigate.

I have twice nominated Anthraquinone to NTP's Office of Chemical Nomination and Selection in an effort to obtain a valid scientific study to replace NTP's egregiously flawed existing technical report. These letters are attached as an appendix. I respectfully request this Subcommittee's assistance in obtaining a valid scientific evaluation of Anthraquinone to correct NTP Technical Report 494. Safeguards would certainly need to be put into place at NTP to insure the scientific validity of a new study conducted there.

In summary, I cannot imagine that I happened to stumble upon the only two instances of needlessly burdensome regulation based on bad science. I feel quite certain that many companies in many different industries in the United States are suffering under unnecessary regulatory burdens based upon the same indifference to sound science and lack of scientific integrity.

APPENDIX

Two letters submitted to NTP's Office of Chemical Nomination and Selection nominating Anthraquinone for a valid scientific study to replace NTP Technical Report 494

Each letter is 7 pages – a total of 14 pages appended.

Chemical Products Corporation

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December 5, 2008

Office of Chemical Nomination and Selection
National Toxicology Program/NIEHS
MD EC-31
P.O. Box 12233
Research Triangle Park, NC 27709

Subject: Nomination of Anthraquinone, CAS # 84-65-1, for study - Replacement of scientifically untenable NTP Technical Report 494

Dear Sir or Madam:

The National Toxicology Program has demonstrated a strong interest in naturally occurring quinones containing the anthraquinone ring, as a class. Anthraquinone, CAS #84-6-1, also known as 9,10-anthraquinone or 9,10-dioxoanthracene, is the parent compound of this class.

Unfortunately, animal studies conducted by NTP in the mid-1990s employed an Anthraquinone test article contaminated with mutagenic 9-nitroanthracene (anthraquinone is not a mutagen). Uncorrected scientific misconduct on the part of individuals within NTP has resulted in publication of scientifically

untenable conclusions regarding the carcinogenic activity of Anthraquinone in NTP Technical Report 494 (TR494)[1]. Innes et al. (1969)[2] found no carcinogenic activity for Anthraquinone in mice, and Huff et al. (1996)[3] predicted that Anthraquinone would not be carcinogenic based upon structural characteristics of its primary metabolite, 2-hydroxyanthraquinone; the test article employed in the TR494 studies was so contaminated as to confound the interpretation of the results of those studies.

The carcinogenic potential of anthraquinone was evaluated by Innes et al. (1969) in two strains of mice. At 7 days of age and continuing through 28 days of age, groups of 18 male or 18 female $B6C3F_1$ or $B6AKRF_1$ mice received 464 mg anthraquinone/kg body weight daily by gavage. After 28 days, these groups received 1,206 ppm anthraquinone in feed for 18 months. No increase in tumors in either strain of mice was associated with administration of anthraquinone.

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1 Toxicology and Carcinogenesis Studies of Anthraquinone (CAS No. 84-65-1) In F344/N Rats and $B6C3F_1$ Mice (Feed Studies); National Toxicology Program Technical Report 494; NIH publication 05-3953.
2 Innes, J.R.M., Ulland, B.M., Valerio, M.G., Petrucelli, L., Fishbein, L., Hart, E.R., Pallotta, A.J., Bates, R.R., Falk, H.L., Gart, J.J., Klein, M., Mitchell, I., and Peters, J. (1969). Bioassay of pesticides and industrial chemicals for tumorigenicity in mice: A preliminary note. J. Natl. Cancer Inst. 42, 1101-1114.
3 Huff, James; Weisburger, Elizabeth; and Fung, Victor A.; "Multicomponent Criteria for Predicting Carcinogenicity: Dataset of 30 NTP Chemicals"; Environmental Health Perspectives Supplements Volume 104; Number S5; October 1996.

Huff et al. (1996) predicted that Anthraquinone would not be carcinogenic based upon multicomponent criteria for predicting carcinogenicity, including structural considerations of Anthraquinone's primary metabolite, 2-hydroxyanthraquinone.

In the mid-1990s NTP conducted animal tests using an Anthraquinone test article manufactured by the nitric acid oxidation of anthracene which was contaminated with mutagenic 9-nitroanthracene (Anthraquinone is not a mutagen). A 1999 TR494, which incorrectly declared the test substance, Anthraquinone, to be a mutagen, and concluded that there was clear evidence of carcinogenic activity in both male and female mice, was withdrawn in September 2003 because it failed to recognize the mutagenic contamination in the non-mutagenic test article[4].

