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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 5, 2003

[8:34 a.m.]

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

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P R O C E E D I N G S

DR. HEERINGA: Good morning. Welcome to the third day of the meeting of the FIFRA science Advisory Panel and the discussion of the Preliminary Probabilistic Exposure and Risk Assessment for Children Who contact CCA-Treated Wood on Playsets and Decks and CCA-Containing Soil Around These Structures.

I'm Steve Heeringaj. I'm the session chair for this meeting of the SAP. I'm a permanent member of the SAP Panel. I am a research scientist and director of the Statistical Design Group at the University of Michigan's Institute for Social Research. My area of specialty is in applied statistics, biostatistics, and populations based-research.

I'd like the other members of the Panel to introduce themselves. Dr. Matsumura just arriving.

DR. MATSUMURA: Good morning. My name is Fumio Matsumura. I'm a professor of environmental toxicology. And my area of expertise is in general toxicology, molecular toxicology, and biochemical toxicology.

DR. Thrall: Good morning. Mary Anna Thrall, professor of veterinary pathology at Colorado State University.

DR. RIVIERE: Jim Riviere, professor of pharmacology, North Carolina State University

DR. ADGATE: John Adgate. University of Minnesota school of Public Health, Division of Environmental and Occupational Health, exposure analysis and risk assessment.

DR. FREEMAN: Natalie Freeman, Robert wood Johnson Medical School; children's activity patterns and exposure to metals and pesticides

DR. STEINBERG: JJ Steinberg. Albert Einstein College of Medicine. I'm a professor there and involved in environmental toxicology.

DR. STYBLO: Miroslav Styblo. Associate professor of pediatrics and nutrition, University of North Carolina Chapel Hill. Metabolism of arsenic and molecular mechanism of arsenic toxicity.

DR. WAUCHOPE: I'm Don Wauchope. I'm a chemist

with the USDA agriculture research service in Tifton, Georgia. And my research area is pesticide fate and behavior in the environment.

DR. LEBOW: Stan Lebow. Scientist with the USDA Forest Service out of Madison, Wisconsin, research on environmental impacts of wood preservative and wood preservative evaluations.

DR. STILWELL: Dave Stilwell, Connecticut Agricultural Experiment Station. And I have experience with dislodgeable arsenic and arsenic in soil.

DR. REED: Nu-May Ruby Reed, California Environmental Protection Agency. I'm a toxicologist doing pesticide risk assessment.

DR. RYAN: I'm Barry Ryan, professor of environmental and occupational health at the School of Environmental and Public Health at Emory University. My special expertise is in environment exposure assessment.

DR. MACINTOSH: I'm David MacIntosh. I'm a senior scientist at Environmental Health and Engineering in Newton, Massachusetts. And I work in the area of

exposure analysis and risk assessment.

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

DR. HATTIS: Dale Hattis, research professor at Clark University, specializing in issues of risk modeling and variability and uncertainty.

DR. PORTIER: Ken Portier, associate professor of statistics, University of Florida, specializing in environmental sampling statistical issues in probabilistic risk assessment.

DR. MACDONALD: Peter Macdonald. I'm a professor of mathematics and statistics at McMaster University in Canada, general expertise in applied statistics.

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

DR. HEERINGA: Thanks again to the members of the panel.

And I want to, before we turn for the agenda for the morning, which is a continuation of the questions, I want to ask Mr. Lewis, Paul Lewis, the designated public official, and I believe Larry Dorsey, the secretary for the Science Advisory Panel, if they have any announcements that they'd like to make.

MR. DORSEY: Thank you, Steve. I'd just like comment to the Panel. We're monitoring the weather conditions. I think in Washington, we're going to be fine. It appears to be in the 30s today. We're also checking your various airport to make sure they're still open. I want to assure you that you'll be taken care of. We've checked at the hotel. There are rooms tonight in case somebody doesn't make a flight. There are connections. So what I'm going to suggest, if at noon if you are concerned that an airport is open or a connection might not be made, would you please check in the break-out room. We have a person from MegaTech there that is checking SATO Travel for you. I think everybody will be fine. But we just want to make sure your comfort level is

okay. And if you have any questions, please ask me or check me in the break-out room. Thank you, very much.

DR. HEERINGA: We'll check everyone's risk tolerance on the weather here. Paul, Mr. Lewis.

MR. LEWIS: Thank you, Dr. Heeringa. Welcome to the third and final day of our meeting of the FIFRA Advisory Panel. I think we can all agree we had some challenging and interesting discussion in the past several days.

As I mentioned, FIFRA SAP operates under the guidance of the Federal Advisory Committee Act. Again,k this is an open meeting. All materials for this meeting is available in our docket including the report that will summarize the Panel's deliberations that began yesterday afternoon and will continue today.

For members of the panel, as Mr. Dorsey mentioned, please, if anyone needs to leave early today for the meeting, please approach me beforehand and provide your comments to the lead discussant for the question or questions that you're assigned to. That way we can have

earmarks as we begin writing our report. Thank you.

Dr. Heeringa.

DR. HEERINGA: One last final administrative note. I'd like extend my thanks to Dr. Matsumura for filling in yesterday afternoon while I was in College Park. Thank you very much.

At this point in time, before we turn to the questions, we'd like to give the staff of the Environmental Protection Agency a chance to either present points of clarification from discussion on the past two days or comments to sort of direct our responses, items that we may have missed or items of interest that you'd like to provide.

Mr. William Jordan of the EPA,

DR. JORDAN: Thank you, Dr. Heeringa.

My name is Bill Jordan. I'm a senior policy advisor in the Office of the Pesticide Programs. And on behalf of all the folks from EPA, we want to express our appreciation to the Panel for your comments. So far, we've found them very thoughtful, very helpful, and they

will help us to do a better job in the next iteration of the risk assessment.

In our sense, the way in which the Panel is approaching the discussion of these issues gives us ample opportunity to respond to areas where you have questions and clarify some of the points that AZ raised in the public comments. So we are happy to continue with that approach, and, frankly, don't want to delay matters any longer than necessary. Even know you did come to Washington to enjoy the weather.

Let's go ahead and tackle the questions.

DR. HEERINGA: Very good. Okay. Without further adieu, let's move on. I believe we are at issue No. 4. Is this right, Paul?

MR. LEWIS: That is correct.

DR. HEERINGA: Issue No. 4. Mr. Jordan, would you, please, read the question. Excuse me. I'm sorry. Dr. Ozkaynak.

DR. OZKAYNAK: EPA's draft CCA exposure assessment includes a formal sensitivity and uncertainty

analysis as well as discussion of various sources of uncertainty in the model analyses.

Question A: THE panel is requested to comment on the utility and suitability of the statistical diagnostic tools used by SHEDS for analyzing model results (e.g., variability analyses, sensitive analysis, uncertainty analyses).

DR. HEERINGA: And our lead discussant to respond to the questions on this issue is Dr. MacIntosh.

DR. MACINTOSH: First, I'd like to say that this issue, the associate discussants are Dr. Ryan, Dr. Francis, Dr. Hattis, and Dr. Portiere. And given this is the third day we're here, we've had the chance to talk about this together. And I've received both written and verbal input from each of them and have attempted to incorporate that, their comments as well as mine into a single initial response. So I'll read that and then ask each of them to provide any additional comments as we go along.

Results from the SHEDS-Wood model runs were

analyzed to identify the influence of model inputs on model output. More specifically, the Agency used a series of sensitivity analyses to identify the model inputs with the greatest influence on interindividual variation of estimated CCA-absorbed doses. Likewise, the Agency used a similar set analytical methods to determine the model inputs that contributed most to uncertainty in the model output. I'm going to talk about each of those in turn.

With respect to the sensitivity, the SHEDS-Wood model developers used two approaches. The first, they referred, or maybe we did, I'm not sure, as the scaling approach. This is where they altered or perturbed each input by a factor of 2 up and a factor of 2 down and did that individually for each input and ran the model and compared the output by looking at the median and the upper and lower bounds of the 90 percent confidence interval on that population. Maybe not a confidence level.

We found that this scaling approach was useful because it is easy. One reason is because it's easy to understand that type of perturbation to the inputs. It's

intuitive and you can work with it.

On the other hand, we found that it has some limitations principally because of issues related to scale with respect to that actual dynamic range of the input parameters themselves. The scaling up and down by a factor of 2 invokes a parametric response essential. In that sense, the range of the variables as measured by the standard deviation is more relevant in a parametric sense.

That said, it's also important to note that some of the variables do not display variability while others display a considerable range. Thus, in this factor of 2 sensitivity analysis approach, the scaling approach, one may be seeing a sensitivity in response of the model that's an artifact of including too much variability; or likewise, an artifact of including too little variability. For this reason that SHEDS-Wood developers should consider foregoing this factor of 2 method altogether where possible.

In some cases scarce data may necessitate the factor of 2 or a similar approach but we express some

reservations, nevertheless, that the variables deemed most sensitive may be misspecified under this scaling approach.

