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FIFRA SCIENTIFIC ADVISORY PANEL (SAP)

OPEN MEETING

DRAFT PRELIMINARY PROBABILISTIC EXPOSURE AND RISK ASSESSMENT FOR CHILDREN WHO CONTACT CCA-TREATED WOOD ON PLAYSETS AND DECKS AND CCA-CONTAINING SOIL AROUND THESE STRUCTURES

December 3, 2003

[8:33 a.m.]

Sheraton Crystal City Hotel
1800 Jefferson Davis Highway
Arlington, Virginia 22202

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P R O C E D I N G S

DR. HEERINGA: Good morning and welcome to the meeting of the FIFRA Scientific Advisory Panel Open on the Draft Preliminary Probabilistic Exposure and Risk Assessment for Children who Contact CCA-Treated Wood on Playsets and Decks and CCA-Containing Soil Around these Structures. A long title.

I'm Steven Herringa, the session chair. I'm a research scientist at the Institute for Social Research at the University of Michigan. We have individuals here to respond to questions of specific scientific interest. And so I would like to go around the table at this point and have the members of the science advisory Panel introduce themselves and give a little background. Dr. Matsumura.

DR. MATSUMURA: Good morning my name is Fumio Matsumura. I'm a professor of environmental toxicology and director of the environmental health sciences. My area of expertise is toxicology. I'm interested in the pesticides and dioxins.

DR. THRALL: Mary Anna Thrall. I'm a professor of veterinary pathology at Colorado State University.

DR. KISSEL: John Kissel, University of Washington, Department of Environmental and Occupational Health Sciences. I do human exposure assessment.

DR. RIVIERE: Jim Riviere. I'm a distinguished professor of Pharmacology and Director of a Chemical Toxicology Research Center, North Carolina State University. Areas, pharmacokinetics and dermal absorption.

DR. ADGATE: John Adgate. University of Minnesota School of Public Health, exposure and risk analysis.

DR. FREEMAN: Natalie Freeman, Robert Wood Johnson Medical School, childrens activity patterns and exposure to metals and pesticides.

DR. BATES: Michael Bates. I'm an epidemiologist in the school of public health at the University of California at Berkeley.

DR. STEINBERG: JJ Steinberg, Albert Einstein College of Medicine. I'm professor there, director of the autopsy service and in environmental toxicology.

DR. STYBLO: Miroslav Styblo. I'm a research associate professor of pediatrics and nutrition at the University of North Carolina, Chapel Hill. And my expertise is in the area of arsenic metabolism and molecule effects.

DR. CHOU: Good morning. I'm Selene Jen Chou from the Agency for Toxic Substances and Disease Registry. I'm the chemical manager for the tox profile for arsenic. And I'm also interested in human health risk assessment.

DR. WAUCHOPE: I'm Don Wauchope. I'm with the U.S. Department of Agriculture, Ag Research Service in Tifton, Georgia. I do research on environmental impact of pesticides and simulation modeling of pesticides.

DR. LEBOW: Stan Lebow. Forest Service, Forest Products Laboratory out of Madison, Wisconsin. Research on wood preservative evaluation and environmental impacts.

DR. STILWELL: Dave Stilwell at the Connecticut Agricultural Experiment Station. And I've done work on dislodgeable residues on CCA wood and arsenic around structures built using CCA wood.

DR. REED: I'm Nu-May Ruby Reed. Staff Toxicologist, Pesticide Regulation, California EPA. Id do pesticide research.

DR. RYAN: My name is Barry Ryan. I'm a professor in environmental and occupational health at Emory University. And my expertise is in multimedia environmental exposure assessment.

DR. FRANCIS: I'm Marcie Francis. And I'm a senior research scientist at Battelle specializing in human exposure assessment and exposure modeling.

DR. HATTIS: I'm Dale Hattis with Clark University. I'm a research professor. And I'm a risk assessment modeler with primary specialization in issues of uncertainty and variability and differences between children and adults in susceptibility.

DR. PORTIER: I'm Ken Portier, Associate Professor of Statistics at the University of Florida Institute of Food and Agricultural Sciences. My expertise is in applied statistics, environmental sampling and statistical and PRA.

DR. MCDONALD: Peter Macdonald from McMaster University in Canada, Professor of Mathematics and Statistics. I have general expertise in applied statistics.

DR. HEERINGA: Thank you very much. And again, I think as you have heard now, we have a considerable amount of expertise combined here on the science advisory Panel. And in addition we'll be hearing from experts in a number of different areas, both within the Agency and through public comments from experts from industry and also from the general public and private sector. So I think for the next three days, there will be plenty of expertise in this room.

Our job here is to get at scientific discussions

related to the issues of risk exposure and probabilistic risk assessment for CCA-treated wood. We'll be focusing on science, issues of policy. Of course as I've indicated to the Panel earlier, there is somewhat of a gray line here. But we will be focusing on science. And I will try to keep us directed to the scientific discussions related to the exposure and risk assessment reports that we've been assembled here to review.

With those comments, I'd like to turn the mike over to our designated federal official for this meeting, Mr. Paul Lewis.

MR. LEWIS: Thank you. Again, I'm Paul Lewis and I'll be serving as the designated federal official to the FIFRA SAP for this meeting.

I want to first thank Dr. Heeringa for agreeing to serve as session chair and also to members of the Panel and the public who attend this important meeting of the FIFRA SAP to review the Agency's Draft Preliminary Probabilistic Exposure and Risk Assessment for Children

Who Contact CCA-treated Wood.

We appreciate the time and effort of the Panel members in preparing for the meeting and taking into account their busy schedules and the amount of material that we provided to you to review as you prepare for this meeting.

By way of background FIFRA SAP is a federal advisory committee and provides independent scientific peer review and advice to the Panel on pesticides and pesticide-related issues regarding impact of proposed regulatory actions on human health and the environment.

The FIFRA SAP only provides advice and recommendations to the Agency. Decision-making and implementation authority remains with Agency. FIFRA established what is called the permanent Panel for the SAP which consists of seven members. Three of our members are here today, Dr. Heeringa, Dr. Matsumura, and Dr. Thrall.

The expertise on the Panel is also augmented through a science review board. And science review board

members serve as ad hoc temporary members of the FIFRA SAP providing additional scientific input to assist in reviews connected by the Panel.

As the designated federal official, I serve as liaison between the Agency and the Panel. I am also responsible for ensuring provisions of the Federal Advisory Committee Act in relation to this meeting.

The Federal Advisory Committee Act of 1972 established a system of governing the creation, operation, and termination of executive branch advisory committees. The FIFRA SAP is subject to all requirements of FACA. And these include open meetings, timely public notice of the meeting and document availability. In this case documents are available through our pesticide programs docket and the major background documents and relevant material is also available on our web site.

As the designated federal official, a critical responsibility is to work with appropriate Agency officials to ensure all appropriate ethics regulations are

satisfied. In that capacity, Panel members are briefed with provisions of federal conflict of interest laws. Each participant has filed a standard government financial disclosure report.

And, I, along with our deputy ethics officer for the Office of Prevention, Pesticides and Toxic Substances, in consultation with the Office of General Council, have reviewed the report to ensure all ethics requirements are met. And for your information, a sample copy of this form is available on our FIFRA SAP web site.

The Panel will review challenging science issues over the next several days. And we have noted a full agenda, and meeting times are approximate. Thus, we may not adhere to exact times as noted due to Panel discussions and the public comments that will be occurring beginning this afternoon.

We strive to ensure adequate time for panel presentations, public comments to be presented, and Panel deliberations. For presenters and panel members, public

commentors, please identify yourself and speak into the microphones since the meeting is indeed being recorded. And copies of the presentation materials and presentations will be available in the Office of Programs docket within the next few days.

For members of the public requesting time to make a public comment, please limit your comments to five minutes unless prior arrangement has been arranged. For those who have not preregistered at this time, please notify either myself or my colleagues of the FIFRA SAP staff that is sitting to the right of me here if you're interested in making a public comment.

As I mentioned previously, there is a public docket for this meeting and all background materials, questions posed to the Panel by the Agency and other documents related to this SAP meeting are available in docket. Overheads will be available in a few days.

Background documents are also available on our web site and the agenda lists contact information for both

those documents via our Docket Office and our web site.

For members of the press, Mr. Douglas Parsons, Director of Communications Media Office OPTS is available. And, Mr. Parsons, can you introduce yourself?

For those of you from the press who have inquiries, please direct your questions to Mr. Parsons. He will be available today to respond to any press inquiries.

At the conclusion of the meeting, the SAP will prepare a report as a response to questions posed by the Agency, background materials, presentations, and public comments. And the report will serve as meeting minutes.

We anticipate the meeting minutes will be completed in approximately six weeks after the meeting.

In closing, I would like to again thank the Chair, Dr. Heeringa, and the fellow members of the Panel here for the time that you spent preparing for this meeting. And I'm looking forward to very challenging and interesting deliberations over the next three days.

DR. HEERINGA: Thank you very much, Paul.

Before we begin with the mornings presentations, I just want to make one administrative comment. The sessions are being recorded; and, therefore, if you either as a presenter or a discussant or a public commentor come to the mike, be sure to introduce yourself and your affiliation before you begin. That way we have that on the tape for appropriate transcription later if needed.

With those minor administrative things out of the way, I have the pleasure of introducing Mr. Joseph Merenda who is the Director of the Office of Science Coordination and Policy of the EPA for some introductory remarks. Joe.

MR. MERENDA: Thank you, Steve.

Good morning. And it's a distinct pleasure on my part to welcome all of you as members of the FIFRA Scientific Advisory Panel for this meeting as well as members of the public who will be observing and those who are make public comments to this session.

Independent external scientific peer review is a very critical part of EPA's scientific and regulatory a processes. It's something at EPA we consider to be one of our most important activities. And one that I'm pleased to tell you our new EPA Administrator Mike Levit gave a presentation yesterday to EPA employees at headquarters.

And one of the points that he made during that presentation was the importance of sound science to the Agency's activity. So I can assure you that our new administrator holds in this in high regard, as have previous leaders of the EPA, the value of the service that you as members of this FIFRA Scientific Advisory Panel will be providing over the next few days.

This is certainly a very complex topic that you will be discussing. And the breath of expertise that is reflected on this Panel is, I think, indicative of the range of the issues that need to be covered.

So I don't want to protract the welcoming remarks and take any time away from the important

discussions that will go on. Let me just wrap up by thanking you all for your service on this Panel. And I very much look forward to hearing your comments.

DR. HEERINGA: Thank you very much, Mr. Merenda. At this point in time, we'd like to begin with the opening of the actual presentations and to provide an introduction, we have Mr. William Jordon of the Office of Pesticide Programs at the EPA. Bill.

DR. JORDAN: Thank you, Dr. Herringa.

What I am doing is those of who you have looked at the agenda notice two sets of remarks. The first is an introduction which is really a job that normally would be handled by our office director, Jim Jones. Both he and the deputy officer director, Ann Lindsey, are in Vancouver and are, therefore, unavailable. They did want me to say on their behalf how much they appreciate the work that the Panel does and to express as best I could the way in which you play a role and to say how genuinely grateful we are for what you do.

And I took that charge seriously. And I'm going to take a few minutes to just try to tell you how much I really appreciate it.

My role in the Office of Pesticide Programs is the senior policy advisor. And in that position, I get a chance to work with most of the divisions in the pesticide program as we develop policy documents. A large part of what we do obviously is scientific. So whenever we're coming to the Science Advisory Panel for a presentation, I work with the scientists who have prepared the analyses, the risk assessments for the Panel to review.

And although we always try to do a good job on the work we produce in the Pesticide Office, and at this time we are not only just the Pesticide Office but also the Office of Research and Development. When we come to the Scientific Advisory Panel, we work extra hard because we hold ourselves to a higher standard because we know when we undergo peer review from the SAP, that we're going to be getting the benefit of the thinking and advice of

really the best people in the fields that are represented on the Panel.

And not just the best people in the fields in the United States, but really in the world. We have drawn today as we have in past panels people from other countries because we want to try to get really the best advice that we possibly can. We know that when we get a job, when we get advice that says we've done a good job, it validates of the work of months, or in some cases as this one, years of effort by large groups of people. And it means an enormous amount to us to hear that we have done our work thoroughly, well, and to meet the high standards that you bring when you review it.

But sometimes it happens that you say, gee, you could have done something differently, you could have done a better job, you could have looked into another area or another aspect. We also appreciate that because, frankly, we do not bring to you simple issues. We don't bring to you things that have obvious answers. We bring to you the

toughest and most controversial matters that we're working on and often at the cutting edge of science.

And so when you were able to pull together advice and say to EPA, try going down this road, that, too, is extremely valuable and appreciated because it helps us to figure where to go next. And so when we get the reports from the Panel at end of the work that you do, we read it closely, we study it. We then set about developing plans to figure out how we will follow through on the advice you have given us.

Now, we don't always do everything that you suggest. Sometimes the research done in some of our reports seems to suggest we go in a direction that, frankly, we don't have the resources or time to do because of the regulatory situation within which we work. But we always look and appreciate that kind of advice because it can set the agenda for work done by the Office of Research and Develop and can let us know in several years where we might look for work outside the Agency to begin to help us

frame a different and better course.

For all the hard work that we do, we also know that you do a lot of hard work, both here in the sessions and also in preparation. We have marveled constantly at how thoughtful and thorough the comments are that we receive in the public meetings, and we know that just didn't spring full blown from your mind as you sat here listening to our presentations but really reflected hours and days of work that you put in reading the background materials and preparing your thoughts for presentation here.

And we appreciate that the work doesn't end when the public sessions come to a close, that you spend time reviewing the draft reports and making sure that the thoughts that you've tried to convey are presented clearly, that inconsistencies are noted and ironed out, and that the reports that we get meet high standards of clarity and thoughtfulness. So we know you do a lot of work, and it is greatly, greatly appreciated.

I want to take a moment and say thank you to Dr. Heeringa who, as I understand it, is serving as the chair for the first time on the SAP. And we know you're a veteran of many sessions. And we look forward to having you serve as the chair through this one.

And also to the other permanent members of the SAP, Dr. Thrall and Dr. Matsumura. And we note that there are a lot of familiar faces among the ad hoc members. And to those of you who are returning to the SAP after some time away or maybe even just this seems like a great hobby to you or whatever, we want to say thank you; and we hope that you find this rewarding.

We expect that's the case. Dr. Reed and Dr. Freeman and Dr. Hattis and Dr. Steinberg and I'm sure others of you have been here as well. We really do appreciate the fact that you're willing to come back time after time. And the continuity that that provides in terms of the recommendations also makes it possible for these meetings to go forward.

And, finally, for those of you who are here for the first time, let me say that we also appreciate your taking time out of your schedules, often very busy schedules. And we hope, like the others who have agreed to be here multiple times, that you'll find it rewarding and that you'll find the issues challenging and that you'll consider accepting a call if in the future we find that your expertise would help us do a better job.

No set of introductory remarks and thank yous would be complete without acknowledging the work that Paul Lewis and Larry Dorsey and the rest of the team who help put these meetings together do. The SAP team has the job making it appear effortless. And when they do their job well, which is every meeting, you probably aren't aware of how hard they work and how many details they take care of.

I have seen backstage the management and effort that they have put in and the countless hours tending to numerous details so that this meeting comes off smoothly, that not only the Panel members have a positive experience

but so, too, do the members of the audience and the folks who are making presentations for EPA. So Larry, Paul, the rest of the team, thank you all very much for the work that you do.

DR. HEERINGA: Thank you, Mr. Jordon. Just a comment. If you look at the points of origin for many of us, Wisconsin, Minnesota, Michigan, New England, we come for the weather I think.

DR. JORDAN: Well, that too.

Let me turn now to the next part of my remarks which have to do with setting a context for the presentations that will follow. We're here today to review the preliminary probabilistic assessment of risks from exposure to CCA residues encountered by children who are playing on or otherwise active near or on treated decks and playsets.

CCA as most of you know is a wood preservative. And it is used in treating wood that in turn is put into decks and playsets. And children may be exposed to

residues of CCA orally or dermally as a consequence of their contact with CCA residues in soil or residues that are on the surface of the wood with which they have come in contact.

Let me just briefly review a little bit of the history of CCA and our attempts to assess the risks of exposure for children. This is our third time to come back to the Scientific Advisory Panel. The past two visits have been very helpful. And my colleagues will be talking in detail about the history, so I'll only touch briefly on that.

Let me say that in 2001, EPA developed a deterministic risk assessment for CCA in children in playsets and decks. And one of the key recommendations that came out of that SAP meeting was that EPA investigate modeling techniques to try to prepare a probabilistic risk assessment that showed the variability in exposure and risk that children encounter.

And so after going over the data available and

working with our colleagues in the Office of Research and Development, we came back in August 2002. At that session the Office of Research and Development presented the stochastic human exposure and dose simulation model, SHEDS-Wood. Although, I'm also tempted to call it wood SHEDS-Wood.

The work that the Office of Research and Development has done on SHEDS-Wood is really groundbreaking. We believe that it is going to be a very useful tool not only for dealing with CCA risk assessments, also it will help us in the future in dealing with other exposure assessments. So we took the model and asked you all in the SAP for your advice about how to make that model better, and we got a number of very valuable suggestions both about the modeling methodology and also the data we were using for the CCA present assessment itself. And it is based on the work that we've done since then to respond to the recommendations and incorporate new information that we come back to you this time around for

review of our preliminary probabilistic risk assessment.

I want to say a word also about the status of CCA. In February 2002, EPA announced a voluntary decision by the industry, the wood-treating industry, and the companies that make CCA to move away from using that product to treat wood in residential settings. The transition will affect virtually all residential uses of wood treated with CCA, including wood used in playsets, decks, picnic tables, landscaping timbers, pretty much anything that you might find around a home, a school or in a park at the beach in a boardwalk, for example.

And it is as a consequence of that effective December 31 of this year, this month, no wood manufacture may treat wood with CCA for most residential uses. So we think that the kinds of exposures that are addressed in this preliminary risk assessment will in the future come to an end. There will be no new decks or playsets built. Although obviously, decks and playsets that have already been constructed from CCA-treated products, wood products,

will continue to be out there. So it is our purpose in this assessment to try to understand and characterize the risks that might be associated with existing structures.

Even though from a regulatory point of view, there's not much that EPA can do with regard to the existing treated structures. We do think that the work that we're doing here is valuable for several different reasons. First of all, as I mentioned, we think that it's helpful to understand what risks may be associated with the existing CCA-treated structures. So we're going to take the preliminary risk assessment that we're doing here, the advice that we get from you, and develop a final risk assessment that or revised risk assessment that we hope will help inform public policy and choices about what to do in that area.

An important part of that is examination of mitigation measures such as the use of sealants that will, we hope and we think, mitigate some of the risks that may be going on. And in that regard, EPA in cooperation with

the Consumer Product Safety Commission is conducting a study to determine whether different types of wood sealants on CCA-treated wood would have the effect of reducing exposure. The data are not in. We expect the study -- it's underway now. And we expect to have the results in the Spring of 2005. And so those data will in the future provide us a better basis for understanding and characterizing the eventual risk.

So a part of what we're doing today is continuing to try to understand what the risks are for existing structures.

A second thing that I should note is that CCA will have other uses. Not in the residential area, necessarily, but we at EPA will continue to look at arsenic and chromium. So the insights and advice that we get from the Panel will be useful in that review.

And, finally, the SHEDS-Wood model itself is a tool that we think will be extraordinarily valuable in the future in dealing with other wood preservatives, and,

frankly, with some adaptation, can probably be useful in a number of other areas. So understanding what advice you have for continuing to improve that model will be helpful to us as we go forward in other aspects of our risk assessment not only in the pesticide area but in other parts of EPA.

I want to wrap up these introductory remarks by saying that the work that we're doing here today is not just the Office of Pesticides Programs. In fact, in large part, the credit for any good work goes to our colleagues in the Office of Research and Development. As you'll hear, they've been working on the SHEDS-Wood model for a long time. And they have worked very, very closely with us.

It is an example of the kind of collaborative effort with the Office of Research and Development that has helped us in the Office of Pesticide Programs feel as if we're able to stay on the cutting edge of science and take advantage of some of the best thinking in the Agency.

And for their work we are immensely grateful.

So let me stop here and turn it over to so we can begin the substantive presentations on the CCA probabilistic risk assessment.

DR. HEERINGA: Thank you very much, Mr. Jordon.

At this point in time, we'll begin our first of the presentations by the Agency on the SHEDS-Wood model and the expose and risk assessment. And our first speaker is Dr. Haluk Ozkaynak. He's from the Office of Research and Development at EPA. Haluk.

DR. OZKAYNAK: Thank you. Good morning. I'd like to send greetings from my colleagues from the Office of Pesticide Program and Office of Science Coordination and Policy and welcome you today also on behalf of EPA's Office of Research and Development.

I'd like to also express my deep appreciation to all of the Panel members for coming to this important meeting especially during the very busy pre-holiday period. This shows everyone's keen interest in the topic

and their concern regarding the scientific and public issues surrounding the CCA problem.

We have a couple of very busy days ahead of us, so I won't take too long going over the background issues. However, I wanted to give you a quick overview of the ORD SHEDS-Wood program to put the following presentations in perspective. Can I have first slide, please?

As Bill noted, SHEDS-Wood stands for stochastic human exposure and dose simulation models. Those are the acronyms. And this model has been a product now of nearly five years of research conducted at ORD's National Exposure Research Lab. It actually began in the area of developing a human exposure model for the particulate matter problem as well as the pesticide exposure problem. So the first versions of the SHEDS-Wood model have been developed for the PM and in the pesticide context.

And over the last couple of years, we've been also working on the air toxins. So there is a parallel effort going on in the SHEDS-Wood air toxins.

The SHEDS-Wood program has sort of started with similar philosophy and construct in mind. So even though we have different applications of the SHEDS-Wood program namely for PM pesticides, wood, and air toxins, all of the SHEDS-Wood models have common construct and compatible structure. SHEDS-Wood is a two-dimensional Monte Carlo simulation model which incorporates both variability and uncertainty in model inputs as well as outputs. Thus it's a unique tool of the Agency for assessing potential human exposures to environmental contaminants.

The model that we will be presenting today, the SHEDS-Wood model, that effort began a couple years ago around November 2001 following OPPs antimicrobial divisions request. SHEDS-Wood model is an extension of the SHEDS-Wood pesticide model, specifically configured for the CCA problem.

SHEDS-Wood simulates childrens exposure and dose from contact with wood preservative treated playsets and decks. The model evaluates both dermal soil and wood and

nondietary ingestion routes, specifically hand-to-mouth and soil ingestion pathways. SHEDS-Wood model does not include inhalation or the dietary ingestion pathways. However, the SHEDS pesticide model does.

Like the other SHEDS model, SHEDS-Wood model utilized EPA's consolidated human activity data base, or the CHAD data base, to simulate the activities of individual children. And the model generates realistic exposure and dose profiles using pathway-specific exposure factors for each microactivity that's linked with the CHAD diaries.

Now, how do we arrive at this meeting? We received during the previous SAP, the August 2002 SAP, a number of useful comments and recommendations. In addition, we have received a fair amount of comments from public and extensive review comments that we also received during this past August, August 2003, from a ORD, an external review off the preliminary document.

And all of these comments and all of the input

that we have received over the course of the past six months and year and a half, have now been incorporated in the revised document, the September 25 document, on probability exposure and dose for CCA.

During OPPs review process, ORD also received comments from the CCA registrant representatives and on the September report. And those comments that were received have been reviewed and responded in a separate document dated November 4, 2003, addendum document, which is about a 20-page documents which we also have copies available to you. And it's provided to the public.

Now I'd like to introduce my colleague on my right, Dr. Valerie Zartarian, who will introduce the SHEDS team who worked on the CCA problem and begin the technical presentation on the probabilistic exposure and dose modeling for CCA. Valerie.

DR. ZARTARIAN: Thank you. Good morning, Mr. Chair, members of the Panel, fellow colleagues, and ladies and gentlemen.

First, I'd like to gratefully acknowledging my colleagues on the SHEDS-Wood CCA assessment. Dr. Jianping Xue who took the lead on co-development, statistical analyses, and model simulations. Could you stand up and identify yourself?

Dr. Haluk Ozkaynak, you just heard from sitting on my left, who provided oversight and guidance on the entire assessment as well as assistance distribution fitting. Dr. Winston Dang, who's sitting on my right, who provided assistance with model inputs and guidance with the population definition as well as exposure scenarios.

And my colleagues from ManTech, Environmental Technology, Dr. Graham Glen and Luther Smith, who assisted with the SHEDS-Wood coding, the model analyses, distribution fitting, and report writing. Would you stand up? Thank you. You'll be hearing from all of them over the next several days.

What I'm going to try to cover in the next hour or so are changes that we have made to the SHEDS-Wood

model and analyses since last year's SAP meeting as my colleagues mentioned to address Panel member, public, and peer review comments. We'll define the specific population and exposure scenario that we considered, present the SHEDS-Wood methodology specific to the CCA assessment including the algorithms for assessing exposure and absorbed dose, and describe the statistical methods for conducting sensitivity and uncertainty analyses, and discussing data sources, methods for distribution fitting, the distributions for key input variables, and the type of model outputs. And you'll hear the specific results in the next talk after the break.

As was mentioned previously, a number of changes have been made to the SHEDS-Wood since the August 2002 SAP meeting. And we grouped these in three areas: activity diary assembly, changes to model inputs, and internal algorithms.

With respect to activity diary assembly, we made changes such as altering the mapping from CHAD locations

to the SHEDS-Wood categories, for example, including day care centers as possible locations for contact, using new probabilities based on actual longitudinal activity data for switching between high, medium, and low potential exposure categories for the children based on time spent outdoors.

In the area of model inputs, we now allow the use of Beta, Weibull, and Gamma distributions per the SAP recommendation and replaced the assumed dermal transfer coefficient with new experimental data.

With respect to internal algorithms, some of the changes that we made include updating the body weight and hand size monthly, rather than annually, applying a new methodology for assigning contact events within a day, revising the dermal exposure and residue ingestion equations per SAP recommendations, and modifying our methods for conducting uncertainty analyses to sample parameter pairs to preserve correlations.

The next several slides summarize the analyses

that were conducted since the last year's meeting. And these are grouped in baseline simulations, special simulations, sensitivity and uncertainty analyses, and supporting analyses that were conducted external to the SHEDS-Wood.

For the baseline simulations, we focused on the target population which I'll define in a moment. In particular we looked specifically at arsenic and chromium, whereas last year we looked at a hypothetical chemical. This is chemical specific for children assumed to not have pica behavior. That was conducted in a special simulation. And also as part of the baseline simulations, we did assume random daily hand washing. And I point that out because special simulations include additional hand washing after play activities. And we used what we're calling baseline input values, some of which were altered for special runs. So for the special -- and also part of the baseline simulations include stability of model results using different sample sizes.

For the special simulations, we looked at the age group of 1 to 13 years per the SAP recommendation. We also looked at a lower dermal absorption rate and increased GI absorption rate different from the baseline values. We considered hypothetical exposure mitigation scenarios by simulating residue reduction via sealants and additional hand washing after play events. We looked at children exposed to public playsets only and also children who exhibit pica soil ingestion behavior.

For sensitivity and uncertainty analyses, we varied each variable up and down by a standard deviation as well as by a factor of 2 per the SAP recommendation. And we fixed activity diaries in doing the sensitivity analyses. We also looked at the impact of the selection of the input distributions.

Supporting analysis conducted external to the model included examining the impact of geographic location and season in the CHAD diaries. We justified our sample size for bootstrap sampling with the modified approach, as

well as the use of eight diaries for the construction of longitudinal activity diaries. And the other analyses listed there.