A substantially revised February 2004 TR494 contained the same conclusions as the withdrawn 1999 report, but included new information that (1) "pure" anthraquinone is not mutagenic, (2) the TR494 test article was contaminated with mutagenic 9-nitroanthracene, (3) the TR494 test article had been found to be mutagenic to Salmonella typhimurium strains TA98 and TA100 without metabolic activation[5], and

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4 HHS Information Quality Web Site. Information Requests for Corrections and HHS' Responses. Item 5. 2003. http://aspe.hhs.gov/infoQuality/requests.shtml

5 Butterworth, B.E., Mathre, O.B., and Ballinger, K.; "The preparation of anthraquinone used in the National Toxicology Program cancer bioassay was contaminated with the mutagen 9-nitroanthracene"; Mutagenesis 16, 169-177; 2001.

(4) the primary anthraquinone metabolite, 2-hydroxyanthraquinone, had been found by NTP to be mutagenic to TA98 without S9 activation in a 2003 preincubation mutagenicity assay, thus, being cited as the mutagen potentially responsible for the observed tumors. NTP concealed an earlier negative preincubation assay for 2-hydroxyanthraquinone[6][7] in conflict with its finding. Nevertheless, on February 18, 2004 the NTP's Technical Reports Review Subcommittee restricted the conclusions in TR494 to "anthracene-derived anthraquinone", in reference to the obsolete TR494 test article production method which contributed mutagenic contaminants. No anthracene-derived Anthraquinone has been available commercially within the U.S. for many years.

In an unprecedented action, NTP commissioned further mutagenicity testing in the summer of 2004 after the February 2004 peer review. To remove the "anthracene-derived anthraquinone" restriction from the conclusions presented in the final TR494, NTP presented a new negative mutagenicity assay conducted in the summer of 2004 to NTP's December 9, 2004 Technical Reports Review

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6 Tikkanen, L.; Matsushima, T.; Natori, S.; "Mutagenicity of anthraquinones in the Salmonella preincubation test"; Mutation Research; 116(3-4):297-304; March 1983. This paper also presents a negative assay for Anthraquinone which NTP ignored in 1999, but later had to accept as accurate.

7 Page 91 in TR494 states specifically that Tikkanen et al. (1983) did not perform testing without S9; in fact, negative preincubation assays in strains TA98, TA100 and TA 2637 were reported without S9 activation.

Subcommittee for "Sample A07496"as a conclusive demonstration that the TR494 test article, "Anthraquinone, Lot 5893", had not been mutagenic after all. False information was provided to the peer review panel to overcome a concern expressed by one of the reviewers that mutagenic impurities might have decomposed during the more than 7 years which had elapsed since the conclusion of the animal studies[8]. This new information was incorporated into the final TR494 and the "anthracene-derived anthraquinone" limitation on the conclusions was removed.

Investigation has revealed that "Sample A07496" has been falsely presented as being an aliquot of the TR494 test article "Anthraquinone Lot 5893". The Test Article Receipt and Transfer Report from BioReliance Testing Laboratories (BTL), the laboratory which performed the 2004 mutagenicity assay for NTP, shows that "Sample A07496" was not labeled "Anthraquinone, Lot 5893", the TR494 test article, when it was received by BTL and assigned sample number A07496[9].

In a remarkable perpetuation of scientific misconduct, NIEHS's September 22, 2008 Information Quality response confirmed that any aliquot of the TR494 test article would be labeled "Anthraquinone, Lot 5893" when shipped from the

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8 HHS Information Quality Web Site. Information Requests for Corrections and HHS' Responses. Item 28 at section c. http://aspe.hhs.gov/infoQuality/requests.shtml

9 BioReliance Testing Laboratories Test Article Receipt and Transfer Reports; Documents Responsive to NIH FOI No. 33011; 7 pages; attachment to item c2. at Item 28 in http://aspe.hhs.gov/infoQuality/requests.shtml

Battelle Columbus Laboratories test article repository, but ignored the BTL Test Article Receipt and Transfer Report submitted to document the fact that "Sample A07496" was not so labeled when it was received by BTL for mutagenicity assay[10]. Enforcement of the HHS Information Quality Guidelines appears to be moribund; NIEHS is currently turning a blind eye to scientific misconduct within its own ranks.