In that plus-or-minus-one standard deviation method that was also used, we found this method to be appealing because that change in that input variable is normalized with respect to the variability assigned to the parameter. In other words, that scaling afford by perturbing the variable plus-or-minus-one standard deviation also includes information on that likely range of the variable.

We noted, though, that in cases where there's limited data the plus-or-minus-one standard deviation approach sometimes gave negative results, that is in the case of a skewed distribution, because it seemed to us that a parametric approaching the arithmetic mean and the arithmetic standard deviation was used. Therefore, we think it might be more useful to instead of perturbing the variables by a plus-or-minus-one standard deviation, to instead just use something like the 16th percentile and the 84th percentile. That way you're ensured not to go

into these negative ranges. In fact, Dr. Hattis indicated that that indeed was that intention of the 2000 SAP in their recommendation.

Lastly with respect to that sensitivity analysis, the model developers used a stepwise regression approach in which case they rank the models with respect to their contributions to variability by the partial r squared associated with each term. Clearly, this is a more rigorous statistical tool than that two previous methods. And among other benefits, you can attempt to reflect sensitivity of one input while controlling for the influences of other inputs and, therefore, yield a potentially more accurate and useful characterization.

However, regression analyses require assumptions about that distributions of the dependent and independent variables, for example, independence and normality. And the extent to which these assumptions are not met, the results of the regression analysis are subject to some limitation.

We think that the Agency should acknowledge

these potential limitations and determine the extent to which their conclusions could be influenced by statistical considerations.

Lastly, that stepwise regression approach is useful for only the nonpoint parameters as useful but parameters some of which could be important too.

Looking at that uncertainty analyses that were done, we have many of the same comments. Just to refreshing everyone's memory there, for examining the relationship between uncertainty in a model input with the model outputs, the developers used Spearman and Pierson correlation analysis looking at associations between the mean value for inputs and the mean value for outputs. And they also used stepwise linear regression reporting again that partial r-squared. And essentially because the Pierson and stepwise regression are also two parametric, the comments that we had about the stepwise previously apply here too.

So in conclusion with Question A and my synthesis of comments here, we find that in general, the

analysis of the SHED-Wood model results has been approached in a useful and suitable manner. As of yet, there is no scientific consensus on the single best method to analyze output for that model for these purposes. Therefore, the use of several different methods to examine relationships between inputs and outputs that were used in this case are considered to be appropriate.

And importantly, the results of the different methods for the sensitivity and the uncertainty analyses are reasonably consistent suggesting that the conclusion drawn from these analyses are robust with respect to the choice of analytical method. We find that comforting. Nevertheless, the results of the sensitivity and uncertainty analysis may be limited by discrepancies between the data the choice of that statistical tool referred to earlier.

So I'll turn this over.

DR. HEERINGA: Thank you very much, Dr. MacIntosh. Are there any additional comments from the associate discussants? Comments from any other members of

the Panel?

Thank you very much. I think we can move on to Part B.

DR. OZKAYNAK: Question B: Is the bootstrap approach that is used for fitting uncertainty distributions, which has been revised in response to prior SAP comments, implemented properly, or are there alternative approaches that are recommended?

DR. HEERINGA: Dr. MacIntosh.

DR. MACINTOSH: Thank you very much. A much shorter answer this time.

It appears that bootstrap approach is implemented appropriately. Alternative approaches are available for fitting uncertainty distributions from available data. However, in our judgement, alternative approaches are unlikely to yield results that are sufficiently different to make an appreciable difference in the over all results.

In addition, addressing other sources of uncertainty in the data and model may yield more

substantive improvements in the modeling system and its results for this particular application. For example, the bootstrap approach cannot be used to express uncertainty for variables for which there are few data. And therefore, spending time on that may be more beneficial than exploring alternatives to that bootstrap approach.

DR. HEERINGA: Thank you very much. Any other comments from that Panel? Dr. Hattis.

DR. HATTIS: I would just like to add in response to Question D below, we'll talk -- the bootstrap approach, I think, is likely to adequately capture fluctuations due to sample size. And to some extent, the analysts' subjective impression of the strength of their data from the data they have in front of them, there are some additional sources of uncertainty in particular the possibility of systematic errors, unrepresentativeness of the population studied, that sort of thing, that are likely not captured. And we'll talk a little bit more about ways of assessing that in Question D below.

DR. HEERINGA: Very good. Dr. Macdonald.

DR. MACDONALD: I'd like Dr. Hattis to explain what you mean by sensitivity to sample size. Which sample are you talking about?

DR. HATTIS: Essentially the sample size of the set of data that they have what's represented as B in the terminology of the -- essentially, this is captured by that number of iteration or the number of draws from that nonparametric distributions -- bootstrap -- for that nonparametric bootstrap that is done. So essentially, if one has only three values, the spread and you sample three values from a defined distribution for a parametric bootstrap or from the empirical distribution for a nonparametric, you get a wider spread of sets-of-three values of fitted parameters from sets-of-three values than you would from sets-of-thirty values. And that's the sense in which I'm using the term "sample size."

DR. MACDONALD: You're referring then not to the size of the bootstrap sample but the size of the sample in which the original distribution was based.

DR. HATTIS: Well, I guess I'm referring to the

size of the bootstrap sample which is inspired by the author's evaluation of the size of the data sets that's contributing to their distributions.

DR. MACDONALD: Well, as report coordinator, I'm responsible for making this clear in the final version. I trust that it will be by then.

DR. HEERINGA: Just to complete that comment, I think that the issue of the influence of the sample of the underlying data of which that bootstrap is formulated and that size of the bootstrap samples themselves used to simulate the bootstrap distribution will be clarified by Dr. Macdonald.

Any other comments? Okay. Question C.

DR. OZKAYNAK: Question C: Are the uncertainty distributions assigned to chemical and non-chemical specific model input parameters appropriate?

DR. MACINTOSH: To say that we would limit in response to this particular subquestion to those parameters that were treated uncertain in a probabilistic sense.

In cases where that available data were applicable, in other words, specific to the model use and representation of an appropriate U.S. population of children that you intended to model, then the uncertainty distributions described in the SHEDS-Wood report are probably reasonable and generally appear appropriate. And as we said in a previous question, it's our judgment those distributions are fairly robust to the method chosen to represent the uncertainty.

That said, I want to make a quick side note. Again according to Dr. Hattis who had served on the previous SAP on this issue, his recollection is that the SAP recommended the uncertainty analysis include modifying the distributional form of an uncertainty expression in addition to simply altering the parameters for a given type.

Now, in cases where the available data are not specific to their use in the model or representative of the U.S. population or the model population here which is largely the case for the parameters in this model, then

the uncertainty distributions generated by the bootstrap method may not be appropriate. We learned for example that the videography studies used to quantify hand-to-mouth frequency included few, if any, children on public playsets, residential playsets, residential decks and the soil around them.

We also know that absorption rates used in the model were based upon animal models exposed to certain concentrations of CCA or arsenic; and yet there appeared to be little consideration of animal-to-human extrapolation or possible concentration-dependent effects in the uncertainty analyses. Other examples exist. They will be identified by the SAP and considered for inclusion in our final report.

DR. HEERINGA: Yes.

DR. XUE: I would like to respond for one item in terms of the form of distribution raised by 2002 SAP. We do did some analyses. Because first of all, we cannot systematically to do certain analyses in terms of change of form of a distribution. But after sensitivity by

scaled down standard deviation by a factor of 2 we've identified the important key input. Then we change the distribution because we fit the distribution. Sometimes we fit five distribution to set one of it. Then we change that distribution.

I'd like to show slide X-4, X-4, 47. So they have, when we fit the distribution for the residue on the transfer efficiency, because this is a deck concentration and that transfer efficiency. This is the most important one. We change it from log normal into Weibull distribution to see what's effective on total exposure. We found that the effect is very, very -- is also very robust and not much changed. So this is the distribution we did. And this results, we already gave it to SAP Panel. You can look at this analysis.

DR. HEERINGA: Thank you. And just to be clear here, that based on underlying data for this transfer coefficient, you fitted to a maximum likelihood or method of moments, initially a log normal distribution, and alternately a Weibull distribution; and simulations were

run on those two input distributions.

DR. XUE: Correct. So this is the result. Here, I can't see clearly. One is I remember one is the residue concentration in the deck, and the playset concentration in the deck. And also another one is transfer efficiency. These are the three most important input for all SHEDS model.

DR. HEERINGA: Thank you very much.

DR. OZKAYNAK: I also want to clarify or perhaps maybe request a clarification. I think that maybe I misunderstood what Dr. MacIntosh said. We have taken at heart the recommendations from Dr. Hattis and the SAP from last year. And we have indeed come up with new forms of distributions. And as Dr. Xue reported now, we have looked at alternatives and how they influence the results. So we have looked at other forms of distributions, and they're not assumed in prescribed sets of which we have done the previous SAP.