Next two slides, please. The study population that we have defined for this assessment is 1- to 6-year-old children in the United States who contact CCA-treated wood residues and or soil containing arsenic or chromium at public playsets at a minimum.

A subset of these children also contacts CCA-treated wood residues and or soil containing arsenic or chromium from residential playsets and/or residential decks. We picked this age group for the baseline simulations, 1- to 6-year olds, because of greater hand-to-mouth contact for children less than 7 years of age. And also this age group was consistent with other CCA assessments. However, as I mentioned previously, special analyses were conducted for the 1 to 13 year old age group.

Public playsets were the primary focus, the

prime source considered. And there were several reasons for that. More potential time at schools and day care centers, more available data for public than home playsets, and also on public playsets, playgrounds were the focus of CPSC and other groups.

Given the lack of data on playset and deck contact days and exposed skin surface and geographic area warm and cold climate bounding scenarios to represent two extremes. The warm climate bounding scenario assumes surface area of hands, face, arms, legs and assumes the feet and torso exposed throughout year, and greater assumed contact days. In the cold climate bonding scenarios, the surface area assumes only the surface of the hands and face are exposed throughout the year and lower contact days.

These bounding climate scenarios are not intended to be specific to any particular geographic location in the U.S. However, they are intended to be realistic bounding estimates for the U.S. population.

The three exposure time periods that we considered are short-term, intermediate term, lifetime. And we also considered four primary exposure pathways relevant to CCA-treated wood and nearby soil, dermal residue contact, determine soil contact, soil ingestion, and residue ingestion.

SHEDS simulates individuals by selecting time location activity diaries from CHAD as Dr. Ozkaynak mentioned. And these diaries include sequences of information that people report about where they are and what they're doing over a course of a day or several days. It then applies an algorithm for simulating longitudinal one year diaries for a child based on the CHAD diaries.

Exposure time series are then generated by randomly sampling user-supplied concentrations and exposure factors into the pathway-specific exposure equations for each of the activity location combinations in the one-year diary.

SHEDS-Wood, these exposure profiles, are

combined with user-supplied daily absorption rates to obtain pathway specific absorbed dose profiles. And then metrics of interest, for example, ADD or LADD are extracted from individual profiles. And this process for the individual is repeated thousands of times to generate population distributions as shown in the bottom right box.

SHEDS has the option of 1- or 2-stage Monte Carlo simulation to assess variability and/or uncertainty in the exposure dose estimates.

Thus the very brief overview of the general SHEDS methodology. So now I'm going to step through the steps that are specific to the SHEDS-Wood algorithm and the CCA assessment that we conducted.

Again, the EPA CHAD diaries are the basis for simulating the children in this assessment. There are 4 CHAD studies that provide children's diaries for ages 1 to 6 years. University of Michigan National Human Activity Pattern Survey, California Air Resources Board Survey, and the Cincinnati Study.

In these four studies, there are 4,259 children ages 1 to 6. In the SHEDS-Wood assessment, we used 2,536. Those are the children that reported time in suitable outdoor locations for this assessment which I will define shortly. Because we considered 1- to 6-year olds for the baseline assessment, there are 12 age gender cohorts. And we have found that age and gender are important predictors for time spent outdoors and there are roughly 200 children in each of these age gender cohorts using the CHAD diaries.

The age-gender cohorts in SHEDS-Wood are proportional to the U.S. census. We used weights from the census to sample for the cohort sizes in our assessment.

So the very first step in the process is to select a cohort and a potential exposure category for an individual child. And by potential exposure category, I'm referring to a high, medium, or low potential exposure which allows for more consistent matching of children's diaries across seasons and years. So a high potential

exposure category would mean that a child tends to have high outdoor time on most but not all days within a year and also tends to have a high outdoor time from year to year, and, thereafter, high potential exposure.

And the way that we do this is we randomly assign a simulated child. Before we even select a diary, we randomly assign them to a high, medium, or low potential exposure category. At the same time, we sort the CHAD diaries by their outdoor times. So we have low, medium, and high categories for the CHAD diaries.

For a given simulated child, we use 8 CHAD diaries that are selected randomly and independently using a probability matrix I'll show in the next slide. And the child is then assigned to the same category from one year to the next.

This is the probability matrix that I just mentioned. The left-hand column represents the category that the child is randomly assigned to: low, medium, or high potential exposure. The other three columns

represent the probabilities of selecting a CHAD diary with low, medium, or high outdoor time. For example, a child that's randomly assigned as a high potential exposure child, would have 18 percent chance of drawing a low outdoor time diary, a 34 percent chance of drawing a medium outdoor time diary, and a 48 percent chance of drawing a high outdoor time diary for any of the eight diaries selected to construct the one-year profile.

To assess these category shift probabilities that you're looking at, the results from a Harvard Longitudinal Activity Data Set from Southern California children were analyzed by Dr. Xue and his colleagues. Based on these probabilities, SHEDS-Wood allows low, medium, and high outdoor time diaries to be chosen for weekends and weekdays within a season. And it allows them to change from season to season as you'll see on the next slide.

So the next step is to assemble the child's one-year diary. And to do this, we developed an approach

using eight diaries which is intended to capture the relationship between inter- and intravariability. And we believe it does this based on the time data for time outdoors from that Southern California study of 160 children I just mentioned.

So eight CHAD diaries are used to simulate a year for the given cohort. And these are sampled again independently for each child based on the probability matrix you just saw. We have one diary from each of the four seasons and one from weekend and weekday within each season. And the basis for doing this was that statistical analyses show that day of week and season are two of the most important variables for compiling a longitudinal activity diary.

We then fixed the weekday diaries and the two weekend diaries and repeat the seven-day activity pattern within each season. But I want to emphasize that even though the same CHAD diary is used for several consecutive days in constructing the one-year diary, the number and

duration of exposure events varies from day to day because of user-specified inputs.

The next step is to assign the contact days for the child. Once we have the one-year activity diary constructed, SHEDS-Wood assigns contact days within the year for that child. Possible contact days are determined by days in the year-long activity with what we're calling "suitable locations." And suitable locations are defined as locations with the potential for contact with CCA-treated wood and/or soil from playsets or deck.

So these include residences, outdoor locations, child care facilities, amusement parks, school grounds, play grounds. The average one-year CHAD diary has 185 days with possible public playset contact time. But this ranges from 25 to 366 days with the method that we used to construct the one-year diary. And there are 260 days on average for decks and home playsets.

So the user sets the fraction of those possible contact days that become simulated contact days in

SHEDS-Wood. So the number of contact days per year depends on two things: The number of days in the one-year and the child's one-year profile with diary time and suitable locations and the probability of contact occurring on those days.

And to determine the probability of contact on those days for the warm climate scenario, we assumed is 126 days per year in the warm and 54 in the cold. And this is based on an assumption of seven days per week minus rained out days in the warm climate scenario; three days per week of play time minus rained out days in the cold scenario.

And given the average number of days per year in CHAD with possible contact, this results in a 68 percent probability of contact with public playsets in the warm scenario and a 29 percent probability of contact on possible contact days for the cold climate scenario.

So once we know when the contact days are, the next step is for SHEDS-Wood to assign the wood and soil

contact events within each contact day. A contact event is defined as a CHAD location in which a child touches wood or soil on or around a treated playset or deck. And these typically range for 1 to 60 minutes in CHAD and on average, while a child is awake, about 30 minutes.

The user supplied input determines the frequency and duration of contact events. And the reason we do this is that the CHAD diaries do not indicate contact. They're not detailed enough to indicate contact with CCA-treated wood structures. So the model simulates contacts events probabilistically in a subset of the suitable CHAD locations.

There's also a distinction in the model between wood and soil contact events. And this is based on the user specified fraction of time on or near the treated wood that the child touches wood versus soil. So the model steps through a sequence of diary activities in chronological order and assigns the contact events within the day.

Once the longitudinal activities diaries are generated and the contact events assigned, SHEDS-Wood then generates the child's route-specific exposure profiles. And these are time series that preserve the within day peak and variation over time. And they're helpful for analyzing source-to-dose relationships and also looking at impact of various potential exposure reduction strategies such as hand washing and bathing at particular times.

Exposure in this assessment is defined as contact between a chemical and a person. And it is quantified as the mass on the skin or in the GI tract.

In SHEDS-Wood is always carried over from day to day for both dermal and GI routes. The GI route is voided at 6 a.m. each day. SHEDS-Wood follows the child through his or her annual diary, simulating route-specific exposures. And there are 12 exposure time series that are tracked for each person in SHEDS for the four pathways and also for each public playset, home playsets, and decks.

To do this, SHEDS-Woods samples model input

parameter values from user-specified probability distributions. And then it combines activity information with concentrations and exposure factors into route-specific exposure and dose equations. And these, as you'll see shortly with some figures, these profiles account for removal as well as loading processes. The removal processes include hand washing, bathing, hand-to-mouth ingestion and absorption into the blood.

This is a hypothetical dermal exposure profile for the dermal contact with wood surface residues. This is on the X axis time; on the Y axis is exposure mass. This is again hypothetical for a two-day time period for a single hypothetical child just to give you an illustration of what the code is actually doing for this particular pathway.

You can see several lines one for hand exposure, one for body exposure, and one for total exposure. And you'll see increases when exposure or addition takes place on the skin. And you can see a removal processes

indicated by hand washing and bathing events.

The hand and body are modeled separately. And the reason for that is because we're trying to keep track of ingestion of residues on the hands as well. The hands profile as you can see, hand exposure is affected by washing, bathing, and hand-to-mouth except during sleeping. And the body is affected by bathing events only.

The exposure also decreases slowly due to the assumed dermal absorption rate in the model. It's tough to see on the figure. But while they're sleeping, there is a slight decrease.

Oh, and one more thing on that slide. The additions, the jumps on the profile to add dermal exposure to the skin are obtained combining residue concentrations, residue-to-skin transfer efficiency, and surface area contacted.

The next profile illustrates dermal exposure from soil. And the basic equation for the additions you

see in the figure is by combining soil concentrations, soil skin adherence factor, and exposed skin surface area. So this profile looks very similar to the dermal residue exposure profile because the loading and removal processes are very similar for residues and soil. But the numerical values are different because of the differences in input values.

This is the profile for GI tract exposure from residue ingestion. Once the child is awake and they have dermal hand exposure as you saw a couple of slides ago, there is a fairly constant transfer from the hands to the GI tract. This stops during sleep events. And the GI tract is also reduced by absorption into the blood and void at 6 a.m. each day. So you can see a steeper decrease during the sleep activity. This is due to a higher assumed GI absorption rate than the dermal.

And the primary equation for the increases on this curve are derived by combining the dermal expose that you saw previously, the dermal hand loading, times the

surface area contacted. From one hand-to-mouth contact, it's the dermal hand loading times the surface area of the skin mouthed times the saliva removal efficiency.

This is the GI tract exposure from soil ingestion. The main equation involves combining soil concentration times soil ingestion rate. And this only increases when the child is at the deck or playset with direct soil ingestion and there's an immediate rise on the curve.

This slide describes dose simulation in the SHEDS-Wood model. Absorbed dose is defined here as mass entering the blood. The total daily absorbed dose is reported in SHEDS-Wood at the end of each day. So we have a counter for the total daily dose that we reset each day. But I want to emphasize that we're not zeroing the mass in the blood each day. We're simply resetting the counter for the amount that gets into the blood each day.

SHEDS-Wood does not quantify concentration in the blood because we do not have currently a

pharmacokinetic model. The absorbed dose profile is then estimated by applying absorption fractions to each route-specific exposure profile. And the change in the absorbed dose is proportional to existing exposure. However,, absorption into the body is one of several competing processes as you saw, removal processes for exposure. So the absorbed dose is not simultaneous with the contact with the source.

This is an illustration of the daily total absorbed dose with the absorbed on the Y axis and time on the X axis. This is a running total again of what enters the body. That's what is being tracked. And absorption is zero only if all of the dermal and GI tract exposures happen to be zero at the same time. And then it starts with any nonzero exposure.

So, again, this illustrates two days. You can see two starts of a new day at in the middle and at the end of the X axis. And again the GI tract void is indicated. The reported daily value immediately at the

end of the first day is followed by resetting the counter. So that's the vertical line that drops down. And then there's an immediate rise at the beginning of Day 2 and that illustrates the carry-over exposure from the previous day.

So this is an illustration of the corresponding one-year absorbed dose profile for the generated exposure dose profile for an individual child. And again this is derived from applying an absorption fraction to the exposure profile for the child, the one-year exposure profile. The values that are plotted on this are the reported daily values for absorbed doses as you just saw.

The next step is to compute the outputs for one child by averaging the absorbed dose. So once we have the absorbed dose profiles, we compute the outputs of interest, for example, short-term, average, intermediate term, or lifetime values. And the lifetime values are -- short-term are derived with the 15-day averaging period; intermediate term with 90; and the lifetime values are

computed by computing the one-year profiles as we just saw and then stringing together six one-year profiles for the ages 1 to 6 for the baseline runs by correlating high, medium, and low potential exposure children.

And then for the baseline runs, we assign zero dose for 7 to 75 years for that simulated child. And we compute the child's lifetime average daily dose over the 75 years.

The Steps 1 to 7 that I just went through all focus on one child. To obtain population estimates, the steps are repeated many times using Monte Carlo sampling. With one-stage Monte Carlo sampling, we repeat the random sampling of inputs for different individuals but from fixed input distributions.

And for the CCA assessment, we use the 1,500 samples which we found provided stable results at both the mean and upper percentiles.

For two-stage Monte Carlo stimulations, we repeated the sampling. This repeats sampling for

different individuals but also allows us to vary the input distributions to account for uncertainty in the model inputs. And for the CCA assessment, we used about 200 uncertainty runs or 200 sets of input parameters accounting for uncertainty, and 480 simulated children per uncertainty run which gave us 40 children per each of the 12 age gender cohorts.

We used several approaches for conducting sensitivity analyses. In the first approach, we fixed diaries and varied each input independently one at a time. First, we fixed all the input variables as point estimates at what we're calling the "medium values." And then for each independent variable, we did it two ways. First, multiplying by a factor of two and one half to obtain what we're calling the high-end dose and low doses. And then to address the SAP comments, we also did it by adding and subtracting one standard deviation.

We have 33 independent variables in this assessment. And we set them to low, immediate, and high

values. So this yielded a data size of about 32,000. And this approach yields the information on the magnitude of the sensitivity of each input to the dose.

With the second approach, we used multivariant stepwise regression to all of the data, the 32,160 data points generated with the first approach. And independent variables were ranked by their partial R squared to assess their relative importance. The results from these two complimentary approaches were analyzed together to rank the importance of inputs with respects to variability.

For conducting uncertainty analyses, we conducted three types of statistical methods and also two graphical methods to assess the uncertainty. The mean of the 480 realizations for each of the input variables computed along with the mean absorbed dose was derived for each of the 200 uncertainty runs. And two types of correlation coefficients were ranked, Spearman and Pearson. We also applied multivariate stepwise regression using the 200 means for each input and output.

And as well as those analyses, we developed two forms of graphical analyses of uncertainty. The first one is three complete CDFs corresponding to the 5th, 50th and 95th percentile of the uncertainty runs ranked by their medians. You'll see illustrations of these later. The second one are three CDFs reflecting selected variability percentiles, 200 from each of the 200 uncertainty runs.

As I just mentioned there are 33 SHEDS-Wood inputs for the CCA assessment. And these are grouped in activity factors, concentrations and residues, dose factors and exposure factors. Activity factors include the fraction of children with treated home playsets and decks, the fraction of outdoor time that a child plays on or around treated playsets and decks, the number of days per year that a child plays on or around treated playsets and decks, and the fraction of time that a child is on or around the treated structure contacts residues versus soil.

Inputs also include soil concentrations near

playsets and decks and wood surface residues. Dose factors include dermal absorption fraction and GI absorption fraction for residues in soil.

Exposure factors include residue to skin transfer efficiency, the hand-to-mouth dermal transfer fraction otherwise known as saliva removal efficiency; the fraction of the skin that's contacted. I won't read all of them.

This lists the sources of data that are used for the different types of inputs. For activity patterns, the CHAD diaries and also information from the census. Also available literature for other microactivity information such as hand-to-mouth frequency as well as Agency derived estimates, for example, fraction of time on the playsets versus the soil.

Wood residues were derived from new hand wipe studies from the American Chemistry Council and the Consumer Products Safety Commission. And we also used environmental working group woodblock data for

uncertainty. And the new wood residue studies were also used to develop residue to skin transfer efficiency and maximum dermal loading.

Soil concentrations were obtained from published literature. Exposure factors came from SAP recommendations, published data, and the Office of Pesticides Standard Operating Procedures. And dose factors came from SAP recommendations, published data, and new data from Wester, et al., and the CCA task force.

I'll briefly mention the new data considered. However, Dr. Dang will be discussing these in more detail. Surface residues on the wood again came from hand wipe studies conducted by the American Chemistry Council which had larger sample size than previous studies, relative bioavailability studies conducted with swine for wood surface residues and soil residues were obtained by the CCA Task Force as recommended by the 2001 SAP; and also new data for dermal absorption was conducted with a monkey study; and a chemical complex study was conducted by Nico,

et al., to look at the effect of wood matrix on skin absorption and bioavailability. Again you'll be hearing more about those from Dr. Dang.

So the next slide talks about how we assign variability distributions to the SHEDS-Wood inputs. Where data were available, we used point estimates, for example, for the average number of contact days or the fraction of children who have treated decks or treated home playsets. When the values were restricted between zero and one for the input, we used Beta distributions.

And these were based on a foundational triangle distribution with a peak at the mean and the maximum and minimum at plus or minus a stand deviation. And this approach for using the Beta distributions was developed in response to the 2002 SAP comments about problems with using the triangular uniform distributions for limited data sets.

Where more data were available, we used Weibull or log normal distributions. For example, some of the

inputs we used this for were hand-to-mouth frequency, soil concentrations, surface residues, and the soil skin adherence factor. And we fit these distributions using the method of moments or maximum likelihood estimation and we applied goodness-of-fit test to verify the selection.

The 2002 SAP suggested that the parametric bootstrap approach we presented last year was arbitrary in the choice of sample size and also lacked correlation in the parameters. So we revised this approach. I'll go through the steps here. And then I'll show a few illustrations in the next couple of slides.

The first step is to fit apparent variability distribution estimating the two parameters. For example, if it was log normal, the geometric mean and the GSD to all data from the original N studies using the method of moments. The next step is to fit a variability distribution to data in each of the end studies using that shape of the parent distribution. And we examine the scatter plot of the N v1 and v2 values to give us a sense

of the uncertainty scale.

The next step is to sample B data points from the parent distribution K times where B is the bootstrap sample size and K is the number of samples of parameter pairs to save for the uncertainty runs. So what we're really trying to do here is optimize B and then sample the K uncertainty pairs.

So for each of the K sets of the B data points, we fit a parent distribution and compute parameter values of interest to obtain the K v1 v2 pairs. Next we overlay the scatter plot of those K pairs with the N pairs obtained in Step 2. And then we repeated Steps 3 through 5 with different values of B until the two scatter plots match in spread.

And, again, repeating the steps is to find a suitable B value to capture the uncertainty from the different studies available. And we found that a B value of 4 or 5 was suitable for very small or highly uncertain data sets. A value of 10 was typically used for slightly

larger data sets, and 15 or 20 for even larger or less uncertain data sets.

K was typically 150 to 200 to achieve sufficient randomization as well as consider computation time.

For those of you following along in your handout, I moved the next slide to after these figures because I wanted to show you an illustration of how we fit uncertainty distributions and variability distributions for several cases. This first case is where we really didn't have data and we had to use best estimates for fraction of time that the child contacts the deck versus the soil when playing on or around a treated deck.

We first assumed a triangular distribution with a minimum .7, mode .9, and a maximum of 1. And then we fit a Beta distribution which as you can see had a similar shape but allows the value to range from zero to 1. So again, start with the foundational triangle with best estimates and then fit a Beta distribution. And this gives us a Beta distribution with parameters 39.6 and 4.4,

which you'll see on the next slide.

It's hard to see. It's a black dot. But it's in the red cloud. That's the point to develop the uncertainty cloud that captures the parameters from the actual data. In this case, the 39.6, 4.4. So again the important thing to notice is real data is located within the cloud, that parameters 1 and 2 are correlated so we're using the pairs rather than independent draws, and the bootstrap sample size here was 5 to reflect the fact that we have no available data and used our best judgment.

The next slide is a different example where we actually had quite a bit of data and that was for the maximum dermal arsenic loading. This is for the cold climate scenario. So the original data are the black dots. You can see that we tried to fit several types of the distributions. The original data consisted of data from the American Chemistry Council and the Consumer Product Safety Commission here. And the best fit, as you can see in this case was the log normal distribution.

If you look at the next slide, the next slide is the associated uncertainty distribution for that variable. And, again, what you're looking at is an uncertainty cloud that includes log normal parameters for the original data sets. So it's hard to distinguish the big dots from the little ones.

But the point is that the cloud captures the geometric mean and GSD for all of the ACC and CPSC data together as well as the parameters for the ACC data and cold climate, which is the black dot, and the CPSC data, which is the plus sign that is about 3, three and a half. And the smaller dots are the bootstrap values. And in this case, the bootstrap sample size was 15 to reflect more confidence in the available data.

And the other point on here that I need to mention is that we have ACC data in the warm climate as well which is at about two and a half. And the point of that is that the approach we've taken to determine the B value is really semiquantitative. It includes the

original data sets, but we also try to use professional judgement to consider uncertainty looking at other data sets as well as professional judgement.

So once we've established the uncertainty distributions with the approach I just described using bootstrapping, the next step is to sample parameter pairs from the uncertainty distributions. So at the start of each uncertainty iteration in SHEDS-Wood, one of those K v1 v2 parameter pairs is randomly selected for each of the SHEDS-Wood input variables.

Using this parameter pairs, SHEDS-Wood runs a simulation -- the user runs a simulation with the model of N individuals. And we used 480 for our assessment.

The selected v1 v2 pairs defined the finds variability distributions that are used for a given uncertainty iteration. All simulated individuals within one uncertainty iteration randomly draw values from these K variability distributions. Then we repeat these steps M times. In our case, it was about 200, 200 uncertainty

runs. And we examined those 200 cumulative distribution functions. And you'll see a number of those in the next presentation.

And the last slide here is just a summary of the types of all model outputs, population, cumulative density functions in graphical form, summary statistics tables, percent contribution by route which we generated with pie charts, CDFs, as well as tables which were in the report. Sensitivity analysis tables, uncertainty analysis tables and CDFs. And all of these types of outputs for the special simulation results as well. And again after the break, you'll be seeing a number of actual results simulated by SHEDS-Wood for the CCA assessment.

DR. HEERINGA: Thank you, Dr. Zartarian. That's an excellent presentation. At this point, one of the critical aspects we will turn to in the session tomorrow with responses to actual questions. But here we have a chance for Panel members to ask questions of clarification or fact of the presenters. I'd open the floor at this

point to any members of the SAP who would you like to direct questions to Dr. Zartarian.

Yes, Dr. MacIntosh. Please use the mike and state your name for the record.

DR. MACINTOSH: I'm Dave MacIntosh. I'm glad that you showed us some of detail of the bootstrapping technique. I found it difficult actually to look -- or the quality of the plots in the report are not very good. Right. So just like you said, it's hard to see the various points or the types points on that plot. It is in here, too. Do you have a copy that we can look at that's more clear. Do you have an electronic version we could look at?

DR. ZARTARIAN: We have an electronic version that shows it. I don't know if the report you have is in color or not.

DR. MACINTOSH: No.

DR. ZARTARIAN: You do have some.

DR. MACINTOSH: If you go on the web, is it

better? We may have a solution. Okay.

DR. XUE: There is a problem for the resolution is for that problem because this process generated by SAS. But when you convert in the JPEG file, SAS lost the resolution. If we look at the SAS output it is very clear. But when you transform into the JPEG file because it is like the resolution would be not --

DR. HEERINGA: Okay. Thank you very much. This is a technical point. And I think that we'll do two things, we'll actually look at the PDF file on CD-ROM. And then potentially, if that's not satisfactory for Dr. MacIntosh, we'll have a chance to actually look at the plots that are produced directly.

DR. MACINTOSH: Thanks.

DR. HEERINGA: Dr. McDonald.

DR. MCDONALD: The slide conducting sensitivity analyses, you have the statement, 33 independent variables set to low, medium, and high values, 480 simulations per run implies up 32,160 data size. I don't see where you're

getting 32,160. It seems a bit low to me if you're doing all possible combinations. Could you please clarify what's happening there?

DR. ZARTARIAN: I'll turn it over to Dr. Xue from EPA.

DR. XUE: Basically, that is how you cannot multiply three. One is the baseline. When your medium are not the same because you have three case lower, medium and high. For medium one, you always -- you need run once because you don't need to run three times all the time. These were fixed. So you basically the number you look at is the number from the two multiplied by 33 multiplied 48 plus 1. So this is calculation at these numbers.

DR. MCDONALD: Doesn't it need to be 2 to the power 33?

DR. XUE: Not positive. Because what we do is that the one I just give you an example. For one parameter, we run three times. One is lower, medium, and

high. So these three. And the second plot then 3 multiplied by 480. Second one, you only run two because the median will not change it because you're only changing it one parameter at a time.

For second time, you only run lower and high. So second time would be 2 multiplied 480. Then for third one, the same way. So their number is 33 multiplied 2 and multiply 480 plus the 480. So this is where the number comes from.

DR. HEERINGA: Possibly it sounds like we have a calculation issue. But maybe we'll have a chance to look at that and come back to the Panel. Obviously, if there's some clarification, we would want to have it publicly stated. We have another answer.

DR. HEERINGA: Yes. Please state your name.

DR. GLEN: Graham Glen with ManTech. It's not 2 to the power 33 because we're not simultaneously allowing more than one parameter to be at its high value or its low value. We're only allowing one to vary and keeping the

other 32 at this medium values. I hope that clears it up.

DR. HEERINGA: So this is conditional on fixing all other parameters at a constant value and median. Dr. Hattis, did you have a question?

DR. HATTIS: You've done an extensive analysis of the hand-to-mouth pathway, direct dermal absorption pathway, and the comparable pathways, a total of eight pathways including both soil on the hand. It occurs to me that there might be a couple of other ones. Primarily, pathways that involved initial contact of children's clothing with the decks or playsets followed by either transfer to the hand or other things. So either contact with clothes with the playset or contact of clothes with the soil undoubtedly happens.

Is there any source of information that you've seen that will other allow you to evaluate those other primary routes originating in transfer to clothes?

DR. ZARTARIAN: I believe we acknowledged that in the report that there are other pathways that we do not

consider such as the one you mentioned, track-in from pets, for example, direct mouthing on wood structures. But because of the lack of data and we assume that those pathways were not as relevant or as critical as the ones that we considered, we did not address them in this assessment.

DR. HEERINGA: Dr. Steinberg.

DR. STEINBERG: On your schematic there was a bath that occurred after each day period. Was there an assumption of a daily bathing or bath of each child after exposure?

DR. ZARTARIAN: No. In the previous version of SHEDS-Wood, we did force a daily bathing event. In the revised version per SAP recommendations, we used the CHAD bathing events where they were available. And refresh me, Luther. In the cases where there were long stretches between baths, we used available data on frequency of bathing events.

Did you want to clarify that further?

DR. HEERINGA: Please, step up to the mike and state your name.

