EPA Tools and Resources webinar

Integrated Risk Information System (IRIS): Current Assessments and Recent Developments transcript

Speaker: Lisa Matthews

Our presenter today is Gina Perovich, who is the IRIS Program deputy director. Before she starts her presentation, I want to introduce Dr. John Vanderberg who is the director of EPA's Human Health Risk Assessment Research Program, of which IRIS is a part, and John is located in EPA at Research Triangle Park, North Carolina. John, thank you for providing some opening remarks for us today.

[Sound check interruption]

Speaker: John Vanderberg

Thank you very much Lisa for the introduction. Again, I am the National Program Director of EPA's Human Health Risk Assessment Program, which is one of the six national programs we have in the Office of Research and Development to support the various science developments and applications for the Agency as well as our state and local agencies/colleagues. The Human Health Risk Assessment Program has four major components. First off, we develop science methods [and] this is where we look at new systematic review, the development of new dose-response methods, such as benchmark dose-model, which many of you may have used. We're also looking at the interpretation and application of new types of science from new technologies, such as high throughput screening in the risk assessment context, and also the evaluation of the world's literature if you will through our health and environmental research online system. So in addition to developing sort of the science methods, we apply those in essentially three major areas. One of them is in the integrated science assessment for the major of the criteria air pollutants, and those are done here in North Carolina through my division, I am a division director as well. The second area is our provisional peer reviewed toxicity values, which are supporting superfund site managers and for other purposes, as well as essentially supporting community evaluation of potential risks in the environment as well as cumulative risk assessment. The other area of our major sort of product line is the Integrated Risk Information System (IRIS) program and this has been an area of considerable interest and importance to support Agency decisions as well as those again at state and local agencies and other stakeholders around the world. I'm very pleased this afternoon that Gina Perovich, who is the deputy director of the IRIS division will be presenting to you. Gina has been with the IRIS program for three years, and has actually worked in the National Center for Environmental Assessment where the program resides for the last eight years. She has worked with the Office of Research and Development for the past sixteen years, and she is an excellent speaker so I'm looking forward to her comments. So Gina, let me turn it to you.

[Sound check interruption]

Speaker: Gina Perovich

Okay so I'm Gina [and] am the Deputy Director the for IRIS program that is managed out of the IRIS Division out of EPA's National Center for Environmental Assessment. This is located out of EPA's Office of Research and Development.

I am going to take you through some information on the program today, in three parts. The first thing I'm going to do is talk to you a little bit about IRIS, I'll provide you with a little bit of background, and then I'll talk about current updates and process changes. If it's been awhile since you've engaged with the program or picked up an IRIS assessment, things look pretty different. We've made a lot to changes to the program in the last five years, and so I'll go through that and try to orient folks and cover the developments that have occurred. I'll also highlight a few chemicals of interest and just share with you some examples of what the information looks like on the database, and I'll wrap up with a little blurb about current efforts in the program. So I'll go ahead and get us started

IRIS stands for Integrated Risk Information System, and IRIS is the program that provides information on potential adverse health effects that could result from exposure to chemical substances found in the environment. Each IRIS assessment can cover a chemical, or a group of chemicals, or even a complex mixture. IRIS assessments are the preferred source of toxicity information used by the EPA, and they're an important source of toxicity information that are used by state and local health agencies, other federal agencies, and different international health organizations. The toxicity values that EPA provides through these IRIS assessments – well let me back up for one second – the way an IRIS assessment is created is what we do is we search the literature that's out there, the available literature on a chemical, we bring all of that information together, we synthesis that, we analyze that, and then we make some calls about hazard characterization and then we provide some toxicity values. The toxicity values are provided in the form of reference doses for ingestion and reference concentrations for inhalation. Those are levels below which we don't intend – or we don't believe that you will see adverse health effects. Those levels are used by EPA's program and regional offices to set standards and to clean up hazardous waste sites and such. We also provide risk characterization for cancer. We provide hazard characterization, oral slope factors, and inhalation unit risks. The oral slope factors providing information about risk from ingestion and inhalation providing the risks that would come with breathing that chemical over an associated period of time. IRIS is actually a database, and information is posted on the IRIS database in the form of an IRIS summary, and then supporting documents and those documents are called toxicological reviews or chemical assessments. The IRIS database provides qualitative and quantitative information for over 550 substances.