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

DR. OZKAYNAK: Thank you.

DR. HEERINGA: Dr. Hattis.

DR. HATTIS: I can say that we're gratified by the responsiveness of this study team to our earlier suggestions.

DR. HEERINGA: I guess we can move on to Question D.

DR. OZKAYNAK: Question D: The Panel is requested to comment on whether the modeling approach and documentation appropriately identify and address critical sources of uncertainty in the model and the resulting exposure estimates. Does EPA's documentation adequately describe the uncertainties inherent in the data used for modeling and the influence of these uncertainties on interpretation of the modeling results?

DR. HEERINGA: Dr. MacIntosh.

DR. MACINTOSH: In general, we found that the EPA's documentation contains a reasonable, although sometimes limited, description of the uncertainties inherent in the data and the influence of those

uncertainties on the interpretation of the modeling results. That the uncertainty analysis has potentially important limitations is suggested by the uncertainty bounds described in that exposure assessment report.

For example, that 90 percent confidence interval for uncertainty about the median lifetime average daily dose of arsenic ranged over a factor of 4. And this range of uncertainty struck many members of the SAP as surprisingly narrow. And Dr. Ozkaynak made a similar observation during his comments on the strengths and limitations of the modeling implementation.

The unexpectedly small range of uncertainty may in part be a result of the decision to use only the bootstrap approach to characterize uncertainty, and thereby was necessarily limited to parameters for which data were available to support that type of analysis. This strategy means that some potentially important and highly uncertain variables were omitted from the uncertainty analysis.

Some examples are the average number of days per

year that a child plays on or around a treated public playset, the fraction of children with a CCA-treated residential playset, the average number of days per year that a child plays on or around that CCA-treated residential playset, the fraction of children with a CCA-treated residential deck, the average number of days that a child plays on that deck, and also the 8-day diary location activity information.

Also omitted from that uncertainty analysis is a lack of knowledge about the appropriate scenarios to include in the model and the algorithms and corresponding used to simulate certain physical events. At least some of these scenarios and algorithms were identified in the materials submitted to SAP members prior to the meeting and during the public comment period during this meeting.

And some examples are as follows. Exposures associated with water and mulch that we heard about yesterday, effectiveness of sealants as a function of time, wood condition, and other factors for containing CCA residues, potential of unloading events from the skin,

assumptions about the arsenic chemical form and oxidase on available for transfer of CCA residue to skin, and subsequent absorption perhaps associated with that leaching suggested by the changing chromium to arsenic rations described in the public comments by Dr. Ruby and other.

Also transient changes in exposure conditions that could have a substantial influence on short-term exposures including sanding, sawing, changes in pH associated with maintenance of decks.

In addition, same factor I mentioned before: the absorption fraction as related, the Agency chose to use an absorption fraction approach. But there are alternatives such as a physical model of dermal absorption that is described in EPA's guidance for dermal exposure assessment.

At this time, the SAP can only speculate about the influence of these types of uncertainty on the model results. It's clear, however, that additional and potentially critical sources of uncertainty remain to be

addressed.

DR. HEERINGA: Thank you very much, Dr. MacIntosh. Any additional contributions from associates? Dr. Hattis.

DR. HATTIS: Yes. I had, first, another odd observation from the data that maybe you folks would like to comment on or comment on later when you do the next iteration. And that is looking at Figure 37 on page is 50, the uncertainty plot for the --

DR. HEERINGA: In that exposure report?

DR. HATTIS: Yeah, in the exposure report. That's right. In that average daily dose for arsenic in warm climates. What I noticed is that there didn't seem to be much increase in the spread between the 5th percentile and 95th uncertainty percentiles between the left-hand curve and the center of curve or between the right-hand in the center of the curve. So essentially what I intuitively expected would be that extreme percentiles the distribution should be more uncertain than that center of the distribution. And I don't see it.

So I'm obviously -- my intuition is obviously wrong, and I'd like to know why it's wrong. If you have a feel for that and can respond soon, than that would be great. But you don't have to.

DR. XUE: This is one of my explanation because this figure is just from three populations, not adjusted for the whole population. This is base mainly look at the variability. And for answer to your question, another thing. Because it comes from three separated populations, so these results is not stable at all. This figure in terms of the uncertainty. The different one is not stable because it only come from three populations selected by media to get this.

DR. HATTIS: Okay. I'm not completely getting it, but that's all right.

DR. XUE: If you look at that next figure, this is for -- I think that lower is a little bit high.

DR. HATTIS: Yeah, okay. There may be a little bit more spread.

DR. XUE: For that first figure, it's just when

we do this, we select a (inaudible) media, selected three populations. Three from -- if we run 300, we only select three, three ones. Then we put their variability there. So this is the results for uncertainties not stable.

DR. OZKAYNAK: There are 298 sets of CDFs. So these are selected three out of the 298.

DR. HATTIS: Oh, yes. What I thought this was was a plot of the uncertainty percentiles across that 180.

DR. OZKAYNAK: That's that second one.

DR. XUE: That one.

DR. HATTIS: And that shows a little more spread. All right. Evidently in my quick reading, I didn't quite grasp it.

DR. HEERINGA: Thank you for that clarification. I think that's important. I think most of us would expect to see these bounds flare as we approach that extreme percentiles particularly on the upper end if it's a skewed distribution.

DR. PORTIER: I wanted some clarification. You generated 480 individuals, and then you modified the

parameters as you ran them through or you ran the same 480 individuals. I was looking at this 480 individuals and 189 uncertainty runs. Right?

DR. XUE: So basically what we do is that we first have one set of parameters. This comes from bootstrap, each pair. Then use each pair number, run 480s. Then we get the results and we study the results. Next time from another pair, we get another run. Then we run another 480. Run about 300 times.

DR. PORTIER: Right. You need to change the write up on page 80 to clarify that. It sounds like you first generated 480 and then those 480 were passed through 189 scenarios rather than you generate 480 individuals to 189 different parameterization scenario which is what we expected to occur. Right.

DR. OZKAYNAK: Sure. We'll make sure that we clarify that.

DR. HEERINGA: Thank you. And we'll be sure in our PANEL report to include that recommendation, specific suggestion.

DR. HATTIS: I have a little amplification of the Uncertainty, overall uncertainty issue, some of which was captured in your earlier discussion but not quite all.

Generally, it's likely that overall uncertainties are under stated because, first, influential variables for which no variability estimates were made also not subject to the bootstrap which was covered earlier. And, second, any procedure that relies on internal fluctuation within a data set will tend to incorporate only random error and neglects sources of systematic error among studies such as unrepresentativeness of the study population for the target population of exposed children.

For example, your 160 Los Angeles children might be representative of the whole nation, and it might differ somewhat. And that's true for many of the cases. Pennsylvania boards might not fully reflect all of the cold climate boards, et cetera.

And there's no way you can get any information directly on that subject from the fluctuations within that

Pennsylvania data set. And this is not a well recognized and analyzed problem within the statistical community, I must say.

But going back, to deal with that first point, that is that lack of uncertainty estimates for that single point parameters. I mean basically the only feasible approach is to use professional judgement or a formal expert solicitation, but that can be expensive, to arrive at some reasonable estimate of uncertainty, perhaps informed by estimates of uncertainty for other parameters for which you have more information. Although that's a little hazardous.

For that second problem, that is the systematic error, the magnitude of unsuspected systematic error in procedures for inflating conventional standard error types estimates of uncertainty have been empirically studied in a series of papers by Alec Schlecter, who is a Russian emigre physicist who recently passed on.

The basic observation -- this is from highly sophisticated statistical folks. These are physicists,

measuring elementary particle properties like the weight of a particular bosun or the speed of light. The observation is that when newer, more accurate measurements are made, they wander systematically farther from that previously estimated confidence limits than would be expected by chance. So the idea is that we can use some empirical observations of how accurate our standard error type estimates of uncertainty are to inflate the estimates of uncertainty that we get from the purely observation of random error.

This is almost never done. Okay. But if you want to describe uncertainty. And this is where I think part of the cutting edge is or some would say beyond the cutting edge. But nevertheless, if you want to be that truth about uncertainty, I think some expansion of the random fluctuation calculated uncertainties is in order. And I've described to some extent very limited applications of this in some papers of mine.

Ideally, you would want to draw the rules for such expansion from experience within the types of

environmental parameters that you're dealing with rather than measurements of physical parameters of physicists. But I think that you can confidently say that the biologists and engineers for making the physical measurements are likely to be no more free of systematic error relative to random error than the physicists are.

So you could use at least the physicists estimates of how to inflate as a starting point if you want to do something sooner and say, for sensitivity analysis, how much would our uncertainty inflate in recognition of that. It turns out that the shape of the uncertainty distribution is indicated not as Gaussian but some exponential shape. But I provide in a paper ways of easily converting between Gaussian and these expanded confidence limits. So it's not hard to do in calculation terms.

