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EXAMINING THE SCIENTIFIC AND OPERATIONAL INTEGRITY OF EPA'S IRIS PROGRAM

JOINT HEARING

BEFORE THE

SUBCOMMITTEE ON ENVIRONMENT &
SUBCOMMITTEE ON OVERSIGHT

COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

HOUSE OF REPRESENTATIVES

ONE HUNDRED FIFTEENTH CONGRESS

FIRST SESSION

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EXAMINING THE SCIENTIFIC AND OPERATIONAL INTEGRITY OF EPA'S IRIS PROGRAM

Wednesday, September 6, 2017

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON ENVIRONMENT AND
SUBCOMMITTEE ON OSVERSIGHT,
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY,
Washington, D.C.

The Subcommittees met, pursuant to call, at 10:04 a.m., in Room 2318 of the Rayburn House Office Building, Hon. Andy Biggs [Chairman of the Subcommittee on Environment] presiding.

LAMAR S. SMITH, Texas
CHAIRMAN

EDDIE BERNICE JOHNSON, Texas
RANKING MEMBER

Congress of the United States
House of Representatives
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Subcommittees on Environment and Oversight

Examining the Scientific and Operational Integrity of EPA's IRIS Program

Wednesday, September 6, 2017
10:00 a.m.
2318 Rayburn House Office Building

Witnesses

Dr. Kenneth Mundt, Principal, Ramboll Environ

Dr. James Bus, Senior Managing Scientist, Exponent

Dr. Thomas Burke, Johns Hopkins University

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY

HEARING CHARTER

August 31, 2017

TO: Members, Subcommittee on Environment and Subcommittee on Oversight

FROM: Majority Staff, Committee on Science, Space, and Technology

SUBJECT: Joint Subcommittee Hearing: "Examining the Scientific and Operational Integrity of EPA's IRIS Program"

The Subcommittee on Environment and the Subcommittee on Oversight of the Committee on Science, Space, and Technology will hold a joint hearing titled *Examining the Scientific and Operational Integrity of EPA's IRIS Program* on Wednesday, September 6, 2017, at 10:00 a.m. in Room 2318 of the Rayburn House Office Building.

Hearing Purpose:

The purpose of this hearing is to examine the U.S. Environmental Protection Agency's Integrated Risk Information System (IRIS) program. This hearing will focus on the scientific and operational integrity issues as they relate to the functionality and goals of the IRIS program.

Witness List

- **Dr. Kenneth Mundt,** *Principal, Ramboll Environ*
- **Dr. James Bus,** *Senior Managing Scientist, Exponent*
- **Dr. Thomas Burke,** *Professor, Bloomberg School of Public Health, Johns Hopkins*

Staff Contact

For questions related to the hearing, please contact the Majority Staff at 202-225-6371.

Chairman BIGGS. Good morning. Welcome to the Subcommittee on Environment and Oversight in the House Committee on Science, Space, and Technology, our hearing on "Examining the Scientific and Operational Integrity of the EPA's IRIS Program."

I'm grateful to be back. Good to see so many back, and I know others will be coming, and I hope all of you had a productive work period in your districts.

The Subcommittee on Environment and Oversight will come to order. Without objection, the Chair is authorized to declare recesses of the Subcommittee at any time.

Welcome to today's hearing titled "Examining the Scientific and Operational Integrity of EPA's IRIS Program." I recognize myself for five minutes for an opening statement.

Welcome to our Subcommittee hearing titled "Examining the Scientific and Operational Integrity of EPA's IRIS Program." Today, we will hear from witnesses who are experts in the fields of epidemiology and toxicology and learn about their interactions with EPA's IRIS program. The original purpose of IRIS was simply to identify and characterize the health hazards of chemicals that are found in the environment. However, this program has long suffered from a lack of scientific transparency and an inability to produce work in a timely manner.

Even worse, IRIS appears to have been used by the previous Administration as cover for unjustified and unscientific regulatory action, something well outside of the scope of the program's mandate.

I'm far from the only one raising the alarm. In fact, both the National Academy of Science and the Government Accountability Office have been critical of the management of the IRIS program.

In February of this year, GAO again included IRIS on its annual high-risk list, which identifies federal programs that have greater than normal vulnerabilities to fraud, waste, abuse, and mismanagement.

In both 2011 and 2014, NAS made numerous recommendations for IRIS that have never been fully implemented. For example, NAS found that IRIS assessment methods and reporting continue to be a concern, especially in light of the extremely long process that IRIS takes to choose chemicals and complete its evaluations.

Despite the numerous deficiencies that were highlighted in both the GAO and NAS reports, IRIS fails to show any sign of improvement. It is now the role of Congress, as the ultimate steward of taxpayer dollars, to carefully assess whether IRIS can even be salvaged. I myself remain very skeptical and simply cannot support the program in its current form.

What I find most troubling is that IRIS may be providing conflicting or duplicative information and creating confusion for Americans regarding either the harm or lack of harm that any given chemical may possess. If that is indeed the case, IRIS poses a threat to the public's trust and safety and simply cannot be allowed to continue to operate.

I'm also deeply concerned by the fact that we can actually point to cases in which determinations by IRIS have been inappropriately used to make regulatory decisions. For example, the previous Administration took action against a chemical manufacturer in Louisiana based on a faulty IRIS determination, even though that

particular company was currently in compliance with all emissions regulations put forward under the Clean Air Act. Actions like the one initiated by IRIS in Louisiana do not inspire confidence in our federal agencies.

This Committee is committed to ensuring that EPA uses the best available science. IRIS, it appears, has failed to use even passable science on many occasions, and what is so troubling is that even when IRIS administrators are alerted to this fundamental problem, they take absolutely no corrective action.

We must also be committed to ensuring that EPA's actions are based on the highest levels of scientific integrity. The fact that IRIS has been subjected to continued scrutiny of its scientific processes and continued requests for Information Quality Act reviews should send a clear signal that the program is failing and is in serious danger of irrevocably subverting its mission.

All those concerns aside—and they are considerable—I am hopeful that the witnesses before us today can provide Congress with information to better inform actions that this Committee may take. We all want to ensure the protection of American citizens from the potentially harmful impacts of chemicals. If IRIS is the appropriate program to do that, we in Congress must ensure that it is properly organized and makes informed decisions.

Moreover, we must ensure that IRIS efforts—the efforts of IRIS to evaluate chemicals are based on real-world threats, not theoretical ones.

I would briefly take a moment to point out that the existence of or changes to the IRIS program would not have an impact on the continued effectiveness of EPA's Risk Management program.

I look forward to learning more from our distinguished panel today, and have no doubt that this will be a wide-ranging and fascinating discussion. I thank each of our witnesses for being here today.

[The prepared statement of Chairman Biggs follows:]

COMMITTEE ON
SCIENCE, SPACE, & TECHNOLOGY
Lamar Smith, Chairman

For Immediate Release
September 6, 2017

Media Contact: Thea McDonald
(202) 225-6371

Statement of Environment Subcommittee Chairman Andy Biggs (R-Ariz.)
Examining the Scientific and Operational Integrity of EPA's IRIS Program

Chairman Biggs: Good morning and welcome to today's joint subcommittee hearing, entitled "Examining the Scientific and Operational Integrity of EPA's IRIS Program." Today, we will hear from witnesses who are experts in the fields of epidemiology and toxicology and learn about their interactions with EPA's IRIS program.

The original purpose of IRIS was simply to "identify and characterize the health hazards of chemicals that are found in the environment." However, this program has long suffered from a lack of scientific transparency and an inability to produce work in a timely manner. Even worse, IRIS appears to have been used by the previous administration as cover for unjustified and unscientific regulatory action, something well outside of the scope of the program's mandate.

And I'm far from the only one raising the alarm. In fact, both the National Academy of Science and the Government Accountability Office have been critical of the management of the IRIS program. In February of this year, GAO again included IRIS on its annual "high risk" list, which identifies federal programs that have greater than normal vulnerabilities to fraud, waste, abuse, and mismanagement.

In both 2011 and 2014, NAS made numerous recommendations for IRIS that have never been fully implemented. For example, NAS found that IRIS assessment methods and reporting continue to be a concern, especially in light of the extremely long process that IRIS takes to choose chemicals and complete its evaluations.

Despite the numerous deficiencies that were highlighted in both the GAO and NAS reports, IRIS fails to show any sign of improvement. It is now the role of Congress, as the ultimate steward of taxpayer dollars, to carefully assess whether IRIS can even be salvaged. I myself remain very skeptical and simply cannot support the program in its current form.

What I find most troubling is that IRIS may be providing conflicting or duplicative information and creating confusion for Americans regarding either the harm—or lack of harm—that any given chemical may possess. If that is indeed the case, IRIS poses a threat to the public's trust and safety and simply cannot be allowed to continue to operate.

I am also deeply concerned by the fact that we can actually point to cases in which determinations by IRIS have been inappropriately used to make regulatory decisions.

For example, the previous administration took action against a chemical manufacturer in Louisiana based on a faulty IRIS determination, even though that particular company was currently in compliance with all emissions regulations put forward under the Clean Air Act.

Actions like the one initiated by IRIS in Louisiana do not inspire confidence in our federal agencies. This Committee is committed to ensuring that EPA uses the best available science. IRIS, it appears, has failed to use even passable science on many occasions, and what is so troubling is that even when IRIS administrators are alerted to this fundamental problem, they take absolutely no corrective action.

We must also be committed to ensuring that EPA's actions are based on the highest levels of scientific integrity. The fact that IRIS has been subjected to continued scrutiny of its scientific processes and continued requests for Information Quality Act reviews should send a clear signal that the program is failing and is in serious danger of irrevocably subverting its mission.

All those concerns aside – and they are considerable – I am hopeful that the witnesses before us today can provide Congress with information to better inform actions that this Committee may take.

We all want to ensure the protection of American citizens from the potentially harmful impacts of chemicals. If IRIS is the appropriate program to do that, we in Congress must ensure that it is properly organized and makes informed decisions. Moreover, we must ensure that IRIS efforts to evaluate chemicals are based on real-world threats, not theoretical ones.

I look forward to learning more from our distinguished witnesses and have no doubt that this will be a wide-ranging and fascinating discussion.

###

Chairman BIGGS. And with that, I yield back the balance of my time and recognize now the Ranking Member of the Environment Subcommittee, the gentlewoman from Oregon, for an opening statement.

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

Mr. Chairman, this Committee has a long tradition of examining the Environmental Protection Agency's Integrated Risk Information System, or IRIS. The last time this Committee held a hearing on it was back in 2014, and at that hearing, I said that this Committee needs to allow the EPA to fulfill its mission of protecting the public's health from environmental hazards. Producing assessments of chemicals that may cause harm to our constituents and our communities is critical to that mission.

I am disappointed that today, this Committee is once again headed in the wrong direction. Rather than undermining important public health assessments, we should be supporting and in fact strengthening the EPA's efforts to protect Americans from unsafe chemical exposure. Given that the Committee has not held a hearing on this issue in three years, it is troubling that today the Majority is calling two witnesses with clear interests in a particular outcome, but did not call the EPA or the GAO. This does not seem to me like a hearing to investigate how we can best protect our constituents' health, which is what we should be doing, but instead an attempt to look for a basis for weakening or eliminating the IRIS program. That is unacceptable.

It's also perplexing that the Majority is hosting a hearing to emphasize industry-held criticisms of the IRIS program at a time when independent organizations that have investigated the IRIS program are citing its notable improvements. And Mr. Chairman, you said that IRIS has failed to show any signs of improvement, but just last week, the independent EPA Science Advisory Board, or the SAB, wrote a letter to Administrator Pruitt praising the progress of the IRIS program. That letter said, "The SAB has observed significant enhancements in the IRIS program over the last few years, with impactful changes over the past year, and marked progress over the past six months. The changes are so extensive and positive that they constitute a virtual reinvention of IRIS," and I'll repeat that last line: "The changes are so extensive and positive that they constitute a virtual reinvention of IRIS."

The work of IRIS is especially critical to protecting the health of our Nation's children. The human health assessments developed through the program provide vital information that aids the EPA in its decision making, and also informs state and local governments and public health professionals. Fundamentally the IRIS program helps those tasked with protecting the public's health to make the best decisions they can by using the best available science to determine the potential harmful effects of chemical exposures. That is precisely why this Committee has taken an interest in the activities of IRIS in the past, particularly when the program was not living up to its potential.

In response to a request from Congress, the National Academies reviewed the IRIS program and released a report, two months prior to our 2014 hearing, which made recommendations for improvements that EPA should implement. What is the status of those rec-

ommendations, what progress has the program made, and what improvements are still needed? Those are the questions we should be asking the EPA and the National Academies. Unfortunately, the Majority did not invite anyone from the EPA or the National Academies to offer any answers.

Mr. Chairman, the IRIS program is too important for there not to be a thoughtful examination of its status and a fuller review of the recent progress it has made. This Committee has the important role of providing oversight of the Administration's efforts in its jurisdiction.

During the Obama Administration, this Committee held dozens and dozens of hearings investigating actions of the Administration, and the EPA, including the EPA Administrator, was here to answer. Yet, now that there is a Republican Administration, this Committee has failed to have a single hearing with any of the presidential appointments in its jurisdiction.

During the Obama Administration, Administrator Pruitt testified in front of this Committee in his role as Oklahoma's Attorney General and was highly critical of the EPA. Now that he is the EPA Administrator, the American people deserve the opportunity to hear his priorities for the EPA. This Committee must fulfill its duty of providing oversight of the agencies in its jurisdiction.

Mr. Chairman, will you commit to holding a Full Committee hearing on a legislative day this year with EPA Administrator Pruitt?

Chairman BIGGS. Is the gentlewoman done?

Ms. BONAMICI. No, I'm asking, Mr. Chairman, will you commit to holding a Full Committee hearing on a legislative day this year with EPA Administrator Pruitt? He has not been before this Committee yet.

Chairman BIGGS. Well, I appreciate you asking me a question in public that you've never broached with me in private, which I consider to be highly improper and highly unusual, frankly, and I'm happy to discuss with you in private.

Ms. BONAMICI. Thank you, Mr. Chairman.

And finally, Mr. Chairman, I ask that the letter from EPA's Science Advisory Board, which I referenced earlier, be made a part of the record.

Thank you, and I yield back.

[The prepared statement of Ms. Bonamici follows:]

OPENING STATEMENT
Ranking Member Suzanne Bonamici (D-OR)
of the Subcommittee on Environment

House Committee on Science, Space, and Technology
Subcommittee on Environment
Subcommittee on Oversight
"Examining the Scientific and Operational Integrity of EPA's IRIS Program"

September 6, 2017

Mr. Chairman, this Committee has a long tradition of examining the Environmental Protection Agency's Integrated Risk Information System, or IRIS. The last time this Committee held a hearing on it was back in 2014. At that hearing, I said that this Committee needs to allow the EPA to fulfill its mission of protecting the public's health from environmental hazards. Producing assessments of chemicals that may cause harm to our constituents and our communities is critical to that mission.

I am disappointed that, today, this Committee is once again headed in the wrong direction. Rather than undermining important public health assessments, we should be supporting and in fact strengthening the EPA's efforts to protect Americans from unsafe chemical exposure. Given that the Committee has not held a hearing on this issue in three years, it is troubling that today the Majority called two witnesses with clear interests in a particular outcome, but did not call the EPA or the GAO. This does not seem to me like a hearing to investigate how to best protect our constituent's health, which is what we should be doing, but instead an attempt to look for a basis for weakening or eliminating the IRIS program. That is unacceptable.

It is also perplexing that the Majority is hosting a hearing to emphasize industry-held criticisms of the IRIS program at a time when the independent organizations that have investigated the IRIS program are citing its notable improvements. Just last week, the independent EPA Science Advisory Board - "the SAB" - wrote a letter to Administrator Pruitt praising the progress of the IRIS program. That letter said, quote – "The SAB has observed significant enhancements in the IRIS program over the past few years, with impactful changes over the past year, and marked progress over the past six months. The changes are so extensive and positive that they constitute a virtual reinvention of IRIS." I will repeat that last line: "The changes are so extensive and positive that they constitute a virtual reinvention of IRIS."

The work of IRIS is especially critical to protecting the health of our nation's children. The human health assessments developed through the program provide vital information that aids the EPA in its decision making, and also informs state and local governments and public health professionals. Fundamentally the IRIS program helps those tasked with protecting the public's health to make the best decisions they can by using the best available science to determine the potential harmful effects of chemical exposures.

That is precisely why this Committee has taken an interest in the activities of IRIS in the past, particularly when the program was not living up to its potential. In response to a request from

Congress, the National Academies reviewed the IRIS program and released a report, two months prior to our 2014 hearing, which made recommendations for improvements that EPA should implement. What is the status of those recommendations, what progress has the program made, and what improvements are still needed? Those are the questions we should be asking EPA and the National Academies. Unfortunately, the Majority did not invite anyone from EPA or the National Academies to offer any answers.

Mr. Chairman, the IRIS program is too important for there not to be a thoughtful examination of its status and a fuller review of the recent progress it has made. This Committee has the important role of providing oversight of the Administration's efforts in its jurisdiction. During the Obama Administration this Committee held dozens and dozens of hearings investigating actions of the Administration, and the EPA was here to answer. Yet, now that there is a Republican Administration, this Committee has failed to have a single hearing with any of the presidential appointees in its jurisdiction. During the Obama Administration, Administrator Pruitt testified in front of this Committee in his role as Oklahoma's Attorney General and was highly critical of the EPA. Now that he is the EPA Administrator, the American people deserve the opportunity to hear his priorities for the EPA. This Committee must fulfill its duty of providing oversight of the agencies in its jurisdiction.

Mr. Chairman, will you commit to holding a Full Committee hearing on a legislative day this year with EPA Administrator Pruitt?

Finally, Mr. Chairman, I ask that the letter from EPA's SAB, which I referenced earlier, be made part of the record.

Thank you. I yield back.

Chairman BIGGS. Thank you, Ms. Bonamici. Thank you.

And now we're going to recognize the Chairman of the Subcommittee on Oversight, Mr. LaHood, for his opening statement.

Mr. LAHOOD. Thank you, Chairman Biggs, and good morning, and welcome to today's Joint Subcommittee hearing on "Examining EPA's Integrated Risk Information System Program."

Today, we will hear from expert witnesses highlighting various examples of why oversight of the IRIS program is critical to restoring scientific integrity to the agency. I would like to thank the witnesses in advance for their testimony today.

EPA created IRIS in 1985 under no statutory authority, defining no safeguards, timelines, or binding requirements with which the program must adhere. EPA intended for the program to "foster consistency in the evaluation of chemical toxicity across the Agency."

However, since 2011 multiple reports have been issued raising glaring deficiencies in the program that to this day have gone unaddressed. As we will hear today from witnesses, there are many questions and issues that have been raised about IRIS assessments being based on sound science. There are multiple instances of the IRIS program relying on outdated or flawed studies to complete assessments, neglecting to obtain or use the scientifically critical raw supporting data related to risk assessments. Moreover, IRIS has failed to adapt mode-of-action science utilized by other offices within EPA, which we will hear today from Dr. Bus.

More troubling, it appears that quasi-regulatory decisions have been based off the assessments completed by the IRIS program. The fact that many of these assessments may be faulty illustrates why oversight is so important to the function of our government.

An accredited scientific body, The National Academy of Sciences, has raised serious questions and concerns about IRIS. The GAO has included IRIS on its biennial High Risk List since 2009, and this Committee sent EPA a letter last year raising similar concerns. These combined efforts have resulted in little, if any, improvement to the IRIS program. By holding this hearing today and diving deeper into the issue at hand, I hope to continue an oversight of the IRIS program to bring attention to the scientific integrity issues that need to be addressed here today.

And Mr. Chairman, I would also add, I know a number of issues have been raised already here this morning. I would just mention that the Minority mentioned the EPA's Science Advisory Board letter to Administrator Pruitt as evidence the IRIS program has been improved significantly. This letter was sent to Administrator Pruitt last Friday, September 1st, less than 36 hours after the Science Advisory Board meeting and two days after the public notice of today's hearing. The Board was not tasked with providing official review or comment on the presentation highlighting changes to the IRIS program. It appears that the SAB recognizes that issues have existed in the past with regard to the IRIS program and that issues still persist currently. Given the speed with which this letter was sent, I find it difficult for the letter to carry much weight toward establishing any significant progress with the IRIS program.

Moreover, this letter fails to provide for any meaningful scientific scrutiny of reviews completed in the past where scientific integrity

issues have been raised, which is one of the major issues with the program and why we are here today, Mr. Chairman.

With that, I yield back. Thank you.

[The prepared statement of Mr. LaHood follows:]

COMMITTEE ON
SCIENCE, SPACE, & TECHNOLOGY
Lamar Smith, Chairman

For Immediate Release
September 6, 2017

Media Contact: Thea McDonald
(202) 225-6371

Statement of Oversight Subcommittee Chairman Darin LaHood (R-Ill.)
Examining the Scientific and Operational Integrity of EPA's IRIS Program

Chairman LaHood: Good morning and welcome to today's Joint Subcommittee hearing "Examining EPA's Integrated Risk Information System Program." Today, we will hear from expert witnesses highlighting various examples of why oversight of the IRIS program is critical to restoring scientific integrity to the agency. I would like to thank the witnesses in advance for their testimony today.

EPA created IRIS in 1985 under no statutory authority, defining no safeguards, timelines, or binding requirements with which the program must adhere. EPA intended for the program to "foster consistency in the evaluation of chemical toxicity across the Agency." However, since 2011 multiple reports have been issued raising glaring deficiencies in the program that to this day have gone un-addressed.

As we will hear from witnesses today, IRIS assessments are not based on sound science. There are multiple instances of the IRIS program relying on outdated or flawed studies to complete assessments, neglecting to obtain or use the scientifically critical raw supporting data related to risk assessments. Moreover, IRIS has failed to adapt "mode of action" science utilized by other offices within EPA, which we will hear more about from Dr. Bus.

More troubling, it appears that quasi-regulatory decisions have been based off the assessments completed by the IRIS program. The fact that many of these assessments may be faulty illustrates why oversight is so important to the function of our government.

An accredited scientific body, The National Academy of Sciences has raised serious questions and concerns about IRIS; the GAO has included IRIS on its biennial High Risk List since 2009; and this Committee sent EPA a letter last year raising similar concerns. These combined efforts have resulted in little, if any, improvement. By holding this hearing today and diving deeper into the issue at hand I hope to continue our oversight of the IRIS program to bring attention to the scientific integrity issues that need to be addressed.

###

Chairman BIGGS. Thank you, Mr. LaHood.

I now recognize the Ranking Member of the Subcommittee on Oversight, Mr. Beyer, for his opening statement.

Mr. BEYER. Thank you, Chairman Biggs, and thank you, Chairman Biggs and Chairman LaHood, for this hearing.

And I too must convey my disappointment with this hearing and the apparent purpose. I'm encouraged by my friend Chairman LaHood's comments that he believes it's the appropriate role for this Committee to have oversight of IRIS but this—I fear this isn't a hearing about oversight. This is going to be a hearing about how to—not a hearing about how to improve the critical function of the EPA's Integrated Risk Information System, not a hearing to actually determine the facts about the remarkable progress they've recently made. This appears to be a hearing for industry.

The letter that the EPA's Science Advisory Board wrote to EPA Administrator Pruitt last week touted the progress made by the IRIS program and its importance in protecting the public health. To quote: "The SAB members in attendance voted unanimously that I communicate to you their enthusiasm for the IRIS program's progress." However, the Majority has not invited anyone from the SAB or the National Academies of Sciences or the GAO or the EPA to testify about the significant improvements the program has made. And I don't think that it undercuts the validity or the importance of the SAB's letter to suggest that it was at least partially a reaction to the announcement of this hearing. Of course it was. When they saw this was coming up, they thought it was important to note all the progress that had been made.

The Majority has instead chosen to ignore this progress and invite two industry scientists as witnesses, who undoubtedly criticize the IRIS program and the EPA in general, and despite assurances from Majority staff that this hearing is simply about hearing from stakeholders, the real intent seems to coincide with a call by industry to eliminate IRIS altogether. For example, if I could ask one slide to be put up? I note that our Chairman Biggs recently offered an amendment to H.A. 3354, the Appropriations Act of 2018, that would zero out all funding for EPA's IRIS program, effectively abolishing it.

I believe this hearing should be viewed in the larger context of what it actually is, which is another attack on the American public's environmental health, another opportunity for industry consultants and industry-paid scientists to attempt to weakness the effectiveness of the EPA, the only federal agency charged with protecting the environment and the health of the American people.

You know, whatever efforts this Administration takes to impede progress made to the EPA's IRIS program, reduce its role in identifying harmful chemicals, or eliminate this program altogether, those efforts unfortunately fit neatly into the anti-science agenda already unveiled by this Administration. Since the Trump Administration came to office less than eight months ago, political appointees at EPA are now reviewing grants to conduct scientific studies, rather than actual scientists as has been the tradition through Democratic and Republican Presidents in the past. The EPA has withdrawn a data request to industry regarding methane emissions from the oil and gas industry, which is a growing and

dangerous problem. Administrator Scott Pruitt has made it known he wants more industry representatives on the Agency's scientific advisory boards, an effort that will undermine the health and safety of the American public and damage the environment. Key positions at the EPA are now being filled with individuals with deep ties to industry, rather than qualified scientists or qualified public health experts. Senior federal officials and scientists have resigned in protest over the direction of the Trump Administration and the actions of the EPA Administrator, and the EPA and other federal agencies have scrubbed references to climate change from their websites and some federal offices have reportedly banned the use of the term.

So it really disheartens me that the Science Committee is not investigating important scientific issues that have a real world impact on the health and safety of our citizens across the country, their exposure to chemical pollutants, and the human health implications of a warming climate. Rather, the Committee seems resolved to providing a forum for industry scientists to advocate for policies and procedures that will please the industries they work for, but cause harm to the environment and the public health of all Americans across the political spectrum.

Thank you, Mr. Chairman. I yield back.

[The prepared statement of Mr. Beyer follows:]

OPENING STATEMENT
Ranking Member Donald Beyer (D-VA)
of the Subcommittee on Oversight

House Committee on Science, Space and Technology
Subcommittee on Environment
Subcommittee on Oversight
"Examining the Scientific and Operational Integrity of EPA's IRIS Program"
September 6, 2017

Thank you Chairman Biggs and Chairman LaHood. Unfortunately, I too must convey my disappointment with this hearing and the apparent purpose for this hearing. This is not a hearing about oversight. This is not a hearing about how to improve the critical function of the EPA's Integrated Risk Information System (IRIS) program. This is not a hearing constructed to actually determine the facts about the problems this program has had in the past and the remarkable progress they have recently made. This appears to be a hearing for industry.

The letter that the EPA's Science Advisory Board (SAB) wrote to EPA Administrator Scott Pruitt just last week touted the progress made by the IRIS program and its importance in protecting the public's health. The letter to Administrator Pruitt, written by the Chair of the SAB, said - quote: "The SAB members in attendance voted unanimously that I communicate to you their enthusiasm for the IRIS program's progress." However, the Majority has not invited anyone from the SAB or the National Academies of Sciences or the Government Accountability Office (GAO) or the EPA to testify about the significant improvements the program has made.

The Majority has instead chosen to ignore this progress and invited two industry scientists as witnesses, who undoubtedly will criticize the IRIS program and the EPA in general. And despite assurances from Majority staff that this hearing is simply about hearing from "stakeholders" about the IRIS program, the real intent seems to coincide with a calling by industry to eliminate IRIS altogether.

I would note that Chairman Biggs recently offered an Amendment to H.R. 3354 – the Department of the Interior, Environment, and Related Agencies Appropriations Act of 2018 that would zero out all funding for the EPA's IRIS program, effectively abolishing it. It appears that this hearing had a pre-determined outcome from the start, and was never intended to be a thoughtful examination of the EPA's IRIS program. It appears to be some sort of pre-text for eliminating the program altogether.

I believe this hearing should be viewed in the larger context of what it actually is: another attack on the American public's environmental health, and another opportunity for industry consultants and industry-paid scientists to attempt to weaken the effectiveness of the EPA, the only federal Agency charged with protecting the environment and the health of the American people. Some Trump Administration officials have also called for eliminating the IRIS program, a move supported by some from industry and industry-friendly groups such as the Competitive Enterprise Institute (CEI). The efforts by these individuals and groups to eliminate, or drastically

curtail the budget and staff of IRIS, seem to be part and parcel of this Administration's war against the environment and science, and appears to be part of this hearing's agenda too.

Whatever efforts this Administration takes to impede progress made to the EPA's IRIS program, reduce its role in identifying harmful chemicals, or eliminate this program altogether, those efforts fit neatly into the anti-science agenda already unveiled by this Administration.

Since the Trump Administration came to office less than eight months ago:

- Political appointees at EPA are now reviewing grants to conduct scientific studies, rather than actual scientists' as has been the tradition in the past.

- The EPA has withdrawn a data request to industry regarding methane emissions from the oil and gas industry, which has been a growing and dangerous problem.

- EPA Administrator Scott Pruitt has made it known he wants more industry representatives on the Agency's scientific advisory boards, an effort that will undermine the health and safety of the American public and damage the environment.

- Key positions at the EPA are now being filled by individuals with deep ties to industry, rather than qualified scientists or public health experts.

- Senior federal officials and scientists have resigned in protest over the direction of the Trump Administration and the actions of EPA Administrator Scott Pruitt.

- The EPA and other federal agencies have scrubbed references to climate change from their websites and some federal offices have reportedly banned the use of the term.

It disheartens me that the Science Committee is not investigating important scientific issues that have a real world impact on the health and safety of citizens across this country, their exposure to chemical pollutants, for instance, and the human health implications of a warming climate. Rather, the Committee seems resolved to providing a forum for industry scientists to advocate for policies and procedures that will please the industries they work for, but cause harm to the environment and the public health of all Americans across the political spectrum.

Thank you, I yield back.

Chairman BIGGS. Thank you, Mr. Beyer.

I now recognize the Ranking Member of the Full Committee, Ms. Johnson.

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

I too must say that I'm disappointed, but I'm really not surprised that we are holding this hearing today. Sadly, I have had to make this statement too many times in the last four years.

How can we, in good conscience, title this hearing as an examination of the scientific and operational integrity of EPA's IRIS program, when there is no one here from EPA here to testify? I don't think we can. How do we conduct the necessary oversight for this program when the Government Accountability Office is not present to answer questions about their recent review of IRIS? I don't know that we can. How are we serving the best interests of our constituents, and of all Americans, when the National Academies of Sciences is not present to discuss their report upon which the last three years. worth of reforms to IRIS were based upon? I don't think we are. How can we have an honest discussion about this program while ignoring the key entities that have reviewed it and studied its recent improvements? I don't think we can.