So I'd like to touch base on where IRIS falls in the risk assessment paradigm. So IRIS assessments are chemical assessments/toxicological reviews/hazard assessments, they are not risk assessments. So if you actually look across the risk assessment paradigm, beginning with hazard identification and then ending with risk management [then] IRIS is here towards the left. IRIS provides hazard identification and dose response assessments. This information is then used by program offices, local agencies, state agencies [and] other risk assessors; they combine that with exposure information and then add in decisions concerning risk characterization and risk management. I just want to be clear about what IRIS is and what IRIS does and does not do. We don't address any of the programmatic/political risk considerations/risk management decisions – that's not us – we're providing the science and we're providing the numbers and those are being folded into the decisions by others.

The program has really changed in the last few years, and that is largely due to a review we received from the National Academy of Sciences in 2011. In 2011 we asked the Academies to review our draft formaldehyde IRIS assessment and they did that. In doing so, the NRC provided recommendations for improving the development of all IRIS assessments in general. A couple of those examples are here on this slide. For example, the NRC required a further discussion of the methods of the assessment. They

wanted to hear more about the criteria we used to exclude and include studies in our hazard characterization and evaluation. So remember, we are synthesizing this great body of literature and then we're coming up with conclusions and what they thought was that we could better articulate how we made those decisions and what criteria we used. They asked us to use some more standardized evidence tables to provide the information. These assessments were traditionally very large, some of the big ones could be 700 to 1,000 pages - so a lot to get through. A couple of the things the Academy focused on were streamlining issues, so using standardized evidence tables and rigorously editing the documents to reduce the volume of text and reduce redundancies. We employed some uniformed approaches to evaluate strengths and weaknesses of the study, and we did everything that we could to summarize all these data findings in tables to make this more accessible to the reader instead of wading through this 1,000-page document. It's important to note that since 2011 IRIS has been moving. The NRC did not tell EPA to stop developing IRIS assessments or to stop this program until all of these changes were fully implemented, so what we've done is implemented these along the way without slowing down our progress – or attempting [to] not slow down our progress – some of this inevitable lead us having to stop and focus on a few things.

So our new document structure is very different now. The assessments are broken down into two discrete parts, we have hazard identification and the dose response analysis. We have made them more concise, they are rigorously edited to reduce redundancy. There's a preamble included now in the front of the IRIS assessment that really explains how the assessment is crafted [and] what considerations are looked at, and identifies any issues that are pertinent to that particular assessment. There's an executive summary now that's a lot more user friendly and readable than the old IRIS summary that provides the major conclusions and key issues upfront. We did incorporate the use of evidence tables and exposure-response arrays. We added text that focuses more on analysis and synthesis of all of the evidence, rather than a step-by-step litany of study descriptions, and we standardized our weight of evidence characterization for all health effects.

We further enhanced the IRIS process in 2013, coming on the heels of that NRC review, and we had a couple of goals in doing so. One was to improve the fundamental science in our assessments. We did that by implementing systematic review, so we have now a structured systematic way that we look at and evaluate literature for inclusion or exclusion into an assessment. We also strengthened our peer review process at the same time. IRIS assessments were historically reviewed by different bodies including the NRC and EPA's own Scientific Advisory Board (SAB), which is housed by EPA. But we also had some contractor led peer review, so what was happening was that we were getting a lot of different advice from a lot of different groups, which was not helping with consistency across the program. So we had put in place a chemical assessment advisory committee, called the CAAC, which is under EPA's SAB or science advisory board. This is a separate panel that is dedicated specifically to reviewing IRIS assessments, so this is really nice, so we have a standing panel of folks that we go back to over and over again to get input on IRIS assessments. They do the peer review, and then that panel is augmented with different expertise as needed. That is a very hands-off thing to learn a little bit more about the peer review process. The SAB runs their own website, talks about their process, takes public comment [and] it's pretty separated from what we do here in the program and necessarily so, so we can keep that arm's length relationship and that space between us and our peer reviewers. We also wanted to increase capacity and productivity to better meet stakeholder needs. These assessments are large, they are complex – extremely complex, and they take a long time to complete. One of the reasons that these

assessments are viewed as the gold standard for risk information or toxicity information is because they are so thoroughly done and they go through so many different levels of review – both within the Agency, throughout the federal community, high level peer reviews – and this all takes time. We are aware that we are not putting out assessments quickly enough. We get tons of requests for chemicals that need to be assessed and we want to increase capacity and productivity to better meet stakeholders' needs. We also wanted to increase transparency, so any issues that come up in the assessment, any of the controversial science issues or calls that need to be made are identified and debated early, so not later in the process when we're trying to finalize the assessment, but bringing those things out in the beginning and having those debates early and often. We also wanted to increase stakeholder engagement.