But it seems to me that one interesting observation is that we would observe that the existing estimates of uncertainty and various parameter distributions that you just made can offer an invaluable

opportunity to explore and calibrate this possible avenue of uncertainty evaluation if, for example, you make improved estimates and representation measurements of key model parameters as suggested in some detail by Dr. Chassion yesterday. This would provide the basis for assessing the degree of under estimation of uncertainty that results from that techniques you've just applied in making these estimates.

So what I want to say is these are valuable uncertainty estimates. Even if they later prove to be wrong, even if you later find that, like the you have understated the uncertainty, it give you a clue as to how to inflate more appropriately uncertainty estimates for future studies. So I would urge that even if you think that there's not, even beside the relevance of improved estimates of these parameters for decision-making on CCA, you should also look at it as a research effort in now evaluating this brand new, well, relatively new, tool for uncertainty analysis that you've created.

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

I would like to ask if there are any other comments from the Panel.

DR. XUE: I just clarify one point about the bootstrap. We did not use the actual sample size others that B for bootstrap because we know that the data limitation. And that's why we part of this uncertainty and use all of the data available so that I'll make sure all this data is different data source were included. And when we don't have data, we have give as much uncertainty as possible. We also know that they have limitation, random -- and we already ask other people to do more research on this uncertainty.

DR. HEERINGA: Very good. I think that's clear in the exposure and that sample sizes for modified actually reflects the relationship to that quality of input data. So that comes through.

DR. HATTIS: A subjective evaluation of how much systematic error and random error there might be. The experience is that subjective estimates of uncertainty as well tend to understate real uncertainty. And it's

measured a couple of different ways. And this also reinforces that desirability of taking the opportunity of new measurements to calibrate this.

DR. HEERINGA: Thank you very much. At this point in time, we're ready to move on to Question E.

DR. OZKAYNAK: Question E: Does the Panel recommend performing any additional uncertainty analyses to evaluate the impacts of using alternative input distributions on the modeling results (e.g., to address uncertainties in various factors determining the frequency of children's exposures to CCA-treated wood in playsets and decks)?

DR. HEERINGA: Dr. MacIntosh.

DR. MACINTOSH: Well, the short answer to that Question E is yes. And we've just heard from Dr. Hattis and others about possible approaches to performing additional uncertainty analyses.

In a related topic, we think it's also important that the Agency articulate the purpose of this uncertainty analysis because the purpose is closely related to the

methods that is used to characterize uncertainty. In other words, having a clear purpose is important for establishing the conceptual framework for describing uncertainty. And as a results, it aids in defining the scope and methods of the analysis.

For example, the purpose could be to characterize the entire likelihood function of plausible, hypothetical population-based, probability distributions for CCA absorbed dose or exposure.

this purpose might be of greatest interest to an EPA program office such as OPP. The current exposure assessment does not appear to have this purpose, however, because we know that potentially exposure scenarios and exposure-related mechanisms and parameters were not included in that formal uncertainty analysis.

It reminds me of the venerable parable about the man who lost his keys along a dark under street and is looking for them under the street light or the lamppost. When asked why he's looking there, the man replies, because that's where the light is. As a result, he has

little chance of finding his keys. All right. And by analogy, the current uncertainty analysis is limited to where that data are sufficient to support the bootstrap analysis methodology. As a result, this strategy has little for finding the true range of possible and plausible exposure distributions for the model population.

Similarly, however, the purpose of the uncertainty analysis could be to characterize uncertainty associated with relatively data rich parameters within the historical model framework and CCA-exposure scenarios of SHEDS-Wood. Even though much more limited in scope than the first example, this purpose is fine. And it clearly has scientific utility.

In my opinion, this second example of purpose is approximately an accurate description of the uncertainty analysis that's contained in that report. As such, I think that purpose should be clearly, again, articulated in the report, so that the reader has some idea of what's represented by this uncertainty. And even the goals of the uncertainty analysis.

At that same time, the readers and users of the results should be cautioned against a false sense of security about that accuracy about that uncertainty analysis. Methods to assess the impact of data posit can be suggested, and Dr. Hattis, suggested one. There are others. We note that we find it fortunate that we actually don't have to --in the words of Dr. Ryan -- bell the cat here. And we don't envy the task that SHEDS-Wood team would have to undertake to perform this.

However, we also note, and this following up on a comment by Dr. Hattis, without knowledge of these components of uncertainty and variability, it's very likely the uncertainty in the estimates made is itself underestimated. Additional comments?

DR. HEERINGA: Thank you very much. Are there any additional comments from the discussants?

I think in our report we will try to be clear on this distinction on the uncertainty analysis is essentially as conducted here as I interpret it is related to testing the uncertainty associated with the building of

the distributional assumptions based on the available data; and there is clearly this other area of uncertainty that none of us really want to be stuck with, and that is the selectivity and the potentially nonrepresentativeness of the particular data which we are building our uncertainty models. But, clearly, it has to be done in stages. And I think that clarification is a good one.

Any others? Yes, Dr. Macdonald.

DR. MACDONALD: A general comment I think to all of the activities described in this issue that when you're trying to study a system that has a large number of inputs and particularly when you're trying to see which inputs are most critical and which ones are less critical, I think we need attention to principles of experimental design. Certainly in a case like this where you have a large number of variables and can assume that there's a limited number of interactions to Gucci type of fractional factorials probably appropriate and one would hope would be more efficient in leading to conclusions.

DR. HEERINGA: Thank you very much, Peter. Any

other comments from that Panel on this particular question?

Seeing none, I recommend that we move on to Issue No. 5.

DR. OZKAYNAK: Issue 5: Special Model Simulations.

A number of special simulations with the SHEDS-Wood model were conducted in order to examine the importance of specific exposure scenarios or the impact of certain input assumptions. For example, some to these analyses included conducting separate simulations for children exposed to public playsets only, modeling exposures of the 7-13 year old age group, and studying exposures of children exhibiting pica behavior.

Additional analyses were also conducted to examine the impacts of using data or assumptions about increased GI absorption, decreased dermal absorption, lowering the transferable wood residue concentrations by sealants, and hand washing after play events. the results from these special analyses were not significantly

different than the baseline model results, except for the large impact of assuming the use of sealants would greatly reduce wood residues.

Question A: The Panel is requested to comment on the appropriateness of the justifications made in characterizing the key factors or inputs for each of these special simulations. Did the Agency provide adequate technical rationale and justification for its choices for these alternative exposure scenarios or input distributions? Do the results from these special analyses reflect proper use of available information?

DR. HEERINGA: Dr. Kissel is the lead discussant on this question.

DR. KISSEL: To some extent some of these things have already come up in prior discussion. And I think the wording of the question is perhaps too formal for what we're actually dealing with here.

Generally, the feedback I got was that we were satisfied that EPA had run an assortment of test cases, sort of what-if scenarios, that examined the overall case

and that the list was more or less appropriate. We do have a couple of suggestions for additional scenarios but general there was satisfaction that things were done appropriately.

When you're given these kind of questions which are, well, we don't really know too much about that so what if sort of thing, there is no formal measure of whether that's appropriate or inappropriate. It's a professional judgment sort of issue, and I don't think we have too much argument about that way things were done.

Do you think A is where we should discuss other possible scenarios, or is that B?

DR. HEERINGA: Maybe just leave it for B.

DR. KISSEL: Okay.

DR. KISSEL: Any the associated discussants want to add anything to that?

DR. HEERINGA: That question relates to the special simulations including that pica behavior. Dr. Freeman.

DR. FREEMAN: This is relevant to pica. This

has to do with the sealant reductions. I think what the model does -- and you can correct me if I'm wrong -- is it assumes that the sealant is replaced consistently enough so the reduction is continuous for the exposure lifetime of the child. And from some of the presentation we had yesterday, this becomes questionable. I'm not sure how much effect it would have on your model if you tried to put in that sort of variability.

DR. XUE: You're correct. We assume that the change is 90 percent average for lifetime.

DR. HEERINGA: Thank you very much. The two sealant effectiveness simulations are quite extreme in that they virtually limit the residue exposures to zero in one case and 5 percent of the prevalent values in the other case. So in some ways they look like, I think, sort of extreme cases with regard to residue reductions.

DR. OZKAYNAK: That was that intention to sort of test out what would be the implications of using a very effective sealant in terms of not only the exposure dose predictions but also that associated risks. Since we did

not have sealant-specific, actual sealant information in terms of effectiveness across multiple seasons and years, we just selected those hypothetical scenarios just to do a bounding analysis.

DR. HEERINGA: And given the importance of residue ingestion in the total exposure pathway, it very much looks like a scenario not only for sealants but for an assumption of very, very different sort of concentrations or uptakes in residues as well.

Any other comments from the Panel members?

DR. HATTIS: I just would reinforce the idea. I think it was a useful set of supplementary analyses and reasonably well done.