I would also note that just last week the EPA's independent Science Advisory Board—the SAB—sent a letter to EPA Administrator Scott Pruitt praising the progress the IRIS program has made. The letter said, in part, and I quote: "The Board commends the Agency for making such significant improvements over a short period of time. We are optimistic that the restructured IRIS program will strengthen the scientific foundations of risk assessment and protect the health and safety of the American public." But we are not here to hear that today. Instead, the Majority has invited two industry scientists to voice their criticisms of IRIS.

Let me be clear, industry perspectives should not be excluded from scientific discussions on environmental issues at the EPA, and they are not now and nor have they ever been. The current membership of EPA's Science Advisory Board, for instance, includes representatives from the Dow Chemical Company, Procter and Gamble, and Exxon Mobil. However, I'm concerned that industry, the leadership of this Committee, and now this Administration, are seeking to let industry drive the science upon which critical decisions about protecting the public's health and the environment are made.

The current criticisms of the EPA's IRIS program by industry highlight that point. We have seen this tactic used by industry before, and I'm sure that we'll see it repeated in the future.

Mr. Chairman, not only can we do better, we must do better. The American people deserve a Congress that is working for them, and with them, not against them, and certainly not for the interests of wealthy polluting industries. I hope that one day soon our Committee will be a forum for a balanced discussion on the critical issues under our jurisdiction. Unfortunately, today's hearing falls well short of that mark.

My last point—the response from the Majority to my statement may be that Minority Members are permitted to invite one witness to these hearings and that we could have invited anyone we wanted to, such as a representative of the EPA, the SAB or the GAO

or the National Academies. My response to that, Mr. Chairman is that I don't believe it is the job of the Minority to do the Majority's job for them. It is clear that all of those entities should be represented at today's hearing, not just the single witness allocated for the Minority. If we are serious about conducting credible oversight of IRIS, I would hope that the Majority will commit to a follow-up hearing so that those voices may be heard.

I thank you, and I yield back.

[The prepared statement of Ms. Johnson follows:]

OPENING STATEMENT
Ranking Member Eddie Bernice Johnson (D-TX)

House Committee on Science, Space, and Technology
Subcommittee on Environment
Subcommittee on Oversight
"Examining the Scientific and Operational Integrity of EPA's IRIS Program"
September 6, 2017

Mr. Chairman, I am disappointed, but I am not surprised, that we are holding this hearing today. Sadly, I have had to make this statement too many times in the last four years. How can we, in good conscience, title this hearing as an examination of the scientific and operational integrity of EPA's IRIS program, when there is no one from EPA here to testify? We cannot.

How do we conduct the necessary oversight of this program, when the Government Accountability Office (GAO) is not present to answer questions about their recent review of IRIS? We do not.

How are we serving the best interests of our constituents, and of all Americans, when the National Academies of Sciences is not present to discuss their report upon which the last three years' worth of reforms to IRIS were based upon? We are not.

How can we have an honest discussion about this program while ignoring the key entities that have reviewed it and studied its recent improvements? We simply can't.

I would also note that just last week the EPA's independent Science Advisory Board (SAB) sent a letter to EPA Administrator Scott Pruitt praising the progress the IRIS program has made. The letter said, in part – and I quote: "The Board commends the Agency for making such significant improvements over a short period of time. We are optimistic that the restructured IRIS program will strengthen the scientific foundations of risk assessment and protect the health and safety of the American public." But we're not hearing from the SAB either. Instead, the Majority has invited two industry scientists to voice their criticisms of IRIS.

Let me be clear, industry perspectives should not be excluded from scientific discussions on environmental issues at the EPA – and they are not now, nor have they ever been. The current membership of EPA's Science Advisory Board, for instance, includes representatives from the Dow Chemical Company, Procter & Gamble, and Exxon Mobil. However, I am concerned that industry, the leadership of this Committee, and now this Administration, are seeking to let industry drive the science upon which critical decisions about protecting the public's health and the environment are made. The current criticisms of the EPA's IRIS program by industry highlight that point. We have seen this tactic used by industry before and I am sure we will see it repeated in the future.

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Thank you. I yield back.

Chairman BIGGS. Thank you. I thank the gentlewoman.

I want to now introduce our witnesses, the three with impeccable scientific backgrounds and expertise, and I'm grateful that each of you would take time to be here today. When you give your testimony, at some points you'll get five minutes, and I'll stand up and dance as you get close so you know you're near the end.

Dr. Kenneth Mundt is our first witness. He is the Principal at Ramboll Environ, where he serves as the Health Sciences Global Practice Area Leader and Director of Applied Epidemiology. Additionally, Dr. Mundt is an Adjunct Faculty Member at the University of North Carolina and the University of Massachusetts-Amherst. He received a bachelor's degree from Dartmouth College and a Ph.D. in epidemiology from the University of North Carolina at Chapel Hill.

Our next witness today is Dr. James Bus, Senior Managing Scientist at Exponent. Dr. Bus has over 23 years' experience as a Consulting Toxicologist in the Toxicology and Environmental Research and Consulting Unit at the Dow Chemical Company and serves as an Adjunct Professor in the Department of Pharmacology and Toxicology at Michigan State University. He received a bachelor's degree in medicinal chemistry and a Ph.D. in pharmacology from Michigan State University.

And our final witness today is Dr. Thomas Burke, Professor at Johns Hopkins Bloomberg School of Public Health. Dr. Burke also serves as the Director of the Johns Hopkins Risk Sciences and Public Policy Institute. He received a master's of public health from the University of Texas and a Ph.D. from the University of Pennsylvania.

And I now recognize Dr. Mundt for five minutes to present his testimony. Dr. Mundt.

TESTIMONY OF DR. KENNETH MUNDT,
PRINCIPAL, RAMBOLL ENVIRON

Dr. MUNDT. Good morning.

Chairman BIGGS. You're going to need to press the "talk" button. There you go. Thanks.

Dr. MUNDT. Good morning. Thank you, Mr. Chairman. My name is Kenneth Mundt. I'm an Epidemiologist and Health Sciences Practice Network Leader at Ramboll Environ.

My career has focused on evaluating health risks of chemicals, particularly in the workplace. Thank you and the Committees for the opportunity today to provide the highlights of a scientific evaluation of the 2010 IRIS Toxicological Review of Chloroprene that colleagues at Ramboll and Environ and I recently completed. Our evaluation of the IRIS review illustrates how important good science is to understanding human health risks and highlights some issues that need to be addressed.

IRIS is responsible for evaluating the potential human health effects of chemical exposures. However, as noted, the IRIS review process has been criticized by expert panels of the National Research Council of the National Academy of Sciences. In particular, the NAS emphasized the importance of transparency and rigor in the IRIS review methods. Our evaluation of the IRIS review of chloroprene identified several scientific problems impacting the

evaluation of chloroprene as a human carcinogen, and leading to the derivation of an inhalation unit risk, or IUR, that is 156 times greater than the IUR we derived.

The following were among the key scientific problems we found with that IRIS review. First, EPA failed to critically evaluate the quality of each epidemiological study of chloroprene-exposed workers, which resulted in giving equal weight to all studies, both good and bad. Suggestive positive associations were reported among the weakest studies with the greatest limitations. However, the largest and best study demonstrated no increased risk of liver or lung cancers. The NAS reviews provided guidance on study selection, methods for evaluating study quality, accounting for various forms of bias that impact study findings, and integrating evidence so that stronger studies are given greater weight.

Second, the EPA ignored the strongest study's conclusion: "Persons exposed to chloroprene or vinyl chloride at the levels encountered in the four study sites did not have elevated risk of mortality from any of the causes of death including all cancers combined and lung and liver cancers, the cancer sites of a priori interest." In contrast, the IRIS review noted "Relative risk estimates for liver cancer while not statistically significant increased with increasing exposure indicating a dose response trend." However, this trend also was not statistically significant and provides no evidence of increased risk.

Third, and most importantly, EPA did not fully account for large and well-recognized differences between mice and humans. Mice appear to be far more sensitive to chloroprene than other animals, or even humans, which can be explained by differences in pharmacokinetics. Accounting for these differences using standard methods applied by EPA and IRIS reviews of other chemicals dramatically reduced the estimated IUR.

Ultimately, applying standard EPA methodology and conservative assumptions we derived the revised IUR. Compared with ours, the EPA IUR was 156 times higher. Simply put, the EPA's IUR is extremely large, scientifically implausible, and has significant real-world consequences. Correction of the IUR is especially critically given that it has prompted lawsuits and enforcement actions.

Our critical review and integration of the published epidemiological and toxicological evidence on chloroprene also highlights the need to reconsider EPA's classification of chloroprene. The IRIS review classified chloroprene as "likely to be carcinogenic to humans" based on five stated criteria. We determined that three of these criteria are not supported by a weight of evidence analysis, and a fourth, the structural similarities to other chemicals was not informative. It also underscores the importance of some of the improvement recommended by the NAS.

As the Committee looks at how EPA can be expending resources more efficiently and how to improve the IRIS program as a whole, the chloroprene example may help identify specific areas where scientific and procedural flaws may be targeted and remedied.

There's nothing that precludes the EPA from using credible outside scientific resources to foster constructive scientific debate and

enhance their evaluation and decision-making capabilities. In doing so, EPA will better achieve justifiable scientific conclusions.

Thank you.

[The prepared statement of Dr. Mundt follows:]

The Committee on Science, Space, and Technology's Subcommittee on Environment and Subcommittee on Oversight of the U.S. House of Representatives

September 6th Hearing

Examining the Scientific and Operational Integrity of EPA's Iris Program

THE IRIS REVIEW PROCESS: CHLOROPRENE AND THE CRITICALITY OF GOOD SCIENCE

Dr. Kenneth Mundt

Dr. Sonja Sax

Dr. P. Robinan Gentry

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RAMBOLL ENVIRON

The IRIS Review Process: Chloroprene and the criticality of good science

Overview

The US Environmental Protection Agency (EPA) Integrated Risk Information System (IRIS) compiles and evaluates available scientific studies to determine the potential for chemicals to cause human health effects, and to conduct risk assessments that indicate the exposure levels at which risk of health effects is increased. These evaluations are relied upon by federal, state, local as well as international regulatory and public health agencies. Therefore, the validity of the IRIS evaluations is paramount. Over the last decade the methods used in and ultimate quality of IRIS reviews have been criticized by numerous entities, most notably, by expert panels of the National Academy of Sciences (NRC 2011, 2014).

EPA's 2010 IRIS Toxicological Review of Chloroprene (Final Report) (hereafter, "the 2010 Review")[1] serves as one example where several of the more recent concerns expressed by two National Research Council (NRC) Committees of the National Academy of Sciences (NAS) can impact the quality of the scientific evaluation and lead to the derivation and publication of official risk numbers (intended to quantify the relationship between chloroprene exposure and the risk of human cancers), which in the case of chloroprene are not scientifically valid. For example, the Inhalation Unit Risk (IUR) that EPA published for chloroprene appears to be *156 times* greater than a more scientifically accurately derived value. Furthermore, EPA's extreme IUR for chloroprene – a chemical EPA did not even classify as a "known" human carcinogen due to uncertainty - is orders of magnitude higher than the IURs for other chemicals for which the integration of evidence demonstrates carcinogenicity in humans (such as benzene and vinyl chloride) and are classified as "known" human carcinogens. Clearly, EPA's IUR for chloroprene needs to be corrected.

Based on a detailed critical evaluation of the 2010 Review conducted by Ramboll Environ US Corporation (Ramboll Environ), and sponsored by Denka Performance Elastomer LLC ("DPE"), several scientific errors and other problems were identified that likely gave rise to the extreme IUR value that EPA derived. The most important of these scientific issues include the following:

- The 2010 Review failed to critically evaluate the quality of each of the published epidemiological studies on workers highly exposed to chloroprene and apparently gave equal weight to all studies regardless of quality. Workers' exposure to chloroprene is expected to be thousands of times higher than that of the general public. Suggestive associations are reported among the weakest studies (including studies from Armenia, Russia and China); in contrast, the stronger studies (primarily from the US and UK) do not demonstrate increased cancer risks. EPA noted: "In humans, significant increases in liver cancer

[1] U.S. EPA. IRIS Toxicological Review of Chloroprene (Final Report). U.S. Environmental Protection Agency, Washington, DC, EPA/635/R-09/010F, 2010.

mortality were observed in four occupational epidemiology studies (out of nine total studies)." The four studies did not include the highest quality study.

- The 2010 Review ignored the conclusion of the highest quality and most informative epidemiological study published to date: "We conclude that persons exposed to chloroprene or vinyl chloride at the levels encountered in the four study sites did not have elevated risks of mortality from any of the causes of death examined, including all cancers combined and lung and liver cancer, the cancer sites of *a priori* interest" (Marsh et al., 2007a, 2007b). Rather, the 2010 Review highlighted out of context statistical results based on small subgroups of workers, even though none of the risk estimates was statistically significant (i.e., likely arose due to chance). EPA noted: "Relative risk estimates for liver cancer (while not statistically significant) increased with increasing exposure, indicating a dose-response trend." However, even the reported "trend" was not statistically significant (p=0.09).
- The 2010 Review failed to properly account for large and well-recognized differences between mice and humans in deriving the IUR. The National Toxicology Program (NTP) conducted a study in which male and female mice of a specific strain, as well as male and female rats, were exposed to high concentrations of chloroprene. More tumors were observed in the exposed mice than the unexposed mice, and more in mice compared to rats, with the mouse data then used as the main data for estimating potential cancer risk to humans. However, scientific evidence providing significant and well-documented physiological and metabolic differences between mice and humans were not fully considered. Furthermore, the effects driving the estimates of cancer risk (lung cancer observed in female mice) were not elevated with chloroprene exposure in experiments using rats or hamsters, suggesting that mice are not equivalent to humans and far more sensitive to chloroprene than other animals or humans.

Ramboll Environ, using published data and standard EPA risk assessment methods that properly account for these large differences between female mice and humans (and that EPA has used in IUR calculations for other chemicals), derived a corrected IUR, demonstrating that the EPA IUR was overestimated 156-fold. Other quantitative evaluations in the 2010 Review (e.g., Reference Concentration) also are likely to be incorrect if the interspecies differences are not fully appreciated.

As emphasized in reviews by prominent scientific committees, most notably those of the NAS (NRC 2011, 2014), significant improvements to the IRIS review methods and process are needed, including greater transparency. Additionally, fuller engagement of scientists most knowledgeable about the chemicals under review – including those potentially funded by industry – would contribute to scientific quality and help identify and correct scientific errors before reviews are finalized.

Regardless of future improvements, some IRIS Reviews that are in progress (e.g., formaldehyde) or have been finalized (e.g., chloroprene) need to be validated, with mechanisms for correcting past errors. Regulations and other decisions based on the erroneous IUR for chloroprene, for example, will not be based on sound science, and likely will have serious impacts. Scientifically, the magnitude of this difference

between the published and recalculated IUR is very large, and clearly warrants re-evaluation and correction.

Impetus for Ramboll Environ's evaluation of the 2010 Review

In December 2015, EPA finalized and published the 2011 National Air Toxics Assessment (NATA), which indicated an extremely high off-site air pollution cancer risk from emissions of chloroprene from what is now DPE's Neoprene production facility in LaPlace, Louisiana. The NATA was derived based on the IUR from the 2010 Review and the emission profile of the Neoprene facility. The NATA findings precipitated adverse public opinion, enforcement actions, and a class action lawsuit, all of which potentially have serious economic implications for DPE and the community.

Immediately after the release of the NATA cancer risk conclusions, DPE asked Ramboll Environ to conduct an independent evaluation of the 2010 Review, including a critical review and synthesis of all relevant published epidemiological and toxicological literature, with a focus on validating EPA's cancer IUR as reported in the 2010 Review. DPE recognized Ramboll Environ's scientific work and interaction with the IRIS program regarding the IRIS Draft Formaldehyde Toxicological Review, which was the focus of the NRC 2011 peer review and their criticisms of the IRIS process and methods.

Highlights of the Ramboll Environ evaluation as of one year ago were presented to EPA on August 9, 2016 at an event EPA entitled, "IRIS Assessment of Chloroprene," and attended by 13 EPA representatives – including the Acting Director of EPA's National Center for Environmental Assessment (NCEA) and the Director of IRIS – plus three representatives of the Louisiana Department of Environmental Quality. Ramboll Environ's presentation to the group can be found at the following link: https://cfpub.epa.gov/ncea/iris2/events.cfm. A follow-up letter to Dr. Vandenberg is included as an Attachment. This letter highlights some of the difficulties encountered in seeking a correction of the 2010 Review.

Subsequently, the full Ramboll Environ report was submitted to EPA as part of a request for correction, and is available at the following link: https://www.epa.gov/quality/rfc-17002. This report lays out the exact approach used in calculating an IUR for chloroprene using the best scientific methods used by EPA in other chemical evaluations, and considering the quality of the epidemiological and toxicological evidence used in evaluating chloroprene's carcinogenicity and risk numbers.

Ramboll Environ's evaluation of the 2010 Review

In the 2010 Review, EPA classified chloroprene as "likely to be carcinogenic to humans" and not the more definitive "known to be a human carcinogen," primarily based on EPA's recognition that the evidence was insufficient to classify it as a known human carcinogen. However, even classifying chloroprene as "likely to be carcinogenic to humans" was subject to and influenced by questionable interpretations of the published epidemiological and toxicological evidence.

Nevertheless, EPA proceeded to derive an IUR for chloroprene that is the 5th highest IUR (not including carcinogenic metals or coke oven emissions) EPA ever has developed, even among chemicals EPA or the World Health Organization's (WHO's) International Agency for Research on Cancer (IARC) classifies as "known" or likely/probable human carcinogens. Specifically, the IUR for lifetime exposure to chloroprene derived by EPA is 5×10^{-4} per microgram per cubic meter ($\mu g/m^3$).

The chloroprene IUR is sufficiently large that EPA should have realized prior to publishing the 2010 Review that the value was anomalous. Despite the fact that the 2010 Review underwent several peer-reviews, the large and obvious discrepancy between EPA's IUR for chloroprene and other IURs derived by EPA appears to have gone further unnoticed or unreported. The reasons for this are not clear, but call into question the quality of the peer-review process that IRIS has relied upon to draw conclusions regarding the potential for cancer risk in humans.

The main objective for the Ramboll Environ scientific evaluation of the 2010 Review was to evaluate the IUR for chloroprene as derived by EPA, and to provide improved and transparent scientific methods, interpretations and risk calculations to facilitate scientifically justified corrections for EPA's consideration.

The main elements of the Ramboll Environ assessment are presented below in four sections: Epidemiological Evidence; Toxicological Evidence; Chloroprene Carcinogenicity Classification; and, Deriving the Chloroprene IUR.

Epidemiological Evidence

A critical piece to understanding the potential cancer effects in humans from exposure to chloroprene is a rigorous evaluation of the occupational epidemiological literature. Workers involved in producing and directly using chloroprene are likely the most highly exposed individuals, and the occupational setting facilitates epidemiological methods for enumerating cohorts of workers, estimating levels of exposure and following workers over time to observe the rates at which various outcomes, including cancers, occur. The epidemiological evidence relevant to chloroprene carcinogenicity and that EPA correctly identified includes findings from occupational cohorts from the US, France, Ireland, Armenia, Russia and China. However, the 2010 Review of the epidemiological literature was methodologically irregular, particularly with respect to how individual study quality was assessed and weighted in the overall weight-of-evidence assessment. In fact, it is not clear whether EPA critically evaluated the quality of each of the published epidemiological studies on workers highly exposed to chloroprene and their respective cancer risks, and if so, the methods and rationale for how this was done were not transparent. For example, where suggestive positive associations are seen is among the weakest studies (including studies from Armenia, Russia and China); in contrast, the stronger studies (primarily from the US and UK) do not demonstrate increased cancer risks. The NRC recommendations regarding the IRIS review process (2011, 2014) underscore the importance of considering the quality of individual studies, giving greater weight to high-quality studies in the weight-of-evidence evaluation, and providing transparency in applying and documenting these methods.

A critical review of the same literature cited in the 2010 Review had already been published by Bukowski, as of 2009. The Table below is adapted from a similar table in that publication:

Table: Quality Rankings for Cohort Studies of Cancer Risks from Occupational Chloroprene Exposure

EPA Criteria	Marsh et al. (2007 a,b) Study				Other Studies			
	Kentucky[1]	North Ireland[1]	Louisiana[1]	France-Mort*[1]	Armenia[2]	France-Incid**[3]	Russia[4]	China[5]
Clear objectives	H‡	H	H	H	H	H-M	H	M
Comparison groups	H	H-M	H-M	M	M	M	M-L	L
Exposure	H	H	H	H	M	M	L	L
Follow-up	H	H-M	H	H-M	M-L	M-L	M-L	M-L
Case ascertainment	H	H-M	H-M	H-M	M	M	M	H-M
Control of bias	H-M	H-M	H-M	M	M-L	M	M	M-L
Sample size	H	H	M	L	M-L	L	H-M	M-L
Data collection and evaluation	H	H	H	H	M	M	M-L	M-L
Adequate response	H	H	H	H	M	M	M	H-M
Documentation of results	H	H	H	H	M-L	M	M	L
Overall rank (1=best)	**1**	**2**	**3**	**4**	**5**	**5**	**5**	**6**

Source: Bukowski 2009 * Mort=Mortality ** Incid=Incidence ‡ Subjective estimate of study quality for each specific criterion H=high, M=medium, L=low; 1 – Marsh et al. 2007; 2 – Bulbulyan et al. 1999; 3 – Colonna and Laydevant 2001; 4 – Bulbulyan et al. 1998; 5 – Li et al. 1989

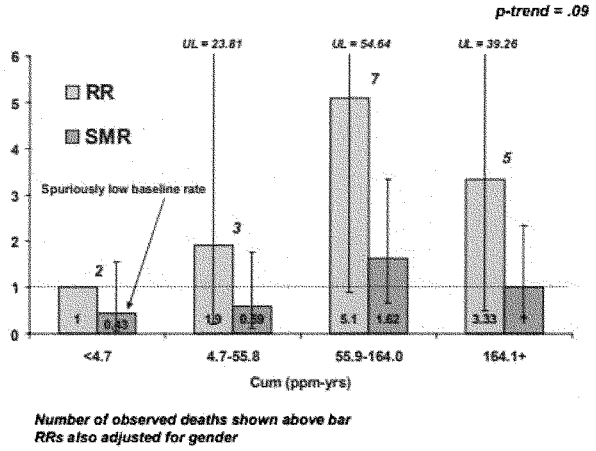
From this evaluation of individual study quality, it is clear that the first four studies received predominately "high" or "high-medium" ratings, in contrast with the final four studies that received predominately "medium" or lower ratings (Bukowski 2009). The Marsh et al. study (2007a, 2007b) combined the data from these four high-quality studies, and represent the most methodologically rigorous epidemiological evidence available to date. This study has the largest overall cohort size and the most rigorous follow-up, providing the greatest statistical power to detect an increased cancer risk should one exist. In contrast with the low-quality studies, the Marsh et al. study (2007a, 2007b) has the most comprehensive exposure assessment, including assessment and consideration of exposure to other occupational carcinogens (i.e., potentially confounding agents) such as vinyl chloride.

Importantly, the Marsh et al. (2007a, 2007b) study reported no excess occurrence of lung or liver cancers among chloroprene exposed workers when compared to the general population reference group. For all exposed workers at all plants combined, observed liver cancer mortality was 72% of what would be expected based on rates in the unexposed general population (this is expressed by the standardized mortality ratio, or SMR). The comparable finding for all exposed workers in the largest plant

(Louisville) was 90% of expected. Both these values demonstrate no increased risk for liver cancer. By exposure sub-group, none of the SMRs was statistically significantly elevated, and three of the four were below 1.0 (the value when observed and expected are equal). Furthermore, there was no statistically significant trend of increasing risk with increasing exposure (see Figure).

Figure

Liver Cancer RRs and SMRs by Cumulative CD Exposure, Louisville



Source: Figure from comments submitted by Andrea V. Malinowski to EPA, Docket ID No. EPA-HQ-ORD-2009-0217, based on data from Marsh et al. 2007b

For lung cancers – the cancer site that provided the highest incidence in the mouse and was hypothesized to be relevant to chloroprene exposure – the Marsh et al. study (2007a, 2007b) documented a statistically significant 25% *deficit* of lung cancer mortality for all plants combined. Specifically, the pooled study data observed 112 fewer lung cancer deaths than would be expected based on unexposed population rates. Findings for each of the four individual plants were consistent (i.e., suggesting a deficit) although only one – Louisville, the largest plant – had a statistically significant deficit (89 fewer lung cancer deaths observed than expected). In contrast, EPA noted in the IRIS review that several studies reported higher SMRs for lung cancer among workers exposed to chloroprene, although few of the associations were significant and none of the studies controlled for confounding by smoking status, a strong indicator of lung cancer.

Nevertheless, EPA appears to have given no more weight to the most recent and rigorous epidemiological evidence (Marsh et al., 2007a, 2007b) showing no increased occurrence of liver and lung cancer than to the poorer quality Russian, Armenian, and Chinese studies, all of which had significant limitations. These limitations had been identified by others than Bukowski (2009). Rice and Boffetta (2001) conducted a review that included cohorts from the US (Pell 1978), China (Li et al. 1989), Russia (Bulbulyan et al. 1998) and Armenia (Bulbulyan et al. 1999) and noted significant methodological limitations in these studies, including unclear documentation for cohort enumeration, inadequate reference rates for standardized ratios, a lack of detailed histopathology of liver cancer cases, and limited or no information on potential co-exposures. They also remarked that the occupational chloroprene exposure assessment was poor for all published studies at that time, and the statistical power of the available studies was low due to the small number of observed cancers of interest.

In addition to discounting the Marsh et al. (2007a, 2007b) study findings relative to the weaker evidence, EPA also appears to have misinterpreted the Marsh et al. (2007b) results. Specifically, the 2010 Review interpreted a statistical correlation between exposure level and liver cancer risk relative to a comparison subgroup where the comparison group exhibited anomalously fewer cancers than expected, creating the appearance of an increased risk in the higher exposure groups (see Figure). Specifically, note that the 2 observed liver cancer deaths represent less than half the expected number. In turn, using this as the referent or comparison group effectively inflates the other categories by a factor of 2.3. Furthermore, that there were only two liver cancer deaths in this category contributed to large instability in all categories due to chance alone, i.e., the impact of one fewer or one more liver cancer death in this category would spuriously generate conflicting results.

The issues summarized here suggest that EPA's 2010 Review relied on incomplete evaluation and misinterpretation of the published epidemiological evidence. Properly evaluated, interpreted and weighted, the weight of epidemiological evidence does not demonstrate an association between occupational chloroprene exposure and increased incidence of liver or lung cancer.

Separate from the evaluation of the 2010 Review, Ramboll Environ examined cancer incidence data from the Louisiana Tumor Registry, comparing rates for St. John the Baptist Parish where the DPE Neoprene plant is located, with those of the state of Louisiana. For all cancers combined, the rate in the five most recent years in St. John the Baptist Parish was 463.2, compared with 478.7 for the state of Louisiana, that is, cancer rates in St. John the Baptist Parish were about 3% below the state average. For lung cancers, the rate in St. John the Baptist Parish was 60.1 compared with 70.5 for the state of Louisiana, that is, lung cancer rates in St. John the Baptist Parish are 14.7% lower than the state average. Too few liver cancers have occurred in St. John the Baptist Parish to be publically reported.[2] Though these official data are at best an indirect indicator of a population impact of the DPE facility operations, they do not provide evidence that the parish in which the DPE facility operates has elevated cancer rates.

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[2] https://statecancerprofiles.cancer.gov/incidencerates/index.php?stateFIPS=22&cancer=001&race=00&sex=0&age=001&type=incd&sortVariableName=rate&sortOrder=default#results.

Toxicological Evidence

As with the epidemiological studies, the toxicological evidence also should be evaluated in ways that adhere to EPA's own standard risk evaluation methodologies and conform to the NRC recommendations. The 2010 Review relied on the animal toxicological data as basis for deriving the chloroprene IUR, and specifically, the animal studies conducted by the National Toxicology Program (NTP 1998). Overall, this study, which included both mice and rats, demonstrated very little consistency across species in tumor incidence and tumor locations, but also demonstrated a unique sensitivity in a particular strain of female mice in which lung tumors appeared to be the most sensitive endpoint. Findings were specific to mice and not generalizable across the other animal species tested, including rats and hamsters. Given the striking differences in response in mice compared to other laboratory species, it is critically important to identify and evaluate possible differences in pharmacokinetics between animal species and to consider differences between mice and humans. The impact of this on the IUR is substantial, as discussed below.

In addition to revisiting the reliance on the animal dataset for the estimation of the IUR, a more rigorous re-evaluation and integration of the cytotoxic and genotoxic evidence for chloroprene is needed, consistent with NRC (2011, 2014) recommendations. The Ramboll Environ evaluation of the published toxicological literature found that the evidence from these studies indicates that chloroprene acts through a different mode of action (MOA) than 1,3-butadiene, a structurally similar known human carcinogen, but used for comparison and to draw conclusions by EPA in the 2010 Review. Using the NRC (2011, 2014) recommendations as guidelines, review of chloroprene's genotoxicity profile appears to lack several attributes necessary to conclude that there is a mutagenic MOA. Instead, the evidence supports site-specific cytotoxicity as a more likely MOA. This contradicts EPA's conclusion that chloroprene acts *via* a mutagenic MOA, and alone inflated EPA's IUR by about 60%.

Chloroprene Carcinogenicity Classification

The 2010 Review determined that chloroprene was "likely to be carcinogenic to humans" based on EPA's conclusions of (1) statistically significant and dose-related information from the NTP (1998) chronic inhalation bioassay data demonstrating the early appearance of tumors, development of malignant tumors, and the occurrence of multiple tumors within and across animal species; (2) evidence of an association between liver cancer risk and occupational exposure to chloroprene; (3) suggestive evidence of an association between lung cancer risk and occupational exposure; (4) a proposed mutagenic mode of action (MOA); and (5) structural similarities between chloroprene and known human carcinogens, 1,3-butadiene and vinyl chloride. As has been demonstrated in this report, three of the five EPA conclusions are not supported by the weight of evidence, and the fourth—structural similarities—has been shown not to be informative, as the evidence available for the chemicals demonstrates different modes of action.

The Ramboll Environ evaluation of the 2010 Review demonstrated considerable misinterpretation of the available science to support the "likely to be carcinogenic to humans" classification. For example, the epidemiological evidence, based on an appropriate weight-of-evidence approach, fails to demonstrate clearly increased risks among exposed occupational groups and the general population, and a weak difference between exposed and unexposed workers reflecting a deficit among the least exposed. The claim that chloroprene is mutagenic is not supported by the overall evidence. Although there are structural similarities between chloroprene and 1,3-butadiene or vinyl chloride, the toxicological evidence that supports possible modes of action demonstrates substantial differences between chloroprene, vinyl chloride, and 1,3-butadiene. Little discussion of critical uncertainties in relying on the mouse data from NTP (1998) to predict the potential for carcinogenic risk in humans is offered in the 2010 Review, given ample evidence of important pharmacokinetic differences between mice and other species.