This is a diagram that outlines the IRIS process, and it's a seven step process. This blue in the background here is the original process, the underlying process, and it starts with scoping and problem formation, it goes to draft development. Our assessments then undergo an Agency review step, and we'll revise that based on Agency review comments, interagency reviews – so other federal agencies and the Executive Office of the President. We then release the document for public comment, peer review, revise the assessment post-peer review, have a final check-in with our agency and interagency partners, and post the assessment – and that [process] has pretty much stood. When we referred to enhancements and kind of tweaking this process, we increased stakeholder engagement, which are those pink boxes here (on slide), we initiated early public science meetings on problem formulation and key issues – we didn't used to do that – so now we will hold a public meeting here to discuss key issues with the public stakeholders [and] the scientific community and to identify those early issues before we do draft development. Along the way for draft development now, we will be releasing several pieces over the web and asking for comments there. We will be releasing protocols, literature searches, study evaluation criteria – things that talk about how we plan to do the assessment and getting input there before we go [on] with the rest of the process. The other change that's here is separating out public comment from external peer review. If you were to look at an older IRIS process slide, we realized the assessment for public comment and peer review at the same time – we don't do that anymore. We now release it for public comment, we have another public meeting in here, and we discuss the public comments and revise the document prior to going to peer review. So there are many many many places now, more than there were, to engage with us as we craft assessments. Here under draft development, we have made some changes too. This is where we apply the principles of systemic review now to identify and evaluate the studies, to integrate the evidence and derive our toxicity values. This is a more structured [and] repeatable process than it was.

So the public science meetings I mentioned – we'd like to have the scientific community and the public participate in discussions of draft materials that we provide for IRIS assessments under development. It's important to gain scientific perspectives at this meeting, and we do that, and then we consider these perspectives as these assessments are in progress. We hold four such meetings in 2016, and we plan to hold about four in 2017. They are held about once a quarter, and the assessments that we'll be covering in 2016 are still to be determined. These are meetings that are kind of on the books in a regular/semi-regular sort of way, and when we get closer to that – about 90 days out – we will announce more details and exactly which chemicals we will be covering at those meetings.

So how else can you learn about IRIS – stakeholder notification and participation is again something I mentioned we tried to increase in the 2013 enhancements. There are many ways that we notify folks

who are interested in IRIS about what's going on with the program. We have a Human Health Risk Assessment Research Program monthly bulletins that you can sign up for that goes out and highlights activities within the program. Again, that's HHRA – the program that John talked about, so you'll get more updates than just the IRIS program. There's one that's specific to IRIS, so there's an IRIS email bulletin that regularly update stakeholders about opportunities to engage with the program, [it] announces newly released drafts and assessments. We have an IRIS website that provides all of this information, we announce our public comment periods in the Federal Register, and there are still more opportunities for folks to participate. In addition to the steps that I pointed out and the formal public comment periods and the formal public meetings, you can submit comments and materials to the docket at any time, you can attend and participate in the public meetings and scientific workshops. Periodically, if we're going to put on scientific workshops, we will ask for comments on potential topics and speakers for those workshops, [and] we do that for the chemical specific ones as well. You can also nominate peer reviewers and comment and engage through the SAB's peer review process, and they post that information on their website when we release a chemical to them and they kind of handle the process from there. There are ways for you to get involved through the peer review process as well.

Some of what we're providing now in the enhanced IRIS is the new scientific content. Traditionally, this is the same risk assessment paradigm that I mentioned before, highlighting that IRIS was over here on this side. Traditionally, we've provided a wide variety of information across many chapters, and now we have divided it specifically into hazard identification and dose response assessment. Some of what we are providing that's new is organ and system specific RfDs and RfCs. As I explained before about the reference doses and the toxicity values, old IRIS assessments would just provide one value - an overall value based on an endpoint for an assessment. Now what we're doing for the effects that warrant it, [is that] we're providing effects specific or system specific values. This is helpful, we heard this from our stakeholders, and from regions and local risk assessors – this is helpful for people who might be dealing with mixtures or cumulative risk assessments, where you want to compare apples and apples [and] you maybe want to look across all of the reproductive effects of multiple chemicals at one site – so having an overall RfD that's based on development might not help you – you might be really interested in what the value looks like for reproductive. To the extent that's possible, we do that now.