DR. STILWELL: Are we going to introduce the mouthing one on this one?

DR. HEERINGA: Sounds like there's interest in moving on to Part B.

DR. OZKAYNAK: Yes, we can't wait.

Question B: Do any of the findings from these special analyses necessitate the Agency to consider

revising certain scenarios or inputs to that baseline assessment?

DR. KISSEL: This is where I think we want to address either new scenarios or modifications of the special scenarios that are here. And two that we have, one would include modification of soil pica to include more generalized pica which I'll let Natalie give the justification for that.

And that one was some modification of the sealant scenarios to deal with decline in that sealant capacity over time. And I'll let Dr. Stilwell address that one.

Natalie, do you want to say something about pica?

DR. HEERINGA: Dr. Freeman.

DR. FREEMAN: I think some of it I had actually had said yesterday. There is soil ingestion that other children do, but it is not like pica. And that the pica children would not be that ones who are consuming from this sort of environment.

Related to this is, in one of your special models where you use the sealant, you ended up reducing the surface residues but not necessarily the soil concentrations. So that you end up driving perhaps artificially that effect of soil consumption under those situations because, presumably if a lot of the soil contaminants are due to runoff, you would have also reduced those levels as well and so that the proportions that is attributable to contact with that deck may not be as reduced as much relative to soil as you have in your special models.

DR. HEERINGA: With regard to the alternates on sealants, is there any clarification? That really is attacking the residue transfer, residue exposure part of the model. It doesn't attack or address the contact time which is .another is there any consideration at all of scenarios which would alter that distribution of potential exposure times on sets as another sort of product parameter in the total exposure route?

I'm asking a generic question here. Consider

it. I guess I see no response.

DR. HATTIS: I guess one could consider padding or some other way of protecting the surfaces that children are most likely to contact directly.

DR. HEERINGA: One thought that I had, we have these two very large input parameters, very important input parameters to the exposure stream. One of them is the modeling of how much time children actually spend in contact with CCA-treated wood. And that one, I don't think our available data is going to do a more to inform us on. And one of the things that I had thought about on Wednesday when we asked about looking at this annual distribution of exposure time.

What you might do if you are doing these scenarios, say for residue or sealants, is to actually look at that distribution of exposures for children in terms of total exposure time on decks, and then fix certain points in that distribution. Somebody who is sort of in the 20th percentile of the total annual exposure to CC A, and say for a child that spends X amount of time a

year on these decks, what is the difference. I guess it's sort of a partial simulation where you're conditioning on an exposure time. And I think that might actually be informative of this issue that we're struggling with. And I think some of the public commentors were struggling with it.

We are compounding uncertainty on several different parameters. And to be able to see the uncertainty associated with one important parameter is the other, we might want to actually look at the distribution of one, fix certain profiles in that distribution, and then look at that effect of the sealant or residue reductions appropriately. Just a way of sort of, I think, in a very, very complex uncertainty environment of sort of parcelling out the uncertainty sort of one stage at a time. I think maybe that is the best we can do at this point. Dr. Freeman.

DR. FREEMAN: That got me thinking about something that's been going around in my head for a while. Most of the observational studies suggest that about

somewhere between a third or even less of mouthing occurs outdoors for little kids. In some cases, it's close to zero. So you reduce it from 10 times an hour to one to two to three times an hour at most in terms of rates. The contacts haven't been well quantified simply because we have such poor data. Only four kids that I know of where we can actually quantify touches to Playscapes.

The loadings that you get on that hands, if you look at Dr. Kissel's work with soil or with David Cayman's work or Charles Rhodes's work with dust, the suggestion is that, and you have it in your model, that there is a maximum loading that is allowable. And then after that maximum loading occurs, there is, as the child goes through his daily activities, there's a constant dislodging and reloading if it's a particle characteristic.

If it's a fluid-type thing, I don't know how it works. But with particles this constant shifting. If that mouthing doesn't -- and serious mouthing we very rarely see it outdoors in any of these environment unless

the kid is very upset. So the liquefied mouthings seems to occur indoors.

So you're having this situation. You've been playing on that Playscape, 20 minutes or 40 minutes later, you have touched your bicycle, you've touched the door to your house, you've touched a gazillions things, and then you settle to eat your Doritos and watch television, and that's when you're going to be doing your ingestion.

But what are you ingesting at that point? Are you ingesting the residues that you picked up at the Playscape or have so many different contacts and removals occurred between the time of the contact with the wood and the time that you're actually do being serious mouthing that what you're ingesting is something else. And I'm not sure how you can handle that at this point basically because of data lack.

DR. XUE: Basically, we discussed this. But we don't know how to do it because there are no data how to do this way -- otherwise we would underestimate. If we give over estimate because not data people, we did not see

any model do it this way. And the other which is that data is any data available to see what was unloading process or something. There's no data at all. That is why we did this approach.

DR. HEERINGA: Dr. Ozkaynak.

DR. OZKAYNAK: Just to add one more talk to that. Is that even if available studies had looked at loading and unloading in prescribed settings but they've been really well regimented experiments, so it would be necessarily translate into complicated children's play activities. So it's very hard, even if we have one or two piece of information from limited experimental studies, to make that quantum leap and assume that that is going to be the case for children's typical daily activities of contact and mouthing and eating food and other complicated behaviors.

DR. ZARTARIAN: One additional thought. Maybe we can incorporate some of those ideas when we try to expand the uncertainty and the maximum determine loading.

DR. HEERINGA: I think that would be good. Just

a comment too as I tell students in social sciences, humans by nature are the most variable subjects we could ever choose to study. And thanks heavens for that. But children, even more than adults, are even more variable than humans as a general population. In terms of quantification, it's probably the toughest of all statistical and data measurement problems.

DR. HATTIS: That part of that question. It seems that newer data on dermal absorption probably should cause some rethinking, you know, or at least cause you to consider revising the central estimates of dermal absorption and perhaps expanding the uncertainty of the parameter.

DR. HEERINGA: I think at this time, we're ready to move on to issue. --

DR. STILWELL: Hold on.

DR. HEERINGA: Pardon me.

DR. STILWELL: One thing I'd like the EPA on Issue 5, I believe there might be some data for month-to-wood activity that I believe was referenced by

the Environmental Working Group and that would be an additional scenario or pathway to consider. And for that wood, I guess we going to just agree on some sort of compromise where you have some scenario where wood works effective for one year and then starts to decay for maybe a couple of more years and then they repaint and it goes back to some 90-percent reduction.

So you have kind of like a little step function and that sort of thing, that probably would be more a reasonable interpretation than having the wood work perfectly forever.

DR. HEERINGA: Thank you very much, Dr. Stilwell. Yes, Dr. MacIntosh.

DR. MACINTOSH: One additional comment on this, trying to take a step back from looking at these special analyses as one by one basically. And it seems to me that the special analyses came out of the previous SAP recommendations. As such, they're considered different or additional to what as done previously. Also when I look at it, I don't see much difference between these special

analyses and the sensitivity analyses except that only certain parameters were modified or those values were modifies and they were modified in a unique way as opposed to treating all the variables in a standard way in the analysis. So I wonder if this isn't just another type of sensitivity analysis, and as such for readable maybe it should be incorporated into the other sensitivity analysis approach.

But more importantly in my mind, there is a serious limitation of this one-at-a-time variable approach which you lose all the information that might be contained about sensitivity of the model results to joint changes in variables. All right. And it bothers me to see over and over in the report, well, we made this change in the model because of a request for a special analysis and we didn't see much affect on the output. And when I see that 10 times, I go, well, what other together. Right? If it's a factor of 2 or factor of one and a half change 10 times over in both directions, then the effect overall may be large.

And it becomes -- you risk some type of pie in the sky totally naive analysis if you start joining all these together. But nevertheless, I think it become more a realistic representation of what we don't know. And there's some value in that.

DR. OZKAYNAK: I appreciate the comment. And I think that we have done in a few instances a sensitivity analysis or special analysis where we looked at that influence of multiple variable changes. The problem with doing more than one variable change simulations is that you have need joint probabilities as conditional probabilities for all these different scenarios occurring in various complicated mathematical form. And I think it's very challenging to a prior guess how those conditional events can occur when you're taking about multiple changes.

DR. HEERINGA: That's correct.

DR. ZARTARIAN: I'm just going back to Dr. Stilwell's suggestion. I thought that was a good one to consider a step function for residue reduction. But the

effectiveness of sealants depends on the sealant itself as well as people's behavior with respect to how often they apply them. And I'm wondering if Dr. Stilwell or any other members of the panel know of any data sets regarding how often people do seal their decks to give us an idea of what step function to use for that.

DR. XUE: This is Dr. Xue from EPA.

DR. HEERINGA: Just a second. Dr. Lebow and Dr. Stilwell, I think.