Scientific misconduct on the part of NTP staff resulted in the existing NTP Technical Report 494 (TR494) being approved at its third peer review on December 9, 2004. Accepted scientific and ethical standards have not been enforced within NTP, as demonstrated by NIH's September 22, 2008 Information Quality response regarding deficiencies in TR494 as described above. Materially false information remains an integral part of TR494, and the accuracy of the prediction by Huff et al. (1996) that anthraquinone is not a carcinogen has yet to be tested in a scientifically-sound study.

We respectfully submit that the February 18, 2004 NTP Technical Reports Review Subcommittee was correct in its *de facto* determination that mutagenic impurities confounded the results of the TR494 animal studies (hence, the restriction of the conclusions presented to only "anthracene-derived anthraquinone"). We nominate Anthraquinone, CAS

10 HHS Information Quality Web Site. Information Requests for Corrections and HHS' Responses. Item 28 at section c. http://aspe.hhs.gov/infoQuality/requests.shtml

84-65-1, produced by either of the dominant present industrial manufacturing processes – the Friedel-Crafts process or the Diels-Alder process - for study to obtain a scientifically-sound determination of the carcinogenic potential of anthraquinone containing only biologically innocuous impurities.

Chemical Products Corporation markets Anthraquinone to the pulp and paper industry.

Sincerely,

Jerry A. Cook

Jerry A. Cook
Technical Director

Chemical Products Corporation

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November 24, 2009

Office of Chemical Nomination and Selection
National Toxicology Program/NIEHS
MD EC-31
P.O. Box 12233
Research Triangle Park , NC 27709

Subject:

Nomination of Anthraquinone, CAS # 84-65-1, for long-term bioassay – NTP Technical Report 494 has been recognized as deficient

Dear Sir or Madam:

The international scientific community has recognized that NTP Technical Report 494 does not represent sound science. Professor Alan R. Boobis et al. state in the October 2009 issue of Toxicologic Pathology, ***"The data for anthraquinone are considered suspect because other carcinogenicity studies were negative, and the NTP carcinogenicity study used a batch of***

anthraquinone contaminated with the potent mutagen 9-nitroanthracene at a level of 1,200 ppm (Butterworth, Mathre, and Ballinger 2001). (A purified sample was negative in the Ames test.) Certainly, it can be said that the material used by the NTP was mutagenic..." ("A Data-Based Assessment of Alternative Strategies for Identification of Potential Human Cancer Hazards"; Alan R. Boobis, Samuel M. Cohen, Nancy G. Doerrer, Sheila M. Galloway, Patrick J. Haley, Gordon C. Hard, Frederick G. Hess, James S. Macdonald, Stéphane Thibault, Douglas C. Wolf and Jayne Wright; Toxicol Pathol; 37; 714-732; 2009 - at page 719).

The deficient NTP carcinogenicity study referenced by Professor Boobis et al. is reported in NTP Technical Report 494 (TR494); this report contains a negative mutagenicity assay falsely attributed to the contaminated NTP test material. This false assay was presented as "new information" at the third peer review of this technical report on December 9, 2004 and resulted in acceptance of scientifically untenable conclusions by the Technical Reports Review Subcommittee on that date. Documentary evidence (obtained through a Freedom

of Information Act appeal) of misconduct on the part of NTP scientists Dr. Richard Irwin, Dr. Cynthia Smith, and Dr. John Bucher was willfully ignored by Dr. Joyce Martin when she denied Chemical Products Corporation's Request for Reconsideration under the DHHS Information Quality Guidelines in September 2008.

Rigorous scientific analysis led Professor Boobis et al. to conclude, ***"Certainly, it can be said that the material used by the NTP was mutagenic"***, based on knowledge of the potency of the 9-nitroanthracene contaminant. Professor Boobis at Imperial College London has published over 200 original research papers and is an Editor-in-Chief of Food and Chemical Toxicology. He was deputy chairman of the U.K. Advisory Committee on Pesticides (1999-2002) and is a member of a number of national and international grant review and advisory committees, including the UK Committees on Carcinogenicity and on Toxicity. He was awarded the Order of the British Empire for his work on the risk assessment of pesticides in 2003. He is an Honorary Member of EUROTOX, a Fellow of the British Toxicology Society, and a Fellow of the Institute of

Biology. Fortunately, a commitment to research integrity and correction of the scientific record exists within the international scientific community.