The weight-of-evidence evaluation supports a reclassification. Based on the limited evidence remaining to support the potential carcinogenicity of chloroprene, a more appropriate classification of chloroprene would be "suggestive evidence of carcinogenic potential." In any case, a clearer weight-of-evidence narrative is needed that addresses the current uncertainties.

Deriving the Chloroprene IUR

In the 2010 Review, EPA derived the current chloroprene IUR based on a number of assumptions that are not substantiated by the scientific evidence, contributing to overestimation of an already conservative risk estimate (i.e., one based on the most sensitive species, gender, and endpoint). Specifically, EPA based the chloroprene IUR on a composite estimate of risk based on multiple tumors observed primarily in mice, instead of relying on just the most sensitive endpoints in mice (lung tumors) which is consistent with standard EPA methods. EPA then assumed that the female mouse-based IUR was representative of continuous human exposure, and that lung tumors were a result of systemic rather than portal-of-entry effects; EPA also rounded up calculations at various stages of adjustment, and these were compounded. Finally, EPA applied an age-dependent adjustment factor (ADAF) based on insufficient data to support a claimed mutagenic MOA. All of these assumptions are not supported by the scientific evidence and contributed to unrealistic increases in the final IUR, as presented in the Ramboll Environ report submitted to EPA as part of DPE's Request for Correction.

The most important correction of the IUR is that it should seek to be predictive of human response. At the time of the 2010 Review, Himmelstein et al. (2004a, 2004b) had published a paper that described a physiologically based pharmacokinetic (PBPK) model for chloroprene. The model provided a means to adjust the exposures associated with tumors in the mouse to corresponding human exposures, and the model integrates the available data that explain why the mouse is the most sensitive species and why humans would be comparatively much less sensitive to the effects of chloroprene exposure. The hypothesis that differences in pharmacokinetics are determinants of the observed species differences has been demonstrated for other chemicals reviewed by EPA, including vinyl chloride. In the 2010 Review, EPA

acknowledged that its results would be improved with the use of a PBPK model, but that all of the required data were not available. However, all of the quantitative data necessary to refine and verify the critical metabolic parameters for the existing peer-reviewed PBPK model for chloroprene were published prior to the publication of the 2010 Review. Since then, additional data have been published, and these newer findings further validate the model and its use in demonstrating consistency with the epidemiological evidence, and its use in deriving the chloroprene IUR (Thomas et al. 2013, Yang et al. 2012, Allen et al. 2014). In particular, Allen et al. (2014) derived an IUR based on consideration of pharmacokinetic differences between mice and humans and estimated an IUR that was 100 times lower than EPA's value, using a method which integrates both the animal and human evidence. Importantly, consideration of the IUR reported by Allen et al. (2014) in comparison with IURs for known human carcinogens, such as vinyl chloride and 1,3-butadiene, is consistent with the stronger and more consistent epidemiological evidence of human carcinogenicity for these compounds compared to chloroprene.

Ramboll Environ performed an updated analysis by applying the peer-reviewed published results from validated PBPK models (Yang et al. 2012) to arrive at an IUR that accounts for the known interspecies differences in pharmacokinetics. Standard EPA methodology and conservative assumptions were applied to estimate the potential cancer risks for chloroprene. The revised IUR is $1.1x\ 10^{-2}$ per ppm or 3.2×10^{-6} per $\mu g/m^3$, which is of the same order of magnitude as the IUR derived by Allen et al. (2014), and which better reflects the scientific understanding of potential chloroprene cancer effects in humans. In contrast, the EPA derived an IUR for lifetime exposure to chloroprene of 5×10^{-4} per microgram per cubic meter ($\mu g/m^3$), a value approximately 156 times higher than what Ramboll Environ considers the best estimate using standard EPA methods and available data. The revised value also is consistent with the results from validated PBPK models and comparisons with other structurally relevant compounds, such as vinyl chloride and 1,3-butadiene, that are recognized as known human carcinogens.

There is little scientific support for each of EPA's conservative assumptions and subsequent adjustments. Combining a fuller understanding of interspecies pharmacokinetic differences and validated PBPK models with the results from the strongest epidemiological data provides the scientific grounds for correcting the 2010 IUR and calls into question the strength of the evidence to support a "likely to be carcinogenic to humans" classification. Similar adjustments should also be considered in estimating the chloroprene inhalation reference concentrations (RfC), as species- and strain-specific differences are noted. This will assure that policies and decisions resting on these toxicity values meet the test of sound science, transparent methods, and reproducible findings.

Conclusions

EPA's 2010 Review of chloroprene offers examples of several broader issues with the quality of IRIS Reviews including those of the NAS (NRC 2011, 2014), including evaluation of individual toxicological and epidemiological studies for quality, and transparency in weight-of-evidence integration to validly determine a chemical's potential carcinogenicity and derive accurate risk numbers. For chloroprene, the IUR

that EPA derived in the 2010 Review appears to be at least 100-fold inflated, and, based on a best-methods approach performed and documented by Ramboll Environ, over-estimated by as much as 156-fold. Risk assessments based on this IUR, such as the National Air Toxics Assessment, incorporate the overestimated value leading to grossly exaggerated human cancer risk predictions. This undoubtedly and unnecessarily triggers regulatory and legal action, as well as incites fear in the workers exposed to chloroprene, as well as those in the surrounding communities who may be exposed at much lower concentrations.

As outlined above, the overestimation of the IUR is the product of several scientific shortfalls or errors, including misreading of the epidemiological evidence, the likely erroneous assumption that chloroprene is mutagenic, an under-appreciation and subsequent incomplete consideration of the large pharmacokinetic differences between the female mice and humans, as well as other issues.

Scientifically, updating the IRIS Review of chloroprene is warranted, possibly including reconsideration of the carcinogenicity classification in light of a more accurate interpretation of the epidemiological evidence. However, and more urgently, a correction to the IUR is needed, based on the Ramboll Environ analysis provided to EPA in DPE's recent Request for Correction. The IUR published in the 2010 Review requires correction to address flaws that are consistent with the critique of the IRIS program by NRC. Specifically, an updated IUR should be based on the best available methodology as well as a valid, transparent, and systematic interpretation of the body of published evidence. Although there are variations in how IURs are derived, proper application of established EPA risk assessment methods – including the PBPK model to account for extreme interspecies differences – should generate an IUR that is 100-150+ times lower than that published in the 2010 Review. The methods presented in the Ramboll Environ report could serve as a starting point, reducing the time and resources EPA otherwise would expend.

Correction additionally is critical given that the IUR published in the 2010 Review is being used by EPA to support enforcement actions and underlies a class action lawsuit. The chloroprene example highlights deficiencies in the IRIS process that need to be addressed as soon as possible.

Respectfully submitted,

Kenneth A. Mundt, PhD, FACE

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Attachment

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ENVIRONMENT
& HEALTH

John Vandenberg, PhD
Director of Research at NCEA
109 T.W. Alexander Drive
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Sent via e-mail

RE: FOLLOW-UP TO THE MEETING AT RTP

Dear Dr. Vandenberg,

August 23, 2016

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Thank you for setting up and orchestrating the "listening session" on Tuesday August 9th, 2016 at your offices. Dr. Gentry and I appreciate the opportunity to present the findings from our independent review of chloroprene's potential carcinogenicity, based on all available data and state-of-the-art methods for critically reviewing and synthesizing epidemiology, toxicology and mechanistic studies, and for integrating evidence across these lines of inquiry.

As discussed after our presentation of the science, we acknowledge and appreciate your explanation of the IRIS Program's resource constraints, the complex procedures in place for selecting substances for IRIS review or re-review, as well as what you described as the "full docket" of current and future IRIS reviews. Based on this feedback, we understand that the IRIS Program will not at this time undertake a new review of chloroprene – or consider any revisions to the risk numbers – primarily due to resource constraints.

This, as you can understand, leaves our client, Denka Performance Elastomer, LLC (DPE), in a very difficult position, and unjustifiably so from a scientific standpoint. During our meeting, we outlined important new information demonstrating that an IRIS chloroprene IUR derived today would be vastly different and more compatible with other IURs for other chemicals. As we demonstrated during our meeting, properly employing validated PBPK models leads to an IUR for chloroprene that is more than 100-fold lower than the 2010 IRIS value. In fact, the 2010 IRIS Review of Chloroprene astutely acknowledged this very flaw: "Ideally, a PBPK model for the internal dose(s) of the reactive metabolite(s) would decrease some of the quantitative uncertainty in interspecies extrapolation; however, current PBPK models are inadequate for this purpose" (US EPA, 2010, Section 3)[1]. The information and methods required for chloroprene now have been peer-reviewed, published, and validated, with similar models and methods applied by EPA in comparable risk evaluations (such as vinyl chloride).

[1] US EPA 2010. Toxicological Review of Chloroprene. In support of Summary Information on the Integrated Risk Information System. Washington, DC: U.S. Environmental Protection Agency.

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We also noted what we consider a misinterpretation of the body of epidemiological evidence, largely due to discounting the negative results published from the 2007 Marsh et al. study, which is also the strongest epidemiological study, in favor of results from much weaker studies. The integration of the entirety of epidemiological evidence supports the updated toxicology and mechanistic evidence indicating important and substantial differences between humans and mice, specifically in terms of metabolism, which are directly related to estimating the potential cancer risks for chloroprene. This no longer can be ignored. Taking the most up-to-date information into consideration in the context of using science to inform EPA policy and regulation is entirely consistent with the Agency's very public "mission statement" to ensure that "national efforts to reduce environmental risk are based on the best available scientific information."[2]

Without a commitment on the Agency's part to reexamine the 2010 IRIS assessment's IUR derivation in light of the new information, EPA and the Louisiana Department of Environmental Quality have advised DPE that it will be required to meet extremely stringent emissions limits, which may not be attainable, and that are not based on the best available science. We also have seen that the IUR is being used to inform important regulatory and other federal and state government actions, as well as public statements with respect to the possible cancer risks to people who live and work in the community in which our client's facility is located.

Notwithstanding the IRIS Program's resource constraints, we genuinely look forward to any thoughts or ideas you or Dr. Cogliano might have with respect to how we might work collaboratively with you and the program office within EPA that is relying on the 2010 IRIS Assessment, to timely improve and update the IUR. The IUR for chloroprene (as well as actions that are derivative of that IUR) should be more in line with those of other substances, such as vinyl chloride, that provide stronger evidence than chloroprene of carcinogenicity in humans.

We, too, will be exploring various available avenues, and will keep you informed. One possibility would be for us to file a request for correction (RFC). Our ultimate goal, as I initially mentioned to Dr. Cogliano when I first approached him, is to improve the risk calculation based on currently available science and evidence-based processes, which have evolved since the completion of the 2010 Chloroprene Toxicological Review, and to do so in a way that creates the lowest demands on already limited resources. Thank you again, and I look forward to continuing our discussion.

Yours sincerely

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cc: Dr. Vincent Cogliano

[2] https://www.epa.gov/aboutepa/our-mission-and-what-we-do

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ENVIRONMENT
& HEALTH

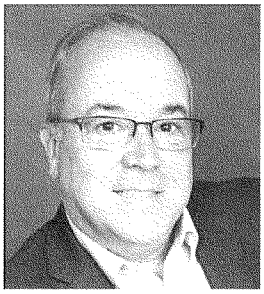
KENNETH A MUNDT

Principal

Dr. Kenneth Mundt is Ramboll's Global Health Sciences Practice Network Leader. He brings over 30 years of experience applying epidemiological concepts and methods to understand human health risks from environmental, occupational and consumer product exposures.

Dr. Mundt specializes in the pragmatic interpretation of epidemiological evidence in evaluating disease causation and supporting science-based regulation and decision-making.

Dr. Mundt served 11 years on the Graduate Faculty of the School of Public Health and Health Sciences, University of Massachusetts at Amherst. He received his PhD in Epidemiology at the University of North Carolina at Chapel Hill, and is a Fellow in the American College of Epidemiology.



EXPERIENCE HIGHLIGHTS

Epidemiological Studies
Managed multidisciplinary teams in designing, conducting and interpreting occupational epidemiological studies of workers involved in rubber, porcelain, chemical and steel industries, as well as military and other professionals.

Health Risks Evaluation and Communication
Responded to observed and perceived health problems related to occupational, environmental and consumer product exposures.

Teaching and Scholarship
Frequent participant in scientific meetings, training courses, and litigation proceedings. Consistent publication record.

Scientific Regulatory Support
Provided scientific evaluation and support to various regulatory and policy processes, including oral and written testimony, statistical re-analysis of data from key studies, preparation of commentaries and technical communications, developing new research opportunities, critical review and meta-analyses of epidemiological evidence, integration of scientific evidence from diverse lines of inquiry, and organize and manage expert panels and topical symposia.

Critical Reviews and Syntheses
Comprehensively identified, systematically critically reviewed and synthesized the epidemiological literature on human health risks associated with numerous occupational, environmental and consumer product exposures.

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Chairman BIGGS. Thank you, Dr. Mundt.

And now I recognize Dr. Bus for five minutes to present his testimony.

TESTIMONY OF DR. JAMES BUS,
SENIOR MANAGING SCIENTIST, EXPONENT

Dr. BUS. Good morning. I am Dr. James Bus, and I'm a Toxicologist with the consulting firm Exponent. I will preface my comments by noting that the increasingly financially and other resource-constrained realities confronting our nation demands nothing less than a cost-effective, transparent and science-based evaluation and regulation of environmental chemicals.

I will briefly highlight three major areas of concern with the IRIS program. First, IRIS has not effectively implemented the National Academy of Sciences recommendation that good risk assessment must start with good problem formulation. Second, IRIS use of chemical mode of action information to better inform its risk assessments is substantially flawed. And third, IRIS frequently does not effectively differentiate between the highest quality science and that of substantially lower quality in its evaluations.

The National Academy has emphasized the importance of the question—what problems are we trying to solve?—as an absolute necessity for focusing the priorities of the IRIS program. Although IRIS has recently implemented problem formulation dialog with the public, the IRIS program has not effectively integrated this key concept into its overall prioritization processes. For example, human exposures to many, if not most chemicals, have been substantially reduced or constrained over the last several decades as a direct result of regulatory and/or industry product stewardship interventions, yet IRIS often overlooks this important progress as a screening mechanism to rule out the need for detailed evaluations. As is commonly said in the practice of toxicology, it is the dose that makes the poison. Thus, more realistic consideration of the relationships of human exposures to doses producing toxicity at much higher doses used in experimental toxicity studies must become a key consideration to answering the practical question of: do real-world exposures indicate a reasonable need for a detailed risk assessment evaluation?

Turning to the second point of concern, and speaking as a toxicologist, extensive taxpayer investments into the toxicological sciences have yielded substantial advances in understanding how chemicals cause toxic effects in animals and in humans. Such mode of action information is essential to establishing the human health relevance of toxicity observed in cell or animal-based toxicity findings. In recognition of the value of mode of action science, the toxicology, risk assessment, and regulatory scientific communities have developed detailed frameworks for credible and transparent translation of these data into chemical risk assessments. While mode of action framework processes have long been included within EPA guidance procedures and are routinely and effectively used by the EPA's Office of Pesticides, the IRIS program has yet to embrace their full practice. Thus, IRIS assessments consistently default to risk decisions that do not reflect the substantial added value of

mode of action science that has long been supported by taxpayer investments.

Finally, the IRIS program has not implemented consistent criteria as have other EPA offices for appropriately waiting study quality as key to meaningful data integration. Too often, poorly conducted and/or described studies carry equal weight to those of far higher quality in the final risk decision. For example, the recent IRIS evaluation of trichloroethylene, a commercially important solvent, relied on published studies from a single university-based laboratory that were subsequently subject to three published error correction that still have not clarified the experimental findings. In addition, not only were the original data from these problematic studies not available for review by the EPA, the study findings also were not reproduced in two much higher-quality studies. In the case of trichloroethylene, the EPA decision to rely on the lower-quality study to drive the risk assessment has created additional environmental remediation costs potentially in the hundreds of millions to even billions of dollars.

Thank you for the opportunity to share my personal perspectives on some of the more serious concerns that continue to plague the IRIS program. Although the IRIS program has recently introduced new evaluation tools aimed at improving the quality of its evaluation, the IRIS program, given its past reluctance to embrace substantive change, will be challenged to efficiently and effectively evolve into a program that meets the expectations of delivering timely, credible and science-based assessment of environmental chemicals.

Thank you.

[The prepared statement of Dr. Bus follows:]

Chairman BIGGS. Thank you, Dr. Bus.

United States House of Representatives Hearing: "Examining the Scientific and Operational Integrity of EPA's IRIS Program", September 6, 2017, 2318 Rayburn House Office Building, Washington, DC.

Committee on Science, Space, and Technology's Subcommittee on Environment and Subcommittee on Oversight.

Oral presentation of James S. Bus, PhD DABT ATS, Exponent, Inc. (support provided by the American Chemistry Council)

Good morning. I am Dr. James Bus, and I am a toxicologist with the consulting firm Exponent. I must preface my comments by noting that the increasingly financially and other resource-constrained realities confronting our nation demands nothing less than a cost-effective, transparent and science-based evaluation and regulation of environmental chemicals.

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Turning to the second point of concern, and speaking as a toxicologist, extensive taxpayer investments in toxicological sciences have yielded substantial advances in understanding how chemicals cause toxic effects in animals and humans. Such mode of action information is essential to establishing the human health relevance of toxicity observed in cell- or animal-based toxicity findings. In recognition of the value of mode of action science, the toxicology, risk assessment and regulatory scientific communities have developed detailed frameworks for credible and transparent translation of these data into chemical risk assessments. While mode of action framework processes have long been included within EPA guidance procedures, and are routinely and effectively used by the EPA Office of Pesticides, the IRIS program has yet to embrace their practice. Thus, IRIS assessments consistently default to risk decisions that do not reflect the substantial added value of mode of action science that has long been supported by taxpayer investments.

Finally, the IRIS program has not implemented consistent criteria, as have other EPA offices, for appropriately weighting study quality as key to meaningful data integration. Too often poorly

conducted and/or described studies carry equal weight to those of far higher quality in the final risk decisions. For example, the recent IRIS evaluation of trichloroethylene, a commercially important solvent, relied on published studies from a single university-based laboratory that were subsequently subject to three published error corrections that have still not clarified the experimental findings. In addition, not only were the original data from the problematic studies not available for review by EPA, the study findings also were not reproduced in two much higher quality studies. In the case of trichloroethylene the EPA decision to rely on the lower quality study to drive the risk assessment has created additional environmental remediation costs potentially in the hundred's of millions to even billions of dollars.

Thank you for the opportunity share my personal perspectives on some of the more serious concerns that continue to plague the IRIS program. Although the IRIS program has recently introduced new evaluation tools aimed at improving the quality of its evaluations, the IRIS program, given its past reluctance to embrace substantive change, will be challenged to efficiently and effectively evolve into a program that meets expectations of delivering timely, credible and science-based risk assessments of environmental chemicals.

Exponent®

James Bus, PhD, DABT, Fellow ATS
Senior Managing Scientist

Professional Profile

Dr. James Bus is a Senior Managing Scientist in Exponent's Health Science Center for Toxicology and Mechanistic Biology. Dr. Bus has over 35 years of toxicology experience focused on research and evidence-based literature analyses informing potential health risks associated with chemical and pesticide exposures. He offers chemical specific and strategic toxicology expertise addressing development, stewardship, and regulatory needs to individual industry clients and business consortia and government and non-governmental agencies. Dr. Bus provides expertise in design, implementation, and interpretation of toxicity tests and mode of action and dose response/exposure evaluations furthering translation of toxicology findings to risk assessment. His expertise includes target-organ and endpoint-specific modes of action, and specific toxicity of chemicals including chlorinated organics, ethylene glycol and glycol ethers, aromatic derivatives benzene, styrene, aniline and others, and pesticides such as 2,4-D. His research interests include toxicokinetic mechanisms mediating dose-dependent expression of chemical toxicity. He has over 120 research and review publications and has received both the Achievement Award and Founder's Award from the Society of Toxicology in recognition of his research and leadership in toxicology.

Dr. Bus' experience includes over 23 years as a consulting toxicologist in the Toxicology and Environmental Research and Consulting unit of The Dow Chemical Company. He previously held positions at the Upjohn Company, the Chemical Industry Institute of Toxicology, and as Assistant Professor of Toxicology at the University of Cincinnati. Across all of these positions he focused on providing consulting and research expertise in support of health risk evaluations of environmental and industrial chemicals and pesticide and pharmaceutical products.

Dr. Bus has served as President of the Society of Toxicology, the American Board of Toxicology, and the Academy of Toxicological Sciences, and as a Director of the International Union of Toxicology. He has served on various toxicology-related advisory Boards and Panels including: ILSI-HESI and ILSI Research Foundation; the American Chemical Council Long-Range Research Strategic Science Team; both EPA ORD Board of Scientific Counselors and Chartered Science Advisory Board; the National Academy of Sciences Board on Environmental Studies and Toxicology; the National Institutes of Environmental Health Sciences/National Toxicology Program Board of Scientific Counselors (Technical Reviews Subcommittee); the FDA National Center for Toxicology Research Science Advisory Board; and Board of Directors of the Hamner Institutes. In addition, Dr. Bus served on the Chemical Substances (TLV) Committee of the American Conference of Governmental and Industrial Hygienists, the Program Committee of the Toxicology Forum, and advisory boards of the University of Michigan and Purdue University. He is an Adjunct Professor in the Department of Pharmacology and Toxicology at Michigan State University.

And now I recognize Dr. Burke for five minutes to present his testimony.

TESTIMONY OF DR. THOMAS BURKE, PROFESSOR, BLOOMBERG SCHOOL OF PUBLIC HEALTH, JOHNS HOPKINS

Dr. BURKE. Thank you for the opportunity to address the Subcommittees today. I'm Tom Burke, Professor at Johns Hopkins, and my views are my own. They don't reflect the university.

First, as a former Houstonian and graduate of the University of Texas School of Public Health in Houston, my thoughts are with all those impacted by Hurricane Harvey.

This hearing is particularly timely as Texans work to recover, restore drinking water and housing, and evaluate the risks from contaminated floodwaters.

Before joining Johns Hopkins, I worked on the frontlines as an environmental and health official for the State of New Jersey, serving three governors. I've also served on the National Academy of Sciences Board on Environmental Studies and Toxicology, the EPA Science Advisory Board, and the Board of scientific Counselors. From 2015 to 2017, I served as the EPA Science Advisor and Deputy Assistant Administrator for Research and Development.

Now, the capacity to evaluate the hazards of toxic chemicals is essential to protecting our public health. It's essential for agencies, public officials, and businesses alike to assure clean air and safe water, to respond to emergencies, and to protect our workers and communities.

The EPA IRIS program is a cornerstone of our national public health capacity. IRIS is charged with the daunting task of synthesizing enormous amounts of scientific information to identify the potential for a chemical to cause adverse health effects. The program provides a consistent and comprehensive source of toxicity data, not just for agency programs but for the regions and state officials, business and industry, and the public.

IRIS is not a regulatory program but the assessments provide essential scientific guidance for agency decisions. Not surprisingly, they're controversial. Don't like the regulation? Attack the science.

There's an important distinction between the IRIS assessment process and the ultimate risk management decision. The assessments 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 risk. Ultimately, the regulatory options are the responsibility of the program offices and the Administrator.

Now, there are challenges to IRIS. The demand for information about the safety of chemicals is constantly growing. One of our greatest environmental challenges is the lack of basic information about health effects. The 2016 bipartisan Lautenberg Chemical Safety Act represents a great step forward but the key to the success will be the scientific capacity of EPA.

Unfortunately, there are inherent scientific uncertainties in toxicology and epidemiology, as we've heard. They present difficult challenges to IRIS. For example, does cancer in a laboratory test animal mean that chemical will cause cancer in humans? If epidemiology studies give conflicting results, which one do we choose? Rigorous stakeholder and peer review is built into the IRIS process

and it's essential for producing credible results and addressing uncertainties.

Now, over the past few years there's been great progress in improving IRIS. As was mentioned, the 2011 formaldehyde report presented a roadmap to improve the process by increasing transparency in the review of evidence. The 2014 follow-up report from the National Academies noted the progress. As has been already stated, the GAO and the EPA Science Advisory Board have also made note of the enormous forward progress that the program has taken.

Now, in conclusion, EPA is a science-based agency. Ultimately, the success and credibility of EPA decision depends upon the quality and integrity of the science behind them. The core mission of EPA is to protect public health. IRIS has a unique and essential role in supporting that mission.

I'd like to close on a personal note. I'd like to acknowledge the great people of IRIS and EPA Office of Research and Development. They're dedicated public servants and world-class scientists. They take on the toughest environmental challenges we face from the dust of the World Trade Center and faucets of Flint to the toxic waters of Katrina and Harvey. They have worked selflessly to protect our Nation's environment and public health. Our health depends on them; our health depends on the IRIS program.

Thank you for the opportunity to speak with you today.

[The prepared statement of Dr. Burke follows:]

Testimony of Thomas A. Burke, PhD, MPH
Jacob I and Irene B. Fabrikant Professor and Chair in Health Risk and Society
Director, Risk Sciences and Public Policy Institute
Johns Hopkins University
Bloomberg School of Public Health

U.S. House of Representatives
Committee on Science, Space, and Technology
Subcommittee on Environment and Subcommittee on Oversight

Hearing on Examining the Scientific and Operational Integrity of EPA's IRIS Program

September 6, 2017

Thank you for the opportunity to address the Subcommittees on Environment and Oversight at today's hearing on EPA's IRIS Program. I am Dr. Thomas Burke, Professor at the Johns Hopkins University Bloomberg School of Public Health. I am also Director of Johns Hopkins Risk Science and Public Policy Institute.

First, as a former Houstonian and graduate of the University of Texas School of Public Health, I want to express my deep sympathy for all those impacted by Hurricane Harvey. Please know that I, and the public health community at Johns Hopkins and throughout the country, stand ready to assist in any way we can. This hearing is particularly timely, as Texas and Louisiana work to protect public health, restore safe drinking water, and evaluate the risks from contaminated floodwaters and chemical releases.

I speak today as an individual, informed by a career devoted to public health and protecting our environment. Before joining the faculty at Johns Hopkins I worked as both an environmental and health official for the State of New Jersey, serving three governors, both republicans and democrats. I have served as a member of the National Academy of Sciences Board on Environmental Science and Toxicology, and a Member of the EPA Science Advisory Board and Board of Scientific Counselors. 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, from January 2015 to January 2017 I served as the EPA Science Advisor and Deputy Assistant Administrator for the Office of Research and Development.

The capacity to evaluate the hazards of toxic chemicals is essential to protecting our public health. It is essential for clean air and safe drinking water, for responding to emergencies, and protecting our communities from harmful exposures. It is equally essential for business, industry, and agriculture to provide safe products, protect workers, and preserve the safety of our food supply.

The IRIS Program

The EPA IRIS Program is a cornerstone of our national capacity to protect public health. IRIS, within the National Center for Environmental Assessment (NCEA), is charged with the daunting task of synthesizing enormous amounts of scientific information to identify the potential for a chemical to cause adverse health effects. The program was started in 1985 to provide a consistent scientific source of toxicity data for the many program offices throughout the Agency and the broader regional and state environmental protection efforts.

IRIS is not a regulatory program, but the assessments provide essential scientific guidance for Agency decisions. There is an important distinction between the IRIS assessment process and the ultimate risk management decision. 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. Ultimately, regulatory options are the responsibility of the program offices and the Administrator.

Challenges to IRIS

The demand for information about the safety of chemicals is constantly growing. Although the actual number is often debated, there are thousands of chemicals in commerce and in our environment. One of our greatest environmental challenges is the lack of basic information on the toxicity and health effects of these chemicals. The 2016 bipartisan passage of the Frank R. Lautenberg Chemical Safety for the 21st Century Act represents a step forward, but the key to success will be the scientific capacity of EPA. IRIS is essential to that capacity.

The IRIS process includes weighing the scientific evidence that a chemical may cause adverse impacts such as developmental and reproductive effects or cancer. IRIS assessments can also be the starting point for many of the agency's most difficult and far-reaching regulatory decisions about chemical pollutants. Not surprisingly, they are also controversial.

Unfortunately, there are inherent uncertainties in toxicology and epidemiology studies that present difficult challenges to IRIS assessments. For example, does finding of cancer in laboratory test animals mean that exposure will cause cancer in humans? If epidemiology studies give conflicting results for an adverse health effect, which study do you choose to characterize the hazard? These vexing questions are examples of the challenges faced by IRIS scientists charged with evaluating and presenting the evidence. Rigorous stakeholder and peer review is built in to the IRIS process and is an essential to

producing credible results, addressing uncertainties, and explaining the scientific basis for conclusions.

The IRIS program is challenging both from a management and science perspective. Over the past few years there has been a tremendous commitment to improvement. This progress is reflected in reviews by the National Academies of Science (NAS), the Government Accountability Office (GAO), and the EPA Science Advisory Board (SAB). The 2011 NAS review of the IRIS Draft Formaldehyde Assessment presented a roadmap to improve the process by increasing transparency and improving the systematic review and of evidence. (1) The follow up NAS report in 2014 credited the program for making steady progress in addressing the recommendations for improvement. The GAO also made recommendations for improvements and has recently noted the progress of the IRIS program. (2) Most recently, the EPA SAB expressed their strong support for the program in a letter to EPA Administrator Pruitt. The Board recognized the progress in responding to NAS recommendations, and noted significant "impactful changes" that "constitute a virtual reinvention of IRIS".

Conclusion

EPA is a science-based agency. Ultimately the success and credibility of EPA decisions depends upon the quality and integrity of the science behind them. The core mission of EPA is to protect public health. IRIS has a unique and essential role in supporting that mission, and the public health efforts of our states and tribes.

I would like to close on a more personal note. During my time at the agency I came to know the great people of EPA ORD and IRIS. They are dedicated and talented public servants and world-class scientists. Their work goes far beyond the tedium IRIS document preparation. They are there to take on the toughest environmental challenges we face. From the dusts of the World Trade Center and the faucets of Flint; to the toxic waters of Katrina and Harvey; they are there, working selflessly to protect our Nation's environment and public health. Our health depends on them.

Thank you for this opportunity to speak with you today.