DR. SMITH: I'm Luther Smith from ManTech Environmental. No, there was not a forced bath each day. If the CHAD diary indicated that the child took a bath, then that was effected. Then the code has a counter in it to record the hours between baths. Then there is a set of mulinomial probabilities that describe how many days a child could go between baths, either one day, two days, up to seven days.

And then you randomly select the number of days between bath. Then once the counter trips at whatever that number of days is, then a bath is enforced so the baths happen at reasonable times of the day based on the diaries.

DR. ZARTARIAN: And the data used for developing those multinomial probabilities came from the soil contact survey.

DR. HEERINGA: Yes. Dr. Francis.

DR. FRANCIS: I just have a clarification question. On the probability matrix for the selecting to the daily diary for the children, you said that the probabilities were based on data from a single study in Southern California of about 160 children.

DR. ZARTARIAN: Yes.

DR. FRANCIS: Why was that study chosen? Is there any way to look at it compared to the CHAD diary data?

DR. ZARTARIAN: The CHAD diaries are typically 2 to 3, 1, 2, or 3, days. That Level 1 day longitudinal study was the most extensive study available to us that included outdoor time information. And that's why we used it to develop the probabilities that we applied to the CHAD situation. There were very few longitudinal, consecutive days.

DR. HEERINGA: Dr. Adgate.

DR. ADGATE: Were. Can you describe real briefly the longest time period in the longitudinal study?

What's the N number of children?

DR. ZARTARIAN: It's 160 children. And I'm going to ask Dr. Xue to answer specific questions about that study.

DR. XUE: This is one year diary from the May 1999 to June 2000. This is a one-year diary.

DR. OZKAYNAK: Seven days for each.

DR. ADGATE: So you got one week once a month. So you got 12 diaries for each child.

DR. ADGATE: It's one week.

DR. OZKAYNAK: One week each so.

DR. XUE: 7 multiplied by 12, average around 16 days, it could be as many as 7 multiplied by 12 days.

DR. ADGATE: Okay.

DR. HEERINGA: There would be one week diary for each month for 12 months.

DR. ADGATE: Right.

DR. HEERINGA: Yes, Dr. Hattis.

DR. HATTIS: One of our charge questions relates

to the stability of different percentiles of the estimates. And I'm seeing on Table 14 in the similar estimates of lifetime average daily dose distributions an N quoted of 728 or 738. Do I take from that that your typical runs were that those numbers of individuals for the variability dimension and 1 hundred for the uncertainty dimension.

DR. ZARTARIAN: Yes, 1,500 for availability, 200 for uncertainty, 480, for each of the 200 uncertainty simulations. 1,500 when we were just doing availability run.

DR. HATTIS: I see. So when you were adjusting a variability with the central uncertainty distributions then that was the 1,500.

DR. ZARTARIAN: Correct.

DR. HATTIS: Simulated children.

DR. ZARTARIAN: Correct.

DR. HATTIS: And the 728 and 738, that's --

DR. ZARTARIAN: I'm not sure where you're

referring to on that.

DR. XUE: Table 14 in the exposure analysis EPA, the separate a deck on the deck, 700 when you look at a table. And the uncertainty, some size is 480, around 200 to around 300 for total. So each variability is 480, some --

DR. HATTIS: I'm a little thick, so you have to be patient with me. For pure variability one which is what the subject of Table 14 is, for example, is that right? We have 14 with and without decks,

EPA: Correct.

DR. HATTIS: And for the full uncertainty runs then the variability dimension gets reduced to 480. Is that right?

EPA: Correct. Time 300.

DR. HATTIS: 300 on the uncertainty dimensions, so 300.

EPA: 480.

DR. HATTIS: The total size of the cases.

EPA: Correct.

DR. HEERINGA: Dr. MacIntosh. Do you have a question?

DR. MACINTOSH: Very often what I have is page 8. It's slide has 3 at the front and assigned contact days for the child. And I was hoping to get some better understanding of what was done here. So that the second using sets act for simulated contact days. Could you elaborate on that with respect to contact days for public playsets?

DR. ZARTARIAN: Right. The actual inputs that the user enters are the average number of days per year with a playset contact and the average number of days with the deck contact. And the warm, 126 days for that input. For the cold climate scenarios, we used 54. And those numbers were derived from 2 things. One was the average number of days per year in the CHAD diaries that had suitable locations or possible contact days. And in the case of public playset contact, that average was 185.

Then we also considered the probability. For warm climate, we assumed that a child typically would play 7 days a week minus 32 percent rained out days. So that's a 68 percent probability times the 185 would give 126 for warm climate. And for the cold climate, 3 days per week minus 32 percent rained out days, which gives 29 percent probability times 185.

DR. MACINTOSH: So let me ask a follow-up question.

DR. HEERINGA: Absolutely, Doctor.

DR. MACINTOSH: Being outdoor others, possibly contact --

DR. ZARTARIAN: With those particular locations, we didn't use all outdoor, what we considered suitable.

DR. MACINTOSH: And then was there for public playsets what is assumed either explicitly or implicitly about the fraction of those that are CCA-treated.

DR. ZARTARIAN: We do not have a separate input for non-CCA-treated versus CCA-treated. CCA-treated we're

assuming that they're all CCA-treated.

DR. MACINTOSH: How about for residential playsets?

DR. ZARTARIAN: Same. Is that correct?

DR. GLEN: Graham Glen with ManTech. We're assuming that 8 percent of the homes have CCA-treated playsets, a larger percentage may have other kinds of playsets. But we're not considering those at all. But when we generate each simulated child, we determine initially whether they have a CCA-treated playset in their home or not and that decision stands throughout simulation.

DR. MACINTOSH: So then is it right that the results from the residential playsets represent cases where some fraction of those children actually have a playset that is CCA-treated but the results for the public playsets, all public playsets, are CCA-treated.

DR. GLEN: The population we're modeling, CCA-treated public playsets, so we're not making any

assessment for children who contact other kinds of public playsets. So therefore 100 percent of the public playsets are treated in the simulated children we're examining.

DR. MACINTOSH: Right.

DR. LEBOW: I had a similar kind of question. I wasn't really following how the number of contact days was derived. I do understand that it's exposed to a treated playset? I'm talking the public exposure. Did the CHAD diary data actually give you data exposed to playsets, or was it just playgrounds.

DR. ZARTARIAN: Playgrounds.

DR. LEBOW: And you assume that when they go to a playground they were on a playset.

DR. ZARTARIAN: Yes.

DR. LEBOW: Most of the playgrounds in my area have a lot of different kinds of structures, kids running around like crazy. I'm not sure, however, how much of the time on a playgrounds they actually play, swings and the sandboxes and that kind of thing. Was there any attempt

to address that?

DR. GLEN: The CHAD diaries are giving us the outdoor time and suitable locations. And then you're applying a user-specified fraction for converting that time to playset contact time. And actually the time in playgrounds is not directly considered. We don't look at the CHAD codes as being in a playground. We just look at the total other outdoor time category.

DR. ZARTARIAN: And that's because there were not enough CHAD diaries with the playground activity to use only those. We compared the outdoor time from CHAD, outdoor children who reported playground time, and we found that those two distributions were similar which justified our use of the outdoor time for all the diaries to get a large enough --

DR. LEBOW: I think I kind of understand that. I guess I'm -- it would seem that tends to lead towards an over estimate of the number of days actually contacting a treated playset. Unless perhaps you're in a day care type

setting, daily sent out to play on a playset. Maybe I'm not completely understanding how the data was derived, 160 days possible contact,

DR. GLEN: It's 835 in other outdoor locations as a mean value.

DR. LEBOW: Vary dramatically, and I understand that. Have any past studies of exposure arrived at a similar number of possible contact days?

DR. GLEN: However, that number is clearly an over estimate as you say because we're using a broader definition of possible contact then would be actual contact.

DR. LEBOW: Right.

DR. GLEN: And, therefore, we're applying this second fraction.

DR. LEBOW: That for example is 68 percent.

DR. GLEN: It is for the warm. It's 29 for the cold.

DR. LEBOW: What occurs to me, and I think that

is the intention of the SHEDS-Wood definition of your population, initially the definition, children with frequent exposure such as a day care or a public school environment. And I wanted to make sure that is still a population not all children who made contact with a treated playset. Do you see any difference between cold and warm?

DR. ZARTARIAN: That is correct. And to answer your first question, the assumption of -- we used the assumption of 7 days per week play on play grounds minus 32 percent for warm and 3 days per week minus rain out days for assumptions in other studies that have been done for CCA.

DR. GLEN: Here because we're constructing year long diaries using only 8 CHAD diaries, and therefore if one of them has contact, many days of the year will. We do not have the ability using that method to model a unique event, for example.

DR. LEBOW: Yeah, I understand that. You have

to work with what data you have. I just wanted to know, you defined those as frequent contact not just any child who is any contact with CCA playset.

DR. ZARTARIAN: Correct.

DR. HEERINGA: Dr. Zartarian, it seems to me that this particular parameter is essentially a -- 2 or 3 different inputs and user specifications. In your exposure assessment do you for each individual child or can you actually compute the total exposure time in a year for these children and look at that distribution for.

After the several steps you have certain durations of time during the year, that somebody is in 48 hours a year, or 24 or 8 hours a year, could that be derived for the --

DR. ZARTARIAN: We have done those analyses, and we could provide them to you.

DR. HEERINGA: I would appreciate seeing that. And common sense statistics on steps to look at what the distribution of actual annual contact times with

CCA-treated are being assumed in this modeling.

DR. ZARTARIAN: Okay.

DR. MCDONALD: Do I understand this correctly? In the diary says this do have contact and by chance they can't, it forces the contacts to be at the very end of the day?

DR. GLEN: What we determined first whether a given diary day is a contact day or not. Then this second random probability check. If this is determined that it should be a contact day, then at least one of the suitable events will become a contact event. And we've stepped through the day. And if we get to the end of the day and none of the prior ones are, then the last one will become a contact event.

DR. MCDONALD: So my question is: Are you sure that doesn't introduce any artifacts?

DR. GLEN: No. It doesn't introduce a time bias because the duration of contact is actually adjusted downward to compensate for the increased selection

probability for the final event in the diary.

DR. MACDONALD: But you have other events GI tract being voided at 6 a.m., and hand wash, and you had it on them all day or at the ends of the day. But maybe this doesn't happen very often so it's not?

DR. GLEN: The time at which contact occurs throughout the day is proportional to the amount of outdoor time on the diary at each hour of the day essentially. So the distribution of exposure times will match that of outdoor times in large numbers. The issue here is how long they have residues on their. Well, the residues will.

DR. MCDONALD: But that will depend on what time of day they had the contact relative to hand washing, bathing.

DR. GLEN: That's right. But the baths are not always going to be at fixed hour like 7 PM. I mean if a child can actually contact new residue after they have a bath, that would carry over into many, 78 hours into the

next day.

DR. REED: I just want to follow up with Dr. Herringa's comment. I'm a little bit lost in terms of in this case, how many hours per year of outdoor activities and contact. But I'm also curious and maybe it's defined in the document. I didn't see it in a obvious way. Could you also give us a sort of a sketch of the distribution of outdoor activities per day instead of just per year? In the CHAD data bases each outdoor event is 1 to 60 minutes, but what is the distribution in general of how many hours per day or how many events per day?

DR. GLEN: The average CHAD diary has close to three hours of outdoor time in total. And it's almost equally described as outdoors at residences and outdoors 1.4 hours in the mean.

DR. REED: Thank you.

DR. HEERINGA: One last clarification. I think that distribution of annual total time exposure to across the simulated children in the exposure assessment would be

extremely valuable. You might even want to just plot that, exposure time aggregated on the X axis and exposure events on the Y axis.

DR. ZARTARIAN: We'll do that.

Dr. HEERINGA: I don't want to make too much extra work. I think that would be extremely useful, applied exposure time and durations and then the more expert individual we're here at the transfers and other type of action reference.

DR. FREEMAN: On your graph on page 10 on dermal exposure, you have dermal exposure sort of incrementing over the course of the day. So that there's some removal and there's always some left. Is the reason that the child does not become a bundle of contacts because you then are resampling a new diary the next day and the loading that exists at the end of the day disappears?

DR. ZARTARIAN: No. The loading does not. It is in fact carried over from one day to the next. And I think bathing is hand washing and bathing. But

particularly bathing is the primary reason that it does not accumulate.

DR. FREEMAN: But you have your bathing removal efficiency as being about I think it was .6, which means that there's always something left over.

DR. GLEN: Has the hand washing, the bathing, is about .1.

DR. FREEMAN: Okay.

DR. GLEN: And another factor that limits constant, there is a maximum dermal loading in the model which prevents accumulates from exceeding a certain threshold.

DR. ZARTARIAN: Maximum dermal loading is based on

DR. RIVIERE: One question on the dermal. Is that constant between hands and the body exposure?

DR. ZARTARIAN: It's the -- it is the same distribution of --

DR. RIVIERE: It is the same.

DR. ZARTARIAN: For the dermal loading, yes, that's the limit for both hands and body.

DR. HEERINGA: Okay. At this point, we'll have other opportunities for questions. Are there any final questions from the Panel? We're approaching the time and the need for a break. We are scheduled for a half-hour break. I think that's awfully generous. And give you 15 minutes hopefully enough for everyone to take. And let's reconvene here at 10:50. Actually that will be 20 minutes, 10:50. Thank you very much.

[Morning recess at 10:30 a.m.

Panel resumed at 11:15 a.m.]

DR. HEERINGA: Welcome back. And at this point in time, we're going to move to the second of our presentations on the SHEDS-Woods exposure analysis, and let Dr. Zartarian make the introductions and the presentation.

DR. ZARTARIAN: Hello, again. I think we can just jump right into the same colleagues as I acknowledged

last time, and they helped me produce these results that I'm going to be showing for variability, sensitivity, and uncertainty analyses.

So the goals of objectives of this presentation are to present the arsenic lifetime average daily dose results, the arsenic and chromium average dose results, identify the relative significance of exposure routes as well as the critical model inputs, and present uncertainty and sensitivity analysis results as well as the result for the special simulations that I talked about in the last presentation.

The bottom line for the arsenic LADD results is that they were central LADD values on the order of 10 to the minus 6th to 10 to the minus 5th milligram per kilogram day with 95th percentiles on the order of 10 to the minus 5th milligram per kilogram per day.

What I'm going try to do here with all these results since there are so many is just read a summary of the key results and then show some selected supporting

figures that illustrate those results.

So on the next slide, this is a CDFs for the arsenic LADD scenario for both playsets and decks, the warm climate bounding scenario versus the cold climate bounding scenario. At the median here for the warm, we have about 6 times 10 to the minus 6 milligram per kilogram per day; and cold is about 3 times 10 to the minus 6. So we're seeing very consistently across percentiles a factor of 2 in the predicted dose for the warm versus the cold climate bonding scenario predictions due to the difference in assumed model inputs for the two situations.

And the other key thing to note is that there are several orders of magnitude between the lower and upper percentiles due to variability in that simulated population.

This is the same situation, Arsenic LADD, but for playsets only rather than playsets and decks. And again the two lines, the red line is for the warm climate

bounding scenario, blue for cold. And this shape of the CDFs is very simply to the previous ones; however, there is a shift in magnitude. If you could just flip back a second to the previous one and then back again. There's a shift down by a factor of about 2 when we take out the decks and again several orders of magnitude variability.

This figure shows that factor of 2 that I just tried to illustrate by flipping between the playsets and the deck, the CDF and the playsets only. The brown line is the arsenic LADD for children with the decks as well as the playsets. And the black line is playsets only. And there's about a factor of 2 spread shown between the two curves.

For the arsenic average daily dose results, we saw central values of both short-term and intermediate term average daily doses on the order of 10 to the minus 5th to 10 to the minus 4th milligram per kilogram per day with 95th percentiles on the order of 10 to the minus 4th milligram per kilogram per day.

These are about one order of magnitude greater than the LADD results that I just showed you. And these are higher as we expect because of the difference in averaging time between the LADD and the ADD time periods.

So now I'm going to show you some CDFs for the arsenic intermediate term and short-term. This is arsenic intermediate term ADD for children with both playsets and decks. Red line is warm. Blue line is the cold bounding scenario values.

So here the median we have about 6.8 times 10 to the minus 5th for the warm, and 3.1 times 10 to the minus 5th for cold. So there's about a factor of 2 to 3 between the warm versus the cold. And as with the LADD CDFs, again several orders of magnitude between upper and lower percentiles.

This is the arsenic intermediate term for playsets warm climate scenario for playsets with decks and children with playsets only. So again the brown line is with deck; black line, without deck. And a factor of 2 to

3 again between the curves.

This is short-term. We just looked at intermediate term. This is arsenic short-term for children with both playsets and decks and the warm versus the cold CDFs. And these short-term results, as we would expect arsenic because of the 15-day versus 90-day averaging time, the results are very similar to the intermediate term results with several orders of magnitude of variability between lower and upper percentiles and about a factor of 2 to 3 between the warm versus cold values.

So this is arsenic short-term average daily dose for the warm climate scenario for playsets and decks versus playsets only. And again a factor of 2 between the curves, 2 to 3 orders of magnitude of variability across low and high percentiles.

Moving onto the chromium results, we found central values of short and intermediate term average daily doses on the order of 10 to the minus 5th to 10 to

the minus 4th milligram per kilogram per day and 95th percentiles on order of 10 to the minus 4th. These chromium results are very similar to the arsenic results because the inputs were very similar between the different scenarios including the arsenic and chromium residue concentrations.

I'll show you the chromium intermediate term average dose CDFs. This is for children with both playsets and decks, warm versus cold scenarios. And at the median here, we have value of about 6 times 10 minus 5th for the warm, and 3.4 times 10 to the minus 5th for cold. So again the warm is greater than the cold -- sorry -- the predicted dose values for chromium dose for the warm climate bounding scenario are about a factor of 1.5 to 2 greater than in the cold climate bounding scenario seen by the distance in the curves. And there again in this case, 2 to 3 orders of magnitude between the lower and upper percentiles.

So that's chromium intermediate term playsets

and decks. The next one is playsets only. And, again, very consistent information, a factor of 1.5 to 2 between the curves and similar range in availability.

And next is chromium immediate term for the warm climate only. This time looking at playsets with decks versus playsets only. And the children with decks had higher chromium doses than the children without decks by a factor of 2 to 3.

The next is chromium short-term for children with playsets and decks, warm versus cold. And again as expected, this is very similar to the immediate term results where the warm scenario results are greater than the cold ones by a factor of about 2. And again several orders of magnitude between lower upper. And one thing to note on this curve is, on the lower CDF, you'll see that line is abruptly stopped. And that's because there was zero exposure that was not plotted. And, in fact, a zero dose can happen with both the short-term and intermediate term because results children have a chance of not being

exposed in the simulated 15- or 90-day time period.

The next one is chromium short-term average daily dose for children contacting playsets only, warm climate results versus cold climate bounding results. And again similar to intermediate term, several order of magnitude variability warm versus cold, difference of a factor of about 2; and also playsets only, a factor of about 2 less than for children with both playsets and decks.

And the next one shows the difference between children with and without decks for the chromium short-term warm scenario. Again here you can see factor of 2 to 3 between the curves.

Next I want to talk about the relative importance of exposure routes as determined by looking at the population CDFs and summary statistics tables as well as the sensitivity and uncertainty analyses.

The most significant exposure route for the population of interest for all of the baseline scenarios

that I defined earlier, that is, arsenic and chromium, warm and cold for all the time periods we considered was residue ingestion via hand-to-mouth contact, followed by dermal residue contact, then soil ingestion, then dermal soil contact.

I also want to note that children with doses in the upper tails of the population distribution exhibited higher contact with public playsets, wood residues, dermal transfer coefficients, and GI absorptions for residues as well as fewer hand washings per day. And that the soil ingestion pathway became relatively more important than residue ingestion when the residues were reduced by 90 or 99.5 percent via hypothetical exposure mitigation scenarios.

So now I want to show a CDF and then a number of pie charts that illustrate these key findings. This is a population CDF for the arsenic lifetime average daily dose case for the warm climate bounding scenario for children contacting both CCA-treated playsets and decks. And this

shows the contribution by exposure pathway.

So the top line is the total. The green line below that is residue ingestion followed by dermal residue contact, the black line below that. And by an order of magnitude lower is the soil ingestion and then dermal soil contact.

And this is just to illustrate the order of importance. And that's consistent across all the percentiles.

And next I want to show a series of pie charts. There's a lot of information; so I'll just try to it summarize the one or two key things to focus on in each of these pie charts.

The first one here is arsenic LADD, the warm climate bounding scenario. This is the mean contribution by pathway for the entire study population. You'll see that 59 percent of the total dose came from the residue ingestion pathway followed by 31 percent from the dermal residue pathway, 8 percent from soil ingestion, and 2

percent from dermal soil contact.

So the two residue pathways totaled to about 90 percent, and the dermal pathway, 10 percent, with residue ingestion being predominant.

The next pie chart is being similar. And for all of these, the black and white pie charts are based on the entire study population, and the color ones are based on the upper 5th percentile of the study population.

So this is similar, the situation, Arsenic LADD, the warm scenario. But this is for the upper 5th percentile of the population. In this case, we have residue ingestion contributing 68 percent which is an increase from the 59 percent for the entire population. And this is because of higher residue ingestion contribution for the most exposed children for the reasons I described earlier: Greater residues, contact time, dermal transfer coefficient, higher dermal transfer coefficient and less hand washing.

The next slide is the arsenic LADD in the cold

climate scenario. We just looked at a couple of warms. This is cold. Main contribution by pathway for the entire study population. And the key thing here is that residue ingestion contributed 85 percent versus the 59 percent that we saw in the corresponding warm scenario.

What we see is that the actual dose values from residue ingestion are similar in magnitude between the cold and warm; however, the contribution due to the residues, there's a greater contribution to residue ingestion for the cold scenario. And that's because the dermal residue contribution is smaller because of the less assumed exposed skin in the cold versus warm climate scenarios. So dermal becomes relatively less important, and the residue ingestion relatively more important.

The next slide is the corresponding scenario but for the upper 5th percentile. And we just see this affect being a bit more pronounced. It was 85 percent on the previous one, and now it's 89 percent for the residue ingestion contribution.

The next one is arsenic short-term ADD for the warm scenario, again, main contribution by pathway for the entire study population. And looking at the pie chart, you'll see 63 percent from residue ingestion as opposed to 59 percent for the LADD warm scenario. The magnitude is higher for the short-term as we would expect and as we saw earlier than the lifetime scenario, but the percent contribution by pathway is similar for this and all the other pathways.

Next one is the arsenic short-term cold. We just saw arsenic short-term warm, so this is short-term cold. And we're seeing residue ingestion contributing 87 percent as opposed to 58 percent for the lifetime scenario cold simulation. And it was 65 percent for the short-term warm scenario.

So the results here are that there is a similar percent contribution between the short-term and the LADD, but there's an order of magnitude difference in the actual magnitude. And also the dermal residue pathway is lower

in the cold again than in the warm because there's less exposed skin surface there. So again, residue ingestion becomes relatively more important, 87 percent versus 63 percent.

Now, moving into chromium pie charts, this is the chromium short-term warm climate scenario for the entire study population. 61 percent contributed by residue ingestion. It was 63 for arsenic. And, again, we're seeing similar results for the short-term arsenic and short-term chromium because both in magnitude and percent contributions because of the similar inputs.

Next one, this is moving back to arsenic lifetime average daily dose for the warm climate scenario. This is showing the impact after an assumed 90 percent residue reduction and hand washing, one of the hypothetical exposure mitigation scenarios.

And what we're seeing here for the first time is soil ingestion being the dominant pathway, 49 percent; where as residue is now 24 percent as opposed to 59

percent for the corresponding baseline run. So as expected with the reduced residues, the contribution from the two residue pathways decreased; and from the two dermal pathways, it increased. Dermal residue is now 20 percent. It was 31 percent previously. And dermal soil is 7 percent. It was 2 percent previously.

And the next slide is the same thing but at the upper 5th percentile of the population. And the results are very similar with residues being less important; soil pathways becoming relatively more important. Even though the actual dose from the soil ingestion contribution is fixed, it becomes relatively more important in the total contribution.

And the next two are the same thing except for an assumed 99.5 percent residue reduction and additional hand washing after a play event. And this shows that with even lower available residue levels reduced by 99.5 percent, the effect is even more pronounced where soil ingestion is now contributing 96 percent to the total

lifetime average daily dose as opposed to 49 percent that we just saw with the 90 percent residue reduction scenario.

And the next slide is the same thing with the 99.5 percent residue reduction in hand washing strategy but at the upper tail of the population. And now it's essentially all the doses essentially coming from soil ingestion.

And we're getting there. Just a few more. The next one is the arsenic lifetime average daily dose for the warm climate scenario. In this case, we lowered the dermal residue absorption from 3 percent to 0.01 percent. And as we expected with the lower dermal rate, the residue ingestion became relatively more important with all other things being equal. It's about 87 percent.

And the next slide is the same thing. The dermal residue absorption reduction scenario at the upper tails and the effect is more pronounced. It is 95 percent contribution here from residue ingestion versus 87 percent

when we looked the at entire population.

That's it for pie charts.

And next we have identification of important model inputs. We found that the four highest ranked variables from both sensitivity and uncertainty analyses results considered together were wood surface residue to skin transfer efficiency, wood surface residue levels, the fraction of hand surface area mouthed per mouthing event, the GI absorption fraction for residues.

Additional variables that were important as indicated by the sensitivity analyses were maximum dermal loading, the average number of days per year that a child plays on or around CCA playsets, and the frequency of hand washing. And similarly, the additional variables that appeared in the uncertainty analyses were daily soil ingestion rate, the average fraction of nonresidential time that a child plays on or around a CCA-treated playsets, and the frequency of hand wash. So notice that frequency of hand washing appears as addition. They're

not in the top four but as additional variables that were important for most sensitivity and uncertainty analyses.

The next slide summarizes, for variability there were 2 to 3 orders of magnitude in variability of the predicted population dose estimates as we saw on all of the CDFs. And this is primarily due to variability in contact time, wood residues, and exposure and dose factors related particularly to the residue ingestion route, the primary route.

This was based on -- where the variability came from was based on an examination of the extreme low and high dose profiles per last year's SAP recommendation. There was a factor of 4 in the uncertainty of predicted population dose estimates from parameter uncertainty. And this was primarily due to uncertainty in the key variables that I just read pertaining to uncertainty analyses. And I want to emphasize that the factor of 4 is just from the parameter uncertainty. There are additional uncertainties for both the model and scenario selection that we do not

quantify here and Dr. Ozkaynak will be discussing some of these other sources of uncertainty in the next talk.

The next table is an illustration of the sensitivity analysis result. This is arsenic short-term average daily dose scenario for the warm climate bounding scenario. And this is the case where we scaled each independent variable up and down by a factor of a half and two. And what you're seeing here are some of the key independent variables, their unites, and then the stepwise regression -- the rank values, squared rank values from the stepwise regression.

And then the last three columns are the results that have first sensitivity analysis approach I had described where we fix everything at a median value and let each independent variable vary up and down to a high and a low value. So the three columns are the ratio of the dose, the absorbed dose, from the medium to the low scenario, high to medium, and high to low. And, again, we considered the results of both of those approaches in

identifying the critical inputs.

The next slide shows graphically the uncertainty analysis for the arsenic annual average daily dose for the warm climate scenario. And this is showing 3 selected populations, the 5th, 50th, and 95th, ranked by medians. So in the case where we did 200 uncertainty runs with 480 children, simulated children per uncertainty run, you're seeing 480 points on each of these three CDFs. So the uncertainty runs were conducted, and they were ranked. The results were ranked by the median, and we picked the 5th, 50th, and 95th. And what you're seeing here is the complete CDF for each of those three populations of 480 children.