As I mentioned we are implementing systematic review [so] just a little more about the structure and what that looks like, and where that is in here. Identifying pertinent studies, evaluating study methods and quality, integrating the evidence, selecting studies for deriving toxicity values is now all planned out, thought out, and documented in a very systematic way. This isn't really something that we didn't do before, [but] it is just a formal way to document, make those decisions, make it reproducible, and communicate that in a very transparent way [and] not just relying on best professional judgment and the types of descriptions that we used to use. It is a way to really kind of articulate that to the public.

I would like to take a few minutes and walk you through a couple of chemicals. Sometimes when I give talks about IRIS I have people ask me to cover specific chemicals. These are probably the ones that I get the most questions on, the top two or three, and then I've included this one as one that we're currently working on. I just wanted to show you some of the information you can find this information in our database. Trichloroethylene or (TCE) is a chemical that we get a lot of inquiries about. It is a stable, colorless liquid with a chloroform-like odor. It was traditionally used as a dry cleaning chemical but was replaced in the 1950s with another chemical tetrachloroethylene as you'll see in another slide, called PERC. But after it was replaced as a dry cleaning chemical then it was primarily used as a degreasing

agent. It's found in adhesives, paint-stripping materials, and human exposure to this chemical occurs through its widespread presence in ambient air, indoor air, soil and ground water. It's also implicated in intrusion and it is found at something like 1,700 superfund sites.

When you go into the IRIS database and look at the IRIS assessment for Trichloroethylene, you can find the following information – although I went and pulled it out for you – you can find the following information: this assessment was finalized in 2011. We had enough data to evaluate both cancer and effects other than cancer and TCE ended up being characterized as "carcinogenic to humans" by all routes of exposure. These are the values that I've pulled out there, and this is the type of thing that you will see.

PERC was another major assessment that we completed in recent years. Again, as I mentioned this one replaced TCE as a dry cleaning chemical. It's been detected in ground water, surface water, air, food [and] human breast milk. Humans are primarily exposed via inhalation or ingestion of contaminated water. This assessment was finalized in 2012. We determined that PERC was likely to be carcinogenic to humans by all routes of exposure, and we were able to provide information on both cancer and non-cancer effects.

Dioxin is up here. Dioxin is something that we get asked about a lot, and dioxins are fairly ubiquitous coming from anything from industrial sources all the way to natural sources such as forest fires. Humans are primarily exposed via ingestion of contaminated food. We finalized an IRIS assessment for dioxin in 2012. Only non-cancer effects were evaluated though – sometimes we will do that if we don't have enough data or [if] we complete one part and want to move that along quickly then we'll move that part out and move on to assessing the other part later. Our intention was actually to do the cancer assessment for dioxin, and we had announced that on our agenda. Unfortunately, though we are not doing that now, so if you looked at our most recent multi-year agenda – and I'll talk about in a minute, the need for an assessment of dioxin carcinogenicity was revaluated [and] we actually decided to focus on other chemical assessment needs that were identified by EPA program and regional offices to be a higher priority than a dioxin cancer assessment at this time. So we adapt to what's needed as we go.

Naphthalene is a crystalline solid. It's used in moth-balls and toilet deodorant blocks [are] kind of the most common thing I think about when I think about naphthalene. It can be found in coal tar, it's a byproduct of steel, and it's used in the production of certain plastics. Humans are exposed to it primarily through inhalation. This chemical was actually already assessed by IRIS in 1998, but now we're currently reassessing the cancer and non-cancer health effects resulting from exposure to this chemical. In 1998 EPA was unable to determine the carcinogenic potential of naphthalene at that time, so we're relooking at this now. What we did [is] we underwent a problem formulation and scoping step, we released materials for that in 2014 and what we're doing now is trying to put together protocols that will outline the plans for systemic review, study quality evaluation, data extraction, literature searches, everything that we plan to do to go ahead and initiate the assessments. It's taken a little while because we kind of had to figure it out after the Academy had recommended that we do that.