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Thomas A. Burke, Johns Hopkins University Bloomberg School of Public Health
Thomas A. Burke, PhD, MPH, is the Jacob I and Irene B. Fabrikant Professor and Chair in Health Risk and Society at Johns Hopkins University Bloomberg School of Public Health, Department of Health Policy and Management. He holds joint appointments in the Department of Environmental Health Sciences and the School of Medicine Department of Oncology. He is also Director of the Johns Hopkins Risk Sciences and Public Policy Institute. Dr. Burke was nominated by President Barack Obama to serve as EPA Assistant Administrator for the Office of Research and Development. From January 2015 until January 2017 Dr. Burke was the EPA Science Advisor and Deputy Assistant Administrator for Research and Development. His research interests include environmental epidemiology and surveillance, evaluation of population exposures to environmental pollutants, assessment and communication of environmental risks, and application of epidemiology and health risk assessment to public policy. Before joining the University faculty, Dr. Burke was Deputy Commissioner of Health for the State of New Jersey and Director of Science and Research for the New Jersey Department of Environmental Protection. In New Jersey, he directed initiatives that influenced the development of national programs, such as Superfund, the Safe Drinking Water Act, and the Toxics Release Inventory. Dr. Burke served as a member of the National Academy of Sciences Board on Environmental Studies and Toxicology. He was Chair of the National Academy of Sciences Committee on Improving Risk Analysis that produced the report *Science and Decisions*, and chaired the NAS Committee on Human Biomonitoring for Environmental Toxicants and the Committee on Toxicants and Pathogens in Biosolids Applied to Land. He also served on the NAS Committee on the Toxicological Effects of Methylmercury. He is a Fellow of the Society for Risk Analysis and a lifetime National Associate of the National Academies. He was Inaugural Chair of the Advisory Committee to the Director of the CDC National Center for Environmental Health and a member of EPA Science Advisory Board and Board of Scientific Counselors. Dr. Burke received his BS from St. Peter's College, his MPH from the University of Texas and his PhD in epidemiology from the University of Pennsylvania.

Chairman BIGGS. Thank you, Dr. Burke, appreciate that. I appreciate the testimony of all of you, and I now recognize myself for five minutes to ask questions, and I'll start with Dr. Mundt.

Dr. Mundt, in your testimony, you talked about the National Air Toxic Assessment and the findings and impacts that those findings had, and I'm wondering, you mentioned specifically precipitated—the NATA findings precipitated adverse public opinion, enforcement actions and a class-action lawsuit, all of which potentially have serious economic implications for DPE and the community. Can you tell us what impact that had with—and how it relates to IRIS?

Dr. MUNDT. Certainly. The NATA enforcement action requires an exposure standard which is unattainable, largely because it used in its calculations the inhalation unit risk that we believe is at least 100-fold inflated from what the best scientific methods and processes would suggest. So I think the root of that particular problem arises with the erroneous derivation or the poor derivation of the IUR and then using it in a calculation to determine at what levels humans can safely be exposed.

Chairman BIGGS. And I'll continue with Dr. Mundt. The Science Committee has been committed to ensuring that the science of EPA is open and available to the American people, and that's why we passed the HONEST Act, which would require science that EPA uses to make decisions to be publicly available. In your experience, does the IRIS program live up to that transparency in science?

Dr. MUNDT. My experience with IRIS has been primarily with the chemicals chloroprene and formaldehyde. The reviews of both of those, at least the draft review for formaldehyde, were from 2010. And of course, the NAS reacted also to the formaldehyde IRIS draft report identifying many of its problems. So I would say that yes, at least in 2010, there were significant problems that have led to more serious misinterpretations of the science and probably hardships for those who are impacted by those regulatory decisions.

I hear a lot about progress being made and good intentions, and I look forward to seeing new IRIS assessments that have embraced all of those recommendations and quality improvements, but to date, I'm really focusing on what I have seen and what has been relied upon from some of the earlier IRIS assessments.

Chairman BIGGS. And Dr. Bus, in your testimony, you indicated that IRIS frequently does not effectively differentiate between highest quality science and that a substantially lower quality in its evaluations. Can you tell us how that might impact the regulatory environment of EPA and how we distinguish between the highest quality science and the lowest quality?

Dr. BUS. Certainly, and thank you for the question. With respect to quality assessments, there are a number of mechanisms and tools that have been used across the agency, not necessarily specific to IRIS but to other programs of the agency, that are available for rating the quality of the science. Also, the EPA has made extensive investment in terms of development of what they call good laboratory practices and setting up of guidelines for how chemicals should be tested. Those studies are generally regarded as having the highest quality.

But yet often when those studies are considered in the overall context of IRIS evaluation, you find as in the case of trichloroethylene, the default was to a study conducted by a single laboratory that turned out not to be reproduced under two conditions of studies conducted by good laboratory practices and using EPA guidelines for conduct of those studies. The implications of that obviously is incredibly important because depending on what science you use will make a big difference in terms of the outcome of the ultimate risk values that will be derived by the IRIS program, and that of course then ultimately drive the final risk assessment, which I mentioned in the case of trichloroethylene can translate to a very large economic impact. So in the case of trichloroethylene, there are many Superfund sites that had been remediated under the previous trichloroethylene remediation programs that had been regarded as now an acceptable point of remediation, with this new assessment conducted by trichloroethylene by the IRIS program, many of those sites now are facing reopening, each one of them costing in the range of several hundred thousand dollars to remediate to the new level identified by IRIS, and you spread that over the range of about a thousand additional sites that have been to have trichloroethylene associated with them, you can see the dollars add up very rapidly.

But most importantly, that really brings home the message of why it's important that the agency has the proper expertise and means and review to use the highest quality science because the implications are important. Thank you.

Chairman BIGGS. Thank you.

And now my time is expired and so I'll recognize the gentlewoman from Oregon, Ms. Bonamici.

Ms. BONAMICI. Thank you, Mr. Chairman, and thank you to the witnesses.

Dr. Burke, I'm concerned about this Committee's lack of diligent oversight of the agencies in its jurisdiction since President Trump took office in January. In your opinion, how could this Committee best provide constructive oversight of the IRIS program with the goal of protecting public health of the American people? For example, are there informative witnesses we would benefit from hearing from as we try to learn more about the IRIS program?

Dr. BURKE. Thank you very much for the question, and yes, there are. IRIS has a daunting task, as I mentioned, and there are many members of the scientific community including the National Academy of Sciences, the Board on Environmental Studies, as I mentioned, that have been key to making sure IRIS documents may be the most scrutinized and peer-reviewed scientific documents the agency has ever produced. There is a tremendous review process, and there is a tremendous commitment to progress. We've seen a lot of change, as has been mentioned here, and I think you need to get the right kind of folks who have been involved in that change before you to really understand not just how important IRIS is but all the changes that have been made to solidify it, to listen to the comments of people like my colleagues here and to make sure the science is improved in a constant way.

Ms. BONAMICI. Thank you, Dr. Burke. And continuing, the mission of the EPA is to protect human health and the environment,

and we know that, and you've served as a Science Advisor for EPA, and you've been an environmental public health professional your entire career, so I'd like to hear your opinion about the general direction now in this Administration with EPA Administrator Pruitt. Recently we've heard actions—we've heard about actions at the EPA that are raising serious concerns including barring EPA scientists from attending scientific conferences, censoring use of the word "climate change," politicizing the allocation of scientific grants, rejecting the conclusion of EPA scientists in banning some harmful chemicals. So Dr. Burke, many anti-science actions seem to be driving decisions at the EPA, so will you please discuss the public health implications of that for individuals across the country in light of these actions.

Dr. BURKE. Thank you for that question. It was a really comprehensive one. But I can address the public health issues and a concern of the public health community. Obviously there's many great debates about the application of science. We hear this today in IRIS, but across the board, and I think it's important that we follow the evidence. But what I'm concerned about in this quest for regulatory relief is that public health has been the collateral damage here, that we really have taken our eye off the ball and the primary mission of EPA. It's a public health agency, and the science is there to provide the foundations of that public health agency.

Ms. BONAMICI. Thank you very much, and I appreciate that. I've been on this Committee my entire time in Congress, and we've had many conversations about public health, and I share your concerns about losing focus on that important part of the EPA's mission. And I wonder if you—since the time you started at the EPA in 2015 and left earlier this year, how did the IRIS program change during your time with the agency during that period of time?

Dr. BURKE. Thank you for that question too. As my colleagues know, I've been involved in the National Academy overview of—and oversight of the IRIS process, and I am aware that there have been historical problems in the presentation of evidence and the management, and I worked like crazy to make sure we have the best people, that we listen to the Academy, that we begin to address the issue of problem formulation, which actually was part of a report that I chaired at the Academy to improve the IRIS process, and so I worked to get the best people there, to make sure we have the best scientific applications of systematic review, to address many of the concerns that you heard today, and the program is on a wonderful, positive trajectory.

Ms. BONAMICI. Thank you. I appreciate your work.

Mr. Chairman, this hearing really seems incomplete without the participation of the EPA to answer questions about the IRIS program and how the Administration will prioritize the protection of health of the American people. There are many important environmental policies and public health issues that the Committee should be addressing: the effects of sea-level rise, ocean acidification, air quality—we're experiencing that in my home State of Oregon right now with terrible wildfires—coastal resiliency efforts, the broad public health impacts of climate change, but this year the Committee has not hosted a single EPA official to testify about these

important matters. It's unacceptable for this Committee to cede its jurisdiction and responsibilities to provide oversight of the federal agencies that are funded by our constituents. We should not go through an entire year without having an EPA official testify before this Committee, so I look forward to working with the Chairman and Chairman Smith. I hope we can get an Administration official to appear before this Committee as soon as possible.

Thank you, Mr. Chairman. I yield back.

Chairman BIGGS. The gentlewoman's time is expired.

The Chair recognizes Mr. LaHood.

Mr. LAHOOD. Thank you, Mr. Chairman, and I want to thank the witnesses for your valuable testimony here today.

Dr. Mundt, one of the intended steps in the IRIS process is independent expert peer review. I wanted to ask you, do you find that this peer review process adequately facilitates discussion from all relevant stakeholders, and particularly as you look at how IRIS utilizes or does not utilize independent third party?

Dr. MUNDT. Thank you. I think peer review in general is subject to the quality of the individuals selected and the amount of energy and efforts that they put into that peer review. This is true for published literature as well. Journal articles are subject to peer review but the quality of that varies from individual to individual.

I assume that the same is true with the IRIS program, that peer review panels have varied in terms of their quality, and maybe more specifically in terms of their expertise. I've found with formaldehyde and with chloroprene there to be inadequate peer review support on the epidemiological literature and its interpretation. So I think that can be remedied. I think, though, that it will require more systematic assignment of peer reviewers and perhaps even provide some standard expectations or guidance that those peer reviewers deliver upon so that obvious errors or bigger problems or questions of greater concern that deserve scientific debate can be identified earlier in the process and not only after the final drafts have been made public.

Mr. LAHOOD. Thank you. And Dr. Bus, do you want to comment on that also?

Dr. BUS. Thank you, and I would agree certainly that peer review is a very important aspect of the overall program, and one of the real challenges because peer review is often conducted by individuals from the scientific community who are essentially serving as a labor of love in terms of it's not their full-time job requires that they have adequate time by way of example to prepare for these types of reviews. So I can describe a review if you want an illustration of has the agency and the IRIS program really learned its lessons in terms of valuing that input. Two reviews, which were just conducted 3 weeks ago, the actual materials of the entire two reports for them to review were presented to them just 4 weeks before they were scheduled to deliver their final opinion. In my mind, that's woefully inadequately.

Secondly, another example in terms of does the IRIS program, have they really understood that it's important to value the input of outside comment to their overall assessment. The year before those same reviews were conducted, they actually correctly held a public session to solicit public input. At that time, their own invited

experts from the National Academy of Sciences indicated that the key endpoint that they were going to use for those evaluations definitely needed the consultation of an expert pathologist. One year later, this program was reviewed just 3 weeks ago by the EPA Science Advisory Board and it received severe criticism—this is a matter of public record—because the agency, the IRIS program had failed to follow up on that advice from their own National Academy consultant expert invited a year before. So that's an example of where although the IRIS may be talking going down the correct road, they still have a lot of need to actually put that into action, and it's not evident at least to date. Even as of events occurring just in the last several weeks that the IRIS program truly has reflected the advances that they are promoting and as claimed as successes, for instance, by way of to their presentation to the EPA Science Advisory Board.

Mr. LAHOOD. Thank you, Dr. Bus.

Dr. Mundt, I mentioned in my opening statement that IRIS is currently operating without specific statutory authority that would hold the program accountable. Do you believe IRIS would benefit from statutory guidance from Congress? And as a follow-up on that, what else can Congress do to help ensure toxicology risk assessment is reliable and transparent, particularly with the backdrop of the National Academy of Science's study and also the GAO study?

Dr. MUNDT. Thank you. I think it's a challenging question, and the solution is not immediately apparent. However, scientists in general are striving for more or less one thing, that is, understanding the science and incorporating the best science, and so I think if statutory support for deriving the best science could work, then yes, of course, it would. But what this usually means is adequate time, as Dr. Bus mentioned, for proper review, the right scientists who are knowledgeable about the key topics, and also support for engagement, that is, all of the scientific interests and communities. I'm frequently referred to as an industry scientist but I'm really not. I'm an independent scientist looking at the science and often my understanding of the science is as great as anyone's having looked deeply into it yet that is often not welcomed in the circles where these issues have been debated at EPA and specifically at IRIS.

Mr. LAHOOD. Thank you.

Thank you, Mr. Chairman.

Chairman BIGGS. Thank you.

The Chair recognizes the gentleman from Virginia, Mr. Beyer.

Mr. BEYER. Mr. Chairman, thank you very much, and thank you all for the testimonies. It's very interesting.

Dr. Burke, Dr. Bus identified three problems with IRIS, and the first was that they don't use—they're not good with problem formulation, and perfect sense. Do real-world exposures indicate reasonable need for a detailed risk assessment evaluation. Do you agree with his assessment? Is there some reason why IRIS isn't or shouldn't be using that?

Dr. BURKE. Well, first of all, IRIS has moved in the direction of starting with the right questions, and I think Dr. Bus rightly points out that there's a need to ask the right questions, and now

that is built into the process. We don't want to have a number pulled out of the air of some bright line of what an acceptable risk is without providing a context, but let's go back to that example of TCE. TCE is probably one of the most pervasive environmental contaminants this world has ever seen from the drinking waters of Camp Lejeune to the Superfund sites all around the country. I personally have closed water supplies in New Jersey because TCE is such a pervasive environmental contaminant exposing millions of people. These are exactly the kinds of things that should drive our priority-setting process, drive our science, and drive our problem formulation.

Mr. BEYER. It sounds like TCE would meet Dr. Bus's test of real-world exposure demonstrating reasonable need.

Dr. BURKE. Absolutely.

Mr. BEYER. His second concern was that the IRIS program has yet to embrace the practice of mode of action information. Why have they been reluctant to do that? Do you agree that mode of action information is important?

Dr. BURKE. Mode of action information is important, and understanding those mechanisms is part of a major investment the agency has made in our computational toxicology and advancing the science but it's also important that we move ahead when we have evidence of a relationship to a health impact even though the mysteries of mode of action may not be there, and this is not just specific chemicals where we lack this information but we know in the complexities of multiple exposures in the environment and the way that the biology of the human works that this is a very challenging undertaking, and the challenge is, when you're charged with protecting public health, when do you have enough information to move ahead to reduce exposure and to support the regulatory decisions of the agency? So he raises some very important points that have been raised by the National Academy of Sciences, but therein lies the inherent uncertainty of the science base for decision making, and we have to constantly try to improve that, and I think with mode of action, we are doing that.

Mr. BEYER. Great. Thank you.

Dr. Mundt, it's nice to see a Dartmouth English major turns out okay. You had mentioned that there are large pharmacokinetic differences between mice and human beings. Is this an argument that we shouldn't be doing mice experiments, animal experiments? It seems to me that most of my adult life, we've been measuring cancer stuff with smaller animals.

Dr. MUNDT. Thank you. The answer is no, not at all. We should continue to use these very good experiments appropriately, but we have to—and as the previous two speakers have noted, there's been great advances in understanding the way that chemicals cause disease. It turns out the way that chloroprene, for example, causes tumors in mice is very different from rats and hamsters and humans, and that can be taken into the computational toxicological developments now in hand. In fact, in 2010, EPA had access to those methods and chose not to use them, and that was one of the basic points of my written testimony.

So yes, I think there's full agreement here, and none of it suggests that we discontinue animal testing. We should probably re-

duce animal testing to that which is most necessary but it does inform human health risks and can be used if properly extrapolated to humans for risk control and exposure control.

Mr. BEYER. Thank you.

Dr. Burke, a very quick political question. Who was President in 1985 when IRIS was started? I'll go on. That's obvious.

Dr. Bus, your third point was that who—that you need to use the highest quality science, and Dr. Mundt had the Bukowski chart. Who determines the highest quality science?

Dr. BUS. Well, ultimately, obviously the IRIS program pulls together the science story as they believe it reflects the assessment for that compound being evaluated, but then it obviously is subjected to additional reviews by external parties including the science advisory panels as well as the external public such as members of the chemistry industry or other individuals interested or parties interested in that science. And then in the end, it is—it does come down to an issue of judgment although that judgment can be guided by, as I mentioned. There's been extensive investment by the federal government to define what constitutes a high-quality study, so we have a whole set of testing guidelines so that when we do toxicity tests in animals that they're done according to an accepted protocol that the scientific community universally agrees is sensitive and adequate to evaluate that particular endpoint of concern.

And then likewise, we have an additional wide set of guidelines called Good Laboratory Practices to make sure that as those studies are conducted, we're keeping accurate records, and that if the additional other people interested in that science want to actually see the science record of that study, it will be available for them to scrutinize. That is one of the major problems that I certainly highlighted with the example of TCE where we have an example of the study that was driving the overall risk assessment for TCE was based on a study where the scientific records, the raw data, was not even available. The author admitted it was fundamentally lost so it couldn't be—it could not be reobtained for re-analysis. But yet the other two studies conducted of much higher quality studies, there was a full study report conducted according to Good Laboratory Practice according to EPA guidelines that was available for complete detailed review by the scientific community. It's those kinds of judgments that are really used to help differentiate what constitutes a high-quality study versus one of lesser quality studies, and in the end, it is a balancing act for sure, and it also has to deal with, well, how do the higher quality studies perform relative to the lower quality studies. So if you have a consistent pattern of high-quality study performance indicating one type of response but you have an outlier study where you're—of uncertain quality that gives you a totally different response, that certainly weighs in terms of your ultimate decision as to how you would look at that science, so thank you for the question.

Mr. BEYER. Thank you, Mr. Chairman.

Chairman BIGGS. Thank you. The gentleman's time is expired.

Without objection, a letter from Denka Performance Elastomer to Administrator Pruitt requesting that EPA withdraw and correct its IRIS review for chloroprene is entered into the record.

[The information appears in Appendix II]

Chairman BIGGS. I now recognize the gentleman from Kansas, Mr. Marshall

Mr. MARSHALL. Yeah, good morning. I'm a physician and a biochemist, so this is actually a pretty exciting topic to me. It feels like I'm back in college again.

I think my first question is for Dr. Mundt. Chloroprene is neoprene, and that's one of your expertises. I think that you've been researching—I mean, obviously bathing your hands in these hydrocarbons is a little bit different than the different phases so I'm just very curious from a scientific standpoint how does IRIS or EPA deal with just whether the chloroprene is liquid, solid, vapor, and do they extrapolate the carcinogenic based upon perhaps the liquid phase compared to the synthetic—like our life jackets, I assume, are made out of neoprene, it looks like.

Dr. MUNDT. Thank you. I'm not an expert on the chemistry here but I understand that chloroprene is the monomer or the building block of neoprene like vinyl chloride monomer makes polyvinyl chloride. The end product is stable, a very different product.

The only epidemiological studies that looked at—reliably looked at worker exposure were those done or overseen by Gary Marsh, Dr. Marsh from the University of Pittsburgh. Most of those studies were in the United States. One was in Ireland. And they had quantitative exposure estimates of workers to chloroprene from the largest plant in Louisville. There's the basis for what kinds of exposures humans can be exposed to. These are significantly higher than what might be anywhere outside of a plant. These are workers and probably the only people exposed to levels——

Mr. MARSHALL. But they're not extrapolating the liquid product carcinogenic potential as opposed to the way the consumers are using it?

Dr. MUNDT. Well, consumers are typically not exposed to this material. In the workplace, though, the workers were exposed to the vapor, so it's in the air, and the risks are evaluated based on inhalation exposure.

Mr. MARSHALL. The next question for Dr. Bus, if the EPA—if the EPA wants to revise or correct an IRIS assessment, does that ever happen, or how does the process work?

Dr. BUS. Once an IRIS decision is closed, it can be reevaluated obviously because science changes with time. So the presumption would be that if a new piece of science came into the record that significantly impacted an existing IRIS review, that there should be a process available for reopening that IRIS record so that it could be revaluated in the context of that new science. One thing we certainly do know is the IRIS program reviews are not subject—although they're subject to reviews by science advisory panels, they're to subject to any legal review in the courtroom, at least as I understand it.

Mr. MARSHALL. But practically speaking, does that happen? Does the EPA ever go back and look at them and make modifications to IRIS findings?

Dr. MUNDT. With some of its older compounds, yes, they do come back as new science comes onto the table. My understanding is, they have revisited some of their evaluations. But it is a very chal-

lenging process in terms of getting it to be reopened to be reevaluated.

Mr. MARSHALL. Last question is about formaldehyde. I guess I'll go back to Dr. Mundt. There were some concerns about transparency in years past when the IRIS reviewed formaldehyde. Has the EPA improved in your estimation of that transparency process, or what steps else need to be taken to help it be more transparent?

Dr. MUNDT. I would say my interactions with EPA in the last couple of years regarding formaldehyde have been very professional, very cordial. There has been—we made a great effort to point out to IRIS all of the new science in the last six or seven years that has been published and is relevant to their evaluation.

We have asked, however, for IRIS to identify what body of scientific papers are they relying on for the revised formaldehyde assessment, and that information has not been shared with us.

Mr. MARSHALL. So they're not being transparent at this point?

Dr. MUNDT. I would say I can't say that there is any source that I can go to say what is EPA considering today including some of the most recent science that contradicts some of the older science.

Mr. MARSHALL. Did they give you any explanation why they won't be more transparent or what's going on?

Dr. MUNDT. Not specifically. I'm assured that there are many changes underway but I was also told by Dr. Bahadori, now heading the NCEA program, that many of these changes will not have been implemented in time for the formaldehyde reissue or the finalization of formaldehyde.

Mr. MARSHALL. I yield back. Thank you.

Chairman BIGGS. Thank you. The Chair recognizes the gentleman from Florida, Mr. Crist.

Mr. CRIST. Thank you very much, Mr. Chairman, and thank you to our panelists for being here today.

I'm from Florida, as the Chairman noted, which means that obviously with the hurricanes that we've experienced in Texas and one that appears to be bearing down on my home state, these issues are in the forefront of my mind, so Dr. Burke, it leads me to a question for you. Can you explain to me and the Committee how IRIS risk assessments assist in disaster recovery and response, particularly related to hurricanes and flooding?

Dr. BURKE. Sure, and I've been there as a state official on the front lines. I've worked as a federal official with the environmental leadership of all of the 50 states, and the IRIS program is there. We're talking about the documents that those folks prepare today but I think what we're not talking about is the scientific expertise at the IRIS program, the folks that are there when Corpus Christi, Texas, has a question about an inadvertent chemical contamination of their water supply and has to understand what the exposures might be and what the risks might be. They're there when there's a complicated mixture from a release. They're there to provide in the case of Harvey, Region 6, our Dallas—or EPA's Dallas office—excuse me, I don't speak for EPA—but Region 6 with the expertise to understand how to take the samples, to understand the vulnerable populations, and to use the expertise of the IRIS program to really have a strong public health response to environmental disasters that are related to things like extreme weather.

Mr. CRIST. Would emergency responders be able to quickly and safely address the types of chemical spills that we're seeing in the wake of Hurricane Harvey without these risk assessments?

Dr. BURKE. Well, there are many ways that emergency responders need to get information, the first of which is understanding what's on site and whether that's reported and shared with the local communities, and that is not part of the IRIS program, but once things are known, IRIS is a reliable and important database that doesn't just look at cancer in rats and things like that but also looks at the acute exposure risks, the lethal dose, the short-term doses, the neurological effects, the respiratory effects, the irritant effects that we've heard about recently in Texas, and so yes, IRIS is there. It's a backstop for the states. It's an important tool.

Mr. CRIST. So it's safe to say that timely chemical assessments are pretty important in helping communities and families recover from the unthinkable?

Dr. BURKE. They're essential. They're absolutely essential.

Mr. CRIST. Thank you, Dr. Burke. As you know, the Trump Administration has proposed to eliminate the IRIS program among other important science programs as well as significantly cut staff at the EPA. Will the EPA be able to handle the recovery and response efforts after Hurricane Harvey and now after Hurricane Irma with a reduced staff, and how would the elimination or downsizing of the IRIS program affect the long-term recovery of communities affected by storms and flooding?

Dr. BURKE. Well, it will have a profound effect on our national capacity to respond to chemical exposures and understanding those risks, and the unique combinations. For instance, I worked on the toxic combinations of water and what was called the toxic gumbo of Katrina. These are challenging risk assessments that need to be supported by data and good exposure science, and this is the kind of expertise that you have uniquely in IRIS that goes well beyond just the toxic substances program or looking at industrial chemicals. It really supports every aspect of our public health efforts, and it's really important to the state and local officials to have this resource, to have that number to call, to have those programs or the Office of Research and Development and IRIS there to support them.

Mr. CRIST. Thank you very much.

Thank you, Mr. Chairman. I yield.

Chairman BIGGS. Thank you.

The Chair recognizes the gentleman from California, Mr. Rohrabacher.

Mr. ROHRABACHER. Well, thank you very much, and let me just note that we hear charges all the time from people who claim that we are politicizing science by basically supporting positions that are not acceptable to other people who believe that their positions are sacrosanct, I guess, and should not be questioned.

As a young man, I remember very well the whole issue of cyclamates. Do you fellows remember cyclamates? That was the industry—the soda pop industry put enormous amounts of money into developing a new sweetener, and it was cyclamates, and they were—and they got into the drinks and then all of a sudden it was said that cyclamates caused cancer, and they had to pull this out.

It cost the equivalent of billions of dollars today when this whole thing—by the time it was finished, and then of course cyclamates were pulled out and then ten years later after a study, it was found that the cyclamates did not cause the cancer, and the Canadians had never abandoned cyclamates during that whole time. So we have to be very careful because those billions of dollars that were wasted in that particular instance could have been used for something else that was beneficial to us. For example, when the cyclamates were pulled out, I know that what came in was high-fructose corn syrup instead, which may not cause cancer but my wife will not let me have anything that has high-fructose corn syrup in it. Now, whether or not that means because she's afraid of getting fat or whatever it is, the bottom line is, the cyclamates would have been more healthy for me than the high-fructose corn syrup.

So there is harm done by chemicals and there's no doubt about that, and we should—and I'm very proud that Ronald Reagan signed this bill. I was working for Ronald Reagan at the time. I may have had something to do with the statement made on this issue years ago.

But the harm done by cyclamates, or by chemicals and drugs, we also have to recognize there is a danger to be done by not permitting people to use beneficial chemicals and drugs that have had positive impacts on our lives, so we have to really be serious about it, and I would hope that the IRIS program is being serious about it and is not—does not succumb to what we have seen here over and over again as a politicalization of science, and it's not a politicalization that comes from oh, we have to represent some major financial interest but instead it's a politicalization where once an academe that something—and Ph.D.'s, I don't know why they have this inclination but they've spent their life promoting a particular theory or they've come out and gotten grants on a particular theory and they will fight to the death to defend that theory even as more people come up and say well, that actually doesn't fit with what we've newly discovered, and I believe that manmade global warming, the fight in that, people have been denied—over and over again we have seen this over the years—denied research grants but those who claim to be so open-minded and liberal about this, and they've been denied people if they have any question as to whether or not mankind is causing global warming.

So one question. I know we're running out of time here for my question. But the—we need to make sure that people are looking not just at the specific reaction to chemicals but also what is the threshold that someone—because we all ingest chemicals even natural chemicals all the time. The threshold is very important as well as the frequently of exposure, and are we being cautious enough to making sure that we do not take away the beneficial chemical results and chemical—things that chemicals can do for us? Are we—is that issue now being handled correctly by this program, or is this still a problem? And I just—for the whole panel.

Dr. BUS. Thank you for that excellent question, and in fact, it really touches on the issue that Dr. Burke just touched on. The agency is called on on many occasions to deal with some very challenging issues such as events associated with hurricanes. That

means that the staff that they have needs to be put in the right place at the right time, and they certainly cannot be diverted to efforts that ultimately are really not proving, as you say, necessary to improving public health.

Let me give you a practical example of that. There's a compound that's under review right now by the agency called ethyl benzene. This is an intermediate compound, 99 percent of which in terms of its total chemical production is used as a closed system intermediate for the production of styrene, so it's a closed process. You're not going to have much releases to the environment as the result of that use. The other process—the other exposures to ethyl benzene come from its natural component of gasoline, which of course is assessed by other means independent of the ethyl benzene that's contained within it. It's another very small component of mixed xylenes, which is a commonly used solvent, but again, mixed xylenes are assessed for their own toxic independently.

So why is this important? Well, EPA has set off in terms of projecting, and this is as of just a couple of weeks ago, the IRIS program notified that they were going to continue forward with the evaluation of ethyl benzene in terms of developing an IRIS evaluation of it. That's an extensive effort on their part which will consume staff time but yet over a year ago in a public problem formulation session, which was appropriately held for this compound, they were advised that this compound is a chemical intermediate all used in closed system production, and that its exposures, which have been monitored in the air across North America for many years, are less than one part per billion, which is the general air concentration associated with ethyl benzene, but here's the kicker. In the case of ethyl benzene in terms of the animal toxicity studies, the primary endpoint of concern is liver tumors in rats that are seen with ethyl benzene but they occur only at a concentration of 750,000 parts per billion. Now, I would argue when you look at that data set alone, you would say that particular compound might not be worthy where significant resource investment by the agency justifies evaluation of a compound for that concern, and that frees the agency up to make the types of information flow that's necessary for the other critical elements that they're challenged with dealing with on an everyday basis, as Dr. Burke has already mentioned. So it's just one example that's actually currently in progress today so it's again another example of has the IRIS program truly learned and put into action what its words are versus where it's walking the talk. At least from my perspective I have some real concerns that that isn't the case. And the end result of it is, is just as you've just described. The necessary resources of the agency to truly protect public health, which I believe is exactly what they should be doing, are constrained when they're not making wise decisions as to where best to put their time in terms of evaluating the science.

Chairman BIGGS. Thank you, and the gentleman's time is expired.

The Chair recognizes the gentleman from Texas, Mr. Weber.

Mr. WEBER. Thank you, Mr. Chairman.