So in this case, uncertainty is read as the vertical distance between the curves. And you should focus on the change in the curves between the 5th and 95th percentile. This is about a factor of 4. And the variability is read as the distance between the lower and upper percentiles for each individual curve. For example,

it's about two order of magnitude between the 10th and 90th percentile.

So another way of looking at the uncertainty is on the next figure. And this is the same scenario, arsenic annual average daily dose, warm climate scenario. And this shows 3 percentiles across all simulated populations. So what you're looking at here are 200 5th percentiles, and 20 50th percentiles, and 200 95th percentiles from the various uncertainty runs.

And in this case, the horizontal axis represents percentiles of the population variability. And then the vertical distance between the curves represents the uncertainty for each individual percentile. So this is another way of looking at the uncertainty and variability on the same figure.

The next slide summarized the special simulations that we conducted. The bottom line is that the baseline dose results did not significantly change for most of the special simulations that we conducted except

for the case of assumed reduced wood residues.

So, to summarize these findings, most of numbers that we're showing here correspond to the warm climate arsenic runs. They would be somewhat different for the other scenarios. But this is to give you an idea of the special simulation results.

For public playsets only, we found that the dose results were similar for children without decks and the playset component of the dose for children with decks.

For the age group selection, because we had very limited data for children ages 7 to 13 years, in order to consider the doses for 1 to 13 year olds as well as 1 to 6 year olds, we assumed that 7 to 13 year olds had 25 percent, 50 percent, 75 percent, and a hundred percent of the dose of 1 to 6 year olds. And we found that the resulting LADD for the higher age group was 10 to 40 percent times higher.

The children for the scenario where we assumed children had pica behavior, we found that the dose results

were 2 to 3 times higher. We also conducted a simulation assuming that the relative bioavailability for surface residues was increased from 27 percent to a hundred percent to get a bounding estimate on that. We found that the results were 1.8 times higher.

We also did a run where we decreased the dermal absorption from 3 percent to 0.01 percent and found the results 26 to 37 percent lower for the warm scenario and 7 to 23 percent lower for the cold scenario.

The next slide summarizes the special simulations specific to hypothetical exposure mitigation scenarios. And we found with additional hand washing, remember for the baseline runs, there is random hand washing throughout the day. So for the special simulation, we forced a hand washing in the model after a play event. And this reduced the baseline dose results by a factor of 1.3 to 1.7.

When we reduced the wood residues by 90 percent, the corresponding arsenic warm climate results were

reduced by a factor of 6 to 7. And when we reduced them by 99.5 percent, their dose results were reduced by a factor of 11 to 17. And when we combined these scenarios these two mitigation scenarios, 90 percent residue reduction with extra hand washing, we saw a reduction in dose by a factor of 7 and the combined with the 99.5 residue reduction in extra hand washing a factor of 11 to 18.

So the next couple of CDFs illustrates some of these special simulations. This is the arsenic LADD warm climate scenario for children, looking at the special simulation of public playsets only. But you're looking at 3 lines here. The top one is public playsets, home playsets, and decks, children with contact with all three.

The next one, they're hard to distinguish, are public and home playsets and public playsets only. And this is showing that children with decks have a factor of 2 greater dose than children without decks. And that children with public and home playsets contact had about

10 to 20 percent higher dose than children contacting public playsets only.

Also most of the playset exposure came from public playsets. And this was because of the greater contact time.

The next one is a CDF for the scenario where we assumed lower dermal absorption 0.01 percent per day. And the top two lines are the baseline total arsenic LADD. And the one just below that, the red one, is the corresponding total LADD after reducing the dermal absorption. And I guess it's the black line, the dotted line, just below the red one is the baseline dermal residue contribution, dermal residue pathway dose. And the line, that the blue line that's several orders of magnitude below that is the dermal residue contribution after the dermal absorption rate was reduced.

So this shows that while the dermal residue pathway changes by several orders of magnitude when we lower the daily dermal absorption rate, the total was only

reduced by a factor of 3. And that's because, looking back to the pie charts, the dermal residue contribution to the total was over 28 percent. So even though when we reduced the rate, it doesn't make as much of an impact on the total.

The next slide shows the special simulation for the arsenic LADD scenario, warm climate scenario, for the case of assuming 90 percent residue reduction in hand washing. In this case, we've got the -- let's see, the top line is baseline total without any mitigation assumed. And the next line is hand washing. The next line shows the impact of hand washing which reduced it about by 30 to 70 percent. And the bottom two lines are the 90 percent residue reduction which had a big impact, a factor of about 6 to 7. And the line that's overlapping, that is a combination of hand washing and 90 percent residue reduction.

The take-home message on this one is that all the extra additional hand washing did make an impact of

about 30 to 70, the 90 percent residue reduction was far greater.

And the last slide is the corresponding CDF with the case of 99.5 percent residue reduction in hand washing with similar results. In this case, again, the 99.5 percent reduction, a factor of 11 to 17 reduction in the dose. And with the extra hand washing, 11 to 18. It's difficult to see the extra effects of the hand washing. However, they did impact 30 to 70 percent.

So these results, this is it for the CDFs. And I just want to remind everybody that the results that I just showed you are all for the dose milligram per kilogram per day for dose. And what you'll be hearing this afternoon, Dr. Dang will be presenting the corresponding risks estimates that go along with all these results that I just presented in this talk.

And next Dr. Ozkaynak will be discussing the strengths and limitation of this SHEDS-Wood exposure and dose assessment as well as similar probabilistic exposure

and dose modeling assessments.

DR. HEERINGA: Dr. Ozkaynak, possibly before we turn to your presentation. Thank you very much, Dr. Zartarian. That was a very nice presentation. Before we turn to Dr. Ozkaynak's presentation, I'd like to offer the Panel a chance to asks questions of clarification or fact. Dr. Hattis.

DR. HATTIS: Sorry to go back to some of the input distributions. But one that you identified from the sensitivity analysis as being critical, and I think is likely to be critical, is, in fact, the residue distribution that I believe you derive from the ACC data primarily. So I would like to ask essentially to get some of these raw data for the Panel so we can look and see.

You've got a log normal distribution that appears to be asymmetric in log space from Table 10 on page 56. The reported minimum is only about a few fold different than the geometric mean whereas the maximum exceeds the geometric mean by something like 30 or 30 fold

or so. So one possible cause of that would be lower bounds that would be nondetect residues.

So the question is: First, can we get the actual distributional data that you used to form these geometric means and standard deviations? Second, how did you treat nondetects in the statistical modeling of this particular distribution?

DR. XUE: First, yes, we will provide you the data for SAP. Second, there is no issue of no detective issue because almost 100 percent is detected.

DR. HATTIS: So in that case, there appears to be an asymmetry. Did you look for possible biomodality or multimodality as the cause of this asymmetry?

DR. XUE: I don't know. I think I need to look more into this.

DR. HATTIS: Right.

DR. HEERINGA: That's a very good point. Yes, Dr. Bates.

DR. BATES: I'd like to ask a question about the

averaging time for the LADD which I understand is 75 years. And I suspect this is a convention and probably makes about sense when you have a long-term exposure. But in this special situation where it is young children who are being exposed, if there is a carcinogenic risk, it's likely to be manifest somewhat before 75 years.

And I'm just wondering whether by using a 75 year averaging time you're kind of diluting the important exposure. And have you given some consideration as to whether this is biologically appropriate?

DR. ZARTARIAN: Winston.

DR. DANG: Why we used 75 years as a lifetime exposure is based on the average exposure duration for the lifetime in the 75 years. We use the 6 years as exposure duration divide by 75 years. That's basically the Agency's policy here.

DR. BATES: Yes, I understand that. But I'm what I'm asking whether in this special case, it's an appropriate approach.

DR. DANG: We didn't consider that as far as I know. Yeah, I think so. Yeah.

DR. HEERINGA: So the answer at this point is that you used 75 as the divisor for the integrated exposure over the 6 years for the LADD but have not considered approaches at this point or other durations of lifetime exposure.

DR. XUE: I think the last time SAP also raised the issue because at that time we assumed that 1 to 6 year old people were children were exposure on the playground. So people, other model do use from 7, 8, and 9 years old. Because other than this for the hand-to-mouth frequency would be very, very small. So we would not -- we don't need to worry about this. That's why we have another analysis. If we assume that they have still have exposure from 7 to 13 years old, what that risk affect will be, what's the more exposure we'll get. So I think that presented the results in his presentation.

DR. HEERINGA: Dr. Steinberg.

DR. STEINBERG: Are there any significant data gaps that empirical data could help you with in any of this modeling? Is there any one or two things that come to mind that are significant?

DR. XUE: Yes. And the number of days the kids go to playground change by graphical location. And the contact time from the week playground not necessary you could do the present. Maybe do other place. Can probability when you would go playground, you are contacted to the playground.

So I think this is -- right now, I think this is the most important for us and also from what's the probability of the deck for given children the deck. And also the home playset. So if we can have more data, it would differently help us.

DR. HEERINGA: Dr. Ryan.

DR. RYAN: I have three sort of related questions. More a clarification than anything else. I'd just like to get your opinion.

If I look at this these various pie charts, Dr. Zartarian, that you presented, I don't see a lot of difference between the contribution from in the overall population versus those that are in the upper 5 percentile whatever the right number might be. For example, I'm looking at one here for LADD for arsenic that says, 59 percent is residue ingestion for the whole population while 68 percent is that for the upper 50 percentile.

Do you believe these numbers are different from one another? And if they are, why? And if they're not, does that really just say that the contribution is really driven by the concentration that might be found in the soil or whatever they might be ingesting? And then I have a couple of others that are other things. I'd like you to comment on this one.

DR. XUE: Yes. First of all, for all we did not do the systematic statistic to see that this is statistically significant or not because this is effect by some -- others. But we did do some analysis for the high

percent of people to look at how much time compared with avenge time, what is the residue, what's the transfer efficiency. We do fine that these numbers increase, this first points.

Second point is that we look at this is just one. Because if it was statistic, it would look same size. We just show one example. And we look at it from warm weather, warm climate, cold climate, intermediate and the short-term. They have consistent pattern this way. That's why we get at the preliminary conclusion. So this is maybe something due to more contact time of residue concentration or transfer coefficient.

DR. RYAN: So this whole thing kind of could be looked upon as some type of sensitivity analysis on a different percentiles to see what the contributions are. I was struck by how similar the contributions seem to be. You'd think that one or another thing might dominate. Just a comment to be made.

One other comment that I'd like to make is the

availability across the population was stated a number of times as several order of magnitude. If you shrink down what you're looking at a little bit to the 10th to the 90th, those several orders of magnitude shrink down to like 1 or 1 and a half. It seems like there's a lot more -- it's a lot tighter in the 10th to the 90th. And I guess that might be driven by the zero to 10 percentile where I believe, Dr. Zartarian, you said often the case would be there was no exposure of all in an individual during a 15-day averaging period at the very low end so the data get truncated there.

At the upper end, is there any similar thing like these are the people that get exposed every day? I'm just trying to understand what's going on at the far tails. And I think I understand the low tail. And the high tail might be the way to go.

DR. ZARTARIAN: We have some supporting information to answer that question. Dr. Glen is looking for it.

DR. GLEN: Are there supplemental slides available, Set X 4?

Slide 14 I believe talks about the extreme dose profiles. It may be hard to read on this screen.

But what it says is a special one year one run of a thousand children was made to examine which variables were driving the extremes of the variability distribution. The highest children in the sample, the two highest, which is 99.8 percentile, averaged 123 days contact in public playsets which is extremely close to the mean number of day. So that was not a factor.

They did both have home playsets and decks. The playset and deck residue concentrations were significantly elevated and moreso the hand and body transfer coefficients were quite high. We no longer use a single term as a transfer coefficient. It's now a product of four terms. But overall these factor were 6 to 7 times higher in these two children than for the general population.

Also hand washing was significantly lower than the overall average by about a factor of 3. These 2 highest children had a 21 times ADD of the population mean. And it was largely driven by the higher residue concentrations, the higher transfer coefficients, and the lower hand washings not the differences in contact time primarily.

DR. RYAN: Okay. That addresses that. So it is a series of things. It's not just higher concentrations that they might be exposed to which kind of might be --

DR. GLEN: No. The concentrations were only higher by a factor of --

DR. RYAN: Yeah. Just a small factor I see here. But overall it looks like the transfer coefficients were, you know, the chief thing here and maybe a little bit from some of these other things as well. Thank you. And if I could, one more?

DR. HEERINGA: Sure, Dr. Ryan.

DR. RYAN: I'm not the brightest guy in world.

Maybe because I'm the product of the Massachusetts public education system. I'm not sure. Be we have others in the room who are also.

The table on sensitivity analysis where you have the stepwise ranks, the medium, low ratios and so on, could you walk me through that. I don't understand how towards the bottom bathing removal efficiency ends up being less than 1 for some of these ratios and so on.

And could you tell me what is really meant by that stepwise rank process? I'd just like to hear a little bit more clarification. I've read it. But it's not quite sinking in yet.

DR. XUE: For the hand washing, because the more hand washing, the less exposure you will have. So high, that's why ratio is less than one. In terms of stepwise regression, we use the partial R square. So that's why to see that if I change this variable, this independent variable what's effect on depend variable. This one can say that even though this ratio is lower, but

statistically, they're related to the dependent variable.

DR. RYAN: So essentially the numbers less than one are simply because if you wash your hands more, the stuff goes down.

DR. XUE: Correct.

DR. RYAN: And that works for some of the other ones as well. So that's why you get ratios less than one. And the stepwise rank, can you just tell me again what the process is? You make the --

DR. XUE: Contribution based on partial R squared, the distribution for total variance.

DR. RYAN: In the changing process, if it changes --

DR. XUE: Because we put all the data since is the analysis. And then we use the total exposure, a total dose as the dependant variable and all the variable as independent variable. Then we run the step-first regression to which one first selected. And then there would be how partial R square. So we use this --

DR. RYAN: And as you go down this stepwise regression, you keep the previous ones in?

DR. XUE: Yes.

DR. HEERINGA: Thank you very much, Dr. Xue. Dr. Francis.

DR. FRANCIS: My question is actually kind of related to Dr. Ryan's. And it involves your pie charts which are actually kind of interesting. And clearly for most of the, what do you want to call them, the nonspecial cases, the residue ingestion is the most important factor. But if you look at your sensitivity table, the first four values that turn out to be the most important are all of those related to residue ingestion. Correct?

DR. ZARTARIAN: Yes.

DR. FRANCIS: Did you try to produce pie charts, or did you try to look at the data for residue ingestion only to see which ones of these are most important? Say, for example, if you did a pie chart and you changed residue -- if you changed the transfer coefficient by a

factor of whatever plus 2, a factor of 2 up or down, or if you changed -- since your data are actually fairly weak on the hand-to-mouth data, if you made some assumptions about those, did you look at any of the things that effect this biggest proportion of the exposure.

DR. XUE: We do change these variable. But we do not do analysis in terms of the ratio as the dose.

DR. ZARTARIAN: We did not do -- you're asking if we did pathway specific sensitivity analyses. The answer is just no. We just did for the entire, for all pathways collectively.

DR. MCDONALD: One thing I've noted. When we're writing up the final report, we'll have to make sure that ADD children doesn't get misinterpreted as children with special attention deficit disorder behavior. Be careful with the acronyms there.

One question though. We were sent a version of SHEDS-Wood on a CD. Were we actually sent enough so that we can run some of the other analyses that you did

complete with the graphical summaries or the regression analysis that you've been talking about?

DR. XUE: The CD has only the program. For the other analyses, we have additional program. We did not put in the CD.

DR. HEERINGA: So the CD contains only the SAS source code, macro source code, for the SHEDS-Wood not actually an executable version of it. I guess it would be executable.

DR. XUE: Yeah, correct. You only can run and look at the results put analysis program in the CD.

DR. HEERINGA: Sure.

DR. MACINTOSH: Given the importance of the ingestion pathway, following up, I think, with some of Dr. Francis's comments here in some ways. Can you talk about the relevance or applicable of the hand-to-mouth videography data to a child on a playground or on a deck or on a playset?

DR. ZARTARIAN: Just a moment. I'm looking at

the analysis from this sensitivity uncertainty analysis.

Could you clarify the question? Are you asking about the quality of the videography data or the contribution to the dose from that particular variable, the importance of that variable?

DR. MACINTOSH: More the former. Like the kind of the quality. Not necessarily the quality, but more like the relevance. Let me find that variable in the report. Basically the hand-to-mouth frequency. It's on page 74, top of the page. So is this study, Valarie, that you've been involved with, you know, it's the Leckie report and then your '98 paper and then the two Reed papers and the Tolve paper?

So are those children on decks? Are they on playgrounds? Are they on playsets? If so, how many? If not, okay. How do you think that relates to children who are on playgrounds and playsets and decks?

DR. ZARTARIAN: Very good question. I see what you're asking now. There are very few studies available

for frequency of hand-to-mouth activity or surface area of hands mouthed during mouthing events, both of which we needed in SHEDS-Wood. We used available data. I believe all the ones we used were from videography studies, and they were not specific to this study population.

The Leckie, et al., study was, I believe, 20 children both indoors and outdoors in the Bay area of California. I'll have to check on that. It may have just been outdoors. The Zartarian, et al., '98 paper was just four children, migrant children of farm workers in California. The Reed Study was 30 children indoors and outdoors in urban New Jersey. And the Freeman, et al., 2000 study was for children -- we used outdoor -- indoor and door for uncertainty data.

DR. FREEMAN: The four children that I sent you, that was the playset data. There are 19 children were videotaped, but only four were on playsets.

DR. ZARTARIAN: That's right. That's right. So of all the children considered, only the data for four of

the children were specific to playsets.

DR. MACINTOSH: And then how did you synthesize that data?

DR. ZARTARIAN: Most of the studies where we actually had the raw data, we fit a Weibull distribution to those. And then we also used, because we had summary statistics available from the Minnesota children's study and the Black, et al., study; we used those two additional studies for the uncertainty distribution fitting.

DR. MACINTOSH: Okay.

DR. HEERINGA: The Weibull distribution then is just distribution of counter or frequency of mouthings during a fixed interval of time.

DR. ZARTARIAN: Correct. We also used the videography data for the -- sorry -- the Leckie, et al., 2000 study also had some information on the fraction of hands mouthed.

DR. HEERINGA: Thank you very much, Dr. Zartarian.

DR. HATTIS: This is the question about the interface between your exposure assessment and Dr. Dang's risk assessment, particularly for the arsenic. You've in the past stressed the importance of being consistent about the exposure, the terms in which exposure is stated. And your terms exposure means crossing the barrier to the bloodstream essentially.

DR. ZARTARIAN: In this scenario, exposure is the contact and the doses, the crossing into the blood.

DR. HATTIS: Okay. Okay. Fine. But your final outputs are in terms of dose, in terms of milligram per kilogram.

DR. ZARTARIAN: Correct. Absorbed dose.

DR. HATTIS: Absorbed dose.

DR. ZARTARIAN: Yes.

DR. HATTIS: Quite right.

Dr. Dang's calculations of risk utilize Agency potency factors that seem to be based, I believe, on the calculation of concentration in the water in the Taiwan

studies and an assumed amount drank per day. So that there seems to be not exactly the same definition of absorbed dose in the two things. In fact, yours would be -- your term for ingestion is like 27 percent per day on average. And maybe that gets reduced because some of that gets lost with the voiding.

DR. ZARTARIAN: I believe these issues will be discussed in the afternoon session. But Dr. Dang may want to add something.

DR. DANG: We use lifetime average daily dose based on the shift with the model. And regarding that cancer effect, I would like to defer to Dr. Jonathan Chang. Maybe he can be able to answer that question.

DR. CHANG: I think this is a very good question. And when we do the risk assessment and we notice that the absorbed dose and the dosage that is used for the risk assessment has an endpoint, there are in a different kind of basis. And this is reasons that in the exposure assessment part that we do have one basic

assumption. That one is that arsenic -- when we're talking about oral exposure, because it's hazard endpoint is based on the exposed dose, so we just assumed that through oral route 100 percent that exposed is absorbed into the body. So this is the assumptions that we used.

DR. HATTIS: So you didn't take the direct outputs from the study for using, from this dose analysis for your --

DR. CHANG: So I think in the calculation in the model that basically we assume, 100 percent if it's true oral route is absorbed into the body. So, therefore, when we say "absorbed dose," it's equal to the exposed dose.

DR. HATTIS: I'm trying to understand whether we need to ask Dr. Zartarian's group to supply us with different numbers essentially to see whether -- because essentially, to make this conversion between exposure rate, contact rate, by the oral route at least and absorbed dose, there's at least a fact -- there's likely to be at least a factor of four difference. So the issue

is whether in fact the numbers we have reflect this difference.

DR. CHANG: Actually, if we are talking about the oral exposure route and those kind of things, we're assuming basically the number from the exposure models, the SHEDS model result is equivalent to that contact dose to the exposed dose.

DR. HATTIS: But it's not.

DR. DANG: Actually, lifetime average of daily dose has already been justified with bioavailability. I believe that has been presented in exposure assessment for oral with residue and with soil bioavailability studies. So in other words, the baseline lifetime every day daily dose already include indication of the dose by bioavailability already.

DR. HATTIS: Well, that's in the Taiwan study. The model reduces the contact dose by at least this four fold factor.

DR. ZARTARIAN: The SHEDS-Wood model used

bioavailability from a pig study.

DR. DANG: Yes.

DR. ZARTARIAN: Which is a different than --

DR. DANG: That is a different issue.

DR. ZARTARIAN: Yeah, that's different numbers than for the risk.

DR. DANG: It's the Taiwan study basically used arsenic in solution. And what we use it is basically is bioavailability is relative bioavailability is comparable from absorption in what we compare it. The dosing study, what we have, and I'm going to discuss it this afternoon, compared to the water soluble. So one is like -- we find it's about a 29 percent. And for the soil residue is roughly about 47 percent.

DR. HEERINGA: I think there is a question that we'll need to sort out this afternoon because I think the question, as I understand Dr. Hattis, is whether we are compounding the bioavailability coefficients on these exposure estimates. So we just need to understand that

pathway from the SHEDS-Woods exposure estimates and to the actual lifetime average daily doses that are actually being used in the actual risk calculations.

DR. KISSEL: I'm having trouble finding the maximum skin loading of arsenic. Can you point me in the document where that cap, that cut off for skin loading of arsenic is?

DR. GLEN: The maximum dermal loading is not a separate input variable, and, therefore, does not appear in Table 9 or the discussion in the report on inputs. It's calculated from two other inputs, the residue concentrations and the transfer efficiency, I believe. Because it's a derived value in the model, there may not be very much information on it in the report. I'm not sure exactly where it's discussed. I'll have to get back to you.

DR. XUE: The data came from ACC, one is hand -- basically it's the residue in the hand. And also another is the residue from the deck. So we carry this number to

calculate the transfer efficiency. So the transfer efficiency, this is -- because we only have two number we know. One is that the transfer efficiency; one is the of deck residue. So because of the maximum loading, we can get at this from the transfer efficiency and the deck residue. That is why this is not an independent input variable.

DR. KISSEL: I'd still like to know what the number turns out to be.

DR. XUE: The number to be -- we have figure, a supplemental. X-4, Table 9.

DR. KISSEL: There's no units on the X axis there. That's what bothers me.

DR. XUE: The units is microgram per centimeter square.

DR. RIVIERE: Back to the same question I had earlier. Is the hand maximal load the same as the rest of the body?

DR. XUE: Correct.

DR. RIVIERE: So you assume the same transfer efficiency to hand to the rest of the body.

DR. XUE: Correct.

DR. RIVIERE: I guess there will be a time we can talk later, right, about specific points of this.

DR. HEERINGA: Yes, we'll have a chance for general questions after this.

DR. ADGATE: I was just wondering. What it appears is that things that are products are kind of hard to dig up in the report. And it would be nice to see everything that's sort of a product term, the time spent on playsets and on your deck was one example. And this is another. Are there other products like this that are sort of key to the model and model outputs?

DR. ZARTARIAN: We talk about the dermal transfer coefficient a little bit in the report. But we do explicitly say that that's the product of four terms. And we show those explicitly. Those are the only ones I can think of off the top of my head.

DR. RIVIERE: Okay.

DR. HEERINGA: That's a good point. Are there any other questions at this point?

DR. WAUCHOPE: Just a quick general complaint. This is not only place where units are not reported in figures and in tables. I found that frustrating because very often I had no idea what the scale referred to.

DR. ZARTARIAN: Was that in the report or just in the supplemental slides?

DR. WAUCHOPE: In the report, yes.

DR. ZARTARIAN: In the report.

DR. WAUCHOPE: I'll be glad to show you some examples.

DR. ZARTARIAN: If you could, that will be great. Thanks.

DR. HEERINGA: And definitely we'll have a chance in our final report to have an addendum with some of the technical points that need to be clear.

DR. STILWELL: I just have one question on that

extreme dose profile. You found an increased residue concentrations were very important. So is that meaning like for docks and piers and things like that where the arsenic in the wood is much higher? So did you take that into account. Like playgrounds may not always be built with .4-pound CCA wood. There may be higher amounts in there and particularly fishing piers.

DR. ZARTARIAN: We used the available data that was collected that was specifically on playsets and decks and not other structures.

DR. HEERINGA: Any additional questions at this point from the Panel? We will have a chance, of course, not only through the remaining presentations, but even through the response to questions to entertain other points of clarification.

At this point, I have 12:08. And what I'd like to ask Dr. Ozkaynak whether he wants to go before lunch or after lunch.

DR. OZKAYNAK: I think it's really at your

discretion. Either way is fine with me.

DR. HEERINGA: In the interest in staying with our agenda, I think you were scheduled for a presentation of approximately one half hour. I think that what I would prefer to do is that we take a one-hour break for lunch and reconvene at 1:10 at which time we would have your presentation.

In terms of our agenda, and again depending on comments and questions, that would probably put us about 15 minutes to a half hour off schedule. But I think we'll see how the afternoon goes. And for public commentors that are scheduled to present this afternoon, we'll do everything we can to meet your scheduled slot today versus tomorrow that is, not to the minute, since many of you may have travel schedules, too, that's we'd like to honor.

In that case, let's adjourn for the lunch hour, returning here at 1:10 to hear Dr. Ozkaynak's presentation.

[Lunch recess at 12:10 p.m.;

meeting reconvened at 1:13 p.m.]

DR. HEERINGA: Welcome back. We're going to reconvene our session on the Science Advisory Panel meeting on children's exposure to CCA-treated wood and playsets and decks. We're going to be picking up our agenda with a presentation by Dr. Haluk Ozkaynak of the Office of Research and Development on the Strengths and Limitations Probabilistic Exposure and Dose Assessment.

DR. OZKAYNAK: Thank you, Dr. Heeringa.

I'm going to step back a little bit and take a big picture look at the modeling methodologies that we heard this morning.

Certainly, it has been come quite clear from the presentations that we've heard so far and the discussion ensuing them, that the SHEDS-Wood model is a fairly complex model with numerous inputs and multiple pathway of exposures that are being simulated. So it would be helpful for us to examine what are some of the important attributes of this model as well as self-inherent

limitations.

So I tried to organize my brief presentation here in those two categories. First of all, one of the advantages of this model is that it relies upon a probabilistic methodology which has been recommended over the past numerous years now by various scientific panels, specifically, the FIFRA OPP-SAP in 2001 for CCA, has recommended the Agency to consider probabilistic methodologies for exposure and risk assessment.