Professor Boobis et al. have provided an essential correction of the scientific record regarding Anthraquinone. The REACH Substance Information Exchange Forum (SIEF), of which I am a member, will disregard the conclusions presented in TR494 when preparing the REACH registraion dossier for anthraquinone on the basis that they are scientifically untenable. The European Chemicals Agency has been formally requested by the REACH SIEF to confirm the SIEF's determination that TR494 does not represent sound science.

The final TR494, published in September 2005, also misrepresents the scientific record concerning the mutagenicity of anthraquinone's primary metabolite, 2-hydroxyanthraquinone. After the 1999 TR494 had been withdrawn because ***"the presence of this contaminant*** *[9-nitroanthracene]* ***raises doubt as to the effect(s) of anthraquinone itself, or its metabolites, and confounds interpretation of the NTP studies..."*** (NIEHS

Deputy Director Samuel H. Wilson's determination in September 2003), NTP conducted a mutagenicity assay of 2-hydroxyanthraquinone which purported to show that it was mutagenic to Salmonella typhimurium TA98 without metabolic activation. Thus, Dr. Irwin at al. presented 2-hydroxyanthraquinone as a direct acting mutagen produced *in situ* which could be responsible for the carcinogenicity observed in the TR494 studies through a mechanism involving mutagenicity. A conflicting earlier negative preincubation assay of 2-hydroxyanthraquinone in TA98 without metabolic activation was withheld from peer reviewers and its existence is specifically denied in TR494; at page 91, TR494 incorrectly states that Tikkanen et al. (1983) did not perform mutagenicity assays in the absence of S9 metabolic activation; in fact, Tikkanen et al. (1983) reported negative assays of 2-hydroxyanthraquinone in 3 strains - TA98, TA100 and TA 2637 – in the absence of S9 metabolic activation (Tikkanen, L.; Matsushima, T.; Natori, S.; Mutagenicity of anthraquinones in the Salmonella preincubation test; Mutation Research; 116(3-4):297-304; March 1983).

An additional negative assay of 2-hydroxyanthraquinone in TA98 without metabolic activation was reported by Butterworth et al. in August 2004 (Butterworth, B.E., Mathre, O.B., and Ballinger, K.E., Adalsteinsson, O.; Contamination is a Frequent Confounding Factor in Toxicology Studies with Anthraquinone and Related Compounds; Int J Toxicol; *23; No. 5; 335-344; 2004).*

In summary, Anthraquinone is not a mutagen, but the test article employed in the studies conducted by NTP in the mid-1990s contained biologically significant mutagenic contamination – it was found to be mutagenic to Salmonella typhimurium strains TA98 and TA100 without S9 metabolic activation (less so with metabolic activation). Misconduct on the part of NTP scientists resulted in publication of a final technical report which contains a false negative mutagenicity for the TR494 test article and misrepresents the scientific record concerning the mutagenicity of the primary anthraquinone metabolite, 2-hydroxyanthraquinone. The international scientific community has recognized that the conclusions presented in TR494 are scientifically untenable.

We reiterate our nomination of anthraquinone, CAS # 84-65-1, for long-term bioassay by NTP. The failure of NIEHS to withdraw TR494 after being presented conclusive documentation that it is scientifically deficient demonstrates that NIEHS and NTP lack a functioning mechanism to insure research integrity. Thus, a repeated anthraquinone study should be overseen by an impartial scientific body outside of NIEHS.

Anthraquinone, CAS #84-65-1, should be chosen by NTP's Board of Scientific Counselors for study in 2010 for the same reasons that it was chosen by NTP for study in the early 1990s.

Sincerely,

Jerry A. Cook

Jerry A. Cook
Technical Director

November 14, 2011

Dr. Thomas A. Burke
Associate Dean for Public Health Practice and Training
Department of Health Policy and Management
The Johns Hopkins Bloomberg School of Public Health
624 North Broadway, Room 429
Baltimore, MD 21205

Dear Dr. Burke:

Thank you for appearing before the Subcommittee on Environment and the Economy on October 6, 2011, to testify at the hearing entitled "Chemical Risk Assessment: What Works for Jobs and the Economy?"