So that's just an example of some of the chemicals and the types of information you will find in the database. There are a few other developments that I will touch on. You heard me mention the multi-year agenda. This is a list of chemicals that IRIS is working on. Traditionally, we had an agenda that would be set by putting something out on the federal register notice, calling for submissions, we take submissions from the public, federal agencies [and] our own agency. The last time that was done was in

2012, and a large IRIS agenda was put together through that very public process. There were like 70 chemicals that ended up on the IRIS agenda and they weren't really vetted in any particular way – we just took the nominations and made the agenda. It was quickly evident that you can't work on 70 chemicals at once – at least we can't [since] these are very resource intensive. So what we did was we set about trying to reprioritize that agenda. We surveyed the program and regional offices for their assessment needs; we evaluated the resources we would need to put towards each assessment according to scientific discipline and level of complexity; we discussed with senior officials in EPA how we could meet the highest priority needs of their office and their region. Then we re-released the new multi-year agenda in 2015. That can be found on the website at this address.

I'm going to talk to you a little about what's in there. Fifteen chemicals came out of that exercise as having the highest priority, and they were placed into 3 groups based on that – based on what we heard from our program offices. Those will be started over the next few years as resources allow, with the exception of nitrate, nitrite, which were added to the 2015 agenda that weren't in 2012 and PFOS PFAS, all of the other high priority assessments were already on the 2012 IRIS agenda. So it's really truly best described as kind of reprioritizing that 2012 list based on what we can do and what the Agency needs right now. Of course, at the same time, we released the multi-year agendas when we made our announcement about not doing the dioxin cancer assessment – it was just not as a high a priority as some of the other things the Agency needed from us.

This is what the bottom line of the multi-year agenda looks like, so if you want to know what IRIS top priorities are for the coming years, this is it. Based on the feedback that I described - that we solicited, we narrowed it down to 15 chemicals of the highest priority and they are in 3 groups. Group 1, Group 2, Group 3 in order of top priority here, medium, low. But within a group, that's not ranked [so] it's not like Manganese is definitely something that we will start before Vanadium or anything like that. This group is of equal importance to the Agency, but based on what resources we have in the IRIS program and other considerations, we will figure out which ones we can start in here, and same thing goes for this group and this group. So this is where IRIS is headed over the next few years to support the program.

Lastly, I will touch upon efforts that we have ongoing to keep IRIS up-to-date. We are developing a process for updating and maintaining finalized IRIS assessments that would not warrant a full reassessment through this IRIS process. This is one of the ways that we are looking at trying to increase productivity and trying to deliver more information that people need more quickly. Right now, for something like naphthalene that was assessed back in 1998 that I mentioned – we're doing a full reassessment of naphthalene. There are some chemicals that we – like other people – that we would like not to have to do a full reassessment for. Perhaps you go reexamine something that was already reassessed and posted, and you find that only a few new critical studies had come out since the chemical was last assessed. We would like to be able to focus on those studies, and how those studies affect the assessment and maybe issue an update or an appendix. In some cases, we may find that there's not a lot of new data that affects the chemical in which case we could then stamp that chemical reevaluated or something in 2016, letting folks know that that value is still current even if it was assessed 10 years ago. We're calling this the update program, and we're trying to figure out how to make that work, what the best way is to do that, and whether or not we can update pieces of assessments or specific endpoints where there's data, when you don't need to redo a whole reassessment without going through a full blown IRIS process – but that's ongoing. We are also developing a process for archiving pesticide assessments on IRIS that have been more recently

evaluated by EPA's Pesticide Program. We're aware that some of the values on IRIS are out-of-date. We haven't reassessed them and wouldn't go back and reassess those pesticides, but yet we know that pesticide programs have maybe put out their own assessments. We are trying to remove some of those older values from the database without wreaking havoc. That's also something that's ongoing right now. These efforts are really to try to keep that database up-to-date, as I've mentioned there are 550 chemicals on there and some were initially assessed a long time ago.

To wrap up, a little bit of a synopsis on the new enhanced IRIS. We've taken a lot of steps over the last 5 years to really improve the science. We've implemented systematic review, we've provided individual toxicity values for different endpoints and outcomes, [and] we've strengthened our peer review process. We've increased transparency, our assessments are clearer [and] more concise, we've eliminated a lot of redundancy, and we've made the information easier to find and easier to communicate. We've markedly increased our opportunities for public engagement. We hope that all of this will lead to increased productivity in the ways that I've kind of described as we went through. I'd like to mention in closing that IRIS will continue to evolve as we receive public input and peer review advice, and we're dedicated to meeting the needs of our stakeholders.

This is my contact information. Vincent Cogliano is the Director of the IRIS Program [and] I am the Deputy Director. I provided some website information for folks. I hope that people found this helpful, and I'll be happy to answer any questions that folks might have.