National Academy and various EPA Science Advisory Panels have advised the Agency and scientific community the merits and the advantages of probabilistic methodologies especially addressing the variability and uncertainty in the information whether it's on the exposure side or the toxicity or the hazard side.

In response to these recommendations and advice, EPA-ORD has embarked upon, as I mentioned before about five years ago, the SHEDS modeling program. And this modeling effort has been the product of a strong team of

researchers, by the way who are largely present here today, possessing unique expertise in the critical disciplines that are needed to achieve this goal, namely biostatistics, exposure modeling, and computer programming.

The SHEDS model is the only EPA 2-dimensional Monte Carlo exposure and dose model which addresses both the variability and uncertainty in model inputs as well as outputs. The model generates realistic times series of high resolution exposure predictions which are order of minutes to hours that can be linked to PMMK models such ORD's ERDEM model, which stands for the exposure related dose evaluation model.

In essence the SHEDS model allows the dynamic computation of interrelated exposures as we heard this morning. Why do we go through great lengths of constructing these diaries and trying to combine them with the various exposure factor and source information?

One of the main problems is that it's very

difficult to simulate complicated human activity profiles for either children or adults as they move from one microenvironment to another during the course of their daily activities. And then hence change their exposure profiles in a very complicated fashion to sources that can be located either indoor, outdoor, or other microenvironments. As I mentioned before, CCA source ranked is located outdoors. But for other pollutants, we have sources that are indoors as well as other microenvironments, public places, in cars, and other environments. So the SHEDS model either for pesticides or CCA or PM or air toxins, rely on the CHAD diaries which are statistically drawn information that provides on a close to a minute resolution the location and the type of activities the subjects perform so that interrelationship between one time period into another in conjunction with where they are and what they are doing can be incorporated in the simulations and, thus, generating some realistic profiles of updates and absorption of chemicals which may

have different properties in terms of their physical and chemical attributes.

Specifically, the SHEDS-Wood model accounts for dermal removal by bathing and washing, and dermal carryover from one event to the next. And, again, these type of carryover processes in terms of the child moving from one location to another, or the child washing their hands or taking a bath, are derived from the information that's provided to us from the CHAD diaries.

The model mechanistically links hand-to-mouth ingestion with dermal hand exposure. So what's on the hand is correlated with what's ingested when a finger is put into the mouth. And we do not make an arbitrary assumption in terms of the average loading or average nondietary ingestion.

The statistical basis of the model construct and the inputs allows us formulation of empirical confidence estimates for different percentiles of the predicted exposure or dose functions cumulative distribution

functions. And as we heard again this morning, the code especially written in SAS allows the user unique advantages in performing sensitivity and uncertainty analysis for identifying critical model inputs and factors contributing most to model predictions. And we already had some discussions about that this morning.

So that the next question, logical question, becomes why bother with a 2-Dimensional Monte Carlo simulation? Clearly, it's more complex and more involved and more computationally intense. And I asked that question especially after a recent conference that I attended. I heard a suggestion from one of the presenters that one can use perhaps 1-Dimensional Monte Carlo model to proximate the uncertainty bounds associated with the predicted population cumulative density function generated by a one-dimensional model.

And if I look at the figure on the bottom left here, that sort of gives you a hypothetical example of how, if one were to implement this, one would obtain some

approximate ranges for the minimum or maximum associated with the predicted CDFs.

The first thing to note is that if the baseline, let's say the middle CDF, is here, and if one were to somehow figure out all the 33 variables, how to assign minimum values to them. Some of them are obviously unbounded distributions. Or come up with a maximum or upper percentile for each one of them and force the model to take the maximums of all of these variables, then resulting CDFs will be unrealistically on the extreme to the right upper exposure end or extremely low on the lower end.

And I've been actually generous not making these distributions far apart than they probably should be. So in essence that the bounds will be extremely broad and will not be really meaningful in terms of assigning any probability estimates for expected percentage of the observations within a certain interval associated with different percentiles of the distribution.

Theoretically, you know, one can assume that some variables might be correlated. But it's impossible that most these variables will be correlated as such. Whereas if you look at example on the right, if you run a 2-D Monte Carlo, as Dr. Zartarian presented some of the CDFs, you'll have a much narrower and more manageable uncertainty range associated the with the variability or cumulative distribution function.

So in essence, there is no simple way out of doing a 2-D Monte Carlo run if one were to look at the availability and uncertainty explicitly and independently.

One of the things that we're, of course, interested in as scientists and as policy analysts, what are the determinants of high end of exposures. So the SHEDS-Wood model provides a reliable technique to examine sources of high-end exposures. We save all the outputs and the critical input values that go into the input for each of the simulation and iterations so that we can post analyze the various issues, the residues or the transfer

coefficients, or time spent on a deck, to figure out what are the real determinants of high-end exposures, and do they make sense, have we generated some artificially strange combinations; and try to assure ourselves that these are reasonable sets of interrelated inputs that have generated those results.

And one of the things that we're going to hear more this afternoon about is that the probabilistic model, like the SHEDS-Wood model allows, is assessing impacts of alternative exposure reduction scenarios. Especially source-to-dose models make this kind of an evaluation very appealing. And thus provides the regulators some guidance in terms of implications of certain changes in the source strings, behaviors, mitigation measures, and other parameters that are critical for evaluation.

The way the model is constructed, it allows incorporation of data from future diary surveys. And we have a structure in the SHEDS-Wood model that we've already exercised in a few instances that when special

survey data is obtained from certain field studies, we can indeed incorporate that and run it as a special application.

I talked about the sensitivity in the certain analysis, why that will be helpful in terms of identifying the critical drivers of the result or the important variables that may have some limitations and how they may influence the results. But in other users of that information it is actually the people that are in the field and who are interested in collecting further information.

The results from our sensitivity and uncertainty analysis at ORD has actually been used to guide future data collection activities. We really feed that information into design of future measurement studies in areas where we really feel that better information with more precise information would be important in terms of enhancing the reliability of model predictions.

And, finally, in terms of the ultimate strength

of the models, such as the SHEDS-Wood and other probabilistic models, is that they provide a valuable tool for risk management and policy evaluations.

Now, having said all that, those are all great attributes. But at the same time as model developers, we're also aware of the limitations of this these models. And we need to be explicit about those as well.

One of the first problems that one encounters, I think a number of you perhaps already did, it's a fairly computer intensive method and model. And right now it runs on the SAS platform. Ao a knowledge of SAS' platform might not necessarily be required but it is preferable.

The model is input intensive and often requires preprocessing of CHAD diaries and many types of information that is required. And the user needs to understand the model and its inputs well for correct implementation. So it's easy to press buttons and get outputs. But in order to avoid some mistakes and perhaps erroneous interpretations, it will be really important to

know something about the code and the basic structure of the model.

Limitations of information or sample size for key model inputs obviously influence the results. We already talked a little bit about that, and I'm sure we will be examining that issue further.

Now the August 2000 SAP, and we started already talking about it this morning, spent a lot of time in terms of the difficulties of fitting distributions. Clearly fitting variability on certain distributions, the model inputs require a certain amount of knowledge of statistics and experience in interpreting the results. And we're always looking for ways to advance our ability, tools, and skills to be able to do the availability and uncertainty estimation and fitting better each time we revise the cord.

And this is an area that is quite important, especially for a 2-dimensional model such as the SHEDS-Wood model. With a 1-dimensional model, one can

probably lump everything together and might not necessarily worry too much about the separation of source variability from uncertainty. But in this case, we do worry immensely about that.

Identifying and implementing multiple correlations has not been a big issue so far as the SHEDS CCA wood model. But it could be important when the correlation among variables can be high which I mean by something greater than .5 typically. And we have not incurred many of these instances, but that's something to watch out.

And when I talked about fitting distributions to variability uncertainty, the next thing that sort of is a logical problem that is associated with that issue is that what are the techniques for actually implementing that. And, unfortunately, currently there are no standard methods for estimating parameter or model uncertainty. Clearly, there are different techniques, there are useful techniques. But they're not unique and they're prescribed

and they shouldn't be.

The SHEDS-Wood model certainly addresses a certain scenario definition and incorporates certain pathways. And if one were to change either the definitions of either the scenarios or pathways, that may necessitate some code modifications depending on the change involved.

Now, let's talk a little bit about the outputs. The model can generate lot of outputs. And a number of the outputs that are generated are post-processed outputs from the basic SHEDS-Wood model. The question then becomes how do you process those outputs and how do you interpret of these model output results from a 2-D Monte Carlo simulation. It's not always straight forward especially when we're talking about interpolation between the variability and uncertainty in a number of occasions.

One of the things that as a modeler and as a scientist that we like to do is a reality check or comparison of the model results with other published data

or comparable analysis. So the comparison of results with other deterministic or other 1-D model, 1-dimensional Monte Carlo probabilistic models, requires careful consideration. It's not always easy to find the best way of benchmarking or ground-truing these models especially when you're dealing with slightly apples and oranges problem.

The current SHEDS-Wood model does not quantify all sources of uncertainty in the exposure and dose predictions. As Dr. Zartarian alluded to that earlier, there are other sources of uncertainty than just the input or model parameter uncertainty. And some of the more important ones is the model uncertainty or scenario uncertainty.

And some of these include alternative specifications of algorithms, for example, that pertains to the model, uncertainty. And sometimes we're unable to characterize biases or uncertainties other than sample-size-based considerations.

How we define the target population and location or instances of their potential exposures are also important. There are likely conditions of exposure occurring in the natural circumstances. But for us to sort of frame all these likely scenarios in the current construct it is not always that straight forward.

The final point that I want to make here is that it's something that might seem obvious to a number of you, but we run into in our discussion with our colleagues sometimes, is that the model designed to simulate distributions of exposures for hypothetical not actual individuals within the population. These are likely conditions of exposure, since many combinations are statistically hypothetical subject and his or her exposure and do not represent an actual individual.

So those are my sort of general observations of what are some strengths and limitations of the SHEDS-Wood model or similar models, probabilistic exposure models, either 1-D or 2-D Monte Carlo construct. Thank you.

DR. HEERINGA: Thank you, Dr. Ozkaynak. Before we move on to the discussion of the probabilistic risk assessment, does anybody on the Panel have any questions that they'd like to pose in response to Dr. Ozkaynak's presentation?

DR. MACINTOSH: I think this might be a rhetorical question more than anything else. But these uncertainties that you mentioned that are not even attempted to be captured in the analysis for CCA that you've done in the model and scenario uncertainty, how would you encourage the Panel to consider those uncertainties with respect to your expressions, your quantitative expressions of uncertainty?

DR. OZKAYNAK: Well, I think what I would be looking for is some guidance and advice in terms of the Agency characterizing at the very least if not perhaps trying to attempt to bound some of these uncertainties that we may not have incorporated. And I mentioned a number of them. Obviously, totally reramping the code and

writing a totally new code will be totally draconian. And I don't think we're going to go there.

I think that differences in different databases and sometimes there are inherent biases or assumptions, certain databases that one needs to be aware of rather than putting everything in the same pot and fitting distributions. And, of course, we made some of those decisions in terms of when we were pulling together certain data sets to estimate variability as opposed to keeping certain aside to look at the uncertainty rather than collectively looking at everything together.

So I'm just thinking aloud here. They are basically some of the issues that were raised earlier in terms of scenario definition, in terms of the target population, how you define that in terms of other sources of uncertainty that may be related to certain algorithm specification that we have not considered for example.

And then the other information is lack of knowledge or presence of knowledge that might influence us

to look at certain information differently. Those are some general thoughts that I have. But I'm sure the Panel members can maybe think about some other useful suggestions for us to think more about.

The other dimensions of uncertainty, because the bounds on the uncertainty that have been sort of presented to you this morning, are not that wide. And I'm not sure whether that's reasonable or it should be greater than that or whether it should be a factor of 2 or a factor of 4. But it's an important question. But at the same time, it's a very difficult one to determine in a defensible fashion. So how do we make that determination in a defensible fashion is obviously what we're interested in finding out.

DR. HEERINGA: Any other questions to Dr. Ozkaynak?

DR. MACINTOSH: So what models -- models are great. I'm all for models. Models are especially great when you can evaluate their performance. Right. So what

-- and, hopefully, you find out that they perform well. So what has been done to evaluate this model so far? And what parameters or what aspects of it have you even attempted to evaluate?

DR. OZKAYNAK: I think -- I'm trying to remember. Dr. Zartarian, did you mention anything about the model evaluation this morning? I think model comparison is what we've attempted to do.

DR. MACINTOSH: I see.

DR. ZARTARIAN: We did discuss that a little bit in the report. I didn't talk about that this morning. We tried to compare the SHEDS-Wood probabilistic results to results from other mostly deterministic models by pathway where available. We also tried to do some verification of our estimate of the dermal transfer coefficient compared to some other studies. But for more specific details, I'm going to turn it over to Dr. Dang and our colleagues at VERSER who did most of the work on the model evaluation.

DR. DANG: Well, as Dr. Zartarian just mentioned

about different models have different input and values and different assumptions. With it in our report, we mention that we have a table. We show all the different lessons from this input parameters and also the equation's difference. So in other words, it's very difficult to compare one exactly the same as a probability model together with this SHEDS model. But we did at least all the different input evaluations in our report.

And unless we have to specifically mention about which one is, we did mention about a couple of models. One from CPSC, one from California, and the other one is from EWG. And also we compared it also from industry like Gradient and also Exponent in 2001. And also other studies, we compare to the model from Steve Lopez. And they're all included in our reports.

DR. MACINTOSH: Thank you.

DR. OZKAYNAK: Basically, you know we've tried to do a few things. One is to compare the results from the SHEDS model in terms of semi-quantitatively against

the other models. And we couldn't do it exactly for the reasons that I already mentioned in my presentation. And because of the differences in the assumptions in the other models and how we can really exactly compare it to the 2-D Monte Carlo results.

The other thing is that, with any model like this, one complex models with different modules and pathways, it's very, very difficult to do an actual, quote, unquote, "validation" or validation of the model against some real world data. The best way of doing it is to break it down into different modules and different pathways. And as Dr. Zartarian mentioned, we tried to evaluate some of the key components in the model intrinsically as well as externally to other assumptions or to other inputs that have been generated for those same exposure estimates.

So we have sufficient confidence in our algorithms and assumptions that they are realistic and should be consistent with what one expects in a typical

situation. But it's very difficult at this point in the absence of all detailed measurement studies to be able to evaluate the model.

DR. MACINTOSH: May I ask a follow-up?

DR. HEERINGA: Yes.

DR. MACINTOSH: I believe I've seen in the SHEDS pesticide model where you've modeled chlorpyrophos uptake, right, and then compared that to distributions of discreted chlorpyrophos metabolite. Right? And I think you could just compare the distributions, right, since you obviously didn't have the detailed information on the individuals who produced those urines. And it's very useful. Right? It gives you an idea of whether you're in the right range.

And I'm guessing that because you haven't seen the data that -- well, I don't know. First of all, are there biomonitoring data for arsenic that could be applied in a similar way in this study if you indeed put a simple kind of PPBK model on the back end of your exposure model?

DR. OZKAYNAK: Yes. There are some limited biomonitoring data for general population or without specially examining the subset that has contact with CCA. So I think those type of considerations are important and should be sort of looked at.

But again there are going to be limitations of how well that is going to be useful in the context of CCA especially, where as in the chlorpyrophos case, the situation is a little different because that's for the general population. And chlorpyrophos was in wide use in that context. So we could use a good metabolite -- well, I shouldn't say good metabolite. A metabolite of chlorpyrophos to evaluate the reality or the reasonableness of the model predictions.

I think with the current data, trying to make that comparison and evaluation for arsenic, would not be that straight forward.

DR. HEERINGA: Dr. Dang.

DR. DANG: Yes. In the Issue 11, we bring up a

similar question like Dr. MacIntosh mentioned about biomonitoring. So we probably will discuss that tomorrow is multi-tiers.

DR. HEERINGA: Very good. Thank you. Any other questions at this point?

Okay. Thank you very much. Very informative. And at this point in time, I'd like to move on to the next item on the agenda which is the introduction and a presentation of risk analysis results by Dr. Winston Dang of the Office of Pesticide Programs at the EPA. Dr. Dang.

DR. DANG: Thank you. Good afternoon, the Chair and the Panel. My name is Winston Dang. And in the next 15 minutes, I will present a quick overview of the background and try to summarize the purposes to conduct this probabilistic risk assessment. And later on, I will present the results of the risk analysis and the limitation as well as the uncertainties as conclusion.

But before I start, I'd like to introduce my colleagues. Next to me is Dr. Jonathan Chen, and also, Dr. Linda Phillips and Mr. Nathan Mottle from Versar. Both of them, they're probably going to answer the questions. They help me to prepare the data preparation and also to coordinate this risk assessment document.

The first purpose we are going to do this risk assessment is the ideal of tiered approach. And overall of this assessment is from simple to complex and try to complete from a deterministic to probabilistic risk assessment for children who contact CCA-treated playsets and decks.

And secondly, we apply the distribution of Average Daily Dose (ADD) and Lifetime Average Daily Dose (LADD) from SHEDS-Wood to the current Agency's arsenic cancer slope factor and other arsenic and chromium noncancer endpoints to estimate the possible risks.

Third, the third purpose that we present the arsenic and chromium noncancer and the cancer risk

distribution based on the points such as like a mean and a median and a 95th percentile, etc., and the result of the sensitivity and uncertainty analysis of the key assumptions.

Fourth, we are going to seek the expert scientific advice on the data and methodology used in this assessment.

The fifth one, we try to identify and review the possible and reasonable risk mitigation and strategies such as hand washing and sealant. And number six, we will try to inform the public of reasonable risk mitigation strategies in order to minimize the potential risk to children who contact CCA-treated playsets and decks at the residential sites.

Since 2001, EPA started to work on CCA residential risk assessment for reregistration process, the exposure of children who contact the CCA-treated playsets and decks became the major concerns during the assessment process. Since then, several steps were taken.

Step 1, in October 2001 EPA presented the preliminary deterministic exposure assessment methodologies, such as the proposed input values, and exposure routes as well as the noncancer endpoints to SAP.

At that time, our proposed exposure scenarios included two pathways is from wood and a soil source and four scenarios. We're talking about oral and dermal for the wood, and oral and dermal from soil. And the inhalation exposure not included in this assessment, and this issue had been discussed in SAP 2001.

Step 2, after the Panel reviewed the proposed assessment, the Panel recommended a probabilistic rather than deterministic approach should be considered. The panel also provided feedback on Arsenic and Chromium +6 for noncancer endpoint selections.

The Panel also identified and recommended the need for further research on arsenic bioavailability in soil and wood residues or to investigate wood surface and soil residues concentration of arsenic and chromium +6 to

reevaluate the arsenic dermal absorption, to determine the effectiveness of sealant.

The Panel also recommended to conduct biomonitoring study for children who contact CCA-treated wood and recommended to identify any buffering materials for reasonable risk mitigation near play structures.

In November 2001, OPP work with ORD of EPA start to develop the SHEDS-Wood for the probabilistic exposure assessment and a focus on that children contacting playset and the deck only. In August 2002, SHEDS-Wood was presented to SAP meeting for model review. The model was re-evaluated and updated all the input values and identify the distributions. EPA adopted the recommendations from Panel and made the changes for simulation.

Step 3, to design a baseline exposure and risk assessment including the calculated risks for children 1 to 6 years old who contact CCA-treated playsets in warm and cold climates, with and without home decks.

In this assessment, we incorporated a lot of

new data and updated data, such as surface residue concentration, bioavailability, dermal absorption, to refine the key assumptions which we don't have in the year 2001. And then we run special simulations as presented Dr. Zartarian and Dr. Ozkaynak this morning.

Step 4, after 2002 SAP, the probabilistic risk analysis was developed and the risk characterization from the result of the risk distribution was identified. Then the next thing is we compared the risk reduction impacts, based on the strategies for the risk mitigations such as the sealant and the hand washing.

As soon as we finished that report draft, we sent it for peer review and comments by multiple offices within the EPA such as Office of Research and Development, OPPT, the Office of Water, and the Office of Science Coordination and Policy, and Office of Child Health Protection, and OSWER as well as other agencies such as Consumer Product Safety Commission, Canada's PMRA and California's CDPR, also the registrants's error reviews.

After all the comments and peer review, we completed the first draft preliminary probabilistic risk assessment and presented to SAP 2003 today.

The next step, after this SAP, we will carefully review the Panel's comments as well as other public comments to finalize the risk assessment. We also will complete the study of the effectiveness of sealant. We will update the Cancer Slope Factor (CSF) if any new information becomes available.

DR. HEERINGA: Thank you, Dr. Dang. Before we move onto a discussion of the actual report on the probabilistic risk assessment, are there any questions on Dr. Dang's statement of objectives and aims?

We can move on to the next part of your presentation then, Dr. Dang.

DR. DANG: In the next 45 minutes I will present the risk analysis and the outcomes. First, before I present the risk analysis results, I will outline overall presentations into four different categories in this

presentation.

The first one is about the background information. I will walk through a little detailed that background information. I will spend a few minutes discussing the background including the summary of the 2001 and 2002 SAP recommendations and how the EPA responded and some data submitted to the Agency recently have been discussed in this morning's exposure assessment session. So I will just walk through quickly.

And, secondly, I will present the results of arsenic cancer risk analysis which will give the distribution of risk at different scenarios. And also the third, I will present the review of possible and reasonable risk mitigation measures. And then, fourth, is the conclusions.

In 2001 SAP final report, the Panel comments on several issues. First, the Panel considered the bioavailability research is needed from the contaminated soil and wood residues.

The OPP responses, in 2003, two studies had been submitted by ACC, it's the American Chemistry Council, Arsenic Task Force for Relative Bioavailability (RBA) used on juvenile swine as a test animal. One study used the CCA-treated wood residues as the sample source, and another one study used the contaminated soil residues as the sample sources.

For wood residues, the relative bioavailability of arsenic was assessed by comparing the absorption of arsenic from the dislodgeable arsenic material to the reference material such as sodium arsenate. The rest result of 27 percent compared to the original proposed 100 percent presented by OPP to 2001 SAP. This will lower the total doses estimates of about 40-50 percent. For soil residues is about 46 percent and it is compared to original proposed zero to 100 percent.

Second is, the Panel's final report also suggested using arsenic in more appropriate chemical form in dislodgeable residues and in soil in a relevant matrix

should be carried out to improve estimates of dermal absorption.

In 2003, a new dermal absorption study by Wester's lab using environmental weathered CCA-treated wood residues patched on primates was submitted to EPA for review. This new study is a modification of the 1994 study from the same research lab. The results are based on the urinary arsenic data following application of arsenic in CCA-treated wood residues. The results indicated 0.01 percent absorption was found.

The Panel also strongly recommended that chromium speciation studies be conducted in both wood residues and soil samples. In the spring of 2003, ACC Arsenic Task Force submitted a study to estimate the residues concentration of arsenic and chromium +6 on the surface of aged wood decks. That's from 1 to 23 years old.

The result from the speciation of wood residues sampling of chromium +6 are found lower than the detection

limit. This result is consistent with several other published literatures, the Cr+6 will not be present on the wood residues significantly. As long as the fixation process is completed, the total chromium on the wood surface will be dominated by Chromium +3 trivalent.

The Panel also recommends additional research is needed on the amount of soil ingestion to reduce the uncertainty, and include the high end exposure such as pica child. And this morning SHEDS-Wood presentation and also includes that data had been updated.

Number 5, geographic locations should be included in the assessment. The warm and cold climates were included in the exposure assessment this morning. For example, the possible exposure scenarios for the young children living in Southwest, like a warm climates, may experience and encourage high extended periods of time for outdoor activities. The results from SHEDS-Wood exposure assessment, children live in the warm climates regions may have a higher exposure than in the colder regions.

The SAP recommended that EPA immediately take steps to develop the probabilistic mode of exposure. SHEDS-Wood probabilistic model was developed to assess the children contact the CCA-treated playsets and decks since November 2001. The detail has been discussed also this morning.

And Number 7, the Panel also strongly recommended that research be conducted to determine the Transfer Efficiency from the wood surface to skin. In the spring of 2003, the ACC Arsenic Task Force also submitted a study for hand and block wipes to determine the surface concentration of arsenic and chromium. EPA reviewed this study and to calculate the transfer efficiency distribution and combined together with the CPSC study to evaluate the distribution of transfer efficiency.

The Panel recommended that the Agency undertake studies of childhood behavior and the activity patterns to clarify these possible associations with children daily life. And I believe this morning's presentation already

very clearly indicate CHAD was used in SHEDS-Wood exposure assessment as well as the database from Exposure Factors Handbook, and Child-Specific Exposure Factors Handbook, and many other existing published studies to improve the database for key assumptions.

Additional studies are needed for exposure associated with using the buffering material. The Agency agrees with the Panel's recommendation that additional research on the possible mitigation measure by buffering material is still needed.

Based on the existing data and further research, the Panel recommended that the EPA inform the public of the ability of certain sealant that can be used to substantially reduce leachable and dislodgeable CCA chemicals and thus reduce potential exposure to arsenic and chromium.

The current data supported a treatment frequency of once or twice per year may be too frequent. A new study may be needed and may be able to answer the

question. Currently, a two-year sealant effectiveness project is ongoing between ORD/OPP of EPA and CPSC to evaluate the efficacy of commercially available sealant to reduce the arsenic concentration on the surface of the treated wood and to mitigate the risk.

About 10 more recommendation by the 2001 SAP and Agency understands that 2001 deterministic assessment may generate higher uncertainties associated with the studies. But in 2002 and 2003, many key assumptions included in the assessment based on the new data development such as surface residues, bioavailability, and the methodologies have been improved and the updated data have been incorporated into this probabilistic assessment.

The next step is the review SHEDS-Wood model. The detail of this part of assessment has been presented in this morning. I am not going to repeat that. However, for the risk analysis, the distribution of ADD (Average Daily Dose) from SHEDS-Wood is used to calculate the arsenic and chromium short and intermediate term MOE for

noncancer risk. The distribution of Lifetime Average Daily Dose from SHEDS-Wood is used to calculate the lifetime distribution of arsenic cancer risk.

But let me qualify information here before I continue and move to the next slide. The lifetime average daily dose or average daily dose in SHEDS-Wood already justify the bioavailability. As we mentioned before, we have a new study and that baseline exposure dose already been justified when we conducted the risk assessment where the ADD is used, no further justification is necessary.

One other thing I just want to mention is they have a new study. It's called "Chemical Complex Study." This study used X-ray absorption spectroscopy (XAS) to determine the chemical and structural state of arsenic and chromium molecules in CCA-treated wood residue samples. The result of this study indicated the arsenic and chromium form a matrix with the wood structure. And in this study, we have our question to the Panel in Issue No. 8. So we probably will discuss that in more detail in the

question section.

In the next few minutes, I will present the processes and review of the Risk Assessment Results. We will summarize into the four area. Number 1 is the risk assessment equations for cancer and noncancer; B is the hazard endpoints, cancer and noncancer endpoints was selected; C is noncancer risk results MOE for short and intermediate risks; and D is for the cancer risks results.

For the risk assessment questions, as mentioned before, the distributions of ADD and LADD from SHEDS-Wood are used. And for noncancer MOE, the risk equation is: MOE = NOAEL divided by ADD. There are four scenarios as we mentioned this morning. They have wood and for oral, and wood for dermal, and soil for oral and soil for dermal for arsenic risk analysis were performed. For chromium +6 process we only used soil in oral ingestion exposure route was assessed.

For cancer risk, for arsenic only. The cancer risk is LADD times CSF. And using the current Agency

point estimate of 3.67 for the arsenic Cancer Slops Factor.