Dr. Burke, you said you spent some time in Houston. What part?

Dr. BURKE. Actually I was part of the downtown—I lived at the Texas Medical Center in student housing while I was pursuing my degree there, and part of the flood of 1976.

Mr. WEBER. Oh, I got you. Well, don't tell us how old you are now.

Dr. BURKE. I'm pretty old.

Mr. WEBER. You said in your written remarks "the capacity to evaluate chemicals is essential to public health."

Dr. Mundt, you wouldn't disagree with that, would you?

Dr. MUNDT. No, sir.

Mr. WEBER. Dr. Bus, you wouldn't disagree with that, would you?

Dr. BUS. Absolutely—have to do that.

Mr. WEBER. So I'm going to start back at the other end of the table.

Dr. Mundt, have you ever known scientists to be wrong?

Dr. MUNDT. Quite frequently.

Mr. WEBER. Quite frequently?

Dr. Bus, how about you?

Dr. BUS. I would agree, but there are certainly processes now available to help resolve those disagreements among scientists. So for instance, I mentioned mode of action frameworks. They're an excellent way to resolve those types of——

Mr. WEBER. I just want to make the point that scientists—well, let me get Dr. Burke in here first. Have you ever known scientists to be wrong?

Dr. BURKE. I sure have.

Mr. WEBER. Okay. So they're not infallible.

One of the problems that I see with the way the program is that the IRIS assessment is not reviewable by courts. Are you aware of that, Dr. Mundt?

Dr. MUNDT. No, I'm not aware of that.

Mr. WEBER. Dr. Bus?

Dr. BUS. Yes.

Mr. WEBER. Dr. Burke?

Dr. BURKE. I'll pass.

Mr. WEBER. Let's——

Dr. BURKE. I think that the regulatory application of IRIS is certainly consistently reviewed by the courts.

Mr. WEBER. Let me say it this way then. If that were in fact the case, the process is not reviewable by courts, would that be problematic, Dr. Mundt?

Dr. MUNDT. I have——

Mr. WEBER. I mean, if it's not reviewable by courts, do you see that as a problem?

Dr. MUNDT. I was going to say only if it's wrong. If it's right, then of course——

Mr. WEBER. That'd be great, but the courts——

Dr. MUNDT. —if we're wrong, where can you then turn.

Mr. WEBER. I got you.

Dr. Bus, if it's not reviewable by courts, is that problematic?

Dr. BUS. It can be in certain circumstances, yes.

Mr. WEBER. Dr. Burke?

Dr. BURKE. Again, I think the regulatory application is what the focus should be on, and my understanding is that is reviewable by courts, and very often are reviewed by courts.

Mr. WEBER. Let me read something that I have here. A March 2008 GAO report noted that EPA has not been able to "routinely complete critical IRIS assessments." More recently, a 2011 NAS report found that EPA's IRIS claims were not supported by its assessments, they were subjective, and that no clear scientific framework had been used by EPA to reach its conclusions. The NAS also stated that the IRIS program was deficient in meeting the benchmarks of objectivity, scientific accuracy, and transparency necessary to ensure high-quality and reliable assessments. Any of you all familiar with that report? Just a simple question. Dr. Mundt?

Dr. MUNDT. Yes.

Mr. WEBER. Dr. Bus?

Dr. BUS. Yes.

Mr. WEBER. Dr. Burke?

Dr. BURKE. I assume that's from the 2011——

Mr. WEBER. Okay. So does that sound problematic to you, Dr. Mundt?

Dr. MUNDT. I've spent the last five, six years working on that issue with regard to formaldehyde.

Mr. WEBER. To you, Dr. Bus, is that problematic?

Dr. BUS. Very much so.

Mr. WEBER. Dr. Burke?

Dr. BURKE. Yes, and——

Mr. WEBER. Okay. Thank you for that.

Let me go to my fifth question. Dr. Burke, you said that you had personally, I think, closed down some water plants in New Jersey?

Dr. BURKE. Yes, sir.

Mr. WEBER. Is that right? You need to come back to Texas.

You also said that you felt like that the IRIS was critical in emergencies like hurricanes where they can be out there on the ground taking samples. Is that a fair recounting of what you said?

Dr. BURKE. I think it's—yes.

Mr. WEBER. Are you familiar with the TCEQ in Texas, Texas Commission on Environmental Quality?

Dr. BURKE. Yes, I am.

Mr. WEBER. Are you aware that it is the second largest regulatory agency in the world second only to the federal EPA?

Dr. BURKE. I wasn't aware of that but I am familiar with it.

Mr. WEBER. Right. Well, I can tell you, having served in the Texas legislature for two terms, four years—I was on the environment reg committee—I can tell you that's a fact.

Do you think the TCEQ would have a vested interest in having boots on the ground immediately in those areas and assessing those same kinds of situations?

Dr. BURKE. Yeah, I think the state responsibilities are essential, and they have that role.

Mr. WEBER. Okay. Well, I appreciate you all being here today. I think the statements, the evidence and the hearing kind of speaks for itself. Thank you, gentlemen.

I yield back.

Chairman BIGGS. Thank you.

The Chair recognizes the gentleman from Georgia, Mr. Loudermilk.

Mr. LOUDERMILK. Thank you, Mr. Chairman, and thank all the members of the panel for being here.

Dr. Burke, you mentioned that a member of the National Academy of Sciences, you've made recommendations for IRIS for certain reforms. Did I get that right?

Dr. BURKE. Yes, a 2009 report.

Mr. LOUDERMILK. Have they followed through with those reforms that you've recommended?

Dr. BURKE. They are moving forward, yes, in a very responsive way but the reforms are challenging. There're inherent uncertainties in the science, and very often a lack of scientific information that make it challenging, but I'm very satisfied and have been part of pushing them to do just that.

Mr. LOUDERMILK. So those recommendations are 2009, 2017, they still haven't implemented how much—are you projecting how long it's going to take?

Dr. BURKE. I can't speak for how the program is going now but I know that it was a focus of my efforts to improve that program, and they have implemented tremendous improvement.

Mr. LOUDERMILK. Okay. Thank you.

Dr. Mundt, 2017, the GAO in their High Risk Report set out numerous recommendations for IRIS. Others have as well. To your knowledge, has EPA established timelines for the different stages of the assessment process since the GAO report?

Dr. MUNDT. I've not seen any.

Mr. LOUDERMILK. Okay. Dr. Bus, do you know?

Dr. BUS. No.

Mr. LOUDERMILK. Okay. I wouldn't expect if in 2009 they haven't made significant progress in the other recommendations.

Dr. Bus, the 2017 GAO report also indicates that other EPA offices do not exclusively use IRIS assessments for information on toxicity. The use of alternative sources for toxicity information begs the question, are there in fact other sources better equipped to provide information IRIS assessments do not, and are these sources able to make up for IRIS shortfalls? So it appears that EPA doesn't even use its own data. Are you aware of that?

Dr. BUS. Most of the science that the EPA considers in terms of its chemical evaluations is science coming from other sources. They do have their own Office of Research and Development but the vast majority of the science that the ultimately end up incorporating into their assessment comes from either industry sources or from primarily the academic environment. So those are the primary sources of the science that they use.

Mr. LOUDERMILK. I guess what is IRIS used for if EPA typically doesn't use it?

Dr. BUS. The primary purpose of IRIS is to pull together their IRIS evaluations, the objective of which is to develop what they call reference concentrations. So these are concentrations which they believe the public can be—the science says the public can be exposed to without reasonable concern for harm, and likewise, they also do cancer evaluations to say at what level of exposure is it acceptable where you might not be vulnerable to having cancer as a

consequence of exposure to this agent, and that's where the debate often comes in with respect to IRIS evaluation because there the studies that you use as the basis for making those determinations for those key values, the reference concentrations and the reference doses and the cancer values are really what drive the regulatory action.

So by way of example, Dr. Burke mentioned one of the things an emergency provider immediately would ask in the case of a chemical release associated with a hurricane by way of example, is there a reference—an acute reference concentration associated with this material. So if people happen to be exposed to the vapors or a first responder is exposed to the vapors, what do we know about the potential for that to cause that harm. So having that value is useful if you can measure it at the same time.

Now, it's also fair to say that the agency is not the only agency—and here's another issue regarding redundancy. The National Academy of Sciences has an extensive battery of what they call acute emergency guidelines. That's—they have an entire committee devoted to saying in these acute circumstances like chemical releases associate with these natural disasters, the first responders can consult the EGL values and to say what can we expect, you know, as a consequence of exposure to the first responders and then ultimately to the surrounding population as well.

So not having the IRIS there for those acute responses is certainly covered by other areas in the risk assessment community, so for instance, the National Academy and their EGL values.

Mr. LOUDERMILK. Dr. Mundt, is IRIS in need of major reforms or is it duplicative now that we have other resources like Dr. Bus just brought up?

Dr. MUNDT. Well, the range of products IRIS produces is broad. It not only includes the reference concentrations but it's one of the main organizations, the other being the National Institute for Environmental Health Sciences and the National Toxicology Program for classifying substances as carcinogenic. So there's another area where there's some redundancy. I think one of the other could do this but in every case it ought to be done well with high-quality science. So I don't think that all of the functions of IRIS currently could be absorbed by other organizations.

Mr. LOUDERMILK. But we do——

Chairman BIGGS. The gentleman's time is expired.

Mr. LOUDERMILK. —need major reform.

Dr. MUNDT. It's clear that there are major reforms underway because the problems have been recognized. Whether and at what rate they'll be implemented is yet to be seen.

Mr. LOUDERMILK. Thank you, Mr. Chairman.

Chairman BIGGS. Thank you.

The Chair recognizes the gentleman from California, Mr. Takano.

Mr. TAKANO. Thank you, Mr. Chairman.

Dr. Burke, good morning.

Dr. BURKE. Good morning.

Mr. TAKANO. Despite the vital function IRIS provides in assessing the public health dangers of chemicals and recent findings by both GAO and the Academies that EPA has made progress in im-

proving the IRIS process, this Administration proposed to eliminate the program altogether. My first question is, why would that matter? As a former state environmental official and former EPA Science Advisor, you bring a unique perspective to the table regarding the usefulness of IRIS. How does the program help state and local officials, public health professionals and the public? But first answer the question of why would it matter?

Dr. BURKE. Well, it matters tremendously to the frontline people in public health and environmental protection that we have a consistent source of information. I remember the chaos before 1983 when the risk assessment process got started in 1985 when IRIS was established, and we risk returning to 50 different solutions. As strong as some states may be, I think the business community does not want 50 different solutions, 50 different numbers, and certainly the health effects aren't different in the states. And so it would be a chaotic situation if that program were no longer there to respond to the Nation's environmental chemical priorities.

Mr. TAKANO. Well, what impact would eliminating IRIS have on EPA's statutory obligations?

Dr. BURKE. Well, the National Center for Environmental Assessment and the IRIS program really are the starting point for the science. EPA is only as strong as the science that supports its decisions, and EPA has very clear statutory authorities for clean air and clean water and the cleanup of hazardous waste. Each one of these is guided by science whether it's for a cleanup value or a contaminant level for drinking water or an air quality standard. Without IRIS, without the scientific engines that support that mandate, I feel that EPA would fail to meet its public health responsibilities

Mr. TAKANO. Well, based on these impacts, does it make it—does it make sense to reduce overall staff or monetary resources for the IRIS program?

Dr. BURKE. Again, I think it's an essential capacity for not just EPA but the Nation. Reducing that staff is very shortsighted, and I think would have profound effects not just on public health but on our business community as well.

Mr. TAKANO. So it doesn't make sense at all to reduce the staff.

Dr. Burke, as you state in your testimony, the scientific peer review process is essential to producing credible results, addressing uncertainties, and explaining the scientific basis for conclusions. And contrary to what some of my Republican colleagues believe, the peer review process is a critical part of how we conduct science in this country and around the world. Could you expand on your testimony and describe for us exactly why peer review—why the peer review process is built into IRIS and why is it so essential?

Dr. BURKE. Sure. Independent peer review is essential. All of the data, as was said by my colleagues here, that EPA uses is from the academic community, the scientific community, the industry community, and is peer reviewed prior to being part of this synthesis of information, but IRIS documents are subject to the highest levels of peer review, first through committees of the EPA's Science Advisory Board, and very often for the high-profile, high-impact compounds or substances, the National Academy of Sciences, our highest level of scientific expertise in this country, and so it is essential to be independent and it is essential that it be reviewed with the

kind of scrutiny and the kind of updating that was suggested here today.

But I have to mention one very important distinction between stakeholder input and scientific—independent scientific peer review. These are very different things, and sometimes we get confused about having stakeholders express their opinions on things, on the cost of regulations and things like that that is important but very different than the independence of the scientific review, and I fear that we may have gotten these things kind of crossed and what you see is a frustration on the part of stakeholders because they don't like the answer. Because in my experience in 40 years, I have never seen a stakeholder industry come forward with their risk assessment and say EPA, you got it wrong, your number is way too high, this is bad stuff. It's always recommending a more lenient approach with the public's health.

Mr. TAKANO. Thank you, Dr. Burke.

Chairman BIGGS. Thank you.

The Chair recognizes the gentleman from Texas, Mr. Babin.

Mr. BABIN. Thank you, Mr. Chairman. I thank the witnesses as well.

Dr. Bus, do IRIS assessments properly consider real-world regulatory and risk management implications of its hazard assessments?

Dr. BUS. The risk management applications, if I understand it, is actually outside the domain of the IRIS program. Their intention is just—and their objective and their responsibility is to assess the science that ultimately then is translated for use by the risk managers. However, if that science is not pulled together in a way that represents the best reflection of the practice of that science, it will result in poor risk management decisions. So by way of example, I mentioned the trichloroethylene example. I'll come back to that. The risk managers now are faced with the potential option of saying do we need to revisit all of the Superfund sites that had been resolved for trichloroethylene, do they need to be reopened now as a result of this reassessment conducted by the IRIS program. That's how it flows into a risk management decision.

Mr. BABIN. Okay. Thank you. Thank you very much.

And then Dr. Mundt, does IRIS use a weight-of-evidence framework that incorporates all relevant and reliable data?

Dr. MUNDT. This is one of the key criticisms that the earlier NAS committees identified, and I understand there's efforts in place to move toward this. But in the two chemistries that I've been involved with for the last few years, it's clear that that was not the case. The—especially epidemiological human health studies were all considered as equals where there were some that were considerably stronger and others that were considerably weaker. Preferentially, we tend to favor the results from studies that are well conducted, well documented, large numbers, strong exposure assessments and whatever they say, which should drive the assessment.

Mr. BABIN. Okay. Thank you very much.

One more question, and Dr. Bus, if you don't mind, what steps in the current IRIS process are most troublesome to you? You've mentioned some already, but with chemical toxicity, does one proc-

ess fit all or should it be tailored based on the type of chemical and the need for speedy assessment?

Dr. BUS. You've put your finger on certainly several of the key issues. The ability to identify which compounds really need the attention of the agency to the degree of investment that they engage in with an IRIS evaluation certainly is important. The other area in which the IRIS program has struggled with mightily without coming to any effective resolution even as of the last several reviews that have just been released over the last—this summer, and that is, how to use mode of action science, and why is that important? The vast majority of the decisions that are made with respect to evaluating the health effects of chemicals arises from data flowing from animal toxicology studies because we simply don't have often—I'm sure my colleague, Dr. Mundt, would agree—the horsepower in epidemiology necessarily to tease out those health effects so we rely on animal studies. But we also know animals are not little people, and that in some cases they don't behave the same way biologically as do adults, and we can also—because we can put these animals in cages and give them any amount of chemical that we choose, we often use doses that are far disparate from real-world exposures, and now we recognize that doing that kind of science often can generate results that are fundamentally not quantitatively relevant to human risk. So the risk program has, I'll have to admit, over its entire existence struggled mightily with the use of mode of action data, and I don't believe you can hardly point to a single example where mode of action science despite the extensive investment in the scientific community paid for and generate that science where it's ever been effectively used.

Mr. BABIN. I understand. Thank you very much.

I yield back the balance of my time, Mr. Chairman.

Chairman BIGGS. Thank you. The gentleman yields.

And now I thank the witnesses for your testimony. It's very valuable, very insightful, very interesting today, and the members for their questions. The record will remain open for two weeks for additional comments and written questions from members.

This hearing is adjourned.

[Whereupon, at 11:45 a.m., the Subcommittees were adjourned.]

Appendix I

Answers to Post-Hearing Questions

ANSWERS TO POST-HEARING QUESTIONS

Responses by Dr. Kenneth Mundt

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
Subcommittee on Environment
Subcommittee on Oversight

Hearing Questions for the Record
The Honorable Eddie Bernice Johnson

Examining the Scientific and Operational Integrity of EPA's IRIS Program
Questions for Dr. Kenneth Mundt

1. **Dr. Mundt, you provided unusual written testimony to the Committee. Your testimony appears to have been taken largely from an internal research paper you and two colleagues authored on the chloroprene IRIS assessment for your employer, Ramboll Environ. Unfortunately, your co-authors Dr. Sonja Sax and Dr. P. Robinan Gentry were not witnesses at the hearing and as a result Members of the Science Committee had no opportunity to question them at the hearing. However, I believe it is important to understand the potential conflicts of interest that exist regarding your and your two co-authors critique of the EPA's IRIS program.**

   It is correct that my written testimony was co-authored by Drs. Sonja Sax and Robinan Gentry and that my written testimony provided to the Committee summarizes a detailed technical report prepared for Denka Performance Elastomer, LLC (DPE). DPE's sponsorship of our technical review of EPA's 2010 IRIS Toxicological Review of Chloroprene (Final Report) (hereafter, "the 2010 Review") is clearly stated in our written testimony and our independent critical review was a work for hire. With this statement, Drs. Sonja Sax and P. Robinan Gentry hereby confirm that all oral and written testimony provided by me– including responses to questions – is entirely consistent with our understanding of the science, and endorse it as if it were their own.

   a. **Please provide a list of the specific companies, associations or other entities that have funded or otherwise supported your research efforts since 2010, including a brief description of the nature of the research.**

      Ramboll Environ is part of Ramboll, a global environmental engineering and design firm based in Copenhagen and employing 14,000 worldwide. We serve virtually all corporate and public sector entities in most regions around the world. Our Health Sciences Practice also serves a wide range of clients, the majority of which are corporations that manufacture consumer products of all types, including those that produce the raw materials required for these products. A list of the specific clients would be very long and include manufacturers of chemical, pharmaceutical, food, tobacco, cosmetic, transportation, communications, and other goods used by companies and individuals every day. The list also would include many entities with whom we have contracts specifically assuring confidentiality, including prohibitions against divulging their identities. Our corporate policies allow and encourage the provision of sound scientific

evaluations and interpretations to any legal company or government entity that is not engaged in any hate, terrorist or criminal activities. Therefore, it would be reasonable to assume that Ramboll Environ indeed provides professional scientific evaluations and interpretations to all legal, corporate, government or other entities.

The nature of work performed by Ramboll Environ's Health Sciences Practice area includes, but is not limited to, primary research studies, critical reviews and syntheses of the published scientific literature, quantitative risk assessments, workplace health and safety evaluations, compliance audits, environmental assessments, and chemical and product registrations.

b. Please provide identical information for the listed co-authors of your testimony, Dr. Sonja Sax and Dr. Robinan Gentry.

RAMBOLL ENVIRON

ENVIRONMENT & HEALTH

P ROBINAN GENTRY

Principal/Operations Director – Gulf Coast

Dr. Robinan Gentry has over 25 years of experience in toxicological issues relevant in the determination of the potential safety or risk associated with exposure to chemicals in consumer products, pharmaceuticals or the environment. Over her career, she has been a principal investigator or contributing author for numerous safety and risk assessments for both government and industry. The purpose for a number of these assessments has been to incorporate innovative quantitative approaches in the determination of acceptable levels of exposure of humans to chemicals in the environment, pharmaceuticals and consumer products. She is a published author in the development of physiologically-based pharmacokinetic (PBPK) models and their application into both the cancer and non-cancer risk assessment processes. She has also been involved in projects using these types of models to investigate human variability by age and gender, and the potential impact of this variation on risk assessment. Her recent work includes projects that are aimed at understanding the mode of action of adverse effects in animals and the implications to human health, as well as the development of innovative approaches that rely upon *in vitro* data and incorporation of these data into the risk assessment paradigm.

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CREDENTIALS
Diplomate. American Board of Toxicology, 2002; recertified, 2007, 2012

CAREERS

2015- Present
Principal/Senior Toxicologist, Ramboll Environ US Corporation

2011-2014
Principal/Senior Toxicologist, ENVIRON International Corporation

2001-2010
Manager /Senior Toxicologist, ENVIRON International Corporation

2001
Vice President, IFC Consulting

1997-2001
Senior Project Manager, ICF Consulting

1992-1997
Project Manager, ICF Kaiser

1989-1992
Associate Scientist, ICF Kaiser

1987-1989
Analyst, Clement Associates

EDUCATION

2008
PhD, Toxicology
Utrecht University, The Netherlands

1992
MS, Pharmacology/Toxicology
Northeast Louisiana University, United States

1987
BS, Toxicology
Northeast Louisiana University, United States

COURSES/CERTIFICATIONS

Diplomate of the American Board of Toxicology - DABT

PROJECTS

Risk Assessment Issues and Documents

- Principal Investigator for a multi-year project evaluating integration of the available evidence, epidemiological, toxicological and mechanistic, regarding the potential for formaldehyde to cause cancer, specifically leukemias and nasopharyngeal cancer.
- Primary author of a publication evaluating the raw data from a study relied upon heavily by IARC and the USEPA for establishing biological plausibility of leukemia resulting from exposure to formaldehyde.
- Served as the project manager on a work assignment to support USEPA in advancing the evaluation, development and application of PBPK models to be used in deriving IRIS toxicity values, including models for vinyl acetate, n-methylpyrrolidine, and acetaldehyde.
- Served as project manager and senior toxicologist for a work assignment to support USEPA in the revision of chapters one through six of the *Toxicological Review for Antimony and Compounds*. The document shall provide a summary of the state-of-the-science pertaining to potential health effects from antimony and antimony compounds found in the environment. The document will also contain information necessary for the derivations of an oral reference dose (RfD), inhalation reference concentration (RfC), cancer slope factor and inhalation unit risk where feasible, as well as the information that will be used to assign a cancer weight-of-evidence (WOE) classification. The cancer assessment shall include an uncertainty analysis, and an appropriate classification and grouping of antimony compounds (considering their chemical, physical, biological and toxicological properties), for presentation of hazard and dose response analyses.
- Served as project manager and senior toxicologist for a work assignment involving the completion of the IRIS documentation of the carcinogenic potential and potency of methanol for the cancer assessment portion of the USEPA Methanol Toxicological Review. This project included the quantification of the potential carcinogenicity of methanol using dose-response modelling and documentation of uncertainty in these estimates.
- Served as project manager and senior toxicologist for project involving the development of chapters one through four of the IRIS *Toxicological Review for Weathered Toxaphene*. This project involved a comprehensive literature search and provided information that will be used to derive an RfD, RfC, cancer slope factor and inhalation unit risk (where scientifically feasible). This document will also present information used to assign the cancer WOE characterization for weathered toxaphene.

- Served as project manager and toxicologist on a project for the American Chemistry Council (ACC) ACC to incorporate PBPK and other advanced approaches (e.g., Bayesian logic) in the conduct of quantitative dose-response analyses for compounds that act through receptor-mediated modes of action in order to harmonize cancer and non-cancer effects. The case study compound is DEHP and the initial phase was to discern a mode of action for the reproductive effects, enhance a PBPK model to describe the reproductive component, determine the common obligatory precursor and conduct the initial phase of dose-response modelling.
- Served as project manager and toxicologist for a project that involved conducting a review of the available *in vitro* studies of the interactions of arsenic species with genes and proteins involved in cellular control functions (e.g., DNA repair and redox control), as well as genomic/transcriptomic studies conducted with arsenic compounds. Possible biologically-based dose-response modelling approaches were explored and their suitability for an arsenic risk assessment evaluated. Additional data required to implement alternative modelling approaches was also be identified. Multipathway cancer modelling as a potential approach will also be investigated.
- Served as project manager and toxicologist on a project to assist the USEPA and the National Center for Environmental Assessment's Washington office with the development of an approach for the application of a PBPK model in both a cancer and noncancer risk assessment of 1,2-Dichloroethane (DCE). The approach was divided into two phases: an initial phase related to the evaluation of the existing PBPK model, and a second phase that involved the actual application of the model in the risk assessments for 1,2-DCE.
- Served as task manager for the development of revised drinking water criteria documents for radon and uranium, and an ambient water quality criteria document for methylmercury, for the Office of Water and the Office of Science and Technology. This contract involved a critical evaluation of the recent literature for a given chemical in order to summarize the studies in the appropriate section, but also to determine new studies that may be used in a quantitative manner for derivation of RfDs, RfCs, or cancer potency factors. Also served as task manager under the same contract for the development of the IRIS profile and support documentation for chloroform.
- Served as the principal investigator in a project for a private client that involved the application of benchmark modelling to effects observed in the parental generations of a two-generation reproductive study. This project involved the evaluation of the histological information for determination of data sets to be modelling, as well as the potential relevance of these datasets for human health risk assessment.
- Served as a co-investigator in the quantification of a margin of exposure and cancer slope factor, using existing kinetic and mechanism of action data, for a fungicide. This project involved the evaluation of the increases in the incidence of Leydig cell tumors observed in a two-year bioassay conducted with a fungicide in rats. The mode of action data collected for this chemical were reviewed, and based on this review, it was determined that the likely mode of action for this chemical was different in the rat and human. Therefore, for the risk assessment dose-metric adjustments for metabolic differences and for differences in response to LH stimulation (measured by testosterone production) were made, and a margin of exposure and cancer slope factor were quantified.
- Served as a co-investigator in the derivation of an alternative RfD for methylmercury, based on information available from fish-eating populations. Also participated in the development of a document detailing the methodology for peer-review. This innovative assessment involved the integration of Monte Carlo analysis, benchmark modelling and PBPK modelling. Played a key role in the identification of information for the development of distributions for the Monte Carlo analysis.

- Served as a co-investigator in the development of a document evaluating the toxicological and statistical significance of three National Toxicology Program (NTP) bioassays conducted with nickel subsulfide, nickel sulfate hexahydrate and nickel oxide. The results of the NTP bioassays were explained from a mechanistic viewpoint using putative mechanisms of action described in the toxicological literature. Where appropriate, unit risk factors and cancer slope factors were derived using the results of the NTP bioassays as a basis. The potential impact of the NTP data on future allowable air concentrations was also considered.
- Worked on a consortium of universities and corporations to conduct a comprehensive, independently managed review and evaluation of existing Department of Energy (DOE) weapons complex risk assessments to track issues of public concern. Information provided by this consortium will be used by the DOE Office of Environmental Management and Office of Integrated Risk Management, as background in preparing a June 1995 report to Congress describing the risks associated with cleaning up weapons complexes.
- Served as a contributing author of toxicological profiles for the Agency of Toxic Substances and Disease Registry for radon, plutonium and DDT. Prepared a critical evaluation of the available toxicity data, including animal data and epidemiology data, and identification of effect levels. Susceptible populations and data gaps were also discussed.
- Served as a contributing author for the development of the drinking water criteria documents for several radionuclides (including uranium, alpha emitters and beta/gamma emitters). Critically reviewed and summarized the available animal data and human epidemiology data, including dose calculations and effect determinations.
- Served as a co-investigator in a project that involved the development of comparative potencies for polychlorinated biphenyls (PCBs).
- Served as the principal investigator in the development of a cancer potency estimate for Toluene diisocyanate.
- Served as the principal investigator for the development of benchmark dose estimates and cancer potency estimates using dose-response models for numerous private clients, for use in regulatory or litigation related issues.
- Served as the principal investigator in a project for the USEPA that involved the derivation of potency factors for addenda to 49 reportable quantity documents.
- Served as the principal investigator in the derivation of margins of safety and excess lifetime cancer risks for selected volatile organic chemicals (VOCs).
- Served as a co-investigator on a team writing and editing the carcinogenicity sections for addenda to 49 reportable quantity documents for the USEPA.
- Served as the principal investigator on the derivation of reproductive, developmental and fetotoxic RfD's for a new chemical, based on the laboratory testing of that chemical required for registration.
- Served as the principal investigator in the development of cancer potency estimates for 29 chemicals under the Clean Air Act for the office of Air Quality and Planning Standards.
- Served as the principal investigator in the development of absorption factors for three chemicals based on the available literature to be used to adjust toxicity criteria values (RfDs and Q1*s).
- Served as a co-investigator in a quantitative risk assessment for the development of new permissible exposure limits (PELs) for cadmium, on behalf of OSHA.

- Served as a co-investigator in the development of Appropriate Cleanup Performance Criteria (ACPCs) for selected chemicals in groundwater and soil for a client in Florida, as applied to a RCRA Clean Closure Equivalency Demonstration.
- Assisted the state of Minnesota in setting one-hour standards for VOCs in air.

Risk Assessment Methods Research and Development

- Served as the manager of an ongoing project related to the development of a program to implement two-stage models for calculating the probability of nasal squamous cell carcinoma incidence and mortality in the rat due to inhaled formaldehyde. In addition, confidence limits on risk estimates are calculated and simulations carried out under various prescribed scenarios.
- Developed a report which provided a description of the practices, rationale, approaches and case studies of the production, evaluation and quantitative interpretation of PBPK modelling of genetic polymorphisms of drug metabolizing enzymes. This report was based on analyses, publications and workshop materials previously developed by ENVIRON staff.
- Served as the principal investigator in a project for ATSDR, in which the potential impact of pharmacokinetic and benchmark dose modelling in the development of minimal risk levels for noncancer health effects from chemicals was evaluated. The multi-year study demonstrated the use of these techniques for approximately 20 chemicals, and provided guidance on criteria for determining chemicals for which the application of the techniques should be given priority.
- Developed an advisory system to accompany TOX_RISK, a risk assessment software package developed by Clement International. This advisory system is intended to provide the non-risk assessor with information to assist in the conduct of the risk assessment and the interpretation of results.
- Served as the manager of a project that provided re-registration support for a pesticide. Critically evaluated the existing potency factor for this pesticide, and determined if the appropriate methodology and dose-response modelling techniques had been applied.
- Served as a co-investigator in a project conducted for the Office of Water Quality to investigate the use of the methodology reported in the newest USEPA Guidelines for Carcinogen Risk Assessment for the development of ambient water quality criteria for the protection of human health. This project involved the development of ED10s for four chemicals, 2,4-dinitrotoluene, 1,3-dichloropropene, hexachlorobutadiene and lindane. Also considered were the types of information needed to evaluate the possible underlying mechanisms of carcinogenicity and to distinguish between a linear or nonlinear mechanism of carcinogenicity.
- Managed a project involving a detailed review and critical analysis of the draft guidance documents prepared by the Office of Environmental Health Hazard Assessment for the determination of acute toxicity exposure levels for airborne toxicants, as well as the levels developed for five specific chemicals, including benzene, toluene, hydrogen sulfide, ammonia and nickel.
- Served as the principal investigator for a project that compared and contrasted the risk assessment methods used by USEPA for six chemicals, and the risk assessment of those same six chemicals, under California's Proposition 65.
- Served as a co-investigator in a project to evaluate the potential effects of partial lifetime exposure on the current methodology for risk assessment for the Office of Air Quality and Planning Standards.
- Served as a co-investigator in a critical review, for a private client, of an ambient air standard proposed by the state of Louisiana. This involved an evaluation of the current methodology for

deriving the proposed air standard and investigating alternative methodologies for deriving an air standard.