Pursuant to the Rules of the Committee on Energy and Commerce, the hearing record remains open for 10 business days to permit Members to submit additional questions to witnesses, which are attached. The format of your responses to these questions should be as follows: (1) the name of the Member whose question you are addressing, (2) the complete text of the question you are addressing in bold, and then (3) your answer to that question in plain text.

To facilitate the printing of the hearing record, please e-mail your responses, in Word or PDF format, to Alex.Yergin@mail.house.gov by the close of business on Monday, November 14, 2011.

Thank you again for your time and effort preparing and delivering testimony before the Subcommittee.

Sincerely,

John Shimkus
Chairman
Subcommittee on Environment and the Economy

cc: The Honorable Gene Green, Ranking Member,
Subcommittee on Environment and the Economy

Attachment

The Honorable John Shimkus

1. **Your fellow panelist Dr. Honeycutt has alluded to IRIS values contributing to standards that are below background for his state. In your opinion, as a former state official, are there broader economic consequences associated with publishing an IRIS value that is lower than background levels? Will it impacts jobs and the economy?**

First, it is important to recognize that the publication of an IRIS value does not in itself lead to an environmental standard. The value provides an estimate of potential health risks derived from the available scientific data. While an IRIS value contributes to the standards setting process there are many other factors that go into the establishment of enforceable standards such as costs, public health benefits and technological feasibility. Therefore, publishing an IRIS value does not, by itself, have economic consequences, nor should it directly impact jobs and the economy. It is important that the standards setting process consider economic impacts, as well as feasibility, particularly when the hazards of concern occur naturally in the environment. However, as we have learned from naturally occurring radiation such as radium in groundwater, or high levels of radon in homes, there are times when it is important to reduce population exposure in order to safeguard human health.

2. **As a former New Jersey official, you can appreciate the need to clean-up abandoned waste sites. Mayor Christian Bollwage of Elizabeth, NJ, testified before the House Science Committee that there is a vast practical difference between grossly contaminated sites that are Superfund sites and less contaminated sites, known as brownfields, properties that could be cleaned up and redeveloped for the well-being of that community. He further stated that EPA was "less than careful" about how they originally characterized the risk of brownfields to the public, creating an "unpardonable stigma" attached to any site and making cleanup and redevelopment impossible. If there is not some process to eliminate the flaws NAS has found with IRIS assessments, don't you think it will continue to be a practical barrier to cleanup and these kinds of economic success stories from occurring?**

Cleanup and redevelopment of formerly contaminated brown field sites has been a true environmental success story. Throughout the country there have been major redevelopment efforts such as the Hudson River waterfront in New Jersey that have been successful in containing historical pollutants while spurring economic redevelopment. As a former New Jersey state official I am aware of the challenges of redeveloping Superfund sites and the stigma and concerned about long-term risks. I feel that we have made great progress in redeveloping Brownfields and that data from high risk assessments has contributed to managing site risks.

At the present time the long delay in finalizing IRIS values may indeed be frustrating to developers as they decide upon groundwater contamination treatment and excavation and

disposal options. This can also present challenges to the environmental insurance companies. Improvements to the Irish should focus upon ending the endless debate and challenge to published numbers and speeding up the process. However it must be underscored that the ultimate decision-making on Brownfields rests with the program offices at the national regional and state levels.

The Honorable Bill Cassidy

1. **Dr Burke, in your response to a question you stated that the effects of a biological hazard need to be evaluated in the context of the population affected. That said, many EPA recommendations are concerned with effects of a specific substance on a specific population. An example is the increase in mortality caused by ozone on patients with underlying bronchospatic pulmonary disease or an increase in deaths due to myocardial infarction. But Dr. Anastas in earlier testimony stated that when EPA or IRIS calculates such death rates, they do not compare those who die with a cohort with similar underlying co- morbidities, those who die are compared with the general population. Do you agree with this assessment? If not, why not.**

Sensitive subpopulations such as those with existing comorbidities present a difficult challenge for public health officials. For example we know that small children and the elderly are most susceptible to many public health threats. Similarly those with pre-existing respiratory conditions are the targets of many of our air pollution related alerts including ozone. From an epidemiologic perspective we would expect that the impacts of pollution would in fact be much greater on those with pre-existing conditions.