The hazard endpoint selection for the cancer arsenic is the known human carcinogen for lung and bladder. For chromium hexavalent know human carcinogen by the inhalation route only, but this is not relevant to this assessment.

For noncancer endpoints, which originally presented to 2001 SAP, is arsenic is from human study. It had effects like facial edema, gastro symptoms, neuropathy, skin lesions at LOAEL of 0.05 milligram per kilogram per day.

This end point is used to assess short and intermediate risk from both oral and dermal route. And the target MOE is 30. This is based on the human studies.

For chromium +6 the noncancer assessment, the NOAEL of 0.5 mg/kg/day for incidental oral exposure to Chromium +6 was selected based on a developmental study showing increased mortality and increased body weight in

the dams. The target MOE is 100. No dermal endpoint for irritation was identified yet.

For existing decks and playsets, chromium exposure for wood surface is only to trivalent. Because after the complete fixation process, normally the chromium +6 will have a reduction process to chromium +3. And the chromium +6 has been dominant of the service of total chromium.

So in here we have a no oral wood and dermal wood routes for chromium +6 are assessed. And there could be some small exposure due to soil ingestion. So we used a conservative assumption of 10 percent of the total chromium in soil is chromium +6 for the incidental oral ingestion assessment. And this assumption is used for that risk assessment.

In the next few slides, I'm going to be talking about the results of the Noncancer Risk Results. Three basically are presented. We're going to present with cumulative probability density distribution curves.

Second, we're we're going to present with four different exposure points such as mean, median, 95 percentile, and 99 percentile as upper left box is showing. And then the total risk is presented for two broad sources of exposures, soil and wood.

This figure is the cumulative density functions of the short-term, 1 to 30 days, and MOE at warm climate. The blue line is the cumulative density function distribution only is for results without decks. That's only for playsets.

And the red line is the MOE distribution for children who are exposed to the playsets also may contact with the CCA-treated home decks.

If you look to the curve, if you switch to the left, than means the risk is going to be higher. And the red line has a higher short-term risk than the blue line. However, at the upper right box, the MOEs are higher than 30 even at the 99th percentile for both with or without decks.

This figure is the cumulative density functions of the arsenic for intermediate-term. That means about 30 to 180 days MOE distribution at warm climate. Again, the MOEs on the upper right, show that intermediate MOE are larger than 30. That's a target for OPP so for both without and with decks.

This table summarized the arsenic MOEs for playsets only. As mentioned before, the MOEs were calculated based on the different exposure durations, short-term and intermediate, and the different climates, warm and cold climates. The data were presented in this table for mean, median, 95th percentile and 99th percentiles of the distribution. All of the MOEs are larger than OPP's target MOE of 30. Based on the preliminary results in here, it is unlikely for the majority of children who contact the CCA-treated playsets only will experience the short or intermediate adverse effect at this time.

This table also summarized all scenarios compare

to the exposure to playsets only. And this table is similar as the previous slides. And you can see MOEs all were found above the OPP's target MOE of 30 as even as high as the 99.6 percent distribution. For chromium +6, all above the target MOE of 100.

Next I'm going to present the cancer risk results. And the next few slides are the risk analysis results of arsenic cancer assessment.

The cancer risks are present here in the same manner as the noncancer effects. First, we present with cumulative probability density distribution curves. Second, we also present with four different exposure points, mean, median, 95th percentile, and 99th percentile, as on the upper left box showing. And the third, the total risk is shown for two broad source of exposure, soil and wood.

And this figure presented here is for the total baseline risk data for exposure to residues in the soil in warm climates with or without decks. And the switch to

the right represents more risk concern.

This line chart is a comparison of the total arsenic risks from playsets; that's without decks. Or playset and decks; that's with decks for warm climates and from two broad exposure sources. One is soil and residues playset and deck also.

If you look at the distributions here, the red line is the residue risk of the contact the playset and the deck. The red line dot is the risk of the contact of the playset and the deck. And the orange color are for residues risks with playset only. I think probably just offset. The blue represent the total risk from soil source after contact with playsets only, and the green line is the soil risk for deck and playset.

You can see from here that residue risks are greater than soil in approximately one order of magnitude. In this total risk, the residue is the key contributor to the risk distributions.

This table is the cumulative percentiles risk

results for arsenic cancer risk at warm climates. We have two levels of risk ranges are presented, 1E-6 and 1E-5. For 1E-6 for playset only, only 3 percent of hypothetical exposed population is lower than this 1E-6 of the -- For playset and the decks is .3 percent of the hypothetical population is lower than 1E-5. But if we look at the 1E-5 for playsets only, 47 percent is lower than 1E-5 level; for playset and deck, 23 percent is lower than 1E-5 level.

This table is the summary of arsenic cancer risk results of the three exposure points, mean, median, 50th percentile, and 95th percentile. For playset only at warm climate, the mean is 2.3E-5; the median is 1.1E-5; and the 95% percentile is 8.3E-5.

For playsets and decks at warm climate, mean is 4.2E-5; Median is 2.3E-5; and 95th percentile is 1.4E-4. For cold climates in general, the risks are lower than the warm climates.

From the distribution curve -- I'm not showing it in this table -- the mean risk is very close to or

above the 75th percentile point exposures.

In the next few slides, I'm going to walk through and discuss about the some of the reasonable risk mitigation measurements and the results. Number 1, A is sealants; second is about hand washing. And the third is the combination of the skin and hand wash.

And this figure is a comparison of the residue risk source only. I basically tried to learn how the impact of the residues after applying a 90 percent risk exposure concentration reduction and compared to 99.5 percent of surface residue concentration will be reduced.

If you look at the blue Line it is the maximum reduction for 99.5 percent. And the green Line is the moderate. Reduction is about 90 percent exposure concentration reduction. And the red Line is the baseline. It is no mitigation.

From this line chart, you can see that the distribution lines were switched from right to left. That means the risk is mitigated from higher to lower and can

be as high as two to three order of magnitudes. That depends on how is the effectiveness of sealant that was used. And remember, this is only for the residue risk only.

This figure present the risk mitigation by the total risks. This is not only the residue risk; this include the soil. And if you are using the maximum effectiveness sealant of assumed 99.5 percent reduction of residues concentration here.

This figure presented here, after applying the 99.5% effective sealant, the arsenic exposure concentration from the wood surface will lower, switched to the left, and the exposure from the soil become the key contributor. The soil risk become the dominant.

These bar charts are basically the same but it's a little bit clearer. They represent the risks at warm climates for the mean population. The baseline scenario in the left-hand side already includes a certain amount of hand washing.

But then the next one is reduction by 90 percent of exposure concentration. The next one is hand wash only. And the next one is hand wash combination with 90 percent exposure concentration reduction. And then the last one is the hand wash combination with 99.5 exposure concentration reduction.

Again, this table presents the risks under the assumption of 90 percent reduction in residue concentration, and a maximum 99.5 percent reduction in residue concentration. This presents a numeric number for in this table. And the results represented here are the residues risk alone. The sealant has more impact than the total risk from the two sources, wood and residues in soil.

You can see that for the mean, the column, the baseline is about 4.2 times 10-5. And the maximum is down to 2.9. It's about one order of magnitude or larger. For residue only, you can see from 3.0 times 10-5 and down to the 3.5 10-6. This is one order of magnitude. But if you

use the maximum effective, arsenic is going to 9.5 to 10-8. It's almost three orders of magnitude.

The conclusions, the comments and recommendations have been adopted from the 2001 and 2002 SAP, and we also include the comments from researches and scientists from multiple offices within EPA, as well as from other agencies, such as CPSC, California EPA, and Canada PMRA, as well as a comment from registrant error reviews.

Then we used a comprehensive probabilistic model, SHEDS-Wood, which is considered as a product of a strong team of the researchers possessing unique expertise in biostatistics, exposure modeling, and computer programming.

The Conclusion B is we have a comprehensive sensitivity and uncertainty analyses allow for identification of critical model inputs and factors contributing the most to the model predictions. Sensitivity and uncertainty analysis results indicated

that wood surface residue to skin transfer efficiency, wood surface residue concentration, fraction of the hand surface area, and the mouthed per mouthing event, and the GI absorption fraction for residues are the key factors of exposure in the risk.

The climates, the structures, and exposure routes. Risks are greater in warm climate versus cold climate. And the concentration of wood surface residue contributes more risk than soil. The children contacting the playsets and the decks are at a greater risk than playsets only. The dermal route does not impact the risk as oral, but the oral route has the most impact on the risk. Assuming a mean dermal absorption from 3 percent to 0.01 percent only lower the total risk by 26-30 percent.

The Conclusion D, Hand-to-mouth. Hand-to-mouth activities for wood surface residues account for greatest exposures followed by dermal absorption of wood surface residues and incidental soil ingestion and dermal soil contact.

The sealant can play a very important role on the risk reduction strategies. Some as I show in the slides as high as two to three order of magnitude for lowering wood residue risk from wood exposure pathway only.

And additional hand washing after contact with the playset will reduce the risk 25 to 40 percent.

Let me summarized this draft preliminary probabilistic risk assessment and result. Risk at the central mean and median were found to be in the range of 1E-6 to 1E-5. After the 95th percentile, the risk level for exposure to decks and the playsets under warm climate conditions is at 1E-4. And hand washing and applying an effective sealant will reduce the exposure and the risk most significantly from wood surface residues source.

The analysis show that effective sealants and eliminating the contact with soil could reduce risks of all percentiles to acceptable levels.

Thank you.

DR. HEERINGA: Thank you, Dr. Dang, for a comprehensive presentation. At this point I'd like to open it up for members of the Panel to ask questions of clarification or fact for Dr. Dang and his staff.

DR. HATTIS: I guess at this stage I think you've identified three key papers that are all unpublished 2003 papers that at least I don't have yet. So in order to -- these are the Casteel pig feeding studies which is evidently the source of the GI absorption distributional assumptions, the ACC wipe which is evidently the source of the key wood surface residue findings, and the CPSC measurements of the same kind of thing.

So I guess in order to really effectively evaluate your use of these data, I think we need those papers. Can we have them?

DR. DANG: Yes. As a matter of fact, those papers are on the web site.

DR. HATTIS: On the CD?

DR. DANG: On the CD, yes.

DR. HATTIS: Okay. They're on the CD and the biomonitoring. Okay. Yeah, I can't -- I don't know in detail what's on the CD, so I guess I'll look at them on the CD.

DR. DANG: If you don't have it, I'm very happy to give you another one.

DR. HEERINGA: Thank you very much. Yes, I believe there's a references CD which is separate from some of the other materials that we have that should have those papers on it. But if we don't have them, we'll request them.

Yes, Dr. Bates.

DR. BATES: EPA has done an impressive job of evaluating the uncertainty and the exposure analysis. But you've used just one value for the cancer slope factor. And we've been given an extensive evaluation by industry. And they've argued that in fact the value of the EPA is using contains mathematical error which is inadvertently

doubled it. And there is also the National Research Council report of 2001 which actually suggests quite a larger cancer slope factor.

So I'm just wondering how you plan to take this into account because it really will have quite a major impact on the risk.

DR. DANG: Yes, I'd like to refer to Dr. Jonathan Chen. And the slides are X-2. Can you present the Slides X-2, please?

DR. CHEN: I think at this moment I don't need the slides yet. To me I think at this moment -- I'm going to answer this question in two different phases. The first one is that for the probabilistic risk assessment, at this moment Agency does not have the color or more like a guideline or something to do probabilistic risk assessment on the toxicological part. Part of the reason I can think of is that because we do have all different kind of uncertainties and those kind of thing built into the endpoint selection. And if we are going to use

something, those part into the probabilistic risk assessment in general, those parts may cover the whole distribution of the real risk. So at this moment, the toxicological endpoints no matter if it's cancer policy factor or the endpoints that we select for the short-term or intermediate endpoints that we are not doing -- we are still using single point estimate.

So I'm going to answer the second part of the question. After the 2001 LRC published the report, there's a working group organized in the Agency that is trying find out what would be the most appropriate way to address all those comments from the LRC.

So at this moment, the number, the 3.67, used in this risk assessment may change in the final risk assessment because the Agency at this moment does have a group trying to find out what would be the best way to address those comments. So that's my answer.

DR. HEERINGA: Dr. Dang and Dr. Chen, just to follow up on a question that came up this morning. That

3.67 factor, that is relative to a 75 year lifetime exposure.

DR. CHEN: Well, for the cancer potency factor, 75 year basically is an estimated life span of a person. Basically, that is more like a policy. And so the theory behind the cancer potency factor is more like cancer is microsteps. So any kind of single exposure may contribute to a certain extent in the final cancer development. So this is the reason that we use 75. And we may have some kind of uncertainty, but this is more like a policy at this moment that the Agency uses.

DR. HEERINGA: Thank you.

DR. BATES: I just wanted to express a little bit of concern that the risks that are actually presented in some of these presentations come out as they don't include any caveats to the effect that they may change and they're only estimates at this time. And particularly if the cancer slope factor is varied, then there may be dramatic changes.

DR. CHEN: Well, let's see. That is something that we discussed in the risk assessment. And we point out those numbers may change. So the final version of the risk assessment would have something that may differ from the potency factor that is used in the preliminary draft risk assessment. Yeah, it's stated in the document.

DR. BATES: I'm just a bit concerned that these documents sort of get out there without those statements that you've been talking about. I don't think it's actually in this --

DR. CHEN: It's not in the hand out but in the real document.

DR. DANG: Yes, it's in our document, background document executive summary section. We did mention that this is an interim not final.

DR. HATTIS: Just a follow-up on the same subject. Essentially, you characterize, however, the cancer potency factor that's used as a conservative upper limit, upper confidence limit estimate. You also use the

Q1-Star terminology which implies that it's an upper 95 percent confidence limit. You should be aware, I think, and the Panel should be aware, that this is in fact a central estimate derived. It's not an upper confidence limit at all.

DR. CHEN: Basically, it's a central estimate with 95 percent confidence limit.

DR. HATTIS: Yeah, but the value 3.67.

DR. CHEN: The value 3.67.

DR. HATTIS: The value 3.67 is derived from the center not from the upper confidence limit.,

DR. CHEN: Yes.

DR. HATTIS: All right. And it doesn't have all of the conservative factors built into it that often are part of -- based on risk assessments.

DR. CHEN: Right.

DR. HEERINGA: Any other questions or comments?

DR. MACINTOSH: Included in the materials that we were give was this draft paper, a report authored by

Nico where they talk about the arsenic chromium cluster. And I'm wondering how that chemical form bared upon your consideration of the use of that 3.67 cancer slope fact that I believe comes from arsenic in drinking water. Right?

DR. DANG: Yeah, let me answer that question. Then I defer to Dr. Chen on this.

This is one of very interesting studies. And the study show that this is a chemical complex from the arsenic and chromium and wood become a complex. And we don't know how it's going to impact on the risk assessment. That's one of the questions we ask the Panel for the guidance in Issue No. 8. So that is one of the questions we were to get an answer, hopefully, from the Panel here.

DR. CHEN: So I'm going to answer the second part of the question. Well, basically, that one if we're talking about the chemical structure of the arsenic or chromium in the wood, basically, that is talking about the

leachability of the chemical to surface. So at that point, it's more related to the exposure. So if we change, if we change any kind of doses, we change the exposure part. But from the toxicological part, the hazard part, we would not change based on the complex structure so just the exposure part.

DR. MACINTOSH: So then -- I'm not a toxicologist, so these could be very naive questions. But then would you be assuming that the metabolism of that complex would be used the same as the metabolism of trivalent or pentavalent arsenic oxide?

DR. CHEN: I think that is a very interesting question. And to me I think this is a very good time that we can be talking about the reasons that we are putting some kind of relative bioavailability issue. And because when we're talking the cancer potency of arsenic or those kinds of things, basically, we are using the epidemiological study in Taiwanese population, Southwestern Taiwan. And at that point, we're talking

about arsenic in water, arsenic in water.

But at this moment, we're here for risk assessment arsenic in the wood or arsenic in the soil. Basically, they are completely different issues. So we need to have some kind of comparison between the arsenic in wood when compared with arsenic in the water talking about absorption comparison, this is the reason we come up with relative bioavailability.

So that one is, if we're talking about arsenic potency factor, we still state that is original arsenic in the water state. Then we use the relative potency factor -- a relative bioavailability to make the adjustment. This is the reason that we do have a relative bioavailability in the risk assessment.

DR. MACINTOSH: I see. Thank you.

DR. MATSUMURA: I really enjoyed Dr. Dang's presentation. Good to see that you're responding to the last SAP. And that's very nice to see that you are so responsible and responsive. So that's good feedback.

I would like to repeat the same request that Dr. Hattis had. We would like to look at the original data if we can. I have only the data from Wester for instance from the year 1993. And that's not good enough for me to really judge.

And I have a question on that chromate complex. I'd like to know that, too. Because I do not know how you could just generalize based upon the sodium arsenate to judge the toxicology here. Sodium arsenite, it's far more dangerous. And I don't know what the form that you're discussing about. And their absorption is different. Their toxicity and the stresses, they very different. So I would like to make sure that we have the original. That helps very much.

DR. DANG: Yes. We probably have to go back to the office to find that 1993 Wester studies. But the 1993 Wester study -- oh, you do have.

EPA: We do.

DR. DANG: The latest one is the reference in

the CD also.

DR. MATSUMURA: But I didn't see it.

DR. HEERINGA: We'll get it to you.

DR. CHOU: I enjoyed the response to the questions. Actually, I think there are two questions here regarding to the arsenic chromium complex. One is relative bioavailability to sodium arsenide for example. The other one, actually, is the toxicity. Do we know for sure whether the complex has the same toxicity as arsenic? Do we have that kind of data?

And, thirdly, I would like to know when you extract the residue by brushing, is that really a real-life simulation to children's hand touching the wood? What's the exact form of residue, so called residue, that's transformed from the surface of the wood to the children's hand; rather than if you brush it, then you probably would alter the ratio of this complex that's -- it's embedded in the wood surface. Are we really looking at the relevant form of the so called residue? That's the

basic question I'd like to get an answer on.

DR. DANG: Let me try to answer the third question first. The chemical complex form is the study basically that use so-called brush bracer to brush about 1 to 4 years old wood as residues. And we know this could be that different chemical structure compared to the hand from the wood to hand. But it's going to be very difficult to correlate that wood residues from the hand only because that's not sufficient data. Enough stuff, sufficient substantial amount, to conduct bioavailability studies.

So at that time, they submitted a protocol to the Agency. We have several options we can do. We have one that use the hand and then wash and then collect that residue from that. It's what we call soluble arsenic type.

But then the other issue that we'd like to know how is the structure on the surface. That's another question which we don't know. And how is the friction of

the free arsenic on the surface of wood and also how the friction of that that become a complex.

Regarding those toxicity issues, I defer to Dr. Chen to answer this.

DR. CHEN: I think this is a very interesting question. And to me I think the first thing that we are talking about is whether the complex structure whether that is related to any toxicity issue. That one basically is we don't know.

But there's one thing to me I think that complex structure actually address one thing is that once the wood -- once a CCA solution good into wood can go through the fixation step. And in the fixation step, it can form these kind of complex structure. It means that if the fixation step work properly, then suppose that it should keep arsenic and chromium in the wood that would not be able to leach out.

So how to -- so what would be the most appropriate way to interpret that data, to me, I think is

something that we need to discuss. This is the reason that we raise this question to the Panel.

But at this moment, when we talk about arsenic that goes into solution state whether it has the same kind of toxicity when compared with arsenic in the wood residue, that one we don't know. But there's one thing that we are trying to use relative bioavailability study. If you notice, the relative bioavailability study is that use arsenic in the metrics that we are concerned about compared to the animal.

In the meantime, arsenic in the water to animal compared to arsenic in the urine. So those would be more absorbed arsenic to make the comparison. So for that reason, with absorptive with the relative availability to adjust. So it's no matter what kind of form that is in the water or something or in the wood or in the soil, unless those are going to the body, then if we -- if we assume the arsenic is caused by the arsenic content absorbing into the body, then we already make that

adjustment over there.

DR. RIVIERE: I'm not sure about that though. Because I think a bioavailability adjustment will correct for the bioavailability, the absorption of --

DR. CHEN: Yes, I agree.

DR. RIVIERE: -- that big arsenic complex versus the arsenic alone.

However, once it gets in the body, then the toxicologic potency of that arsenic is probably very different between a complex and the arsenic. Is it metabolized? Does metabolize to the same type of arsenic? Does it even come in the urine? The data on the Wester studies is there was nothing detected.

DR. CHEN: Yeah.

DR. RIVIERE: And looking at -- I guess the problem is, and this is a huge data gap to me. There's two of them. One is we don't know anything at all about the absorption of the complex into the body. And, secondly, we don't know what it is in the body. Is it

arsenic or is it that chromium arsenic complex. If it's the chromium arsenic complex, that could easily be distributed and binding to tissues everyone without any urine at all.

DR. CHEN: I agree with you.

DR. RIVIERE: And then we don't know, you know, the toxicity of that chromium arsenic complex to form a potential carcinogenicity perspective. And I just think on the record that that's a huge gap because we essentially have no information at all.

DR. CHEN: Yeah, I agree with you.

DR. STYBLO: Let me just repeat what we said two years ago here. Those of you who met here, remember that this was one of the big issues discussed. And several times it was pointed out that we are not looking at toxicology or biologically facts or metabolism of arsenic, but we are looking at metabolism and toxicology at least three metals taken together not excluding copper.

And as a matter of fact, there are several

studies published, unfortunately, all of them on animals or cultured cells, that show that both synergistic and antagonistic effects could be expected. And, again, not excluding copper which we did two years ago.

And the fact that we repeat this question again two years later just suggests that this is an important question and something needs to be done to get more data regarding the possible metabolic and toxicologic interaction of these three metals whatever chemical form of these metals is.

DR. HATTIS: To comment on this topic, I just had an opportunity to very briefly look at this Casteel pig feeding study. And that does show arsenic coming out in the urine. So the correction that's been made seems to be appropriate that, you know, it's comparing arsenic in the urine resulting from the wood residues that they prepare by rather mild brushing of the wetted wood surface after removing any surface dust there.

So I think the concern that there might be some

other interactions toxicologically is possible, but I think it's considerably lessened by the fact that we're talking about a fraction of stuff coming out in the urine. And it probably not coming out in the urine as any complex form but as inorganic arsenic.

Go right ahead. You want to reply. I still want to direct a question.

DR. STYBLO: I just want to jump in, too, because I don't agree with you.

I don't think the value of 39 percent of relative bioavailability actually says anything about possible toxicologic consequences. For example, it would make a big difference if this arsenic is really excreted as an inorganic arsenic compared with the expression profiles of metabolized after digestion of arsenate. So one big problem with that study is it doesn't show speciation which would greatly improve our knowledge of the metabolism of the particle complex if it is a complex.

DR. HATTIS: We'll talk about this more in the

discussion period. But never the less, there are studies where one administers either trivalent or pentavalent arsenic. And the short answer is they're interconvertable. You don't get exactly the same proportions of the trivalent arsenic.

Anyhow, in March of this year, the EPA proposed as part of its cancer policy for exposures to mitogenic carcinogens for young children be adjusted upward by 10 fold in the case of kids under two and 3 fold in kids between 2 and 15. I didn't notice any mention of that proposal or its possible consequences in your analysis.

DR. CHEN: I think this is a very important question. And, actually, this is a question that we discuss a lot internally. And at this moment, we didn't put any kind of adjustment factor. The reason is, because at this moment, we are -- this cancer policy factor that we are using is derived from the human epidemiological study in Southwestern Taiwan. And that is a large population and has been a longer time of exposure.

So at this moment, the Agency consider it's very possible that epidemiological study already include the most sensitive population exposure to arsenic in the most sensitive pure time. This reason that at this moment the Agency didn't put any adjustment factor for cancer policy factor in this risk assessment. This is my answer.

DR. HATTIS: I'm sure we'll discuss that. Thank you.

DR. HEERINGA: I can see that we're going to have a very energetic discussion on Issue 8, and I look forward to that. Any other questions?

DR. DANG: Yes, can I answer for that Dr. Hattis. Actually, in our paper, we mention that it includes this early life exposure. In our Chapter 3, we did mention about NRC indicates that the mode of action is still insufficient information to make an adjustment on for that early life exposure for cancer risk.

DR. HEERINGA: Not seeing any more questions at this point in time, I'm sure, as I say, we look forward to

the discussions and I'm sure there will be some issues to go through.

If you would proceed, Dr. Dang, with your conclusion on the strengths and limitations.

DR. DANG: In the next 25 minutes, I will discuss the strength as well as the uncertainties and limitation of this risk assessment.

First, the strengths of this risk assessment we categorized into seven major key elements. Number 1, this is a tiered approach and based on SAP guidance. Second, a subpopulations has been evaluated. The third, the scope of data for key assumptions were have the most updated one. Number 4 is the model we used, we have a lot of confidence on those. Number 5 is the results and the risk characterizations. And 6 is risk mitigation strategies. And 7 is discussed through multiple office peer reviewed internally and externally.

The first one, the tiered approach, as I mentioned before, it's a step-by-step tiered approach.

And as we said before in SAP 2001 has provided guidance for methodology and made the comments on the technically refinement of the model in 2002. Most of the SAP recommendations have been able to be adopted.

The primary population of interest for this risk assessment was children in the United States who frequently contact CCA-treated wood residues and/or CCA-containing soil from public playsets. The subsets include children playing on residential playsets, around residential decks.

The focus of this risk assessment was on estimating the risk to children from contact with various sources of the CCA-treated wood.

The data submitted after SAP 2001 and the comments by the public or by the industry have been incorporated. And a comprehensive sensitivity and uncertainly analyses in order to identify the key assumptions and the data gap have been performed. Wood surface residue concentration and hand-to-mouth activity,

for example, were identified as one of the major contributors to the risks.

SHEDS-Wood is a very good model as far as we have confidence on this. It is the only EPA 2-D Monte Carlo exposure and dose model which addresses both variability and uncertainty in model inputs and outputs. Risk analysis based on this SHEDS-Wood model is the product of strong teamwork including the expertise in biostatistics, toxicology, risk assessment, exposure modeling, and computer programming.

This is the result in the risk characterization. Unlike the deterministic risk assessment, in this assessment present the arsenic and chromium based on the risk distribution such as like mean, median, 95th percentile, etc., and the comprehensive results including the sensitivity and uncertainty analysis of the key assumptions.

The eight primary exposure scenarios were considered. The playsets were considered. The oral/wood,

dermal/wood, oral/soil, dermal/soil. And in the decks we used oral/wood, dermal/wood, oral/soil, dermal/soil. And we covered the key exposure scenarios we considered this as the most important scenario and the pathways.

Number 6, the risk mitigation strategy in this report, we also include several assessments including identify and review the possible and reasonable risk mitigation and strategies such as hand washing and sealant.

Number 7, this report has been through multiple office peer review. And it's internal/external, and we incorporate many comments from scientists from multiple offices within the EPA as well as scientists from other agencies, and also including the registrants error review from CCA registrants.

In the next couple of slides, I'm going to be talking about some uncertainties for the inherent. In this model, we have an uncertainty analysis. We have a quantitative result show that 2-D Monte Carlos. But here,

I'm going to walk through basically is qualitative type.

We categorize into six different areas of uncertainties and limitations. Number 1 is potential pathways were not included. Second area is about environmental media. And number 3 is about toxicity data. And number 4 is about chemical fate. And number 5, risk characterization. And number 6 is about data gap.