DR. LEBOW: I'm not sure of any precise data on how often your average person does it. There are recommendations on the labels of the products that usually vary from one to two to three years. Whether people really do it that often or not, I'm not sure anybody knows.

I did want to mention, as you're aware, that you do have your own ongoing studies in this area. And if they're allowed to follow through their completion, you will actually have some kind of data to plug into your reduction factor.

DR. ZARTARIAN: I believe those are more for that effectiveness of the sealants more than for people's behavior with respect to --

DR. LEBOW: Yeah, right. Exactly,yeah.

DR. HEERINGA: Yes, Dr. Xue.

DR. XUE: In terms of the change in multiple one, we do have one we provide this to that SAP panel. So we changed four. We think it's an important one, a very important one. And we think for future model, we will change it. We change the four together and then we have call examine all the results in the supplemental slide. And we already gave to that SAP panel.

DR. HEERINGA: Right.

DR. OZKAYNAK: Can you identify that, the number of that slide?

DR. XUE: This is from page 48 to 83. First one we tell what the change, what the distribution change. Then what the results change of the change on the table on the figure.

DR. HEERINGA: Thank you very much. Dr.

Macdonald.

DR. MACDONALD: This is the sort of study where I would recommend you do a factorial design just to make sure you're systematically doing the different combinations.

DR. HEERINGA: Thank you for mentioning that again. It crossed my mind too. Okay.

At this point, I think any other comments or clarifications? Let's move on to Issue No. 6, then. Dr. Ozkaynak.

DR. OZKAYNAK: Issue 6: Evaluation of the SHEDS-Wood model results.

The Agency has evaluated the probabilistic CCA exposure model results by comparing them to results from other earlier deterministic CCA assessments. In particular, the SHEDS-Wood model results were found to compare well to a deterministic CCA assessment performed by the Gradient Corporation, and SHEDS-Wood upper percentiles compared well to deterministic Consumer Product Safety Commission estimates.

Question A: Has EPA provided adequate documentation of the overall plausibility of the exposure estimates generated by the SHEDS-Wood model for CCA? Are the comparisons with the results of other selected exposure assessments appropriate and appropriately presented? Are there any other types of benchmarking approaching or data to assess the reliability of the overall exposure model or specific model elements?

DR. HEERINGA: And Dr. Reed is our lead discussant on this question.

DR. REED: Well, I don't have a whole lot to say about this because the database for comparison is very limited as the Agency noted also. I think that document adequately convey the limitation of the comparison. I personally don't think that such comparison based on the limitation that it's possible to determine on the plausibility of the model output in this way; however, this is not the only place that you look at the output plausibility. So I don't see this -- as the limitation within the database, I don't see this as an important

component for that evaluation.

I think model comparisons or comparisons of model output, whether it's in part or as a whole, is a viable means for evaluation. The only scenario that I can think of that would give sufficient meaning in the comparison is that it has to have sufficient common denominator in the model output or the logistics of the model.

And one I can think of is that you have to really compare a sort of set of same exposure scenario with the almost identical set of data input which is, you know, nothing of that sort is available right now. And I'm not even sure if at this point there is such an availability of other models, quote, unquote, "other models," for such a comparison.

I sort of grappled with this issue backwards and forwards. And I was thinking that, what if you take a hypothetical exposure scenario and do a hang calculation and a point estimate, essentially taking your new input data that you have now compared to what you have before

and what the other models have before and see how that would compare between a point estimate and the distributional approach.

I kind of gave up on that idea because it still does not mean a whole lot. So I'm coming up with no good suggestion except to say that the comparisons has to be based on sufficient amount of common denominator. The same scenario, same data input would be great.

DR. HEERINGA: Dr. Freeman first, then Dr. Ryan.

DR. FREEMAN: I actually enjoyed sort of going through the tables that you had where you listed the variable, the various other exposure models used, and trying to find out whether there were similarities and differences. And I was saying, okay, you had two variables that drove your study to some extent. To what extent are these same variables and the measures consistent across all the other exposure models that you were comparing with. And there were only two other models that had -- I don't know where my data is -- measurements for those first two variables. One had to do with the

residue levels on the surface. And I can't remember what the second one was offhand.

I thought that was interesting. There were so many different inputs used between the models you were comparing and your own that I didn't know how to handle it. I wasn't sure I was looking at apples and apple or apples and oranges gains. Even things such as how do you quantify exposure to the deck by the child. Is it in days per year? Is it in hours per day? I mean different models used different measures. So I really wasn't sure how to do an adequate job of comparing these things or whether it was even suitable to do it.

DR. RYAN: My essential comment on this is that we're making a comparison here. The best you can do at this point is make a comparison between what you've done and what other people have done. But it's sort of like comparing a bicycle to a Ferrari. It's just very difficult to have these things put on any kind of the same scale.

I was highly encouraged by the fact that the

results you guys got were in line with results that people got doing entirely different things, trying to mimic the same results. So I think you've done what you can do simply because there isn't a lot of stuff to compare this with. And I think the data are just sparse. And that's the way it's going to be until someone else comes up with a different type of stochastic model of this type, developed independently, and so on. The only thing we can do really is try to validate this model based on real data rather than on comparisons with other models. And I think that's what's intended to go forward from here.

DR. OZKAYNAK: Just a lite comment here. I think we'll change our model to SHEDS-Ferrari now.

DR. FRANCIS: If you're talking about the model and looking at comparison of a model to another model, there are probabilistic exposure assessment models out there that can be used. And if you at least supply the same basic data set, you can see how the various models perform. I think a similar kind of thing was done with the organophosphates for EPA.

It seems like, yes, you can in fact, for looking at how the model is performing, compare that to other models which may have slightly different internal means of coming up with the same results. The algorithms may be different. But I think that that would be a very useful thing to do.

DR. HEERINGA: Thank you very much. Yes, Dr. Dang.

DR. DANG: Thank you for the comment on this input values data for the comparison about the models.

We did prepare those Table 51 to 53, a very comprehensive table for information. Actually our purpose, one of the very important purpose is we try to deliver a message about that risk communication in the future, because one cannot compare to the other one in different perception on that risk communication where they're very different from different models. Thank you.

DR. HEERINGA: Dr. Zartarian.

DR. ZARTARIAN: With respect to that suggestion for another model comparison for that CCA assessment. It

is true that there was a model comparison workshop and other aggregate exposure assessments, probabilistic assessment models available. However, what we found in going from our SHEDS pesticides model, which is intended for different uses of pesticides, we really had to develop a separate model to specifically address children's contact with treated wood structures with very different algorithms, very different equations. And I suspect that the other aggregate probabilistic models that are out there, would have to do the same thing. So I don't believe at this time that the state of the science is available to do such a probabilistic model comparison for this assessment,

DR. FRANCIS: Yeah. I agree with you that I think most of them were sort of developed for dietary kinds of exposures. But I know that some of them do have components, for example, for looking at worker-type exposures that I think could be modified relatively easily to deal with children's exposures. The ones that deal with reentry kinds of issues. In a way, this is a reentry

kind of issue. And I think this is something that should be explored by talking to whoever, the other people that you're looked at before for the models. I don't think that it's that much difficult to adapt some of these other models.

DR. PORTIER: I'm going to disagree. You know, you have to stop and think, what would be gained by putting all that effort into building a competing model just to demonstrate that you get roughly that same results. I'd much rather see the Agency spend time on new data and continuing to validate the individual components than building a whole separate model.

I know in academics we do this all the time. We build competing models primarily to show that our model is better. But in this case, I don't know if we really need to show that it's better. They just need to prove that it does the job that we need for it to do for them which is to provide support in their decision-making process. I see where you're coming from. But I guess I don't really see that as a prime direction.

DR. HATTIS: Yeah. I guess I would say it's an appreciable, it's a significant project. So I mean off the top, if you want to apply the three other available modeling frameworks to this, you probably are looking at a million each, I think.

DR. HEERINGA: Just to be clear here, Dr. Francis, Lifeline, Calendex, CARES, some of the models that were considered in this model comparison, those are the types of models that you're talk about. So for those of you who aren't.

DR. OZKAYNAK: Yes. I fully concur with what Dr. Portier said. Actually, just to give you a history of this, about two years ago the OPP antimicrobial division actually started -- I'm sorry. No, no, no, no. The antimicrobial division when the CCA project was proposed in terms of developing modeling looked at available models -- lifeline, CARES, Calendex, and SHEDS -- and talked with, I believe, with that various leaders of these modeling groups and realized that it was going to be a sizeable effort and made the decision to go forward with

that SHEDS-Wood model development.

And it's been a two full-time effort. Two years of a lot of hard work, and you see a number of people sitting here at the table here. And we've been fully concentrating on this effort. It's not a small task. And it's a major effort. So it's not realistic to expect that.

DR. HEERINGA: Dr. MacIntosh and Dr. Ryan.