- Served as a co-investigator in the preparation of an advisory system and database program for weight-of-evidence assessments and quantitative risk assessments.
- Served as a co-investigator in the development the risk assessment methodology for the risk analysis part of a systems engineering analysis computer software program.

Pharmacokinetics and PBPK Modelling

- Served as the principal investigator on a project to conduct work related to the development and application of a PBPK model in the evaluation of the kinetics of ethanol following occupational exposure.
- Provided litigation support in the application of a PBPK model for trichloroethylene to investigate blood concentrations of the parent and metabolite following various occupational exposure scenarios.
- Assisted a private client in the refinement of an existing PBPK model for dichloromethane for performing a cancer risk analysis. This work considered individual data from human exposures used by DiVincenzo and Kaplan (1981), and a modified PBPK model originally published by Andersen et al. (1987). The input data to the risk analysis was the rodent bioassay data as described in the current IRIS database on DCM, as well as human epidemiological data provided by the client. These analyses relied on Bayesian MCSIM statistical methods and incorporation of GST-T1 polymorphisms to calculate cancer risk.
- Served as manager on a project for Health Canada to develop a report addressing critical issues related to the use of PBPK modelling in risk assessment.
- Served as manager of a project assisting USEPA, National Center for Environmental Assessment, in the development of an approach for the application of a PBPK model in both a cancer and noncancer risk assessment of DCE. In the initial phase of this project, the uncertainties in an existing PBPK model for DCE were qualitatively evaluated, and a determination was made of how this model would best be applied to reduce or characterize uncertainties in high-to-low dose extrapolation and cross-species extrapolation, including human and route-to-route extrapolation. The second phase involved the development of estimates of dose metrics for USEPA application using a revised PBPK model in cross-species and route-to-route extrapolation of cancer and non-cancer risk, and a quantitative uncertainty analysis.
- Served as manager of an ongoing project to provide support to the ILSI Children's Risk Assessment Framework Working Group. This support included compiling, reviewing and evaluating the available data on key physiological parameters for life stages (stages of functional maturation), from the perinatal period through adolescence, to develop a consistent and credible data set for PBPK modelling. These data have been integrated with rodent data in a pre-existent database. To explore the issues associated with trying to populate the database, several case studies were conducted on selected parameters (liver weight, liver blood flow, renal clearance and specific enzyme systems) to characterize the nature of available data, as well as data quality issues and specific data deficiencies. A common conclusion of the case studies was that, for the database to be useful, the data that are being incorporated must be critically evaluated with careful consideration given to data quality and representativeness.
- Served as project manager on a joint project with Toxicology Excellence for Risk Assessment (TERA) to conduct a critical literature review in order to compile information for the USEPA relating to age-

related changes in physiological parameters of animals used in PBPK modelling. The review focused upon the parameters previously utilized in models of pregnancy and lactation in rats and mice, and covered the period from initiation of pregnancy (fetal parameters only) through early adulthood of the offspring. The ultimate goals of this work were to provide a state-of-the-science compilation of PBPK parameters; use the actual age-specific, strain-specific data, which reflect any age-specific differences in growth, to replace default algorithms; and identify data gaps for development of age-directed PBPK models.

- Served as a co-investigator in a project using PBPK models to explore the issue of sensitive subpopulations. As part of this project, a PBPK "lifestage" model was developed in which simulations of the changes in tissue dosimetry over the entire lifespan, birth to 75 years, were been conducted for six environmentally relevant chemicals, covering the spectrum of chemical/physical properties. Two focused case studies were also conducted. One focused on the impact of differences in lung morphology and ventilation rate on both local and systemic toxicity as a function of the properties of the chemical. The other focused on the perinatal period, using PBPK models to evaluate *in utero* exposure via placental transfer versus exposure via lactational transfer, to demonstrate critical periods of exposure from a pharmacokinetic perspective.
- Served as a co-investigator in a project conducted for the American Chemistry Council on the application of a PBPK model in a risk assessment for acetone to estimate RfD. A PBPK model previously developed for isopropanol, whose major metabolite is acetone, was applied. Incorporation of a PBPK model into the derivation of the RfD and RfC for acetone allowed for a tissue-based approach rather than an external exposure-based approach, making it possible to derive an oral RfD from an inhalation study. In addition, the use of the PBPK model enabled an assessment of the potential for acetone to produce any of the effects observed in the isopropanol studies, filling some of the data gaps for acetone.
- Worked on a team as a subcontractor to TERA, in conjunction with staff from the University of Georgia, to develop a harmonized PBPK model for trichloroethylene (TCE). ENVIRON staff and University of Georgia staff had previously developed independent PBPK models for TCE. At the request of the US Air Force, this working group has been convened to develop a harmonized PBPK model for TCE, which will be taken through the peer consultation process by TERA.
- Served as a co-investigator in a project using PBPK modelling to investigate the potential impact of polymorphisms in genes that encode xenobiotic metabolizing enzymes. One goal of the project was to estimate the resulting variability in the activities of these enzymes and the incidence of different metabolism phenotypes in a population. The other was to develop an approach for the incorporation of these data into a standard risk assessment. Two case studies were conducted that focused on the metabolism of warfarin and parathion.
- Served as the principal investigator in the development of a PBPK model for multiple species, including rat, rabbit, monkey, dog and human. This project also included a noncompartmental analysis of the plasma data of the chemical of concern in rats, monkeys, rabbits and dogs.
- Served as a co-investigator in the development of a PBPK model for arsenic for EPRI. This model will be an extension of an existing model that will include the capability to simulate pharmacokinetics in the mouse.
- Served as a co-investigator in the development of a PBPK model for acrylic acid. This project involved not only a review of the toxicokinetic and toxicity information for acrylic acid, but also for esters of acrylic acid to provide direct empirical support for the selection of a duration adjustment factor. Responsible for the development of two manuscripts submitted for publication in a peer-reviewed journal.

- Served as a co-investigator in the development of a PBPK model for isopropanol for the Chemical Manufacturers Association. This project involved the extension of a previously developed rat model to develop a human model and to address reproductive/developmental effects observed in rats. In addressing these effects, the model has the capability to simulate internal dose metrics during a two-generation reproductive study.
- Served as the principal investigator of the available pharmacokinetic and toxicological data available for vinyl chloride for the development of a pharmacokinetic model for vinyl chloride assuming two saturable metabolic pathways, to be used by the USEPA in updating their cancer and noncancer risk assessments for vinyl chloride.
- Served as the principal investigator of the available toxicological data for TCE for the development of dose metrics for this data based on published pharmacokinetic information.
- Served as a co-investigator in a project aimed at making quantitative predictions of interindividual differences in susceptibility by using PBPK models. Initially, a systematic and comprehensive review of the literature was conducted to identify any quantitative information related to gender- or age-specific physiological and biochemical factors that could influence susceptibility to chemical exposure. These data were then organized from a pharmacokinetic perspective by process and chemical class to identify key factors likely to have a significant impact on susceptibility as it relates to internal target tissue dose. The next phase of this work consisted of using PBPK models to develop examples of approaches through the development of case studies. The goal of the case studies is to continue to develop a methodology that incorporates PBPK modelling to assess the likelihood that a chemical or class of chemicals may present an age- or gender-specific risk.

Exposure Assessment Documents for Contaminants, Mixtures, Media- or Site-Specific Cases

- Conducted human health risk assessments for private clients at multiple properties in southern Louisiana that were historically or currently used for oil and gas exploration activities. Focus in some areas was to evaluate the impact that may have resulted to the subsurface soil and groundwater beneath closed pits used to store produced water. As necessary, this also involved the collection of biota samples (i.e., various species of fish, crabs, and oysters) from waterbodies close to selected properties to evaluate the potential impact to humans and ecological receptors from of biota.
- Provided technical support on a project involving the development of inhalation provisional advisory levels for the USEPA and National Homeland Security Research Center.
- Managed exposure assessments conducted to estimate the daily intake of anthraquinone from the ingestion of food products stored in paper/paperboard manufactured from pulp containing residual amounts of anthraquinone. This involved the estimation of the migration of anthraquinone from the paper/paperboard to the food which was ingested by a receptor, as well as dermal contact of the receptor to the paper/paperboard and inhalation of volatiles from the paper/paperboard. Estimated potential exposure via ingestion, dermal contact, and/or inhalation for several other products, including drilling mud and fire logs containing residual anthraquinone.
- Participated in the development and preparation of the environmental impact statement for the licensing of the first commercial uranium enrichment facility to be built in Louisiana, and prepared related sections of the Safety Analysis Report (Reg. Guides 4.9 and 3.25, respectively). The scope of this project included evaluation of environmental effects due to uranium isotopes which may be attributed to plant operation, coordination of multi-disciplinary teams to conduct environmental studies, and the establishment of protracted operational effluent and environmental monitoring programs. Issuance of the permit required QA/QC compliance with NQA-1 and USEPA protocols.

- Reviewed the toxicokinetic data for arsenic and selected organic chemicals in drinking water and soil, in order to develop bioavailability factors to adjust for the difference in absorption of arsenic when contained in a soil medium by the oral route and the dermal route for use in a site-related human health risk assessment.
- Served as the principal investigator in the derivation of an action level for dermal contact with PCBs using methodology recommended in the 1986 USEPA Spill Policy Cleanup memorandum and incorporating site-specific information.
- Served as the manager of the human health portion of a multi-media risk assessment as part of the permit application process to burn hazardous waste as a fuel source at a sulfuric acid regeneration plant, consisting of two phases: a screening level assessment and comprehensive assessment.
- Served as the manager of the ecological portion of a multi-media risk assessment as part of the permit application process under the Screening Level Combustor Risk Assessment Guidelines developed by Region VI USEPA.
- Served as a co-investigator for several site-specific risk assessments and provided toxicological support for numerous other applied risk assessment projects at Superfund and other hazardous waste sites for both private and government clients.
- Served as a co-investigator in the toxicity assessment and risk assessment portions of an EIS for the state of California's Department of Transportation to advise the state as they assess their vegetation management program. The risk assessment was conducted for 25 chemicals with both occupational exposure and exposure to the public by multiple pathways.

Analysis, Document and Issue Paper Preparation

- Managed a project to provide support to the ILSI Children's Risk Assessment Framework Working Group. This support included compiling, reviewing and evaluating the available data on key physiological parameters for life stages (stages of functional maturation), from the perinatal period through adolescence, to develop a consistent and credible data set for PBPK modelling.
- Served as the project manager on a project for EPRI that involved conducting a review of the available *in vitro* studies of the interactions of arsenic species with genes and proteins involved in cellular control functions (e.g., DNA repair and redox control), as well as on genomic and transcriptomic studies conducted with arsenic compounds.
- Managed a project for Health Canada to determine an appropriate approach for providing a meaningful comparison of external acetone intakes to endogenously produced levels.
- Served as the project manager on a project to provide support to the ILSI Research Foundation in the development of a children's risk assessment framework case study on perchlorate to: illustrate the use of the framework, test the framework and suggest refinements or clarifications to facilitate further development. The work product will be a publication in the peer-reviewed literature.
- Served as the project manager on a project to aid in the development of age-specific PBPK models for experimental animals. This effort focused on generic physiological values, such as tissue weight (termed tissue volume in the context of PBPK modelling), intake (alveolar ventilation, food intake and water intake) and flows (blood flows to tissues, bile flow, creatinine clearance and glomerular filtration rate). To date, parameters for Sprague Dawley rats and mice of multiple strains have been collected and evaluated for data gaps and patterns. Using this database, we found that food intake in neonates does scale with approximately bw3/4.

- Served as a co-investigator in a project that investigated the mechanism of action of acrylamide and the formation of mesothelial tumors of the scrotal tunica vaginalis in Fischer 344 rats. The potential relationship between these tumors and testicular Leydig cell tumors was also evaluated and the relevance to human health was determined.
- Served as a senior reviewer of data evaluation reports prepared for different types of toxicity studies, including reproductive/developmental toxicity and subchronic and chronic toxicity studies, in a project for the USEPA's Office of Pesticide Programs and Program for Toxic Substances (OPPTS).
- Developed two documents that reported the final histopathological results of two inhalation toxicity studies following several reexaminations of the initial histopathological results, an independent pathology laboratory and a pathology working group.
- Developed a document that summarized the applicable data for the determination of NOAELs/LOAELs for a select class of chemicals to be submitted to the state of California under Proposition 65. The data was selected from a comprehensive toxicological database containing extensive information regarding the health effects, environmental effects and environmental fate for the class of compounds.
- Participated in a toxicological review of data for a new drug. This included reviewing all toxicological data and supporting studies to discern putative mechanism of action of drug and relevance of this mechanism with regard to human health. This review was presented to the USFDA.
- Participated in a toxicological review of a fungicide for a private client. This included conducting a critical toxicological review of bioassay data, mutagenicity, metabolism and pharmacokinetic data to evaluate statistical and biological significance of animal bioassay, and the relevance of these data with respect to human health.
- Participated in the preparation of toxicological profiles for ATSDR. This included a review of the available toxicity data for radon, plutonium and DDT.
- Participated in a review of the current toxicological literature on PCBs, TCDDs and TCDFs to be used as an addendum to an existing document.
- Participated in a review of the literature on the reproductive toxicity of ethylene glycol and glycol ethers.
- Developed toxicological summaries for occupational exposure to 41 mixtures for a private client to be used as supporting documentation for the toxicity information section of the standard material safety data sheet.
- Conducted a critical review of the recently developed RfC for manganese, consisting of a review of the study upon which the RfC was based. The impact of the uncertainty factors used by the USEPA was also considered, as well as the consistency of the derivation of this value compared to RfCs developed from similar studies. Evaluated the impact on the RfC of incorporating the benchmark approach.
- Participated in a critical review of methylmercury data both in animals and humans to identify the endpoints of concern and to select the appropriate data for use in quantitative analyses. Evaluated the strength of the evidence based on consideration of all the data with regard to threshold, endpoints (discrete, continuous, or multivariate) and feasibility for modelling. Neurotoxicity in the developing fetus was also considered. Four data bases were created: studies with dose-response data that could be used in initial dose-response modelling work; studies with dose-response data expressed in terms of body burden or levels in various tissues or compartments that could be used

for dose-response modelling when used as part of a pharmacokinetic model; data on mechanism of action; and pharmacokinetic studies.

- Served as the principal author of nine data evaluation reviews (DERs) for the Office of Pesticide Programs (OPP) of the USEPA.

Consumer Products/Pharmaceuticals

- Provided toxicological support on litigation issues related to the potential safety of second generation antipsychotics.
- Served as a co-investigator in the evaluation of the potential safety of multiple excipients used in the development of a new controlled-release drug to be administered in chronic pain management.
- Served as a co-investigator into the determination of systemic concentrations of PAHs following the use of coal-tar-containing shampoos in the treatment of skin disorders. Based on internal dose metrics, a safety assessment was conducted to evaluate the potential for adverse effects following therapeutic use.
- Served as a co-investigator in the development of a PBPK model for coumarin, a fragrance ingredient. This model was used to evaluate potential human health risk following dermal exposure to coumarin. The significance of this model is that is relies mainly on the use of in vitro data for development of metabolic parameters.
- Served as the principal investigator in a multi-year safety evaluation of the use of various personal care products and the determination of their compliance with California's Proposition 65.
- Served as the principal investigator for a project involving the application of a PBPK model in the determination of the relationship between the inhaled concentration of ethanol and the blood alcohol concentration (BAC). A comparison of the BAC achieved for a limited number of occupational scenarios, with BACs achieved following social alcohol consumption, has also been conducted. The goal of this project is to determine inhalation concentrations that may result in impairment or the potential for developmental effects in the offspring of exposed workers.
- Served as a co-investigator in the evaluation of the potential for adverse effects in children following exposure to lead in consumer products and residential settings.
- Conducted a critical review of the inhalation and oral literature for antimony compounds in order to select appropriate data to use in dose-response modelling to develop a no significant risk (NSRL) for California's Proposition 65. The metal was of concern because of its presence in consumer products developed by a private client. The data base was limited and a number of assumptions were made to develop the NSRL, all of which were clearly indicated.
- Served as a co-investigator in a quantitative risk assessment to address the issue of the presence of trace lead levels in calcium supplements. This investigation was conducted to determine if the current lead levels in calcium supplements exceeded the target internal dose associated with the NSRL developed by the state of California. This investigation considered the issue of comparative bioavailability for lead by the oral and inhalation routes, the influence of calcium and other minerals on that bioavailability, and the impact of pregnancy on calcium and lead bioavailability.
- Prepared and served as a QA reviewer for multiple toxicological data evaluation reviews (TDER) USFDA for studies submitted in support of a food additive petition.

Safety Assessment and Litigation Support

- Investigated and prepared information outlining the modes of action and potential health effects related to different atypical antipsychotic agents. In addition, provided toxicological support in the safety evaluation of the excipients contained in an extended release opiate compound.
- Applied PBPK models to determine potential blood concentrations of volatiles, including PCE, following various inhalation exposure scenarios.
- Applied pharmacokinetic principles to evaluate potential BACs over time related to insurance claims.
- Evaluated potential effects of lead in consumer products and residential settings on blood lead levels in potentially exposed children.
- Consumer Products/Proposition 65: Provided support in several cases for the review of the basis for Proposition 65 NSRLs, conducted product use-specific exposure assessments, conducted risk assessments and advised on warning requirements. This has included coal tar shampoos and acrylamide
- Provided support for Department of Justice Superfund litigation.
- Provided oversight in the organization of a science advisory panel to evaluate ongoing activities related to arsenic research.

Siloxane-specific Experience

- Principal Investigator the development of aggregate global human health risk assessments for D_4 and D_5. The scope of the project included the development of an aggregated global human health risk assessment for D_4 and D_5 separately, that incorporates the requirements of risk assessments conducted by authoritative bodies worldwide. The assessments considered risk scenarios for workers, consumers, and the general population; contained a probabilistic exposure assessment to rank the exposure scenarios; and utilized an existing physiologically-based pharmacokinetic (PBPK) model for the dose-response assessment and calculation of Margins of Safety.
- Principal Investigator in the development of a Systematic Review of the science for D_5 to support a technically rigorous and representative approach to Risk-based Human Health Risk Assessment. The goal of the proposed project, which includes the development of a protocol for conducting a systematic review of the epidemiological and toxicological literature for D_5, will allow for the evaluation of the procedures anticipated by the USEPA in the evaluation of D_5 in the IRIS process.
- Senior Scientist on a Ramboll Environ team that provided support in the development of dossier for D_5 for submission to the EU Scientific Committee on Consumer Safety (SCCS). The toxicology of this substance was evaluated in full and human exposure was assessed using PBPK modelling and aggregate exposure models covering a range of cosmetics products used daily across the world. In addition to supporting the development of the dossier, Ramboll Environ staff also attended a meeting with the EU SCCS to address any questions related to the dossier.
- Participating in the development of case studies for D_4 and D_5 to estimate Kinetically-Derived Maximum Doses (KMDs). These doses both determination of systemic doses of parent compounds or metabolites, as well as the application of statistical methods to identify nonlinearities in external or internal dose, which are important in identifying a point at which nonlinearity is detectable. The identification of these nonlinearities can assist in the development of protocols for toxicity testing.

- Principal on a project to revise the currently published PBPK model for D_4 and D_5 based on recently available results from oral uptake studies. Refinement of the PBPK model will unify the D_4/D_5 models into a single description for assessing risks from cumulative exposure scenarios.
- Prepared manuscripts summarizing groups of studies performed to assess the potential toxicities of a variety of siloxanes, including fluids, gels and elastomers.
- Managed the development of a database containing abstracts and relevant toxicological studies to be submitted to the USEPA in response to an 8A data call-in for a number of siloxanes to satisfy the database requirement for TSCA, as well as the remaining studies conducted by the client. This project involved the review and abstracting of approximately 5,000 toxicological studies and the incorporation of these abstracts into a searchable database.

PUBLICATIONS

2017

Does occupational exposure to formaldehyde cause hematotoxicity and leukemia-specific chromosome changes in cultured myeloid progenitor cells?
Critical Reviews in Toxicology 47(7); 592-602; DOI: 10.1016/j.ecoenv.2017.04.048.
Authors: Mundt KA, Gallagher AE, Dell LD, Natelson EA, Boffetta P, Gentry PR.

2017

Evaluation of triclosan in Minnesota lakes and rivers: Part II – human health risk assessment.
Ecotoxicol Environ Saf 142:588-596; DOI: 10.1080/10408444.2017.1301878
Authors: Yost LJ, Barber TR, Gentry PR, Bock MJ, Lyndall JL, Capdevielle MC, Slezak BP.

2017

A global human health risk assessment for octamethylcyclotetrasiloxane (D4).
Toxicology Letters 2017; DOI:10.1016/j.toxlet.2017.05.019
Authors: Gentry R., Franzen A, Van Landingham C, Greene T, Plotzke K .

2017

Refinement of the oral exposure description in the cyclic siloxane PBPK model for rats and humans: Implications for exposure assessment
Toxicology Letters 2017; DOI: 10.1016/j.toxlet.2017.04.002
Authors: Campbell JL, Andersen M, Van Landingham C, Gentry R, Jensen E, Domoradzki JY,Clewell III HJ

2017

A tissue dose-based comparative exposure assessment of manganese using physiologically based pharmacokinetic modeling—The importance of homeostatic control for an essential metal.
Toxicology and Applied Pharmacology 322 (2017) 27-40; DOI: 010.1016/j.taap.2017.02.015.
Authors: Gentry PR, Van Landingham C, Fuller WG, Sulsky SI, Green TB, Clewell III HJ, Andersen MA, Roels HA, Taylor MD, Keene AM.

2016

The need for transparency and reproducibility in documenting values for regulatory decision making and evaluating causality: The example of formaldehyde.
Regulatory Toxicology and Pharmacology 2016; 81:512-521.
Authors: Van Landingham C, Mundt KA, Allen BC, Gentry PR

2016
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2016
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Authors: Pease CK, Gentry RP

2016
A global human health risk assessment for Decamethylcyclopentasiloxane (D5).
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2015
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Authors: Sweeney LM, Kester JE, Kirman CR, Gentry PR, Banton MI, Bus JS, Gargas ML.

2015
A Preliminary Regional PBPK Model of Lung Metabolism for Improving Species Dependent Descriptions of 1,3-Butadiene and its Metabolites.
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2015
Evaluation of gene expression changes in human primary lung epithelial cells following 24-hr exposures to inorganic arsenic and its methylated metabolites and to arsenic trioxide.
Environmental and Molecular Mutagenesis 2015; [Epub ahead of print].
Authors: Efremenko AY, Seagrave J, Clewell HJ, Van Landingham C, Gentry PR, Yager JW.

2014
A constrained maximum likelihood approach to evaluate the impact of dose metric on cancer risk assessment: Application to β-chloroprene.
Regulatory Toxicology and Pharmacology 2014; 70(1): 203-213.
Authors: Allen BC, Van Landingham C, Yang Y, Youk, AO, Marsh GM, Esmen N, Gentry PR, Clewell HJ 3rd, Himmelstein MW.

2014
Use of mode of action data to inform a dose-response assessment for bladder cancer following exposure to inorganic arsenic.
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Authors: Gentry PR, Yager JW, Clewell RA, Clewell HJ 3rd.

2014

The impact of recent advances in research on arsenic cancer risk assessment.
Regulatory Toxicology and Pharmacology 2014; 69(1): 91-104.
Authors: Gentry PR, Clewell HJ 3rd, Greene TB, Franzen AC, Yager JW.

2014
Potential occupational risk of amines in carbon capture for power generation.
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Authors: Gentry PR, House-Knight T, Harris A, Greene T, Campleman S.

2013
Formaldehyde exposure and leukemia: Critical review and reevaluation of the results from a study that is the focus for evidence of biological plausibility.
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Authors: Gentry PR, Rodricks JV, Turnbull D, Bachand A, Van Landingham C, Shipp AM, Albertini RJ, Irons R.

2013
Evaluation of gene expression changes in human primary uroepithelial cells following 24-hour exposures to inorganic arsenic and its methylated metabolites.
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Authors: Yager JW, Gentry PR, Thomas RS, Pluta L, Efremenko A, Black M, Arnold LL, McKim JM, Wilga P, Gill G, Choe KY, Clewell HJ 3rd.

2012
Physiologically based pharmacokinetic/toxicokinetic modelling.
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2011
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2011
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Authors: Clewell HJ 3rd, Thomas RS, Kenyon EM, Hughes MF, Adair BM, Gentry PR, Yager JW.

2010
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2007
A pharmacokinetic model of the intracellular dosimetry of inhaled nickel.
Journal of Toxicology and Environmental Health, Part A 2007; 70(5): 445-464.
Authors: Hack CE, Covington TR, Lawrence G, Shipp AM, Gentry PR, Yager JW, Clewell HJ 3rd.

2007
Research toward the development of a biologically based dose response assessment for inorganic arsenic carcinogenicity: A progress report.
Toxicology and Applied Pharmacology 2007; 222(3):388-398.
Authors: Clewell HJ, Thomas RS, Gentry PR, Crump KS, Kenyon EM, El-Masri HA, Yager JW.

2006
Acrylamide: Review of toxicity data and dose-response modelling for cancer and noncancer effects.
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Regulatory Toxicology and Pharmacology 2006; 45(1):44-54.
Authors: Marino DJ, Clewell HJ, Gentry PR, Covington TR, Hack CE, David RM, Morgott DA.

2006
Revised assessment of cancer risk to dichloromethane II. Application of probabilistic methods to cancer risk determinations.
Regulatory Toxicology and Pharmacology 2006; 45(1):55-65.
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2006
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Authors: Covington TR, Gentry PR, Van Landingham CB, Andersen ME, Kester JE, Clewell HJ 3rd.

2005
Evaluation of physiologically based pharmacokinetic models in risk assessment: An example with perchloroethylene.
Critical Reviews in Toxicology 2005; 35(5): 413-433.
Authors: Clewell HJ, Gentry PR, Kester JE, Andersen ME.

2005
Comparison of tissue dosimetry in the mouse following chronic exposure to arsenic compounds.
Journal of Toxicology and Environmental Health 2005; 68(5): 329-351.
Authors: Gentry PR, Covington TR, Lawrence G, McDonald T, Snow ET, Germolec D, Moser G, Yager JW, Clewell HJ 3rd.

2004
Evaluation of the potential impact of age- and gender-specific pharmacokinetic differences on tissue dosimetry.
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2004

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2003
Evaluation of the potential impact of pharmacokinetic differences on tissue dosimetry in offspring during pregnancy and lactation.
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Authors: Sarangapani R, Teeguarden JG, Gentry PR, Clewell HJ 3rd, Barton HA, Bogdanffy MS. Gentry PR, Covington TR, Clewell HJ 3rd.

2003
Evaluation of the potential impact of age- and gender-specific lung morphology and ventilation rate on the dosimetry of vapors.
Inhalation Toxicology 2003; 15(10): 987-1016.
Authors: Sarangapani R, Gentry PR, Covington TR, Teeguarden G, Clewell HJ 3rd.

2003
Application of a physiologically-based pharmacokinetic model for reference dose and reference concentration estimation for acetone.
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Authors: Gentry PR, Covington TR, Andersen ME, Clewell HJ 3rd.

2003
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Journal of Toxicology and Environmental Health, Part A 2003; 67(1): 43-71.
Authors: Gentry PR, Covington TR, Mann S, Shipp AM, Yager JW, Clewell HJ 3rd.

2002
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Toxicological Sciences 2002; 70(1):120-139.
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2002
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Regulatory Toxicology and Pharmacology 2002; 35(2 Pt 1):177-197.
Authors: Haber LT, Maier A, Gentry PR, Clewell HJ 3rd, Dourson ML.

2002
Application of a physiologically-based pharmacokinetic model for isopropanol in the derivation of an RfD/RfC.
Regulatory Toxicology and Pharmacology 2002; 36(1): 51-68.
Authors: Gentry PR, Covington TR, Andersen ME, Clewell HJ 3rd.

2002
Review and evaluation of the potential impact of age and gender-specific pharmacokinetic differences on tissue dosimetry.
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Authors: Clewell HJ 3rd, Teeguarden J, McDonald T, Sarangapani R, Lawrence G, Covington T, Gentry R, Shipp A.

2001
Development of a physiologically based pharmacokinetic model of isopropanol and its metabolite acetone.
Toxicological Sciences 2001; 63(2):160-172.
Authors: Clewell HJ 3rd, Gentry PR, Gearhart JM, Covington TR, Banton MI, Andersen ME.

2001
Comparison of cancer risk estimates for vinyl chloride using animal and human data with a PBPK model.
The Science of the Total Environment 2001; 274(1-3): 37-66.
Authors: Clewell HJ 3rd, Gentry PR, Gearhart JM, Allen BC, Andersen ME.

2001
A hybrid computational fluid dynamics and physiologically based pharmacokinetic model for comparison of predicted tissue concentrations of acrylic acid and other vapors in the rat and human nasal cavities following inhalation exposure.
Inhalation Toxicology 2001; 13(5): 359-376.
Authors: Frederick CB, Gentry PR, Bush ML, Lomas LG, Black BA, Finch L, Kimbell JS, Morgan KT, Subramaniam RP, Morris JB, Ultman JS.

2000
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Authors: Clewell HJ 3rd, Crump K, Gentry R, Shipp A.

2000
Determination of a site-specific reference dose for methylmercury for fish-eating populations.
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Authors: Shipp AM, Gentry PR, Lawrence G, Van Landingham C, Covington T, Clewell H, Gribben K, Crump K.

2000
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2000
Application of a hybrid CFD-PBPK nasal dosimetry model in an inhalation risk assessment: an example with acrylic acid.
Toxicological Sciences 2000; 57(2): 312-325.
Authors: Andersen A, Sarangapani R, Gentry R, Clewell HJ 3rd, Covington T, Frederick C.

1999
Requirements for a biologically realistic cancer risk assessment for inorganic arsenic.
International Journal of Toxicology 18(2):131-147.
Authors: Clewell HJ 3rd, Gentry PR, Barton HA, Shipp AM, Yager JW, Andersen ME.