The potential pathways were not included. They have another potential pathway but less common scenarios were not included in this assessment. For example, one is inhalation exposure to particulates for children who are present during sandblasting of CCA-treated surfaces or playing around CCA-containing soil. And secondly that younger children may directly mouth portions of wood play structure or the deck. And third is further research is needed especially in these areas.

This is about environmental media. The concentrations of the dislodgeable residues especially in the soil and wood are highly dependent on fixation process

during the pressure treatment, the ambient temperature, the pH of the soil, the type of the wood, the formulation of the products, and how is the wood finished; is it oil stain, sealant, paint, etc. And also the moisture contents of wood and soil are also one of the key factors to determine the concentration of residues in soil and also on the wood surface.

Another uncertainty is about toxicity data we use. Take for example we use extrapolation from LOAEL to NOAEL or extrapolation based on intraspecies variation, extrapolation of the epidemiological data from adult populations to children, or deterministic point estimated of the toxicity endpoint. And the CSF is characterized as upper-bound.

Next is chemical fate. We assumed the arsenic concentrations are relatively persistent and immobile and assumed the individual to be exposed to the same concentration for the entire duration of the exposure such as a 6 years migration, dispersion, dilution, retardation,

and other transformation processes that may occur over the time.

No data was available describing the change in soils concentrations due to the use of a sealant. And also we have no data to support the individual will contact the soil within 2 feet around the playsets all the time.

Risk Characterization. Only uncertainty of absorbed dose was characterized. The uncertainty of toxicity values were not characterized. So greater uncertainty after combined uncertainty of absorbed dose plus the uncertainty of toxicity that would be greater. And the uncertainty of assumed risk mitigation measurements and also assumed chromium +6 in the soil concentration with a conservative assumption and plus a high end of arsenic cancer endpoint been selected so overall may create the conservative risk estimates here.

Number 6 about Data Gap. The biomonitoring results, as suggested by the SAP 2001, are not available

to confirm the model results. And the sealant data are not yet available to demonstrate which are real effective. And we don't have any soil risk reduction strategies at this time.

And SAP also recommended considering aggregating exposures from drinking water, air, waste, and other sources such as food, are not included in this assessment. There are not data to support the treatment frequency of sealant for maximal reduction.

This is the conclusion of the strengths and uncertainty analysis here. This risk assessment report provided a transparent risk analysis information including the methodology development, data analysis, comprehensive characterization of variability associated with input parameters, quantitative information of the possible risk distributions, and the potential risk mitigation strategies.

Compared to 2001 deterministic assessment, much lower uncertainties are expected in this assessment.

Thank you.

DR. HEERINGA: Thank you, Dr. Dang. At this point are there any questions from the Panel on this, the latest strengths and limitation of the SHEDS-Woods model?

What I'd like to do is I'd like to take a break at this point for 15 minutes. It's about 7 minutes after 3 by my watch, and we'll reconvene here at 3:30. And then we'll begin the period of public comment.

[Break taken at 3:07;

meeting resumed at 3:33 p.m.]

DR. HEERINGA: Welcome back to the continuation of the Science Advisory Panel meeting. At this point in time, we're going to enter the period of public discussion. And we have a number of people who have spoken with Paul and made arrangements for presentation. It is the time for public presentation. If there's any other in the audience who would like to make public comment -- it probably will be tomorrow morning -- please speak to Paul at some point.

Paul has a small administrative note to add before we begin.

MR. LEWIS: Thank you, Dr. Heeringa.

During this afternoon's discussion presentation by the Agency and feedback by the Panel, there was some communication about reference material that be made available for the Panel. For the Panel and the public's interest, all available material is available in our docket. There's actually a reference CD that was provided to the panel that has a number of studies that were discussed this afternoon. They are available in our docket. And they're also available on our web site, a very comprehensive list. So I invite the members of the public to look at that and to see any references you'd like to pursue in your own interest.

Thank you.

DR. HEERINGA: At this point in time, we are going to begin the public comments. And I'd like to invite scheduled commentor, Mike, Dr. Mike Ruby, on behalf

of Exponent to make a presentation.

DR. RUBY: Thank you, Mr. Chairman.

I wanted to talk to you a little bit today about some of the chemistry issues regarding arsenic on CCA-treated wood and in the wood residue that we're been hearing about today.

Before I start that, I wanted to acknowledge some of my collaborators in this. Peter Nico at Cal State University Stanislav, did most of the work regarding X-ray absorption spectroscopy which I'll be talking about today. That was done in collaboration with Scott Fendor at Stanford. Yvette Lowney, one of my coworkers, was also involved in this as was Stewart Holm at Georgia Pacific.

The reason that we got into this examination of the chemistry of arsenic on CCA-treated wood and in the residue was we were starting to get engaged in these dermal absorption studies and we wanted to try to understand how arsenic is present on the CCA-treated wood and in the residue so that we could make sense out of

whatever dermal absorption results we saw.

I would also add that the work that we did here was really building on earlier work. If you go into the literature, you'll find 10, 15 years of publications regarding fixation of arsenic and chromium on CCA-treated wood. And so what really we were doing here was building upon that research and bringing some research tools to bear to understand these chemistry issues.

So these are the materials that we evaluated. We evaluated a new CCA-treated wood that was provided by RTI and a weathered CCA-treated wood, also provided by RTI, that had been part of the deck that was out in the environment for about four years. And then we looked at this dislodgeable residue. That was provided by ACC.

And I would like to point out that residue, the material we looked at, was the same material that was dosed to the monkeys in the dermal study that will be talked about later this afternoon and also was dosed to the swine in the oral viability study which was alluded to

earlier today.

The origin of the CCA-treated wood residue, it's a composite from six decks. Those decks were in Michigan and Georgia. All of them were treated with CCA-treated type C, and they'd been out in the environment for 1 to 4 years. The decks were dismantled, cut into boards of about two-foot length. All the boards were shipped to -- I forget where. But a university where the residue was collected by washing by DI while brushing a soft bristled brush.

And the resultant material was filtered through glass wool and concentrated on rotavap and air-dried. And this produced a fine brown color that people refer to as the dislodgeable residue or just the residue that was used in these various studies.

Here I'm comparing the metal concentrations for arsenic, chromium, copper, iron, and manganese. In the fresh wood, the aged wood, and the residue, note that the concentration units are millimoles per kilogram so we

could compare -- and I'm presenting them that way so you can directly compare molar ratios of arsenic to chromium to copper.

A couple things to point out, the residue was analyzed as is. It was digested to completion and then analyzed for metals content. The fresh and aged wood, we basically took a wood chip off the surface. It was about a centimeter square and about 2 millimeters deep. And that was digested and the metals were analyzed.

One thing I'd like to point out here is that the arsenic to chromium ratio in these materials is pretty constant, the molar ratios. We see that for the arsenic to chromium -- the chromium to arsenic ratio is about 1.5 to 2 in all these materials. And the other thing that really jumps out is the amount of iron in the residue. There really isn't any iron on the fresh wood or the aged wood. This was the first clue that there's something in residue that's not on the wood itself.

This is a photomicrograph taken with an electron

microprobe which is rather similar instrument to a scanning electron microscope. And it's basically -- there's a scale bar down here. That scale bar is 70 microns. And you see the outline of this kind of dark gray shape here. That's a piece of wood.

And what we find when we look at the residue under the scanning electron microscope or the microprobe was that it's primarily composed of wood fragments along with an organic fraction that is composed of soil minerals, and mostly silicates and iron minerals. They make up about 10 percent of the matrix. And then the rest of it is the wood. The wood itself has arsenic distributed on it. And it ranges from about 500 to 3,000 part per million arsenic on the wood surface.

We also see little tiny blebs of material. And there's one up here, right there, which is a chromium, an arsenic chromium oxide. That little bleb right there. And so it looks like a small amount of crystalline material. But what we think is going on here is that most

of the arsenic is distributed on the wood.

And then we have these little blebs of arsenic chromium oxide. And we also occasionally find loose particles where the iron oxides that were in the soil have picked up some of the arsenic from the CCA-treated wood. And so you find iron arsenic oxide in some of these samples.

I'm going to talk now about this X-ray absorption spectroscopy work that we did. This is the advance photon source at Argonne National Lab. And it's a pretty big instrument as you can see. The work that we did was done at this facility and also at Stanford Linear Accelerator.

The way this thing works, basically, real simply, you got electrons going around this ring. And they accelerated them to around the speed of light. And as a result of the curvature of their path, they spin off very high energy X-rays. And those X-rays are focused into a beam that we use to do research and that we

basically bombard this sample with those high energy X-rays.

This is the kind of data that we get out of these kind of experiments, out of X-ray absorption spectroscopy. Basically what happens is you're bombarding your sample and at some characteristic energy, you get an absorption edge. This is just an example. But if it were arsenic that you're looking at, a certain characteristic energy, you would get an absorption edge. And that's called the near-edge structure or XENES, for X-ray absorption near edge structure.

And then after that, you would get some of these squiggly lines. And those are called the fines structure. And basically what's happening here is these high energy X-rays come in and they knock out a core electron on the element. And when that happens, you get this big absorption peak. And then that electron that's been knocked loose, either it flies off or it bounces off something close to the initial target and it bounces back

to the original target. And it's the identity and the distance to those secondary scattering targets that gives you this fine structure here.

So within this fine structure is contained the information about the structural chemistry. So what the arsenic, for example, what are its nearest neighbors and its second nearest neighbors? So I'll show how this comes out with some example data and then some real data.

This is a nice example for chromium of the near edge structure. You can see -- these are two just compounds, model compounds. One is Chrome 6 and it has this very pronounced near-edge structure there. And one is Chrome 3. And so you can see how if you applied this technique to a sample that's either Chrome 3 or Chrom 6, you can very readily tell what you have got.

This is some XAFS data for some iron compounds. The blue line is magnetite and the orange line is gertite. And these are two iron oxides. They have very similar chemical composition. They differ only from the

arguments of the atoms in space. And you can see they produce quite different XAFS spectra. And it's within these squiggly lines that's contained the information on how far apart the iron atom is from the next iron atom. How far apart it is from the first oxygen. That kind of thing.

So this data is for -- it's near-edge structure data. And we're running the residue, which is the white line, the new wood, the aged wood, and then two model compounds, an arsenic 5 standard and an arsenic 3 standard. You can see that the arsenic 3 near-edge, absorption edge, is at a lower energy than you see with all the other compounds. So what this piece of data tells us is that the new wood and the aged wood all have arsenic 5 as the form of arsenic. So it tells us the oxidation state for arsenic.

This is the same set of materials. But in this case, it's the XENES data for chromium. And this case, you can see this very pronounced absorption edge feature

here for the Chrome 6 standard which is entirely lacking in our environmental samples. So what this piece of information tells us is that in the new wood, aged wood, and the residue we have Chrom 3.

And this, I might add, is consistent with the chemical data that's in the literature where people based on the bulk chemistry characteristics realize that when the Chrome 6 reacts with the wood structure chromium is reduced to Chrom 3 in the process of binding to the wood. But this is just a very nice and powerful technique for demonstrating using that direct spectroscopic technique.

This is the XAFS data for arsenic. And you can see -- what I really wanted to point out with this slide is how the residue, the new wood and the aged wood, produce identical XAFS data or fine structure. And thus they have to have the same chemical structure.

And this is the same kind of data for chromium which simply demonstrates that in the case of the chromium the new wood, the aged wood, and the residue all possess

chromium that experienced to the same structural environment.

So those XAFES data that I just showed, those can be taken through a number of chemical transformations. And through that process one gets out coordination number which tells you how many bonds that element has and also the distance to its nearest neighbor or next nearest neighborhood.

So what happens then is you take these fitting parameters for both arsenic and chromium, and you develop a model for a compound that fits the fitting parameters that you see for the arsenic to oxygen distances and the arsenic to chromium distances and then for the chromium as well.

It's actually done in a computer simulation. And it produced this next slide which is our proposed structure for how arsenic and chromium are bound together on the treated wood. So in this structure, the arsenic is represented by this purple thing here. And it's bound to

two chromium molecules in a binuclear bidentate complex. And the chromium is bound through oxygen to a carbon. And that would be the wood structure coming off this way.

This structure fits all of the XAFS data. And it also is consistent with the historical chemical data that we have.

So our conclusions from this research are that the redox states for arsenic and chromium in the residue and on the wood are arsenic 5 and Chrome 3, that arsenic is bound in a metal cluster with two chromiums, and the chromiums are bound to the wood structure. Based on the XAFS data, we believe that the chemistry of the arsenic does not change with either weathering, because the new wood and the aged wood were the same, or with the collection of the residue.

And then as I mentioned, these results are consistent with the chemical results presented by Bull. The 2001 paper is actually a nice review of the chemistry of CCA on treated wood.

So that was it for me.

DR. HEERINGA: Thank you, Dr. Ruby. I think before you leave, I'm sure there are going to be some questions from the Panel. Are there any questions here from the Panel? Yes. Dr. Bates.

DR. BATES: I was just wondering, are you able to quantitate it? Can you say, for example, that all the arsenic and chromium are bound up in that complex, or is it just a proportion, some free arsenic and chromium?

DR. RUBY: This technique, the X-ray absorption spectroscopy allows you to quantitate down to a point. The detection limit for this method is 2 or 3 percent. So that is to say, if you had two or three percent of some other compound in there, it would start to change the spectra.

I think it's likely -- what we know from some of our electron microprobe data, that there some of the iron faces that are in the residue, I think what happened, this residue, of course, came from a deck. And I think what

happens is that soil got tread into the deck. And then when the decks were removed, some of that soil came with the wood particles that are mostly what this residue is. And the iron minerals in that soil residue have picked up some of the arsenic. We know that from some of the microprobe work.

How much of the arsenic is in those iron faces versus on the wood in this arsenic chromium complex, I can't tell you. I think the amount in the iron is relatively small.

DR. HEERINGA: Yes, Dr. Styblo.

DR. STYBLO: I have three questions. First, a simple question. What do you consider aged wood. I think you mentioned 1 to 3 years for samples of wood you analyzed. Why I'm asking is we have a draft paper from Dr. Solo-Gabriele from Florida that shows leakage, very considerable leakage, arsenite, arsenic 3 from aged wood. In that case, aged wood was like 13, 15 years old. Do you expect that speciation of arsenic in those samples can

change that profoundly?

Second question: I didn't see copper in your structure. Could you explain?

And the third, I wasn't very happy about the spectrum or differences between arsenic 3 and arsenic 5 spectrum. I'm not an expert. Could you explain what kind of interferences are possible when analyzing this type of material and how big an error they can include into the analysis of arsenic 5 and arsenic 3.

DR. RUBY: Okay. I will try and remember all of your questions. To start with the first one, the wood that we analyzed had been out in the environment for four years. So it certainly was not as old as the wood that Solo-Gabriele, and I haven't seen that publication or article, was looking at.

In answer to your question about whether the arsenic speciation could have changed in that time, I would be very surprised to see arsenic 5 converting to arsenic 3 in that environment. It's in the presence of

oxygen. There's no strong reducing agents. So I don't know see how that could happen.

DR. STYBLO: How about microbes?

DR. RUBY: That's possible, but I still would be surprised.

Okay. I remember another question. The arsenic 3 versus 5 issue. Can we go back to that slide there. Basically, the energy that this model compound of arsenic 3, which is the brown line, the energy at which you see this near edge take off is characteristic of that oxidation state for arsenic. And there isn't any physical process or a chemical process that would alter that.

This is a very -- you're talking about a very fundamental process in this case. What you're talking about is stripping off a core electron from an atom. And the energy at which that happens is dependent on the chemical environment, so the oxidation state in this case. There isn't any way to shift that peak.

DR. STEINBERG: Let me just maybe ask a little

different question. When you have a mixture of arsenite and arsenate, at what point can you see residue of arsenite?

DR. RUBY: Ah. What happens then is you got your absorption edge for arsenic 5 is there and arsenic 3 is there. And if you had a 50-50 mixture, they would move towards each other. And you would see them in the middle. You would be able to arsenite, arsenic 3, when you started to have 3 to 5 percent.

DR. STEINBERG: Thank you.

DR. HEERINGA: Dr. Matsumura.

DR. MATSUMURA: I have just one question. How stable is the complex of the chromium and the arsenate?

DR. RUBY: Good question. That is I think very important. We think that that structure should be pretty stable except under certain conditions. I think the most likely conditions that would potentially result in arsenic coming off there would be real basic conditions where you have base catalyzed hydrolysis.

In neutral conditions, we think it should be quite stable. We know something about the stability of chromium binding to hydroxyl to oxygen and then carbon from studies where they looked at binding of chromium to various organic compounds. But probably I think the chromium to carbon bond is going to be more stable in this case than the chromium to arsenic bond. Probably the weakness, if it's going to come off, it's going to be the arsenic coming off the chromium bond.

And for that, I think that it should be -- we think it's pretty stable. There are data on arsenic binding to iron compounds in similar forms where we see, you know, pretty stable. But in terms of quantifying that, the stability, that's pretty difficult to do.

DR. HEERINGA: Dr. Styblo.

DR. STYBLO: Just to follow up on this question. The ratios of copper arsenic and chromium in the freshly treated wood and aged wood seem to suggest that arsenic is disappearing or the ratio was in favor of the chromium in

aged wood. Is this a criterion that would suggest that arsenic could be released from the bound?

DR. RUBY: So your question is in the aged wood, the ratio of copper to arsenic.

DR. STYBLO: Arsenic and chromium.

DR. RUBY: Arsenic and chromium. That ratio there is about 2 to 1. And the fresh wood is about 1.5 to 1. So this would imply that chromium is being enriched relative to arsenic. So that would be one interpretation. Yeah.

And I think previously you had asked about copper, where is the copper in all of this. We believe that the copper is binding to the wood independent of the chromium and arsenic. So we don't see it in the absorption spectra for arsenic and chromium.

DR. WAUCHOPE: I've been asked by the Panel to address this particular issue. And not being an X-ray absorption spectroscoper, I submitted your paper to a world-class buddy of mine who does bimolecular. And he

said your basic conclusions are solid. He agreed with the basic conclusions of the paper.

The only complaint that he really had was that, of course, that typically you can probably find more than one molecular structure that will fit the X-ray data which really doesn't affect our conclusions here. It seems to me the issue here then is if we accept the conclusions of the paper that CCA formed, that the arsenic and chromium and CCA form this very stable structure that's basically bound into the lignin, we keep talking about an arsenic chromium complex. But it's really arsenic chromium carbohydrate complex which is probably part of the structure of the lignin.

It sounds to me like it's the few percent that may be the issue. I mean after all, if you've got a kilogram of arsenic in a big wood deck, it doesn't take but a tiny fraction of that to change arsenic in the soil levels. But if you're measuring it in the parts per billion levels, which we are, parts per million at least,

do you think that's a proper interpretation of the results?

DR. RUBY: Let's see. First, I'm gratified to hear that your expert friend was approving of the report. And it is certainly true that with these kind of data one can always find alternative hypotheses.

I would point out that our structure is based not only on the X-ray absorption data but also on the chemistry data that we have in trying to fit all the pieces of the puzzle together in a way that makes sense.

In terms of your question about how important 2 or 3 percent of something soluble would be, I think it depends on the exposure pathway in that, if the exposure pathway is, say, dermal contact with the residue, then it could be I suppose if you think that 2 or 3 percent might be absorbed. But, of course, the aggressiveness of the fluids at the skin surface are not particularly aggressive when you compare them to the GI tract. So if you were to ingest that material and it would experience a more

aggressive environment, then I think that 2 or 3 percent could potentially be more important.

DR. WAUCHOPE: Okay. I appreciate that.

DR. HEERINGA: Dr. Francis.

DR. FRANCIS: Actually, I sort of have two questions. One is how many samples did you look at? You got sort of one composite sample. Is that correct.

DR. RUBY: Of residue.

DR. FRANCIS: Of residue.

DR. RUBY: Yes.

DR. FRANCIS: How many times did you analyze it? Did you just look at it once? Did you look at one piece? Do you understand what I'm saying?

DR. RUBY: Yeah. All of the samples -- we had one sample from each category. And they were all analyzed in duplicate. So we collected duplicate data sets for each of the three samples.

DR. FRANCIS: And you had similar results.

You also alluded to the fact this was the same

residue that was used in the, what is it, the Casteel

DR. RUBY: Yep.

DR. FRANCIS: -- the studies, the monkey. What was the other one for the feeding study?

DR. RUBY: The feeding study was Casteel.

DR. FRANCIS: The pig.

DR. RUBY: In the pigs. And then the dermal study was Ron Wester in the monkeys.

DR. FRANCIS: So he essentially this complex is what? And with maybe some minor components from the other chromium or arsenic compounds is what was fed to pigs.

DR. RUBY: It was the same material.

DR. FRANCIS: Yeah. Okay. All right.

DR. RUBY: Or a split of the same material. I don't know.

DR. FRANCIS: I don't know if I should ask you. Are you a toxicologist?

DR. RUBY: I'm not formally.

DR. FRANCIS: I guess my question is then given

how much arsenic was eliminated from the pigs, is something happening to that complex in the GI tract?

DR. RUBY: I would say it's breaking down.

DR. FRANCIS: Okay. But we have no idea what it's broken down, how it was broken down or what it was broken down into.

DR. RUBY: I would guess as acid catalytes hydrolysis in the stomach could free up the arsenic.

DR. FRANCIS: I'm interested if we're going to be changing the valence state of the arsenic internally. I don't know.

DR. RUBY: I don't know the answer to that either. The GI tract, the small intestine, become a fairly anoxic and it starts to become reducing. You could. But you know you're going to reduce all of the arsenic. I believe you're going to reduce all of the arsenic 5 to arsenic 3 in the liver anyway.

DR. HEERINGA: Dr. Hattis.

DR. HATTIS: You showed us in the early part of

your presentation, you showed us enormous instruments that are capable of creating very fine beams of particles. I guess photons in this case, X-rays, X-ray photons. And then you showed us a micrograph which had a small particle within the wood that you identified as likely the stuff.

When you were doing your experiment, how thick was the beam? Did you focus specifically on those particles that you had identified as the stuff, or did you have a broader beam that would take into account a relatively large sample of the wood?

DR. RUBY: The X-ray absorption work is a bulk analysis. Actually, you will radiate the entire sample and it penetrates. So you're actually -- the data is an average of over all of what's in the sample.

DR. HATTIS: Thank you.

DR. HEERINGA: Yes, Dr. Stilwell.

DR. STILWELL: Yeah. I was wondering how this surface residue relates to a surface residue, say, in a real situation where it's exposed to constant fluxes of

rainwater and sunlight, and it's a changing sort of situation. For example, if you look at the leachates that come out, the ratio is much less than 2 for the chromium to arsenic. So that means that some of the arsenic disassociates away from the complex and is solubilized into the environment.

DR. RUBY: Okay. I believe you.

DR. STILWELL: So that means that there's some reactivity involved with the material. That was one of the questions.

DR. RUBY: It sounds like the issue is stability of the complex over time in the environment.

DR. STILWELL: Right. There's a discrepancy between the 2 to 1 chromium arsenic ratio on the wood and the amount found in leachate studies, meaning that something happens in between the time it goes from the wood and is taken out of the wood and goes into the environment. So some of that time could actually be spent on the surface of the wood prior to the next rain event

meaning that there would be a certain fraction of other material there.

Also the chromium to arsenic ratio on the hand residue were 1.3 in the ACC study. And I don't know how to explain that.

DR. RUBY: It was 1.3 chromiums to each arsenic.

DR. STILWELL: Right. That's what I came up with. I came up with 1.3. Your study was 2.2. Their study was 1.7 on the residues but 1.3 on the hands when they took the amount of chromium and arsenic from the hands.

So what I'm getting at is: How much does this one particular residue, you know, reflect all situations in a real world situation where you're constantly getting the sunlight, the rain, and that sort of thing.

And also just out of curiosity, in low iron soils, would that make the residue more bioavailable? Does the study use that for the bioavailable? So this particular residue had a lot of iron arsenate in it. But

if it had no iron in the residue, maybe that would increase the bioavailability of the material.

So one of the things I was going to ask, too, is if you did any is sequential extraction on the residue? And that's where you take various acidified rain water, 10th molar, acetic acid to find out how reactive it is.

DR. RUBY: We did not do any bulk chemical tests on the residue. In fact, we had barely enough to work with as it was. It was kind of precious material. And we wouldn't have had enough to do bulk chemical testing.

DR. WAUCHOPE: Since I have the microphone, the question I have is about the speck of, I think, it was chromium arsenate that you showed in the micrograph. Did you prove that identification of that crystal?

DR. RUBY: Yes. The electron microprobe is very good at quantifying chemistry. And so it can tell you the percent chromium, the percent oxygen, and the percent arsenic in that little bleb which was about a micron in diameter.

DR. WAUCHOPE: Thank you.

DR. HEERINGA: Dr. Styblo.

DR. STYBLO: Just one curious question. Using a sealant or any other wood preservative, what do you expect would this kind of treatment do in terms of preservation or chemical destruction of the arsenic chromium complex? What would be you're assessment?

DR. RUBY: This is not really my area. But I would recommend not using a sealant that is real basic or a real strong oxidizer because I think that would have the potential to release arsenic from this complex. Other than that, I think it would be a good idea to try to seal the surface potentially.

DR. HEERINGA: Dr. Bates.

DR. BATES: I was just wondering if you know whether this complex is actually formed on the chromium arsenate mixture or whether it has to go into the wood where it's somehow catalyzed?

DR. RUBY: My sense is it has to react with the

wood, that it forms during the reaction with the wood.

DR. BATES: But you don't know that for sure. You haven't checked the mixture.

DR. RUBY: That's based on my reading of the literature.

DR. HEERINGA: I think the question is: Did you actually test the CCA mixture used to preserve the wood?

DR. RUBY: Oh, No. I didn't do that. But my understanding is that the presence of Chrome 6 in that mixture is pretty well characterized.

DR. HEERINGA: Dr. Kissel.

DR. KISSEL: Did I see one of your slides indicate that it was about 90 percent wood and 10 percent mineral in the sample that you had?

DR. RUBY: Yeah, that's our estimate of what that looks like.

DR. KISSEL: Because we have this report that was done by Battelle which is apparently another sample of the same material but this is not your analyst. Right?

This is somebody else.

DR. RUBY: I don't know.

DR. KISSEL: You don't know who did it which is probably a good clue that it's not the person that works with you.

DR. RUBY: Yeah.

DR. KISSEL: This says 96 percent wood and 4 percent mineral. And I guess my question would be: Is that just a difference in the two samples you got, and what does that imply about general variability in these analyses? Or is that an indication of the ability of these techniques to actually detect the sorts of things we're talking about in a sample which was in fact the same as the material you were using?

DR. RUBY: What Battelle had, I wasn't aware of their work. But what they had and what we had was the same thing. I'm sure of that.

But the way that you quantify how much of each phase you have, is you just back way off and you look at

the whole sample and, you know, transpectroscopist can say fairly accurately to you this percent of this phase and this percent of that phase. That's how we did it. There are some more sophisticated programs that can actually size all the particles and calculate how much of each type. We didn't do that. If they did that, then I would go with their number.

DR. KISSEL: They appear to have done it by getting mass fractions of the elements that would only be in soils and then extrapolating to mineral species with hydroxides and other things and making an estimate.

DR. RUBY: I would say if they've got 4 percent and we've got 10 percent, those are probably fairly close to some kind of experimental error on this technique. We'll call it 6.

DR. HEERINGA: Dr. Styblo, one more question.

DR. STYBLO: Since we started talking about the Battelle paper, I wanted to ask this question before. My impression was that you showed pretty low levels of iron

and they have, if I'm right, 9 or almost 10 grams per kilo, 10,000 micrograms per gram. I think you had much less than that. Maybe I'm wrong. What struck me was that you said it was the same sample.