DR. MACINTOSH: To say something in support of the comments of Dr. Portier. It was two years ago, I think, that the ORD and others organized a model comparison workshop. And they had a panel. And I was on that panel. And we compared SHEDS pesticide to Lifeline, I believe it was, and to CARES and also Calendex was there. We went through. And it was for, I think, two or three very specific exposure scenarios to reduce the scope of the problem and make it more tractable.

And we went through some of the most important pathways parameter by parameter and algorithm by algorithm. And found -- first we found that the results

weren't that different among the different models within a factor of three or four or something. And in this range, those are essentially identical. And we found that the differences could be explained quite easily by certain algorithms or certain parameters.

And my guess is if that was done, a similar model comparison was done for CCA-treated wood that we'd reach quite similar results as Dr. Portier suggested. And, again, given the lack of important data that would be inputs, that are inputs, to SHEDS-Wood and likely inputs to these other models, that might be a more effective use of resources, improving the data might be.

DR. RYAN: I would just like to reiterate that I feel like a me-too guy at this point. But I think I said it first.

Essentially, I think if the estimate of a million dollars or something like per is correct, my impression is the money would be better spent getting some more data, data gaps that we see, or trying to understand the variability or uncertainty and some of the parameters.

It's not for which we are simply using point estimates. And I think that's the way the money should be spent. Whether this is the perfect model, the best model that could be put out is a secondary question. What we is need more data to validate the model

DR. HEERINGA: Dr. Reed and Dr. Francis.

DR. REED: Yeah. I totally agree with not sort of rewardable to go back and use CARES and Lifeline and Calendex to make comparison.

But I think maybe there was a little bit sort of confusion because it wasn't clear, or maybe not as clear, in the document in terms of what the comparison is for. After I read it about five or six times, I thought there is merit in comparison, not having going to go back to extraneous effort to do that. But you just want to know if your output is in line with everybody elses estimate even though they were using different algorithms.

So the model construct itself does not have to be the same. You were just looking to see, well, this is my result and this is their result using different

assumptions and what not. And I think there is merit or the value in doing that. Maybe if you could express it more clearly what you're trying to make the comparison for. Certainly there are different kinds of comparison that we've been talking about using different probabilistic models to make comparisons. The purpose is different I think. So if that could be made clearer, I think.

DR. FRANCIS: Okay. I'll perhaps partially my comments. I can't imagine that it would cost a million dollars per. I think that's totally unreasonable. On that other hand, perhaps I am naive to think that the people who put out these models might actually want to be able to show how their models compare and perhaps with not a whole lot of effort. And like I said, I could be naive. Might want to help in the model comparison.

I also agree that I would much rather see in terms of validation a well done biomonitoring study to compare real data to these scenarios. So if you were taking that same pot of money to say whether or not things

were working, I would much rather see real physical data as opposed to modeling kind of data.

DR. HEERINGA: Dr. Ozkaynak.

DR. OZKAYNAK: Just I guess to end with philosophical comment. I agree with Dr. Reed. I think that we need to do a better job in terms of articulating the purpose of the model comparisons and evaluations and what we really intend to do and what we sort of learned from that comparison. The thing is that a lot of the models especially on that aggregate pesticide exposure arena, use very similar algorithms because they've been prescribed so strictly by the Health Effects Division's standard operating procedures. So if all the models are using the same equations and pretty much relying on the same inputs, you expect that unless they make a mathematical error or a computation error, you get the same results.

Now if we compare in that context, like Dr. MacIntosh mentioned, all the models are trying to do the same things. If you get the same results, have you

learned anything. And my answer to that is no because we're all trying to do the same thing. And I remember a number of years ago, I think it was one of the SAPs, Dr. MacGowen was talking about a model comparison exercise in the physics arena in Europe. And there were like six models being compared, and all five of them seemed to agree and one was widely differing than that other ones. And they said in the end when they tried to figure out what was going on, they found that the model indeed that was totally different from the other ones was actually the correct one.

So one has to be very careful, and we're going to try to sort of think through more carefully on these issues in terms of what are the purposes of the model comparisons and one doesn't fall into the pitfall of a false sense of security if the number seem to be from five different calculations seem to be in the same ballpark. We could all be wrong.

DR. HEERINGA: Thank you very much, Dr. Ozkaynak. And I think consistent with the comments, not

only from our group but the others, I think if we do to a model that's very different in form, it can be extremely informative even it produces the same or a different result.

I think the key there is we have to make sure that we're standardizing of definitions of populations and inputs, because otherwise, we're into not just mathematical errors but errors of the concept itself. But I think conditional on that, I very much support what you just said in terms of the value of almost completely orthogonal approach in terms of sort of validating or at least raising possible disagreements.

Any other questions or comments on that?

Okay. What I'd like to do is to move on to Issue No. 7 prior to our break. I believe that this is the last of the issues that deal primarily with the exposure modeling component of the session.

Dr. Ozkaynak.

DR. OZKAYNAK: Issue 7: Overall completeness and acceptability of the SHEDS-Wood probabilistic CCA

exposure assessment.

EPA has revised the August 2002 SHEDS-Wood exposure assessment after carefully considering numerous comments and suggestions that it has received from various parties, including those from the August 2002 FIFRA SAP members, EPA/ORD and EPA Program Office peer-reviewers of the preliminary draft September 2003 report, and from the general public and other external groups.

Question A: In addition to the comments and suggestions already offered by the Panel members under the specific issues raised previously, considering the availability of data and information, does the Panel recognize any critical gaps in information or methodologies that still need to be addressed for the CCA exposure and dose assessment?

DR. HEERINGA: Dr. Hattis is the lead discussant for this question.

DR. HATTIS: I think overall, my assessment that EPA has done a conscientious job in trying to work with the information they have readily -- well, not so readily

available. I was impressed by one aspect of the public presentations yesterday. And that is the presence of the CCA residues apparently from recycled treated wood products and mulch used in playgrounds. It seems to be a worthy subject for separate specialized analysis.

And data gathering, I should say. Data gathering and analysis -- maybe we should put that cart before that horse whatever -- and possible advice to that public once you've done that kind of thing on desirable sources of materials for use in cushing falls in public and home playgrounds.

Other than that, I don't have any particular suggestions to make.

DR. HEERINGA: Dr. Francis, would you like to make a comment?

DR. FRANCIS: Actually, I think most of the comments that have been made previously for previous questions have covered most of the comments that I would have had.

DR. LEBOW: Yeah. I wasn't sure how to

interpret this question in light of all that other issues and questions that kind of overlapped with this one. So some of my comments do overlap, but I think in some cases it's worth repeating them.

I'm not an expert on modeling general at all so my comments are more general and perhaps are observations that could be perceived by the more general reader of the document.

It struck me that there's an awful lot of contact days for these kids, and that this population certainly does not represent all kids that do contact treated playsets or equipment. And in the exposure documents, it does point that out that this is for kids who frequently contact treated playsets. And I think it almost has to be, if you're looking at a mean of 126 contact days, then you're almost talking a day care scenario where the kids are routinely taken to a facility where they go out and play. And that's I think maybe is largely your intent.

I guess what worries me a little is then I see a

little bit of drift off of this definition of population as time goes on. If you look to the risk assessment document, population is redefined as all kids who are exposed to treated playsets or play equipment or desks. So the population drifts between the two documents from frequent or, in my interpretation, very frequent contact, day care setting, to all kids. I think it's on page 3-2 of the risk assessment documents, explicitly redefines the population and leaves out any mention of frequent contact.

So I think while it's fine to model the very high end or the day care subset in explaining the document and how it's meant to be used, you need to be careful that your population stays the same in your interpretation of the results.

The other thing that I guess kind of goes along this same line, and I don't know if this struck anyone else. It certainly did me. This percent of outdoor time on that playset, I understand that was derived somehow from the CHAD diary, although the Chad diaries didn't actually have that specific information. You fit a band

distribution with a mean of between .75 and .8 depending on your warm cold and a median of 90. So you say 90 percent of your outdoor time is on the playset. And this was used for both the residential and nonresidential.

Well, think about that for a second. Why would a kid spend 90 percent of their time within two feet of this playset. And, again, the only scenario I could think where your median value would be that high would be maybe a day care situation where they go, out two hours of play time, it's a small fenced area, all they have is a playset. Then you median might be 90 percent of the time. But otherwise, like a public park, how could you even achieve a 90 percent median. You would literally have to tie these kids to the playset. So I think that that's something that needs to be looked at unless I'm misinterpreting this value.

DR. ZARTARIAN: Yes. This was one of the variables that we didn't have information on and we made use of the CHAD diaries to try to come up with something. That was what we had some available information on

children who do go to playgrounds and their total outdoor time. And we realized that the number was on the high side from how we derived it out of CHAD. And we were debating about whether to change it or use the information from CHAD.

And our justification for keeping it at that value was that, again, the population was defined as frequent users of playgrounds. So we felt that since it was a population that is actively going to playgrounds, that it was reasonable to assume that when they were at the playgrounds, they were very active on the structures. And again it wasn't all outdoor time. It was the nonresidential outdoor time.