Although I am not familiar with the specific studies that Dr. Anastas was referring to, it is standard epidemiologic practice to examine overall mortality rates when comparing populations. Unfortunately, I don't feel that our current surveillance systems allow us to identify the proportion of the population with pre-existing conditions. In fact, our current estimates of population risk most likely underestimate the true health risks to those in our population that have pre-existing disease. I therefore feel there are limitations to our current methodologies that I hope will be improved in the future with improved population health surveillance and refined epidemiologic methods.

The Honorable Doris Matsui

1. **In the last Congress, I introduced legislation, which became law, to limit formaldehyde emissions from composite wood products. In an ideal world, that bill would not have been necessary. Our system for assessing and controlling toxic chemicals should be strong enough to protect human health and the environment without the need for**

chemical specific congressional action. However, it is not, and that is one of the reasons we acted on responsible legislation to protect health and environmental standards.

2. **The recommendations to strengthen IRIS should not be used as an argument against moving forward with important IRIS assessments.**
   a. **Do you believe that formaldehyde is safe?**

As the NAS report has concluded, formaldehyde exposure is associated with a broad range of health effects, ranging from acute respiratory irritation at high levels to increased cancer risk at chronic lower levels of exposure. The safety of formaldehyde depends upon successful control of worker and population exposures. As a member of a CDC panel evaluating formaldehyde exposure in healtheffects in FEMA trailers, I saw firsthand the broad range of health concerns. Given the widespread use of formaldehyde and building materials and consumer products it is important that we move forward in characterizing risks and reducing exposures.

   b. **In your view, how important are the hazard assessments produced by IRIS?**

IRIS assessments are important part of the knowledge base that guides our public health and environmental protection efforts. They provide an important synthesis of scientific information is extremely important for public health decision-making.

   c. **Should these assessments be abandoned or suspended while improvements to the system are made?**

No. Given the importance of these documents for our Nation's public health and environmental programs, I see no reason to shut down the process while we work to improve the quality of reports.

   d. **What should be done to improve the utility and credibility of government hazard assessments?**

The NAS has made many recommendations on improving the quality and credibility of the EPA's hazard assessment and risk assessment process. I feel the NAS report *Science and Decisions* provides detailed recommendations that would vastly improve the application of risk sciences to our decision-making. In addition, there are,many aspects of the NAS formaldehyde report that can improve the process. EPA is currently moving forward to implement many of these recommendations. I feel that the following aspects are key to improving credibility and utility:

- Improved problem formulation to assure that the agency is asking the right scientific questions,

- more inclusive examination of available scientific studies including clear justification of key studies selected to derive health-based values,
- rigorous and transparent peer review,
- reformatting of the reports to be more readable and useful to risk managers and decision makers,
- and, adherence to realistic timelines for completion

It is also important that we work to end the current "battle of the interest groups" that serves as a divisive force, raising doubts about the credibility of EPA's science and contributing to enormous delay in addressing the scientific needs of our decision-makers.

e. What role should cumulative effects play in risk assessment and management?

At the current time our environmental policies are attempting to protect public health one molecule at a time. We set standards for individual substances while ignoring the potential interactive effects of thousands more that may be present in our water, air and food. In addition, we routinely ignore the tremendous differences in susceptibility throughout our population.

The NAS report *Science and Decisions* underscores the need to move toward improved consideration of cumulative effects and susceptible subpopulations to improve risk management. While there are many scientific challenges it is important that we move forward in recognizing the cumulative impacts of environmental exposures, the broad range of susceptibility within our population, and the many social, environmental, and behavioral risk factors that impact the health of our population.

3. Can these assessments form the basis of effective regulation, including controls of toxic chemicals under TSCA?

Effective management of the risks of toxic chemicals must move beyond the one at a time single substance approach. If it is our goal to protect the health of our population we must consider the true goal of our efforts. For example, if it is our goal to better protect children and the unborn, then we must consider the broader range of potential interactions in deciding about chemical safety. If there are 10 pesticides present in a given crop, does it make sense to set health based standards one at a time, or to consider the potential additive or interactive effects of the entire group? If you are taking 10 medicines, isn't it important that your pharmacist and doctor understand and prevent potential adverse interactions?

The science of toxicology is rapidly moving forward to allow us to rapidly and efficiently identify a board range of potential health impacts. In addition, new tests and enable us to test mixtures of compounds and identify potential health effects. Many scientific challenges remain, but cumulative risk assessment is essential to more effective management of chemical hazards.

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