1999
Evaluation of the uncertainty in an oral reference dose for methylmercury due to interindividual variability in pharmacokinetics.
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Authors: Clewell HJ 3rd, Gearhart JM, Gentry PR, Covington TR, Van Landingham CB, Crump KS, Shipp AM.

1998
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Regulatory Toxicology and Pharmacology 1998; 28: 38-44.
Authors: Allen B, Berman D, Van Landingham C. 1998. Authors: Allen BC, Gentry PR, Shipp AM, Van Landingham CB.

1997
Investigation of the potential impact of benchmark dose and pharmacokinetic modelling in noncancer risk assessment.
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1995
Considering pharmacokinetic and mechanistic information in cancer risk assessments for environmental contaminants: Examples with vinyl chloride and trichloroethylene.
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Authors: Clewell HJ 3rd, Gentry PR, Gearhart JM, Allen BC, Andersen ME.

ABSTRACTS

2005
Physiological parameters for early life stages.
The Toxicologist 2005; 84(S-1): 261.
Authors: Olin S, Clewell HJ 3rd, Gentry R, ILSI Working Group.

2005
Issues in the use of PBPK modelling in the development of cancer slope factors for perchloroethylene.
The Toxicologist 84(S-1): 350.
Authors: Kester KE, Gentry P, Covington TR, Clewell HJ 3rd.

2002
Evaluation of the potential impact of age- and gender-specific pharmacokinetic differences on tissue dosimetry.
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Authors: Gentry R, Teeguarden J, Sarangapani R, Covington T, Lawrence G, McDonald T, Shipp A, Clewell J.

2001
Comparison of alternative exposure measures for evaluating the neurological effects of methylmercury in children.
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Authors: Gentry PR, Clewell HJ 3rd, Shipp AM, Yager JW.

2000
Trichloroacetate tissue dosimetry and PPAR alpha-mediated liver cancer induction by trichloroethylene and perchloroethylene.
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2000
Development of a physiologically-based pharmacokinetic (PB-PK) model and human health risk assessment for coumarin.
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Authors: Gentry R, Clewell HJ 3rd, Covington T, Wilson J.

2000
Investigation of the impact of benchmark and PBPK modelling on the derivation of MRLs.
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Authors: Clewell HJ 3rd, Gentry PR, Gearhart JM, Born SL, Lehman-McKeeman LD, Covington TR.

2000
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The Toxicologist 2000; 54(1): 272.
Authors: Lawrence G, Gentry R, Clewell H, Shipp A.

1999
Development of a physiologically-based pharmacokinetic (PB-PK) model for isopropanol and acetone.
The Toxicologist 1999; 48(1-S):144.
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1999
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1998
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Authors: Gentry PR, Shipp AM, Gearhart JM, Crump KS, Clewell HJ 3rd.

1998
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The Toxicologist 1998; 42(1-S): 229
Authors: Shipp AM, Clewell HJ 3rd, Crump KS, Gentry PR, Andersen ME.

MEMBERSHIPS

Society of Toxicology (SOT)

RAMBOLL ENVIRON

ENVIRONMENT
& HEALTH

SONJA SAX

Senior Environmental Health Scientist

Dr. Sonja Sax is an environmental health scientist with over 15 years of exposure and health risk assessment experience. She has particular expertise in airborne gases and particles, and has performed indoor and outdoor air quality investigations, managed several large environmental projects, conducted critical evaluations of toxicology and epidemiology studies, and helped prepare technical and expert reports. Sonja has authored and co-authored several publications, presented her research and consulting work at various conferences and testified before scientific panels, including the Clean Air Science Advisory Committee (CASAC). Sonja earned an MS and doctorate in environmental health from the Harvard T.H. Chan School of Public Health, where she also served as a postdoctoral fellow.

CAREER

2016->>>
Senior Environmental Health Scientist, Ramboll Environ

2005-2015
Senior Project Manager, Gradient
Managed and worked on multiple projects related to evaluation of human exposures and health risks associated with environmental pollutants; routinely conducted air dispersion modeling and exposure assessments to support health risk assessments; reviewed and interpreted epidemiology and toxicology studies for use in preparing expert reports, peer-reviewed publications, regulatory comments, and risk communications.

2003-2005
Postdoctoral Fellow, Harvard School of Public Health
Managed two large exposure assessment projects, developed study protocols, organized field studies, and managed staff. Additional duties included writing grants, analyzing data, and publishing manuscripts in peer-reviewed journals.

1998-2003
Research/Teaching Assistant, Harvard School of Public Health
Designed, conducted, and managed a large air pollution exposure assessment study of inner-city teenagers in New York City and Los Angeles; measured and analyzed indoor, outdoor, and personal concentrations of volatile organic compounds (VOCs), carbonyls, PM2.5, and particle-associated metals. Teaching assistant for an introductory environmental health course.

CONTACT INFORMATION
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Ramboll Environ
28 Amity Street
Suite 2A
Amherst, 01002
United States of America

1995
Intern, Environmental Protection Agency
Analyzed health effects data to assess the impact of ozone concentrations on hospital admissions in Massachusetts.

1994-1997
Research Assistant, Harvard School of Public Health
Proposed, designed, and implemented an indoor air quality study of a green community of homes.

1991-1994
Research Associate, Repligen Corporation
Managed the peptide chemistry lab. Conducted research to improve the synthesis of peptides. Trained and supervised laboratory staff.

EDUCATION
2003
ScD, Environmental Health Sciences
Harvard School of Public Health

1996
MS, Environmental Health Management
Harvard School of Public Health

1991
BA, Biological Chemistry
Wellesley College

LANGUAGE SKILLS
Spanish (mother tongue), **English** (mother tongue)

EXPERIENCE HIGHLIGHTS
Critical Reviews and Syntheses
Conducted an extensive literature search on the toxicity and health effects of several different chemical compounds including cobalt and cobalt alloys found in dental materials, diesel exhaust, carbon black, welding fumes, and sulfur dioxide.

Systematic Reviews
Conducted weight-of-evidence evaluation of cardiovascular and respiratory effects from exposures to ozone. Results of the critical evaluation of toxicology, epidemiology, and mode-of-action studies were published in several peer-reviewed manuscripts.

Litigation Support
Contributed to the preparation of expert reports in litigation projects that involved a variety of different chemical exposures including volatile organic compounds (e.g., vinyl chloride), asbestos, carbon black, particulate matter, sulfur dioxide, and pesticides.

Exposure and Risk Assessment
For numerous projects prepared technical analyses on exposures and potential health effects associated with various pollutants (e.g., particulate matter, sulfur dioxide, nitrogen dioxide, arsenic, and pesticides). Exposure assessments often included air dispersion modeling.

Regulatory Comments
Provided written and oral comments on several occasions to the Clean Air Scientific Advisory Committee (CASAC) on human exposure, epidemiology, toxicology, and mechanistic studies and their bearing on US EPA's National Ambient Air Quality Standards (NAAQS) for particulate matter and ozone.

Indoor Exposure and Risk Assessment
Conducted exposure and risk assessments of residential exposures to various chemicals including formaldehyde from wood products, vapor intrusion of tetrachloroethylene, exposures to mercury from wallboard and concrete, and exposures to flame retardants from various indoor sources.

PUBLICATIONS

2015
Particle size distributions of lead measured in battery manufacturing and secondary smelter facilities and implications in setting workplace lead exposure limits.
Journal of Occupational and Environmental Hygiene (Submitted)
Authors: Petito Boyce C, Sax SN, Cohen JM

2015
Are the Elements of the Proposed Ozone National Ambient Air Quality Standards Informed by the Best Available Science?
Regulatory Toxicology and Pharmacology 72(1):134-140
Authors: Goodman JE, Sax SN, Lange SS, Rhomberg LR

2015
Providing Perspective for Interpreting Cardiovascular Mortality Risks Associated with Ozone Exposures.
Regulatory Toxicology and Pharmacology 72(1):107-116
Authors: Petito Boyce C, Goodman JE, Sax SN, Loftus CT

2015
Rethinking Meta-analysis: Applications for Air Pollution Data and Beyond.
Risk Analysis 35(6):1017-1039
Authors: Goodman JE, Petito Boyce C, Sax SN, Beyer LA, Prueitt RL

2015
Ozone Exposure and Systemic Biomarkers: Evaluation of Evidence for Adverse Cardiovascular Health Impacts.
Critical Reviews in Toxicology 45(5):412-452
Authors: Goodman JE, Prueitt RL, Sax SN, Pizzurro DM, Lynch HN, Zu K, Venditti FJ

2014
Weight-of-evidence Evaluation of Short-term Ozone Exposure and Cardiovascular Effects.
Critical Reviews in Toxicology 44(9):725-790
Authors: Goodman JE, Prueitt RL, Sax SN, Lynch HN, Zu K, Lemay JC, King JM, Venditti FJ

2014
The dubious benefits of further ozone reductions (Op-ed).
The Wall Street Journal May 11, 2014 at http://online.wsj.com/news/articles/SB10001424052702304178104579536120366671620?mg=reno64-wsj
Authors: Goodman JE, Sax S

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Weight-of-evidence Evaluation of Long-term Ozone Exposure and Cardiovascular Effects.
Critical Reviews in Toxicology 44(9):791-822
Authors: Prueitt RL, Lynch HN, Zu K, Sax SN, Venditti FJ, Goodman JE.

2014
Evaluation of adverse human lung function effects in controlled ozone exposure studies.
Journal of Applied Toxicology 34(5):516-24
Authors: Goodman JE, Prueitt RL, Chandalia J, Sax SN

2013
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Circulation 127(4):e432
Authors: Goodman JE, Sax SN

2013
Letter to the editor Re: Air pollution and lung cancer incidence in 17 European cohorts: Prospective analyses from the European Study of Cohorts for Air Pollution Effects (ESCAPE).
The Lancet Oncology 14(11):e439-40
Authors: Sax SN, Zu K, Goodman JE

2013
Letter to the editor Re: Long-Term Residential Exposure to Air Pollution and Lung Cancer Risk.
Epidemiology 25(1):159
Authors: Sax, SN, Goodman JE

2013
Letter re: Equivocal evidence for confounding effects of components of particulate matter on the relationship between ozone and mortality [Letter].
American Journal of Epidemiology 177(12): 1460–1462
Authors: Sax SN, Goodman JE

2012
Potential indoor air exposures and health risks from mercury off-gassing of coal combustion products (CCPs) used in building materials.
Coal Combustion and Gasification Products 4:68-74
Authors: Long CM, Sax SN, Lewis AS

2011
Human health hazards of exposure to new technology diesel exhaust (NTDE).
Toxicologist - Supplement to Toxicological Sciences 120(Suppl. 2)
Authors: Hesterberg TW, Long CM, Sax SN, Lapin CA, Bunn WB, Valberg PA, McClellan RO

2011
Non-chemical stressors and cumulative risk assessment: An overview of current initiatives and potential air pollutant interactions.
International Journal of Environmental Research and Public Health 8(6):2020-2073.
Authors: Lewis AS, Sax SN, Wason SC, Campleman SL

2011
Risk characterization of the brominated flame retardant decabromodiphenyl ethane in indoor dust.
Toxicologist - Supplement to Toxicological Sciences 120(Suppl. 2):271
Authors: Dodge DG, Pollock MC, Sax SN, Petito Boyce C, Goodman JE

2010
Letter re: Xue et al. (2010) article addressing probabilistic modeling of dietary arsenic exposure and dose.
Environmental Health Perspectives 118(8). E-pub ahead of print doi:10.1289/ehp.1002328.
Authors: Petito Boyce C, Lewis AS, Sax SN, Beck BD, Eldan M, Cohen SM

2009
Human exposure to decabromodiphenyl ether, tetrabromobisphenol A, and decabromodiphenyl ethane in indoor dust.
Journal of Environmental Protection Science 3:75-96
Authors: Petito Boyce C, Sax SN, Dodge DG, Pollock MC, Goodman JE

2009
Non-cancer health effects of diesel exhaust (DE): A critical assessment of recent human and animal toxicological literature.
Critical Reviews in Toxicology 39:195-227
Authors: Hesterberg TW, Long CM, Bunn WB, Sax SN, Lapin CA, Valberg PA

2008
Probabilistic analysis of human health risks associated with background concentrations of inorganic arsenic: Use of a margin of exposure approach.
Human and Ecological Risk Assessment 14:1159-1201. **Winner of the HERA Human Risk Assessment Paper of the Year Award in 2008.
Authors: Petito Boyce C, Lewis AS, Sax SN, Eldan ME, Cohen, SM, Beck BD

2007
Trends in the elemental composition of fine particulate matter in Santiago, Chile, from 1998 to 2003.
Journal of the Air & Waste Management Association 57(7):845-855
Authors: Sax SN, Koutrakis P, Rudolph PA, Cereceda-Balic F, Gramsch E, Oyola P

2006
Integrating studies on carcinogenic risk of carbon black: Epidemiology, animal exposures, and mechanism of action.
Journal of Occupational and Environmental Medicine 48(12):1291-1307
Authors: Valberg P, Long CM, Sax SN

2006
A cancer health risk assessment of a cohort of inner-city teenagers in New York City and Los Angeles.
Environmental Health Perspectives 114(10):1558-1566
Authors: Sax SN, Bennett DH, Chillrud SN, Kinney P, Ross J, Spengler JD

2005
Analysis of PM10, PM2.5, and PM2.5-10 concentrations in Santiago, Chile, from 1989 to 2001.
Journal of the Air & Waste Management Association 55(3):342-351.
Authors: Koutrakis P, Sax SN, Sarnat JA, Coull B, Demokritou P, Oyola P, Garcia J, Gramsch E

2004
Differences in source emission rates of volatile organic compounds in inner-city residences of New York City and Los Angeles.
Journal of Exposure Analysis and Environmental Epidemiology 14:S95-S109
Authors: Sax SN, Bennett DH, Chillrud SN, Kinney PL, Spengler JD

2004
Elevated airborne exposures to manganese, chromium and iron from steel dust in New York City's subway system.
Environmental Science & Technology 38:732-737
Authors: Chillrud SN, Epstein D, Ross JM, Sax SN, Pederson D, Spengler JD, Kinney PL

2002
Exposures to multiple air toxics in New York City.
Environmental Health Perspectives 110(Suppl. 4):539-546
Authors: Kinney PL, Chillrud SN, (Sax) Ramstrom S, Ross J

OTHER ACTIVITIES

Technical peer reviewer for the following Journals:
Journal of the Air & Waste Management Association
Journal of Exposure Science and Environmental Epidemiology
Environmental Health Perspectives
Atmospheric Environment
Environmental Pollution

MEMBERSHIPS

Air & Waste Management Association (AWMA)
Society for Risk Analysis (SRA)
Society for Risk Analysis New England Chapter (SRA-NE)
International Society of Exposure Science (ISES)

2. **Dr. Mundt, in your written testimony before the Committee you referenced a "detailed evaluation of the 2010 Review conducted by Ramboll Environ US Corporation" as a starting point for the EPA to begin a re-evaluation of its 2010 IRIS Toxicological Review of Chloroprene.**
    a. **Has this referenced "2010 Review" prepared by Ramboll Environ been published in a scientific journal? If so, please provide the citation to the journal article.**

    Our technical report has not yet been published. We hope to publish a shorter version of the critical portions of the report. In the meantime, DPE is relying upon our technical review to assist them in addressing the EPA Clean Air Act review of the facility, and to assist the Request for Correction of the erroneous and scientifically unsubstantiated determinations from the 2010 Review, particularly the erroneous IUR. We consider our evaluation of the science to be independent and all conclusions to be our own and not guided or influenced by DPE.

    b. **If the chloroprene paper has been published, was it peer-reviewed prior to publication? If so, please detail the process by which the paper was reviewed.**

    Please see previous response.

3. **A June 26, 2017 letter that Denka Performance Elastomer LLC ("Denka") sent to EPA seeks to have EPA "withdraw and correct" its 2010 IRIS toxicology review of chloroprene. In the letter, Denka leans heavily on the findings of a Ramboll Environ report, in which you served as lead author. Your report—Basis for Requesting Correction of the U.S. EPA Toxicology Review of Chloroprene–stated that Denka "asked Ramboll Environ to conduct an independent evaluation of the 2010 [chloroprene] review."**

    a. **Was Ramboll Environ compensated by Denka for producing the aforementioned report? If so, please detail the compensation provided. Please also detail any other compensation or support Ramboll Environ received from any other company, organization, association, entity or individual for researching and/or producing this report.**

    Yes. As stated in our written testimony, Ramboll Environ and DPE entered a business agreement whereby Ramboll Environ was provided usual fees for the performance of the scientific evaluation of the 2010 Review. No other entity has provided financial sponsorship.

    b. **Was this report—*Basis for Requesting Correction of the U.S. EPA Toxicology Review of Chloroprene*—peer reviewed? If so, please indicate the association, organization, or entity who conducted this review.**

    Our technical report has not yet been submitted to any scientific journal, and therefore has not undergone any formal peer-review. Should we submit some or all of the technical report for publication in a scientific journal, it will be subject

to such peer review. As noted above, our aim was to conduct an independent evaluation of the 2010 Review, specifically with respect to EPA's derivation of the IUR. Our report provides a detailed description of how standard conservative EPA risk evaluation methods and data inputs from peer-reviewed publications can be used to derive a scientifically sound IUR. It is important to reiterate that we used standard EPA methodologies, which EPA has used in the evaluation of other IRIS chemicals, and that our technical report transparently describes the methodology and assumptions used to derive the IUR following the recommendations from the NRC best practices. Importantly, the conclusions of the technical report are based on peer-reviewed publications that were published subsequent to the development of the 2010 Review. Certainly EPA may elect to use alternative assumptions and/or methods; however, any IUR that fully and properly considers the known large differences between the way mice and humans process chloroprene will be much closer to the one we calculated than to the one published by EPA in 2010. Our comparison of the potential cancer risks based on our estimated IUR to the results from epidemiological studies indicates that it is more consistent with the epidemiological evidence than the EPA IUR that was published in the 2010 Review.

Responses by Dr. James Bus

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
Subcommittee on Environment
Subcommittee on Oversight

Hearing Questions for the Record
The Honorable Eddie Bernice Johnson

Examining the Scientific and Operational Integrity of EPA's IRIS Program
Questions for Dr. James Bus

1. **In your written testimony, you acknowledge that you received "support" in preparing your testimony from the American Chemistry Council (ACC). Please detail the complete nature of that "support" provided by ACC, including names of the individuals who provided such "support" in the preparation of your testimony. This should include any financial support provided by the ACC, or any support, of any kind, provided by any other organization or individual regarding the preparation of your testimony.**

   The first question posed inquired about the financial support provided by the American Chemistry Council ("ACC"). Through a contract with my employer, Exponent, the ACC provided financial assistance supporting my expenses associated with development and presentation of my comments. The expenses included both time and travel. Also, because I reside in Michigan, the ACC also made the requested copies of my testimony and accompanying biographical information and arranged for the delivery of those materials to congressional staff.

   My comments were entirely my own, and were based entirely on my professional experiences over many years of interactions with the IRIS program. My comments were not reviewed or approved by the ACC. The ACC provided me with background informational documents on the IRIS program, publicly available copies of the EPA NCEA presentation to the Chartered EPA SAB, and the ensuing SAB letter to Congress reflecting its observations on progress of the EPA IRIS program.

2. **Many of the studies you have conducted while employed at Exponent have been funded by industry. Please provide a list of the specific companies, associations, or other entities that have funded, or otherwise supported, your research efforts since you joined**

Exponent in May 2013. Please also include a brief description of the nature of each research effort.

The second question posed asked me to identify the specific companies, associations or other entities that have funded or supported my research efforts since May of 2013. Due to contractual obligations, Exponent cannot release the names of its clients for which I have provided consulting services without the permission of those clients. As noted in my Exponent curriculum vitae, based on my extensive and broad experiences in toxicology, my consulting activities include provision of

> ...chemical specific and strategy toxicology expertise addressing develop, stewardship, and regulatory needs to individual industry clients and business consortia and government and non-governmental agencies. Dr. Bus provides expertise in design, implementation, and interpretation of toxicity tests and mode of action and dose response/exposure evaluations furthering translation of toxicology findings to risk assessments.

In connection with the publications that appear on my *curriculum vitae* (an updated copy of which is enclosed), funding sources are disclosed in the publication as required by the publisher.

Responses by Dr. Thomas Burke

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
Subcommittee on Environment
Subcommittee on Oversight

Hearing Questions for the Record
The Honorable Eddie Bernice Johnson

Examining the Scientific and Operational Integrity of EPA's IRIS Program
Questions for Dr. Burke

1. **How would you respond to those who suggest that IRIS assessments and the IRIS process should be reviewable through the judicial system? Is there an appropriate role or the courts to play in ensuring both EPA, and the IRIS process meet their regulatory obligations? How would that role differ from inserting judicial review in the IRIS process itself, and what, if any, consequences could there be from inserting such judicial review? Do you believe, for instance, that this sort of judicial review could impact the scientific integrity of the IRIS process?**

   I feel that judicial review is not appropriate, since IRIS is not a regulatory or policy process. IRIS synthesizes scientific evidence. Independent peer review of the science is the most appropriate form of review to assure the quality of the science. The transparency of the process is also enhanced by interagency review, the stakeholder and public comment process. There is an appropriate and important role for the courts in assuring that EPA is meeting their regulatory obligations. Judicial system review of EPA regulatory decisions has proven to be important in assuring that the Agency is complying with the law and meeting its responsibilities in protecting health and the environment. While I would need more specific information on how judicial review might be inserted in the IRIS process before answering, I am concerned that may have a number of unintended and costly consequences. Consequences might include major delays in identifying evaluating risks to human health, deterioration of the scientific excellence, integrity, and independence of IRIS, discouragement or even intimidation of scientists, and increased costs to EPA, the courts, as well as chemical manufacturers and other industries and organizations that may be a party to such judicial review. A key principle of scientific integrity is freedom from outside interference. Judicial review could invite interference throughout the process, from the selection of chemical for assessments to the determination of adverse effects from exposure.

2. **Both the 2008 Government Accountability Office (GAO) report and the 2011 National Academies of Sciences (NAS) report reviewing and suggesting changes to the IRIS program were discussed during the hearing. However, more recent reviews**

conducted by both GAO and the Academies would appear to be more relevant to discussing the current state of the IRIS program.

- **How should the 2008 and 2011 reviews be considered when evaluating the current status of the IRIS program and the more recent GOA and NAS reviews?**

  These reports are outdated and do not reflect the great progress that the IRIS program has made in recent years. While they were important in spurring the positive changes in the program, they no longer reflect the current methods, practices and leadership of the IRIS program. The more recent GAO and NAS reviews are more relevant and both reflect the continued progress and responsiveness of the IRIS program.

- How would you respond to those who suggest that the IRIS program suffers from a deficiency in transparency? What is the process for ensuring transparency at IRIS particularly in the six years since the publication of the 2011 National Academies report?

  Again, this criticism likely reflects outdated reviews rather than the current program. The IRIS assessment process may have one of the most rigorous and open review processes in all of government science. The reports have multiple steps that include agency review, interagency science consultation, public comment, external peer review, revision and then further agency and interagency science discussion. In addition, the program releases preliminary materials during draft development including tables showing the results of pertinent studies. The Program also conducts bimonthly public science meetings providing opportunities for public comment, including web access to meeting to promote greater participation. These improvements were noted in the NAS 2014 review.

3. **What are some of the unforeseen consequences if chemical risk assessments conducted by IRIS were to be driven by industry interests, and more importantly, an industry sponsored chemical assessment was given the same weight and authority as independent scientific studies?**

   IRIS does in fact often consider and include industry sponsored studies that have been published in the peer reviewed literature. The program depends upon he editorial staff of the peer reviewed journal to assure the quality and independence of the research. However, many industry-sponsored critiques of IRIS assessments are prepared by consultants without independent peer review or conflict of interest reporting. Clearly, these reports may introduce bias and financial conflict of interest and may lead to delays in finalizing reports and implementation of public health protections.

4. **EPA's IRIS program evaluates dozens and dozens of studies in its assessments of a chemical's risk to human health and the environment. However, not all studies are the same scientific quality and sometimes studies are authored by individuals that**

have inherent financial or other conflicts-of –interests in the subject they are reviewing. The American Chemistry Council (ACC), for instance, fund a large number of studies that examine the potential dangers of chemicals their member companies actually produce or distribute. Even though the scientists they fund to conduct these studies may be well qualified, how does EPA's IRIS program take into account the potential biases and conflicts of interest in evaluating these studies?

As stated in the previous answer, EPA does consider many peer reviewed published industry-sponsored studies. The IRIS programs evaluates the quality of each study in its systematic review of the evidence base. In addition, the rigorous peer review of each assessment and the agency and public review also assist in identifying weaknesses or potential bias in studies. The quality of the science and the independence of the peer review, not the source of the funding, should be the driver of the assessment of the evidence. That said, it is essential to be diligent in identifying potential conflicts of interest throughout the process.

Appendix II

Additional Material for the Record

DOCUMENTS SUBMITTED BY SUBCOMMITTEE ON ENVIRONMENT CHAIRMAN ANDY BIGGS

U.S. HOUSE OF REPRESENTATIVES
COMMITTEE ON SCIENCE, SPACE, AND TECHNOLOGY
Subcommittee on Environment
Subcommittee on Oversight

Additional Comments for the Record
Chairman Andy Biggs

Examining the Scientific and Operational Integrity of EPA's IRIS Program

1.) The Minority criticized the Majority for failing to invite a witness from the IRIS program itself. This criticism is hypocritical because the Minority had every opportunity to invite one.

2.) The Minority repeatedly suggested in the hearing that the Majority is not committed to defending "good science" at EPA, only industry-backed criticisms. Not only is this claim offensive, but it is also demonstrably untrue. Earlier this year, this Committee and the House of Representatives passed the Science Advisory Board Reform Act and the HONEST Act to ensure EPA is relying on the broadest range of experts and drawing on the most transparent data when making its decisions. If signed into law, these bills will strengthen the quality and integrity of the research and peer review process at EPA, not weaken it.

3.) Finally, I would like to reiterate an admission that Rep. Weber was able to elicit from every witness on the panel: scientists make mistakes. The scientific method and scientific advancement is dependent on continual trial, error, and experimentation. While the hearing witnesses may have been quick to admit to the fallibility of scientists, how often does EPA admit its own science is in error? The historical record would suggest far too infrequently, and as we have learned time and again, the agency is slow to course-correct even after such errors are recognized.

Denka Performance Elastomer LLC
560 Highway 44
LaPlace, LA 70068

June 26, 2017

The Honorable Scott Pruitt
Administrator
U.S. Environmental Protection Agency Headquarters
William Jefferson Clinton Building
1200 Pennsylvania Avenue, N.W.
Mail Code: 1101A
Washington, D.C. 20460

Re: Request to Withdraw and Correct the 2010 IRIS Review of Chloroprene

Dear Administrator Pruitt:

I write on behalf of Denka Performance Elastomer LLC (DPE) in support of the request that the U.S. Environmental Protection Agency (EPA) withdraw and correct its Integrated Risk Information System (IRIS) Toxicological Review of Chloroprene (EPA/635/R-09/010F, 2010) (the 2010 IRIS Review). The errors in the 2010 IRIS Review threaten the very survival of DPE's Neoprene production facility in LaPlace, Louisiana (Facility). In particular, based on those errors and EPA's subsequent flawed determinations concerning the risks caused by Facility emissions, EPA is making stringent air pollution control demands concerning the Facility that are technologically impossible to achieve. EPA must expeditiously apply good science in this matter in order to alleviate the public's undue concerns about the risks associated with this Facility and to prevent further significant damage to DPE's business.

Key conclusions of the 2010 IRIS Review are not based on the best available science or sound scientific practices. First, the 2010 IRIS Review rejected the findings of the strongest available epidemiological study, which concluded that there is no increased risk of cancer in workers exposed to chloroprene (some of the study cohorts actually exhibited a *lower* risk of cancer than the control population). Rather than accepting the overall study conclusions, the 2010 IRIS Review relied on select statistically non-significant comparisons of cancer incidence rates among subgroups of the larger epidemiology study to bolster its classification of chloroprene as "likely to be carcinogenic to humans." Second, the 2010 IRIS Review is flawed because it relied on laboratory animal studies, and then used the results for the most sensitive laboratory animal – female mice – as the basis for a series of overly conservative calculations to develop the human inhalation unit risk (IUR). Contrary to sound scientific practice, the 2010 IRIS Review ignored the known differences between humans and a select strain of female laboratory mice, and relied on results in those female mice to estimate an IUR for humans. Third, the 2010 IRIS Review gives chloroprene, which EPA designates only as a "likely" and not a "known" human carcinogen, the fifth highest IUR estimate of any similar chemical, including known human carcinogens, in the IRIS database. DuPont, the former Facility owner, provided similar information and analysis to EPA in comments on the draft IRIS Review, which comments were rejected in 2010. DPE's Request for Correction and the Ramboll Environ report provide new information and weight-of-evidence review not available in 2010.

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After EPA published the 2010 IRIS Review, the National Academies of Sciences' National Research Council (NRC) recommended major reforms in the IRIS process. Congress has repeatedly instructed EPA to implement the NRC's recommendations, and EPA has advised Congress that it is doing so. The 2010 IRIS Review is plagued with flaws similar to those that gave rise to these reform initiatives, and it is extremely important that the 2010 IRIS Review now be corrected in light of its scientific and procedural deficiencies.

These issues are more fully explained in DPE's Request for Correction and in the supporting toxicological and epidemiological expert review prepared by prominent scientists with the consulting firm of Ramboll Environ: Drs. Kenneth Mundt, Robinan Gentry, and Sonja Sax. Their report is entitled *Basis for Requesting Correction of the U.S. EPA Toxicological Review of Chloroprene*, dated June 2017 ("the Ramboll Environ Report," and attached hereto). The Ramboll Environ Report identifies multiple substantive errors in the 2010 IRIS Review and demonstrates that if chloroprene is to be treated as a possible human carcinogen, the 2010 IRIS Review establishes an IUR that is 156 times too high.

By way of background, DPE acquired the Neoprene Facility from DuPont on November 1, 2015. Neoprene is a synthetic rubber utilized in a wide variety of applications, including laptop sleeves, orthopedic braces, electrical insulation, and automotive fan belts. DPE is the only manufacturer of Neoprene in the United States. The Facility is a commercial mainstay of LaPlace, Louisiana. With an annual payroll of $33 million, DPE directly employs 200-250 people in manufacturing jobs and regularly employs between 125 and 150 contractors. DPE also has created 16 new corporate jobs. Additionally, DPE is investing and upgrading the Facility, including taking new measures to reduce its environmental footprint and improve its productivity and competitiveness.