DR. RUBY: Yeah. You mean iron in the residue sample?

DR. STYBLO: Yeah. Well, the results of -- of dislodgeable residues. So I assume it's in dry sample, yeah.

DR. RUBY: And how much was that?

DR. STYBLO: 9,880 micrograms per gram which is milligrams per kilogram.

DR. RUBY: Okay. So it's parts per million.

DR. STYBLO: Almost 10 grams. It looks like the wood with nails.

DR. RUBY: Right. I have another slide. I think it's the first slide after the extra slides where I present the mellow concentrations in parts per million. There we go. So iron concentration in our CCA residue, we

came out at 15,000 part per million.

DR. STYBLO: You are even better.

DR. HEERINGA: I think at this point I'd like to move on. Thank you very much, Dr. Ruby. And I think that is very, very informative. And at this point, I'd like to invite Dr. Yvette Lowney who is also speaking on behalf of Exponent for her comments and presentations.

DR. LOWNEY: My name is Yvette Lowney. I work with Exponent. And I'm here to talk to you about some recent research that was done and discussed earlier today about dermal absorption of arsenic from CCA residues.

This is work that was done by Dr. Ron Wester at UCSF in his labs using his lab techs. Exponent staff, Mike Ruby and myself, helped coordinate their research. The research was funded by Georgia Pacific.

I'm sorry that Dr. Wester isn't here to present this himself. But I'm going to do my best to cover the salient issues and try to address any questions that you have about it.

We entered into this research following EPA's 2001 deterministic assessment. It was really the methodology that EPA put forward for how you would assess exposures to arsenic from CCA-treated playground structures. That assessment didn't actually include concentration inputs, so you couldn't calculate. It didn't calculate actual exposures.

But if you took information that was available about concentrations of arsenic in soils from playgrounds and concentrations of arsenic in residues on wood surfaces, you could do some calculations and come up with exposures. And when we did that, we looked at the relative contribution that was assumed to come from ingestion exposure and dermal exposure.

And as you see in this pie chart, it shows that at that time the calculations were indicating that 50 percent of total exposures were being contributed from dermal absorption. We looked at that and thought that perhaps it didn't make sense.

When the SAP reviewed the EPA assessment in 2001, they looked at those assumptions and the calculations that came out of it and also voiced some concerns. One recommendation was that the EPA use a lower value that would come out of the -- a lower value for dermal absorption that could come out of the same research that was available. But they went on to say that there was an urgent need for further research looking specially at absorption of arsenic from CCA residues. So that is what spurred this research.

Now in the probabilistic exposure assessment that's been conducted, EPA does a couple of things. The first thing they to is take the SAP recommendations of a lower dermal absorption value. The original assessment had used the value of 6.4 which was the upper limit of the values that came out of the Wester '93 research. They recommended that a lower value that also could come out of that research of 2 to 3 percent be used.

So EPA in their baseline assessment in the

probabilistic exposure assessment that they've just conducted, takes those values and fits a beta distribution to the data and incorporate them. They also do a special analysis where they used the results of this newer research that was submitted to them as a report last summer. When they do that, what they find is that the total exposures, when we use the lower dermal absorption value, total exposures drop by approximately 30 percent. And that occurs because, under the new assumptions, dermal absorption of arsenic contributes about 30 percent of total exposure.

I want to point that the value that they incorporated was a value of 0.01 percent in the special analysis as opposed to the 2 to 3 percent in the baseline analysis. And that 0.01 percent value is the upper bound value from the new research.

So this is a pie chart that comes out of the 2003 assessment showing that if you use the 2 to 3 percent with the Beta distribution you have approximately 30

percent of the total exposure being contributed from dermal absorption of residues.

So just to briefly review the data that came out of the earlier Wester research and was used by EPA in 2001 and in the baseline assessment. What they did at the time is that they evaluated the dermal absorption of soluble arsenic in solution and then soluble arsenic mixed with soil. They applied that to the abdomen of Rhesus monkeys and then measured excretion of radio labeled arsenic in the urine. They were able to use a radio-labeled arsenic for this research which allowed them a very low limit of detection.

These are the data that come out of the 1993 Wester research. So what he did at that point in time was he looked at a low-dose group and a high-dose group both for soluble arsenic and for the soluble arsenic mixed with soil. The low-dose group was targeted in a range that he believed would represent background exposures. The high-dose groups were targeted to dose range that would be

associated with environmental exposures.

And you can see that the range of the absorption values vary from about 2 percent up to 6.4 percent. The 6.4 percent value is the value that EPA used in their initial assessment in 2001. The SAP then recommended that they use something more in the range of the 2 to 3.

I want to point out that none of these values are statistically distinct. They're the same despite the fact that the doses range from about 5 orders of magnitude.

So what the new research does, and I refer to it as Wester 2003, to the extent possible, it replicates the 1993 research; however, it uses CCA residue samples instead of the soluble arsenic or soluble arsenic mixed with soil. We had to modify the research design in order to accept environmental samples. It's not really practical to generate CCA residues that are radio-labeled. So we had to make some modifications that would allow us to measure arsenic absorbed from environmental samples.

The primary thing that we needed to do was to lower arsenic in the diet. Monkeys like humans get a significant contribution of exposures to arsenic from the diet. And we realized that we wouldn't be able to see absorption in the range of significance for this assessment if we couldn't lower the background arsenic excretion levels. So we put a lot of work into lowering the arsenic in the diet.

We increased the surface areas exposed over the 1993 research in order to maximize the dose we could apply. We used a 8-hour exposure time that was partly to better mimic what we thought would be children's exposures; and, also, it's really the upper end of what is allowed by the Animal Care and Use Committee. The animals, when they have the residue attached on them, they have to be in restraint chairs. And it's not possible to keep them in restraint for more than 8 hours at this point.

Based on comments from the 2001 SAP, there was a

lot of concern that in the original Wester research he had not established that the soils were really kept in contact with the skin. So we made sure that the residues were kept in contact with the skin. And then we used an ICPMS analytical technique and looked at total arsenic in the urine of these animals.

So why this research model? We have received questions about why we didn't use an in vitro approach. Our goal with doing this was to generate data that directly respond to the earlier Wester research. The 1993 research has been used both in EPA guidance on how to assess dermal exposures to arsenic and also in the CCA assessment. So we thought it was important to maintain that study design as well as we could since that's the data point that we were trying to update.

We also recognized that there is a general preference for in vivo data over in vitro data. In the face of some ambiguity in what the data mean, we assume that from prior experience and discussions with agencies

that in vivo data would be given preference.

We also know from the early 1993 research that Dr. Wester looked at dermal absorption in vivo with his monkey model and also in vitro with human skin samples. And the data that came from his in vitro analyses were actually demonstrated lower dermal absorption than the in vivo data did. So we wanted to make sure that we weren't artificially biasing our data low by using an in vitro model.

And then finally, right now there is really no validated in vitro model for dermal absorption of arsenic. Actually, the reason that we were able to do this research at all, this has been in development for a couple of years. It's been funded by a government grant from CERDEP to develop some in vitro systems for doing site-specific bioavailability testing. And the first step in that is to develop a good in vivo database against which you can validate an in vitro model. So we hope that in the future there will be a validated in vitro model,

but there isn't one at this point in time.

This is a depiction of our study design. We used a cross-over study design which means that we had three monkeys. Each monkey was dosed both with this CCA residue collected from treated wood and the soluble arsenic in solution separated by a two-week washout period.

The material is applied to the abdomen of the monkeys, the dose is kept against their skin for 8 hours. It's then removed. We collected urine for seven days. The information about the concentration of arsenic in the urine is then used to calculate the percent absorption. And then we can also compare it against the data from the application of the soluble arsenic to see what the relative absorption of the residue to the soluble is.

Originally, we had considered doing this research using actual pieces of wood and placing them against the abdomens of the monkey. When we talked with the EPA about doing that, some concerns came up. One was

how the heck were we going to quantify the dose of what we had applied. Secondly, they were concerned that breathability of the wood would alter the absorption. And then most importantly, they were concerned that we wouldn't be able to demonstrate that we had kept this flat piece of wood in good contact with the skin. And if that were true, you would bias your results low.

So once we established, based on the chemistry data that Mike presented a moment ago that the form of arsenic in the collected residue is the same as the form of arsenic on the surface of CCA-treated wood, we realized we could move forward using this collected dislodgeable residue for this research.

This slide shows the doses that were applied. We wanted to apply as much of the CCA residue as we possible could in order to see a signal from it over background. The constraints were that we didn't want to exceed a monolayer of exposure. We know from research on soil, that for very fine soils, you achieve a monolayer of

coverage on the skin at about 5.4 milligrams per square centimeter. So we targeted a dosing rate for the residue that was lower than that.

Then we matched the CCA -- oh, I'm sorry. This second one should actually say "solution." This CCA-soluble solution.

We matched the dose of the solution to the residue dose so that we would be able to compare those directly.

I've included in here the doses that were in the original 1993 research and then, also, what CPSC in their assessment last spring believed that dermal loading of arsenic onto skin surfaces is from treated wood. You can see that our doses are higher on a unit area basis than either the earlier Wester research or the CPSC skin-loading estimate.

I want to go back to the original Wester research where he showed that dermal absorption was essentially the same despite 5 orders of magnitude in

differences of the applied dose. So although our dose is higher than these other expected exposure levels, we don't think that the results that we would get from the research would be appreciably different just based on Wester's earlier research.

Our dosing method was designed to ensure that the dose was evenly distributed across the skin. We wanted to ensure that the material was kept in close contact with the skin. In the 1993 research, Dr. Wester used a Gortex patch to hold the material in place against the skin. And the concern was that as the monkey sat up in the restraint chair, the soils would be falling to the bottom. And in some preliminary research that we did, we saw that this did happen when you applied soils. The soil congregated at the bottom near where the tape was on the skin.

So instead of using the Gortex, we went over to an approaches that uses a Tegaderm patch, which is a product from 3M. It's marketed as New Skin. It's

basically a large vapor permeable membrane that is adhesive. So we used that.

Then we, also, in order to make sure -- we were concerned that even if this bandage is on them, that maybe it would pouch out and the materials would still be able to fall. So we put a stretch elastic bandage called "Spandage," which is essentially like a fishnet stocking, around the monkeys as well.

You'll be able to see from the next slide, we're extremely confident that the dose was both well distributed across the skin surface and kept in direct contact with the surface of the skin.

These are slides, these are pictures of the dosing trials at UCSF. In the first slide, you can see how an area was masked off on the abdomen of the monkeys. The material was sprinkled and then spread to cover that entire area. It was then covered with this clear Tegaderm that basically went from armpit down to hips and kept the material in contact.

And then down here, you can see where we put the Spandage on them. And these guys looked like stuffed turkeys by the time we got the dose on them in terms of just having a very tight fit of the material against their bellies.

This final slide is where the Tegaderm is pulled off. You can see that the material is still well distributed. There is some that came off with the Tegaderm. There was none that fell out anywhere. You could also see that there was none that was at the bottom of the patch area. And even if we tapped the Tegaderm that came off, none of the residue material would sort of puff off. So I feel that we really did a good job of not having too much loaded on there.

These are the data that come out of the research. I'm not going to go into detail about what these are, but just to point out that we have the concentration of the arsenic in the urine; we have the volume of urine. Those are combined to create the mass,

calculate the mass excreted. Those are converted into 24-hour mass. They are corrected for background. And totalled down here to get the total excretion.

We then adjusted that for urinary arsenic excretion fraction. Dr. Wester knows from prior research that approximately 80 percent of an IV dose administered to monkeys is excreted in the urine. So we adjusted the calculated absorbed dose by what we would expect to see excreted in the urine to come up with the percent absorbed.

The next three slides are the results. The orange depicts the results from the application of the soluble arsenic. So time points over here, this is time before the dosing. We dose at time zero. The soluble arsenic is absorbed quickly. After 8 hours, the patch is removed. Excretion comes down quickly and is back to background it approximately 48 to 72 hours post dosing.

I'm going to show you the graphs for all three monkeys. They're all very similar. The blue line shows

you the results that came out from the application of CCA residue. And as you can see, the urinary excretion never increases above background. Basically, it is a flat line.

And earlier today, Dr. Freeman was asking a question about the time course that's predicted out of the SHEDS model for absorbed dose. And as they showed, there's sort of this upward trend, that it continues up over time. And then as you wash, it comes off. That's not consistent with what we saw at all. We saw that the absorbed amount of arsenic never goes up.

This is the second monkey. Slightly longer excretions. Same general pattern. And, again, the third monkey. The soluble arsenic is absorbed rapidly, excreted rapidly, comes back down to background. The CCA residue dose demonstrates no excretion of arsenic above background.

So these are the compiled results. If you take the data that come from each monkey, you have a range of about .5 to 4 percent dermal absorption. Those are very

consistent with the earlier research. The average from this is about 2.7 percent. And with these data, the average is .003 percent absorbed. But I want to point out again that, even for monkey number one where we could calculate an absorbed value, none of those are actually elevated statistically above background.

It is with significant humility that I need to tell you that I do not have IV data for these specific monkeys. When we met with EPA last spring, they specifically requested that we conduct a new IV dosing and data associated with that for this new modified research model. And for a variety of reasons, we don't have those data available yet. I'm hoping to have them any day. I had expected to have them by the end of the summer. I certainly expected to have them by today. We don't have them yet.

However, that said, I believe that getting the results from the in vitro data are unlikely to change the results or the conclusions of this study. If we've

discovered that the percent excreted in the urine changes the calculated percent absorbed will increase or potentially decrease, but the absorption of arsenic CCA from the CCA residue relative to the soluble arsenic won't change. And also the fact that the excretion of arsenic following application of the residue does not result in statistically elevated excretion of arsenic. It won't change.

These are the data. The blue boxes here represent the arsenic excretion levels after dosing with CCA. And this is Monkey 1, Monkey 2, Monkey 3. The red dots show the background urinary arsenic data. And I put these up because I've been fairly careful in saying that, following application of the residue, there is no statistically elevated increase in urinary arsenic excretion.

And it occurred to me that some of you might think, well, maybe it's not statistically elevated, but I bet it's up at the top of the range. And when I look at

these data, I see that that's not true. The urinary arsenic excretion following application of the residue is really well within the range of the background urinary arsenic.

So these are the pie charts that come out using the information from the 2003 assessment if you set the dermal absorption of arsenic to a .0 percent. As you can see, basically, the dermal absorption from residue becomes negligible, less than 1 percent. The total doses decrease, but the relative contributes from residue ingestion increases.

We did not apply -- for this particular pie chart, we didn't apply the lower absorption rate to soil dermal contact. Dermal absorption from soil contact is small compared to the others; however, we do have some late breaking news.

The concentrations of arsenic in the CCA-impacted soils are too low to actually do research with the monkey model. We know that the results we would

get would not be elevated above background. But it would be because we couldn't apply a dose that, even if it was absorbed, we wouldn't be able to see it.

So what we did is we did an extraction test using the wood residue for which we have the dermal absorption data and then some soils. The CCA utility pole soil is the soil that was fed to swine. The Florida CCA soil is a soil that was fed to monkeys by Steve Roberts. And we combined a given mass of each of those with a given volume of human sweat and looked at how much was liberated. And our results told us that relative to the wood residue the solubility of arsenic from the soils was actually lower, 40 percent and 63 percent relative to the residue.

So this suggests to us that it would be appropriate and conservative even to use the .01 percent dermal absorption and apply it also for the soil dermal exposures.

This is a slide that basically illustrates what

I just said. It uses what's called a parallelogram approach that was suggested for Morris for safety evaluations. So we have information on the relationship between residue and dermal absorption. We have information on the solubility relationship between arsenic and residue and soil. So from that we should be able to determine what the dermal absorption value from soil is.

So conclusions, what we did, we conducted animal research specifically targeted at evaluating the dermal absorption of arsenic from CCA-treated wood. We coupled that with the work that Mike Ruby discussed which showed that the nature of arsenic in the residues is the same as the nature of arsenic on the surface of CCA-treated wood. And also helps us to understand why the absorption of the arsenic was lower than from soluble.

And what we learned is that this animal model produces reliable results. That's based on the similarity between the results that we achieved and the results achieved that were achieved by Dr. Wester in '93. So the

soluble arsenic results are consistent with earlier research. And these results indicate that there is negligible dermal absorption of arsenic from CCA residues.

And that's all.

DR. HEERINGA: Thank you very much, Dr. Lowney. Questions from the Panel for Dr. Lowney?

DR. CHOU: I have a couple questions. The Wester 1993 study, we don't know who was going to be doing the public commenting so I didn't bring the papers here. They're upstairs. So just based on my recollection, the Wester 1993 study actually showed a concentration absorption efficiency is concentration dependent.

DR. LOWNEY: Mike, would you go back to one of the earlier slides that shows that. Go ahead. I'm sorry.

DR. CHOU: At the low dose, if you look at the soluble arsenic in solution, at the low dose, at the dose of 0.0004 microgram per centimeters squared, the absorption is 6.4 plus/minus 3.9 percent. At the high dose, at 0.6 microgram per centimeters squared, the

absorption is 2.0 plus/minus 1. 2. And at the 2001 SAP, I was here, there was a discussion whether which one to use, high or low, and, therefore, maybe 4 percent was acceptable.

So my point is it depends on how you interpret the data. From my point of view, that shows the dermal absorption is concentration dependent. And this morning we talk maximum dermal load. We talk about less than 0.5 microgram per centimeter squared. Maybe it's 0.47. I remember seeing the chart with maximum dermal load. We can say it's maybe around .5 micrograms per centimeters squared.

And compared to this current new data, we're talking about 14.3 microgram per centimeter squared. That's way, way high compared to the maximum so-called overload. And if you look at the picture of the dermal patch on the monkey after exposure, there's a lot of material left on the pad itself. So I just want to caution that we need to think about this in terms of are

we really looking at the 14.3 microgram per centimeter squared. That's way overload.

Or maybe we need to account for the overload and also the possibility of concentration dependence. And that could in part explain why you are looking at you have only 0.01 percent absorption.

DR. LOWNEY: I have a couple of thoughts. You can see for either matrix which was applied in the 1993 research that the dose range covered several orders of magnitude. However, the absorption range if you look specifically at those numbers vary by a factor of 2 or 3 at the most. So despite a huge difference in the applied dose, the reported absorption varied very little. And the difference between those absorption values is not statistically different.

And Dr. Wester in his 1993 paper specifies that. That the 6.4 value reported for the low -- well, let's talk about the soil. The 4.5 percent dermal absorption reported for the low-dose group of arsenic mixed with soil

is not statistically different than the 3.2 percent absorption reported for the high-dose group.

None of the four of these are actually statistically different from the other. So this is just an indication of the normal variability across the monkeys. I don't believe it shows a dose dependency. And Dr. Wester would disagree that it shows a dose dependency as well. His paper specifically says they're statistically not different.

And one more point on that. The doses that we applied certainly are higher than what a child would come into contact with while playing on CCA-treated wood. But we could not detect elevated absorbed arsenic even though we have these monkeys on a low arsenic diet. Our children are also exposed to arsenic in the diet. And I just can't imagine that we could load enough arsenic onto anyone to get an absorption value that registers.

DR. RIVIERE: The IV correction data, that's going to be the soluble arsenic again.

DR. LOWNEY: It will be soluble arsenic administered IV.

DR. RIVIERE: I guess the only concern I have and this come up to earlier comments I had before. If the arsenic is absorbed as not arsenic but as chromium arsenic, then the study isn't applicable at all. Because if the chromium arsenite were to distribute into a fecal excretion or a biliary excretion, it would not be picked up at all in the urine.

The question comes again on since it's a negative study -- you did not detect any absorption. I agree. If the arsenic is absorbed as arsenic, I can live with the facts that there is probably minimal absorption. But if the arsenic is absorbed an arsenic complex, then an IV correction dose of the arsenic complex, that urine data can't be used to make any kind of inference on that.

And, secondly, if it is as an arsenic chromium complex, then you might have to start looking in the skin. Is the stuff just permanently bound through keratin or

fat or tape strips or something because it wouldn't show up in the urine.

So, again, any comments on that?

DR. LOWNEY: Our assumption in this research is that in order for arsenic to be absorbed across the skin, it must be solubilized and that it would be free arsenic. The other thought is that that assumption is consistent with combining this absorbed dose information with toxicity data that were derived for soluble arsenic.

DR. MACINTOSH: I'm just curious of that assumption is that it must be solubilized (inaudible).

DR. LOWNEY: The complex is a fairly large molecule, the arsenic is bound through the oxygens to the chromium and then onto the wood. It's a very large molecule. And our skin is designed to be a fairly effective barrier to large molecules. And so the assumption is that in order for the arsenic to penetrate the skin, it could not be in such a large cluster.

DR. STEINBERG: I may have missed it. Could you

tell me what was the anatomic location that you applied the residue?

DR. LOWNEY: It was on the abdomen of the monkeys. So right smack in the middle of their bellies.

DR. STEINBERG: Was the abdomen shaved?

DR. LOWNEY: The abdomen was shaved three days prior to the dose application. We did want to remove the hair; however, we didn't want to have any irritated skin.

DR. STEINBERG: So it was shaved and then you waited three days.

DR. LOWNEY: Correct.

DR. STEINBERG: How old were these monkeys?

DR. LOWNEY: These monkeys were approximately 20 years old which is about the same age as the monkeys that were used in the 1993 research.

DR. STEINBERG: And 20 years, of course, is a pretty old monkey.

DR. LOWNEY: I believe these monkeys can live be about 40. So it's a middle-aged monkey.

DR. STEINBERG: And how thick do you think the skin is on the abdomen?

DR. LOWNEY: I don't know the answer specifically to that question. We had our protocol reviewed extensively. And, actually, EPA, when we sent our proposed protocol, they also sent it out. And one of the comments that came back from one of their reviewers in California was that they thought that the abdomen of the monkey is an appropriate surface area to be used for estimating this value. So that's one part of my answer.

The other is that my understanding from my comparative anatomy book is that the thickness of skin increases with the nakedness of skin. So mammals that are more furry tend to have thinner skin. And as humans are less furry, we likely --

DR. STEINBERG: Fortunately, I can disagree with that. That's not a problem. That's incorrect.

DR. LOWNEY: The final thing is that most of the contact that children achieve is on the surface of their

palms from the direct contact with the material, and the skin of the palms is much thicker.

DR. STEINBERG: Children by nature tend to have much thinner skin almost in every location. Typically, hairy skin, whether shaved or not, is typically thicker. Middle-aged skin tends to be pretty thick. This type of research on monkeys of which not many people in the world presently do is very tricky, and I'd really like to know what groups were able to make some of those as they say ad authoritum assessments.

There may be one very good reason why you may have had essentially flat line and no absorption is because you're dealing with relatively thick skin over an area. I, of course, would like to see that area. If you take a look at many dermal absorption studies on monkeys or injuries on monkeys, depending on how the skin is prepared and how it looks and whether you apply, for example, keratinizing lotion to make sure that it is indeed soft, absorption through that area is dramatically

different.

So it really, not only do you need experts in monkey-type work to do this, but you almost need experts in dermal-monkey-type work to do this. And there's not a lot of those left on the planet. There's a lot of little problems that I see with some of this work.

DR. LOWNEY: Well, I would consider Dr. Wester to be one of the experts in dermal absorption for monkeys. But, also, it's not that we didn't demonstrate absorption of arsenic across the skin. For the soluble arsenic, we did see absorption across the skin in these monkeys.

We could talk about the absolute absorption and maybe that would differ with skin thickness. But the relative absorption of arsenic from the residue is clearly a couple of orders of magnitude lower than absorption of arsenic in solution.

DR. STEINBERG: But I think that proves the case. That once you had a liquid solution you were able to get reasonably good contact even in relatively thick,

hairy skin of a middle-aged or ancient monkey. Whereas when you were using the residues of the relatively thick skin, you would not get that type of absorption. And that, of course, is still different than a young child who may have saliva and other things on their hand and relatively thin skin and, of course, have much more active absorption.

So, again, the models may not be quite equivalent of what one would want to see.

DR. LOWNEY: One of the things that I learned while we were collecting the sweat for our extraction test is that actually children tend to sweat much less than adults do. There's been quite a bit of research done at McMaster University in Canada where they have been looking at how to develop nutritional supplements for sports drinks for children. And what I read into their reports was that they're sort of stymied because actually children don't sweat.

DR. STEINBERG: I'm going to contest that on two

folds. One is that children transpire more. So they lose more fluids through their skin. That's when the transpiration occurs. Secondly, the fluid on their hands would not only be sweat but it, of course, would be saliva and any other things that they have accumulated that would help them absorb some material.

So again, it's a very, very, very complicated model. And I'm not sure I'm convinced that the monkey data that you've shown in the small number of cases is in any way equivalent.

DR. FREEMAN: In the study, would you expect to find any of the arsenic either in fecal material or in hair?

DR. LOWNEY: Some percentage may be excreted other than through the urine. And that's what the adjustment for the urinary arsenic excretion fraction is intended to take into account. So we did adjust it assuming that 80 percent of an absorbed dose would be excreted in the urine. And we are waiting with baited

breath for IV data from this specific model that will allow us to make a more specific adjustment.

Does that answer your question?

DR. FREEMAN: I guess I should have phrased the question a different way. Which is instead of making assumptions about how it should pass out of the organism, it would have been pretty simple with controlled animals to take hair and fecal samples and analyze them as well just to verify.

DR. LOWNEY: Right. We didn't do a complete mass balance with this. We assumed that the urinary arsenic excretion would be representative of the absorbed dose. That's true.

DR. STYBLO: I generally agree with your conclusion that there is less absorption across the skin. I'm not sure of the absorption in the skin which obviously have different toxicological implications. However, just to show you how a complex situation may happen in case of looking at the complex or at the

interaction of two metals. One example, there is already significantly showing excretion of arsenic selenium complex through bile. This complex is believed to be formed maybe in the blood, maybe in the liver.

So just assuming the scenario that arsenic chromium complex is also excreted the kind of complex that would be excreted in bile, you may not see any differences in urine. I'm not saying that's what happens here. It would be helpful to look at other metabolic patterns than just urinary profiles.

DR. LOWNEY: Well, if you come up with a study design and funding, we would love to do that research.

DR. HEERINGA: I think at this point, we've reached 5 p.m., and I'd like to call today's session to a close. I'd like to thank Dr. Ruby and Dr. Lowney for their presentations and obviously engaging in the scientific process interactively here.

And at this point I'd like to make just a few notes before we close. The agenda tomorrow will stay

fairly well in line, we hope, with the published agenda. We have public commentors and discussants who will begin our session at 9 o'clock. There will be a little bit of a follow-up from today's discussion.

We expect to have probably on the order of seven to nine public commentors tomorrow. We're going to have to stay very much on time with these because we have a large list of questions to turn to over the next day and a half. And I think given the numbers of questions and their complexity, that we don't want to sell that process short, too.

Any other things?

MR. LEWIS: Thank you, Dr. Heeringa. At the conclusion of today's meeting, if I can ask my colleagues on the Panel to immediately meet in the workroom to go over some administrative issues for this evening and to continue our discussions for tomorrow. So if we could meet immediately after, about 5 minutes, to go over some planning for tomorrow, I'd appreciate it. Thank you.

DR. HEERINGA: Thank you, Mr. Lewis. I guess with those final comments, we'll adjourn for this evening and we'll plan to see everyone back here tomorrow morning at 8:30. Have a good night.

[Session adjourned at 5:07 p.m.]

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