The base feedstock for Neoprene is chloroprene. The Facility's air permits authorize it to emit chloroprene, and the Facility operates in compliance with those permit limits. However, shortly after DPE's acquisition of the Facility, on December 17, 2015, EPA publicly released its 2011 National Air Toxics Assessment (NATA), which identified the Facility as creating the greatest offsite risk of cancer of any manufacturing facility in the United States. The NATA findings concerning the Facility are based on the scientifically unwarranted and outdated 2010 IRIS Review and the emission profile of the Facility.

Following the public release of the NATA, EPA and the Louisiana Department of Environmental Quality (LDEQ) pressed DPE to reduce emissions to achieve an extraordinarily miniscule ambient air target concentration of 0.2 $\mu g/m^3$ for chloroprene on an annual average basis (which is intended to reflect a 100 in 1,000,000 rate of potential excess cancers in a population exposed to such concentrations continuously for 70 years). The 0.2 $\mu g/m^3$ target is based on a risk assessment that applied the erroneous and scientifically unsubstantiated IUR from the 2010 IRIS Review, and the target reflects more than a four thousand-fold reduction in the applicable Louisiana 8-hour ambient standard for chloroprene. Ramboll Environ's expert scientific opinion is that the appropriate risk-based ambient target should be 156 times larger or 31.2 $\mu g/m^3$. There is no agency rule or even proposed rule requiring the attainment of the 0.2 $\mu g/m^3$ target, yet EPA has advised DPE, LDEQ, and the public that 0.2 $\mu g/m^3$ is the appropriate target.

As a result of the flawed science embodied in the 2010 IRIS Review, and as a result of the NATA findings and the Facility's emission profile, DPE has suffered extraordinary hardship in a number of ways.

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First, despite DPE's concerns about the science behind the 2010 IRIS Review, DPE is currently spending more than $18 million on new pollution controls. On January 6, 2017, DPE entered into an Administrative Order on Consent with LDEQ to reduce chloroprene emissions by approximately 85% below the level of the Facility's 2014 emissions. DPE estimates that the capital cost of these emission reduction devices is approximately $18 million, and the devices will cost hundreds of thousands of dollars per year to operate. Even though DPE is installing the most advanced air pollution controls available, it will still not be able to meet the stringent 0.2 $\mu g/m^3$ target.

Second, because the 2010 IRIS Review is flawed, EPA's very public announcements arising out of that Review and the NATA have created unnecessary public alarm. For example, after issuing the NATA, EPA created a public webpage specifically addressing DPE's chloroprene emissions.[1] Moreover, environmental activists and plaintiffs' lawyers have had numerous meetings in the community about DPE, all based on the faulty assumption that 0.2 $\mu g/m^3$ is the "safe" level for chloroprene. Further, a local citizen's group has formed and has been handing out misleading flyers and protesting near DPE's Facility. The erroneous IUR in the 2010 IRIS Review and the resulting NATA findings have caused DPE enormous reputational damage.

Third, as a result of the NATA findings, EPA Region 6 asked the National Environmental Investigations Center (NEIC) to investigate the regulatory compliance status of the Facility. NEIC sent a team of inspectors to the Facility from June 6-10, 2016, approximately seven months after DPE's acquisition. To be clear, DPE fully respects the important function of the EPA in enforcing environmental requirements. It is simply a fact, however, that as a result of the erroneous IUR and the NATA findings, EPA has initiated an enforcement proceeding against DPE and has devoted an extraordinary amount of resources from the Department of Justice, EPA headquarters, EPA Region 6, and NEIC to developing and pursuing the issues in the NEIC report.

Finally, since acquiring the Facility in November of 2015, DPE's relatively small management team has been buffeted by continuous environmental regulatory demands resulting from the erroneous IUR and the NATA findings. In addition to Facility operation, DPE staff has been in non-stop meetings and negotiations with EPA and LDEQ. DPE's legal and consulting expenses have been enormous, in the millions of dollars. Underlying all of these expenses and burdens on DPE is the erroneous IUR in the 2010 IRIS Review, as applied in the NATA risk assessment.

DPE needs EPA's assistance in the expeditious application of good science to this matter. In meetings with EPA in 2016 concerning the need to correct the 2010 IRIS Review, EPA officials advised DPE that EPA's "queue is full". DPE respectfully requests that EPA review the science underlying the 2010 IRIS Review, withdraw the erroneous IUR, and develop a more accurate toxicological review of chloroprene. We are confident that the Ramboll Environ Report will lead you to these conclusions. Without

[1] *See* https://www.epa.gov/la/laplace-louisiana-background-information.

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this relief, it is uncertain whether DPE will be able to reduce emissions sufficiently to satisfy agency demands, or even continue operation.

Sincerely,

Koki Tabuchi
President and Chief Executive Officer
Denka Performance Elastomer LLC

DOCUMENTS SUBMITTED BY SUBCOMMITTEE ON ENVIRONMENT RANKING MEMBER SUZANNE BONAMIC

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

September 1, 2017

EPA-SAB-17-008

The Honorable E. Scott Pruitt
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, NW
Washington, D.C. 20460

Subject: Science Advisory Board comments on EPA's response to recommendations on the Integrated Risk Information System

Dear Administrator Pruitt:

The EPA Chartered Science Advisory Board (SAB) met on August 29-30, 2017 and, as part of the meeting's agenda, received an update on the restructuring of the Integrated Risk Information System (IRIS). The Board was particularly impressed and pleased with the rapid progress that the Agency has made in responding to recommendations from the National Research Council of the National Academies of Sciences (NAS) and the SAB, with particularly notable improvements in the program over the past year. The SAB members in attendance voted unanimously that I communicate to you their enthusiasm for the IRIS program's progress.

As you may know, the NAS criticized several aspects of the IRIS program in their 2011 review of the formaldehyde assessment, recommending significant changes designed to make IRIS assessments more systematic and transparent.[1] The NAS recommended that the program establish clearer guidelines for study selection, standardize the presentation of studies, use clear weight-of-evidence guidelines, better describe and justify assumptions to determine points of departure, explain modeling processes used to develop risk estimates, and better document the conclusions and estimation of toxicity values. In its 2014 report, the NAS commended EPA for significant progress toward implementing the recommendations of the 2011 report, although there remained additional room for improvement.[2]

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[1] National Research Council. 2011. Review of the Environmental Protection Agency's Draft IRIS Assessment of Formaldehyde. Washington, DC: The National Academies Press. https://doi.org/10.17226/13142.
[2] National Research Council. 2014. Review of EPA's Integrated Risk Information System (IRIS) Process. Washington, DC: The National Academies Press. https://doi.org/10.17226/18764.

The SAB has observed significant enhancements in the IRIS program over the past few years, with impactful changes over the past year, and marked progress over the past six months. The changes are so extensive and positive that they constitute a virtual reinvention of IRIS. For example, it is now standard practice for the program to engage stakeholders in an early scoping and problem formulation phase, thereby allowing stakeholders to provide important input at the very beginning of the process. The program has fully adopted the principles of systematic review, and incorporated automation and publicly available software platforms to modernize the process. Finally, the IRIS documents are now more modular and structured to enhance transparency and readability.

The SAB notes that no other federal entity performs the IRIS functions, and that IRIS helps ensure consistency in chemical assessments within the Agency and across the federal government. IRIS serves the needs of regions, states and tribes, who often lack the ability to perform their own chemical risk assessments. IRIS is also well-positioned to incorporate new evidence streams such as cell-based screening and computational methods into risk assessment, which will be a major advancement over the coming years. The Board commends the Agency for making such significant improvements over a short period of time. We are optimistic that the restructured IRIS program will strengthen the scientific foundations of risk assessment and protect the health and safety of the American public.

Sincerely,

/s/

Dr. Peter S. Thorne, Chair
Science Advisory Board

Enclosure
(1) Roster of SAB Members

NOTICE

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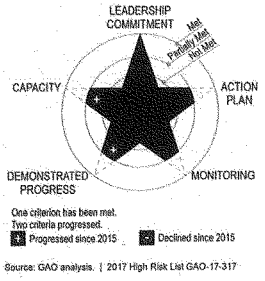
Transforming EPA's Process for Assessing and Controlling Toxic Chemicals

Why Area Is High Risk

The Environmental Protection Agency's (EPA) ability to effectively implement its mission of protecting public health and the environment is critically dependent on assessing the risks posed by chemicals in a credible and timely manner. Such assessments are the cornerstone of scientifically sound environmental decisions, policies, and regulations under a variety of statutes, such as the Safe Drinking Water Act, the Toxic Substances Control Act (TSCA), and the Clean Air Act. EPA conducts assessments of chemicals under its Integrated Risk Information System (IRIS) program. EPA is also authorized under TSCA to obtain information on the risks of chemicals and to control those the agency determines pose an unreasonable risk. Because EPA had not developed sufficient chemical assessment information under these programs to limit exposure to many chemicals that may pose substantial health risks, we added this issue to the High-Risk List in 2009 as a government program in need of broad-based transformation. The Frank R. Lautenberg Chemical Safety for the 21st Century Act, enacted on June 22, 2016, provides EPA with greater authority to address chemical risks, but implementing it will take time.

What GAO Found

Transforming EPA's Processes for Assessing and Controlling Toxic Chemicals



Source: GAO analysis. | 2017 High Risk List GAO-17-317

EPA has again met the criteria for leadership commitment, and its former administrator and top leadership publicly stated their focus on improving the IRIS program and implementing the 2016 TSCA reform legislation through its TSCA program. The agency has begun to align people and resources to address the current and future workload of these programs. For the IRIS program, EPA has partially met the criteria for capacity, an improvement over its previous rating, in part because it issued an IRIS Multi-Year Agenda in December 2015 that focused on the need for IRIS assessments over the next few years. EPA has again not met the criteria for capacity for its TSCA program, and with new TSCA authority, it is unclear if EPA has the people and resources to implement the new law. Overall, EPA needs to continue to determine for both the IRIS and TSCA programs if it has adequate capacity to resolve this high-risk area. EPA needs to work with Congress to ensure that the resources dedicated to IRIS and TSCA activities are sufficient to maintain a viable IRIS database of chemical assessments, and effectively implement TSCA reform activities. EPA has partially met the criteria for having a corrective action plan by issuing an IRIS Multi-Year Agenda. EPA has also partially met the criteria for having a corrective action plan by increasing its efforts to obtain chemical toxicity and exposure data, initiating chemical risk assessments, and reviewing certain new uses of chemicals, but it is too early to tell whether these actions will reduce chemical risks. EPA needs

to continue to implement the TSCA reform legislation and define how it will implement corrective actions to assess and control toxic chemicals.

EPA has now met the criteria for monitoring the IRIS program by finalizing the IRIS Multi-Year Agenda and other actions, including continuing to submit IRIS assessments for independent review to entities with scientific and technical credibility. EPA has not met the criteria for monitoring the TSCA program; to help ensure that the resources dedicated to TSCA are sufficient for effectively implementing the new law, EPA needs to institute a program to monitor and independently validate the effectiveness and sustainability of its initiative to use the new TSCA authorities. For the IRIS program, EPA has now partially met the criteria for demonstrated progress by, among other things, issuing five IRIS assessments since fiscal year 2015—as of January 19, 2017—and making three assessments available for public comment in fiscal year 2016 in preparation for an external peer review meeting associated with that particular assessment. For the TSCA program, EPA has not met the criteria for demonstrated progress. Both the IRIS and TSCA programs need to continue to implement corrective actions to resolve this complex high-risk area.

Passing the Frank R. Lautenberg Chemical Safety for the 21st Century Act may facilitate EPA's effort to improve its processes for assessing and controlling toxic chemicals in the years ahead. The new law provides EPA with greater authority and the ability to take actions that could help EPA implement its mission of protecting human health and the environment. Continued leadership commitment from EPA officials and Congress will be needed to fully implement reforms. Additional work will also be needed to issue a workload analysis to demonstrate capacity, complete a corrective action plan, and demonstrate progress implementing the new legislation.

What Remains to Be Done

Integrated Risk Information System

- We recommended that EPA periodically assess the level of resources that should be dedicated to the Integrated Risk Information System (IRIS) program to meet user needs and maintain a viable database.[1]

[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).

EPA determined the types of IRIS assessments to conduct, based on the needs of EPA's Program Offices and other users, as reported in the IRIS Multi-Year Agenda and in deliberative documents provided to us in October 2016. However, EPA has not established a schedule for regularly revisiting its assessment of resource needs to ensure that priorities are consistent with user needs over time.

- We recommended two actions about EPA's time frames for IRIS assessments.[2] First, we recommended that EPA assess the feasibility and appropriateness of the established time frames for each step in the IRIS assessment process, including whether different time frames should be established for different types of IRIS assessments. Second, should different time frames be necessary, we recommended that EPA establish a written policy that clearly describes the applicability of the time frames for each type of IRIS assessment to provide greater predictability to stakeholders. In July 2013, EPA issued what the agency described as enhancements to the IRIS process to address, in part, these priority recommendations. EPA developed two sets of timelines for the IRIS assessment process and provided us with details about them and its online chemical information tracking system; however, EPA needs to determine whether different time frames should be established.
- We recommended three actions encouraging transparency about the status of planned and ongoing IRIS assessments.[3] First, we recommended that EPA indicate in published IRIS agendas which chemicals it is actively assessing and when it plans to start assessments of the other listed chemicals. Second, we recommended that EPA update the IRIS Substance Assessment Tracking System (IRISTrack) including projected and actual start dates and other information, and to keep this information current. Third, we recommended that EPA publish the IRIS agenda in the Federal Register on an annual basis. In October 2016, EPA officials told us that they believed they had met the intent of these recommendations by publishing an IRIS Multi-Year Agenda in December 2015. However, EPA still needs to provide current and accurate information on chemicals that the agency plans to assess through the IRIS program for IRIS users on an annual basis. The Multi-Year Agenda does not identify projected start dates for new assessments, and

[2]GAO, *Chemical Assessments: Challenges Remain with EPA's Integrated Risk Information System Program,* GAO-12-42 (Washington, D.C.: Dec. 9, 2011).

[3]GAO-12-42.

therefore is not ensuring that current and accurate information on chemicals that EPA plans to assess through IRIS is available to IRIS users. Using the Federal Register to communicate these plans offers greater transparency to the public about the IRIS process than other forms of communication.

- We recommended that EPA develop a strategy to address the needs of its Program Offices and regions when IRIS toxicity assessments are not available.[4] Officials from select EPA offices stated that, in the absence of agency-wide guidance, they used a variety of sources, other than IRIS toxicity assessments to meet their needs, including toxicity information from other EPA offices, or other state or federal agencies. IRIS program officials also stated that there is no agency-wide mechanism for EPA to ensure that chemicals without sufficient scientific data during one nomination period will have such information by subsequent nomination periods. We recognize that the development of EPA's Multi-Year Agenda, issued in December 2015, was a productive effort that EPA told us included an extensive evaluation of user needs. However, the agency does not have a strategy for addressing data gaps or have assurance that its efforts will be sustainable over time. EPA needs to address this priority recommendation by developing: (1) an agency-wide strategy that addresses coordination across EPA offices and with other federal research agencies to help identify and fill data gaps that preclude the agency from conducting IRIS toxicity assessments, and (2) guidance that describes alternative sources of toxicity information and when it would be appropriate to use them when IRIS values are not available, applicable, or current.

Toxic Substances Control Act

After many years of congressional committees considering legislation aimed at reforming the Toxic Substances Control Act (TSCA), in June 2016, Congress passed and the President signed the Frank R. Lautenberg Chemical Safety for the 21st Century Act, which gave EPA greater authority to improve its processes for assessing and controlling toxic chemicals. EPA and Congress need to continue to ensure that the resources dedicated to TSCA activities are sufficient to effectively implement the new law.

[4]GAO, *Chemical Assessments: An Agencywide Strategy May Help EPA Address Unmet Needs for Integrated Risk Information System Assessments*, GAO-13-369 (Washington, D.C.: May 10, 2013).

- We made three priority recommendations to address challenges EPA has faced obtaining toxicity and exposure data, banning or limiting the use of chemicals, and identifying resource needs.[5] First, we recommended that EPA issue a rule to obtain toxicity and exposure data that chemical companies have submitted to the European Chemicals Agency. Second, we recommended that EPA issue a rule to obtain exposure-related data from processors. Third, we recommended that EPA develop strategies for addressing challenges associated with obtaining these data, banning or limiting the use of chemicals, and identifying resource needs. Because EPA has used its authority to limit or ban only five chemicals since TSCA was originally enacted in 1976, in part, because it believed it didn't have enough information, we made these recommendations to address these concerns. The Frank R. Lautenberg Chemical Safety for the 21st Century Act, enacted on June 22, 2016, provides EPA with greater authority to address chemical risks, but implementing it will take time.

With the implementation of the Frank R. Lautenberg Chemical Safety for the 21st Century Act, we believe EPA can make progress on these open recommendations. The act substantially revises TSCA and requires EPA to carry out numerous rulemaking and other activities within the next 2 years. In early 2016, we started a review of the TSCA program. With the passage of TSCA reform, we decided to suspend our review and give EPA time to implement the new law. In October 2016, as part of our recommendation follow-up process, we reviewed information on the new TSCA provisions. EPA officials told us that with new TSCA authority, the agency is better positioned to take action to require chemical companies to report chemical toxicity and exposure data. The new law authorizes EPA to order companies to develop new information relating to a chemical as necessary for prioritization and risk evaluation. This authority may help EPA to gather new information, as necessary, to evaluate hazard and exposure risks. TSCA reform legislation offers promise for EPA implementation of our recommendations and bringing the agency closer to achieving its goal of ensuring the safety of chemicals.

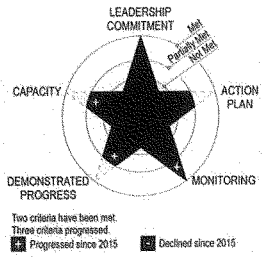
[5]GAO, *Toxic Substances: EPA Has Increased Efforts to Assess and Control Chemicals but Could Strengthen Its Approach*, GAO-13-249 (Washington, D.C.: Mar. 22, 2013).

Additional Details on What GAO Found

IRIS

Transforming EPA's Processes for Assessing and Controlling Toxic Chemicals

EPA's Integrated Risk Information System



Source: GAO analysis. | 2017 High Risk List GAO-17-317

Leadership Commitment

EPA has met the criteria for leadership commitment. In July 2013, the then-EPA Administrator demonstrated leadership commitment to the IRIS program by identifying action on toxics and chemical safety as one of her top seven priorities for the agency. EPA's IRIS database is intended to provide the basic information the agency needs to determine whether it should establish controls to, for example, protect the public from exposure to toxic chemicals in the air, in water, and at hazardous waste sites. "Taking action on toxics and chemical safety" was one of the prior EPA Administrator's priorities for meeting the challenge ahead—a priority that includes the IRIS program. In addition, EPA established an IRIS Executive Review Committee after the 2014 National Research Council report identified the need for quality management of IRIS assessments. According to internal EPA documents, the Executive Review Committee provides a mechanism for the National Center for Environmental Assessment—the center that houses the IRIS program—to endorse IRIS assessments prior to public release, and among other goals, serves to

provide a management-level review for consistency and quality control across assessments. Also, the Office of Research and Development's Deputy Assistant Administrator worked with other EPA Deputy Assistant Administrators in Program Offices, such as the Office of Water and Deputy Regional Administrators, to develop the IRIS Multi-Year Agenda. EPA's top leadership has also demonstrated support for improving the IRIS program by continuing to implement recommendations from us and EPA's Science Advisory Board, and suggestions from the National Academies.

Capacity

EPA has partially met the criteria for capacity, after not meeting the criteria in 2015. In May 2013, we reported that EPA had not recently evaluated the demand for IRIS toxicity assessments with input from users inside and outside EPA. In response to our report, EPA started work on an IRIS Multi-Year Agenda in the summer of 2013 and issued it in December 2015. According to EPA, the purpose of the agenda was to: (1) identify IRIS assessments currently underway and their status; (2) prioritize IRIS assessments that will be initiated over the next few years; and (3) evaluate assessment needs and develop an update process for existing IRIS values. Now that EPA has finalized the agenda, the agency is better informed about how many people and resources to dedicate to the IRIS program.

We have reviewed internal EPA documents on the need for people and resources, and the IRIS program has started to determine if it has the capacity to address the issues it faces. Because of EPA's efforts to develop the Multi-Year Agenda, in October 2016, we closed a priority recommendation we made to EPA in 2008 for the program to determine the types of IRIS assessments to conduct on the basis of the needs of EPA's Program Offices and other users. EPA's actions are a good starting point for EPA's continued process for determining the types of IRIS assessments to conduct on the basis of the needs of EPA's Program Offices and others.

Action Plan

EPA continues to partially meet the criteria for having an action plan to address measures we recommended, and has made progress. For example, by developing the IRIS Multi-Year Agenda and providing us with internal EPA documents, EPA has begun to document how the agency applies its selection criteria for IRIS toxicity assessments, including the circumstances under which Program Offices and Regions may or may not need an IRIS toxicity assessment—a priority recommendation we made in 2013 and closed in October 2016. As of October 2016, EPA officials told us that the agency evaluated user needs for toxicity assessments as

part of its process for developing the Multi-Year Agenda it issued in December 2015. EPA also indicated that the agency used six general criteria to inform the selection of chemicals for assessment or reassessment, and it documented this process in an internal working table as part of its process for developing the agenda. By beginning to document how it applies its IRIS selection criteria, the IRIS program can start to determine a corrective action plan that defines root causes and solutions to move the program forward. EPA needs to be as transparent as possible when applying the selection criteria so that IRIS stakeholders can know how EPA is choosing what assessments to start and why.

Monitoring

EPA has met the criteria for monitoring the IRIS program—after partially meeting the criteria in 2015—by finalizing the IRIS Multi-Year Agenda and other actions. Specifically, the program identified and evaluated demand for the number of IRIS toxicity assessments and resources required to meet users' needs—a priority recommendation we made in 2013 and closed recently based on internal documents provided by EPA. Moreover, EPA presented a plan for how the agency will implement the National Academies' suggestions for improving IRIS assessments in the "roadmap for revision" included in the National Academies' peer review report on the draft formaldehyde assessment. The National Academies' most recent report on the IRIS program, issued in May 2014, independently validates some of the corrective measures the program is implementing. EPA also created the Chemical Assessment Advisory Committee in January 2013, and uses it to provide continuing, consistent review of IRIS assessments and comment on implementing the National Academies' suggestions in specific IRIS assessments—a recommendation we made in December 2011 and closed in the fall of 2016. All of these actions demonstrated EPA's commitment to monitoring the IRIS program.

Demonstrated Progress

EPA has partially met the criteria for demonstrating progress in implementing corrective measures by taking actions, such as releasing the IRIS Multi-Year Agenda that publicly identifies the current and future IRIS assessments. As of January 19, 2017, EPA issued two assessments in fiscal year 2017, two assessments in fiscal year 2016, and one assessment in fiscal year 2015. In addition, EPA made three assessments available for public comment in fiscal year 2016 in preparation for an external peer review meeting associated with that particular assessment.

The IRIS program has also demonstrated progress by establishing Stopping Rules, which, among other things, were implemented to increase flexibility to revise draft assessments as needed after hearing

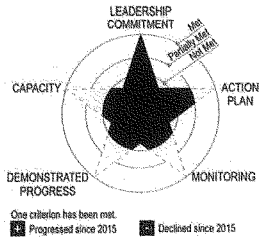
the public's comments prior to peer review. EPA told us that the Stopping Rules also are important to the IRIS process to determine how to include new studies in an assessment without delaying the process or cycling through repeated revisions and re-revisions.

Because of these actions, we closed a 2008 priority recommendation that demonstrated progress in implementing corrective measures. The recommendation called for EPA to conduct IRIS assessments on the basis of peer-reviewed scientific studies available at the time of the assessment, and develop criteria for allowing assessments to be suspended to await the completion of scientific studies only under exceptional circumstances. Although EPA officials told us that the agency has not formally invoked the Stopping Rules in response to a request to delay an assessment to incorporate studies, they told us they apply the rules in their everyday work when deciding whether to include new studies at different points in the IRIS development process. EPA said they would characterize the Stopping Rules as public IRIS policies that are in place to avoid delay for the inclusion of new studies or analysis that they believe would not affect the assessment's conclusions.

TSCA

Transforming EPA's Processes for Assessing and Controlling Toxic Chemicals

Toxic Substances Control Act



Source: GAO analysis. | 2017 High Risk List GAO-17-317

Over the past two decades, we reported that EPA had found much of TSCA difficult to implement—hampering the agency's ability to obtain certain chemical data or place limits on chemicals. For example, EPA has found it difficult to obtain adequate information on toxicity—that is, the degree to which the chemical is harmful or deadly—and exposure levels—the frequency and duration of contact with the chemical. Without this information, it is difficult for EPA to determine whether a chemical poses an unreasonable risk to human health or the environment, and then take any action necessary to regulate such chemicals. The Frank R. Lautenberg Chemical Safety for the 21st Century Act, which reformed TSCA, was enacted on June 22, 2016. The new law provides EPA with greater authority and the ability to take actions that could help EPA implement its mission of protecting human health and the environment.

Leadership Commitment

EPA continues to meet the criteria for leadership commitment because of the former EPA Administrator's explicit support for taking action on toxics,

including TSCA. In addition, the former Administrator and top leadership have expressed support for implementing TSCA reform. For example, the former Administrator said that, as with any major policy reform, this one includes compromises. But the former Administrator noted that the legislation should help EPA's mission to protect public health and the environment.

Capacity

As in 2015, EPA has not met the criteria for capacity because the agency has not yet issued a workload analysis which is needed to determine whether EPA's TSCA program has the capacity—people and resources—to resolve the risk to the program. The TSCA reform legislation requires EPA to report to Congress by December 2016 on its capacity to implement certain aspects of the legislation, including carrying out chemical risk evaluations and issuing rules regulating specific chemicals. In January 2017, EPA issued a report in response to this deadline. The report estimates the costs of carrying out risk evaluations under the TSCA reform legislation and discusses actions underway or planned for increasing EPA's capacity to carry out these evaluations. The report does not, however, contain estimates of EPA's capacity for carrying out risk evaluations or promulgating associated rules. We have previously reported that EPA has found many provisions of TSCA cumbersome and time consuming to implement. It is currently unclear if EPA has the people and resources to implement the new law. We will continue to monitor the program to determine if progress is made and the criteria for capacity are met.

Action Plan

EPA continues to partially meet the criteria for having an action plan. As we reported in 2015, EPA has increased its efforts to obtain chemical toxicity and exposure data, initiate chemical risk assessments, and review certain new uses of chemicals, but it is too early to tell whether these actions will reduce chemical risks. With new TSCA authority, EPA officials stated that the agency is better positioned to take action to require chemical companies to report chemical toxicity and exposure data. Officials also stated that the new law gives the agency additional authorities, including the authority to require companies to develop new information relating to a chemical as necessary for prioritization and risk evaluation. Using both new and previously existing TSCA authorities should enhance the agency's ability to gather new information as necessary to evaluate hazard and exposure risks.

Monitoring

As in 2015, EPA has not met the criteria for monitoring because it is too soon to determine whether EPA's approach to managing chemicals within the new TSCA authorities will position the agency to achieve its goal of

ensuring the safety of chemicals. We will continue to monitor the TSCA program as the agency implements this important legislation.

Demonstrated Progress

As in 2015, EPA has not met the criteria for demonstrating progress, although it has recently begun implementing corrective measures to resolve this high-risk area. For example, the first TSCA reform reporting deadline directed EPA to publish in the Federal Register a list of mercury compounds that will be prohibited from export, not later than 90 days after the date of enactment. That reporting deadline was September 20, 2016; on August 26, 2016, EPA published a list of the mercury compounds that will be prohibited from export effective January 1, 2020. TSCA reform actions required by December 19, 2016, included the following topics and actions: (1) Risk Evaluations: EPA must ensure that risk evaluations are being conducted on 10 chemical substances drawn from the 2014 TSCA Work Plan; (2) Small Business: EPA must review, and potentially revise, its definitions of small businesses for reporting purposes after consulting with the Small Business Administration; and (3) Congressional Report: EPA must submit a report to Congress regarding the agency's capacity to carry out risk evaluations and associated actions.

According to EPA, the promulgation of these rules will better position the agency to increase the rate at which chemicals are evaluated for human and environmental health and safety. As of December 19, 2016, EPA had taken steps to respond to the December deadlines for risk evaluations and small business. Specifically, EPA has announced the first 10 chemicals it will evaluate for potential risks to human health and the environment and published a Federal Register notice on Standards for Small Manufacturers and Processors. In January 2017, EPA took action in response to December deadline 3 by issuing a report: Initial Report to Congress on the EPA's Capacity to Implement Certain Provisions of the Frank R. Lautenberg Chemical Safety for the 21st Century Act. We will continue to monitor EPA as it implements this important piece of chemical legislation and determine if it is satisfying all the criteria for removal from the High-Risk List.

Benefits Achieved by Implementing Our Recommendations

EPA has taken actions to address many of our priority recommendations on chemicals management and Congress has used our work to support legislative deliberations. For example, EPA's efforts, such as developing the IRIS Multi-Year Agenda, addressed a number of our recommendations related to the IRIS program. EPA identified and evaluated demand for the number of IRIS toxicity assessments and resources required to meet users' needs, which was a priority

recommendation we made in 2013 and closed recently based on EPA's actions.

Our work has also supported deliberations by Congress about TSCA and about strengthening EPA's ability to regulate chemicals. For example, as far back as 1994, we reported that Congress should consider setting specific deadlines for reviewing existing chemicals, which the new TSCA legislation would address because it requires EPA to establish a chemical prioritization process, and to initiate risk evaluations of high priority chemicals, among other issues.

Our work since then has addressed a variety of chemical management policy matters for Congress. For example, in 2009, we testified that EPA does not routinely assess the risks of chemicals in commerce, and in 2013, we testified about possible statutory changes to TSCA to give EPA additional authorities to obtain information, and shift more of the burden to chemical companies for demonstrating the safety of their chemicals. Finally, in 2016, Congress passed the Frank R. Lautenberg Chemical Safety for the 21st Century Act, which we found addresses key challenge areas we've identified previously.

GAO Contact

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Related GAO Products

Chemicals Management: Observations on Human Health Risk Assessment and Management by Selected Foreign Programs. GAO-16-111R. Washington, D.C.: October 9, 2015.

Chemical Assessments: Agencies Coordinate Activities, but Additional Action Could Enhance Efforts. GAO-14-763. Washington, D.C.: September 29, 2014.

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Chemical Assessments: An Agencywide Strategy May Help EPA Address Unmet Needs for Integrated Risk Information System Assessments. GAO-13-369. Washington, D.C.: May 10, 2013.

Toxic Substances: EPA Has Increased Efforts to Assess and Control Chemicals but Could Strengthen Its Approach. GAO-13-249. Washington, D.C.: March 22, 2013.

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