DR. LEBOW: I beg to differ. Wasn't it residential also?

DR. ZARTARIAN: Yes. We used the same variable for both.

DR. HEERINGA: Thank you Dr. Lebow. I'm going to direct to Dr. Macdonald.

DR. MACDONALD: I agree with that decision to

just concentrate on the frequent contact children. It's the principle of stratification. There's really no point in simulating the entire population. For example, it just means you're computers are going on hour after hour and not finding any contact events. It's much more effective to be saying, well, we're doing a certain fraction of the population or a certain fraction of the time and just simulate what's going on during contact and then scale those results to apply to the general population later.

The other comment I have is to do with after the presentation yesterday on the ineffectiveness of the sealants. I think that the runs you've done with 90 percent and was it also 99.5 percent sealant effectiveness would be quite misleading to the general public. So perhaps those assumptions should be made a bit more realistic before any results are released.

DR. HEERINGA: Thank you, Dr. Macdonald. I might just add a comment to follow on these last two comments. I think that we've sort of worked around this definition of what the reference population is here.

Intensive users or frequent users, those are terms that really don't have much quantification. And you might translate it into as Dr. Macdonald suggested, sort of a stratified profile analysis of infrequent or occasional uses and quantify that in terms of numbers of hours per week or hours per year because most parents, most play school administrators, most risk assessors can understand that.

I do a little bit of fishing. And fish advisories, you don't eat fish more often than once per week. It's something that I can bring home and relate to my own daily time. So in terms of just saying that this is a population of intensive users and then letting some unknown distribution determine exposures, shows those exposures in terms of either average weekly exposures or total annual exposures in terms of time and then look at the profiles of the exposure distributions for those strata. And then as Peter says, if you need national estimates for risk assessment, you can then try to profile that time of contact distribution based on other sources

and integrate out that way.

Yes. Please identify yourself.

DR. SMITH: Luther Smith. Just as follow-up to Dr. Lebow's comments. I just wanted to point out that not every day is a contact day. And not every possible contact event is a contact event for the children.

DR. OZKAYNAK: There's been a range, again, as we mentioned I think yesterday, across the children that have been simulated here. The potential contact days range anywhere as low as 5 or 10 and 15 to all that way up to 260. So the mean was 126, but not every child is --

DR. LEBOW: Yeah, I understand that the contact days it looks like you've used a fairly normal distribution with a mean of 126. But if you look at your distribution for your percent of outdoor time, it's very heavily weighted towards the upper end. Which I guess if someone like me can look at it and say that doesn't appear real reasonable, then I think a lot of other people will probably be able to reach that same deduction.

And then there was one more point I wanted to

raise. I've started thinking this through. You got these kids on these playsets this many days and this percent of their outdoor time, that means you got an awful lot of kids on these playsets an awful lot, like at a day chair facility. And one of the things I didn't see considered in this modeling effort, and I think Dr. Solo-Gabriele mentioned it yesterday, what happens if you rub the same surface more than once?

You have a very limited surface area actually in a playset that kids touch. They don't uniformly rub the whole structure. They touch the hand rails, the climbing areas, the corners where they turn. And if you go to an older playset, you can actually see these surfaces are worn smooth from kid contact.

It would seem to me if these kids are on there this much and many kids are confined to this area, they're not all touching a fresh surface. In fact, they're probably very infrequently touching a fresh surface.

And I don't know how you figure something like that in. But it would be interesting to do a series of

rubs on the same surface, cleanse the hand, rub it again, do that repeatedly, and see what kind of concentration you get. Because I just don't -- now maybe on a home deck or a home playset it would be a relatively fresh surface. But on a public playset, if you got that much contact time and that many hours and that many kids, it could be a factor.

DR. HEERINGA: Dr. Riviere.

DR. RIVIERE: I'd like to really follow-up on Dr. Lebow's comments. I had no previous exposure to what -- I hadn't read this before. Started off with the risk assessment, the second document, and went to the exposure document. And I did not get at all a clear view that this was restricted to kids who would be 90 percent of the time on a playground contacting this. So I think there's a reality check on this. As you go through this. We've all had situations and it has to go back to what our basic experience is.

The playsets that we've seen in those pictures, even at day care centers, can't hold all those kids at

once. Secondly, you're not going to have kids up for three hours constantly being on those playsets. There's off time; there's lunch times; there's everything else. I think that's something that just sticks out in terms of overall practical experience, that only after I read the exposure assessment and sat through two days here, did I realize that this entire risk assessment is focused on kids who have intimate contact all that time.

And I've at least had that opportunity to read the entire thing. When this goes forward from a public perception, people aren't going to be able to read all of the little caveats in here and how this came up. That's really a sincere problem that efforts should be focused on improving that data.

And based on an earlier comment, I'd also like to really make a point, I'm going to make in Item 10 or 11, that there really needs to be some effort on getting some of this data. Again, year by year, that data is not available so we guesstimate. The data's not available, we guesstimate. There should be some kind of direction that

we really need to get this data, there's needs to be a lot closer interaction, say, with EPA and even industry groups in this line.

As we'll bring up a little later on with the dermal thing, you know, a NF3 is totally unacceptable. It should never even have been presented to come up with something on an estimate. So we really need to get some idea if we're going to have some data in there, that we need to put our effort on finding out how long in a day care center there's actual contact to these surfaces.

DR. HEERINGA: Yes, Dr. Dang.

DR. DANG: I'd like to back one comment from Dr. Peter Macdonald about the 90 percent or 99.5 percent of children may mislead the public. We do not have intention to mislead the public. Actually, this 90 percent we call moderate assumption is based on the 2001 SAP comments, and also it's based from the available literature. It's average existing deck where we can get on the best available data we have.

And you probably know we do have ongoing sealant

studies. And we have to provide this information on the target how much sensitivity we need from those studies. So we hopefully -- 99.5 percent effective the sealant we can kind of find out from the available market. Thank you.

DR. HEERINGA: Thank you, Dr. Dang. Dr. Adgate.

DR. ADGATE: It occurs to me that what most of this discussion is about is sort of clarity and credibility. I guess the problem is that you have this special population but you'll be able to enumerate how big it is probably. But maybe the thing to do is to acknowledge that and say. But I think that's the way you need to think about the problem is how we've created this population, well, how big is it likely to be?

DR. HEERINGA: Mr. Jordan, do you have anything? Dr. Zartarian. And then we'll come back to the Panel members.

DR. ZARTARIAN: I just wanted to go back quickly to the variable that was being discussed, the average fraction of residential outdoor time that a child plays on

or around a CCA-treated residential playset on days when the child plays on or around the CCA-treated residential playset and the similar variable for the public playsets.

The way that we derived this in the absence of other data, we stratified the CHAD diaries by month and analyzed for children ages 1 to 6 years to get the ratio of the reported playground time divided by the total outdoor nonresidential time on days with reported playground events. And that was used as the surrogate variable which yielded the beta distribution with a mean of 75 percent.

So I guess I would put it back to the Panel. If this number seems high, we can do one of several things. Account for that in the uncertainty, additional uncertainty analyses that we do. Or if there's ana alternative approach that the Panel would suggest in the absence of other data for that input.

DR. HEERINGA: Thank you. I think you've stated your source of data, and we'll review that and comment appropriately for that.

DR. GLEN: It might help for clarification to say that the median time and contact with a playset over a course of year is about 14-minutes per day and another 14 on that soil near the playset.

DR. HEERINGA: And that is for the simulated populations --

DR. GLEN: Yes.

DR. HEERINGA: -- represented in these studies.

DR. XUE: I want to make a comment about the kid touching one place. There would be, because only so much playground you can touch. So when we, the data we gathered this, we consider this. We wipe hand. When we gather this concentration, we wipe that hand 20 times. Then -- this is from RTI data. So 20 times we get that loading for hand. This is the data we use. So we already consider about the people that touch that area.

DR. LEBOW: What I meant was wipe that hand once; wash it off; wipe the same spot again; measure that analyte. Keep repeating that process, washing the hand off and then rubbing the same surface over and over again.

What the RTI study did was they just wiped the fresh surface 20 times and how much built up on their hand.

DR. XUE: That's not true because they have limited area, they didn't wash. They have -- the limited area --

DR. LEBOW: They wiped the same surface 20 time.

DR. XUE: Yes, 20 times.

DR. LEBOW: But did they wash their hands between.

DR. XUE: That was 400 centimeters square. Because if you think about hand, the area is 400 feet centimeters square. They keeping touch this area not just the new area all the time.

DR. LEBOW: My question then is: Did they cleanse their hand between those wipes or was that the cumulative amount that they got on their hands after 20 wipes? Were you able to track the amount that the concentration of the hadn went down over time? My interpretation was they wiped it 20 types times. Then they washed it off. They didn't wipe it once; wash it

off, rub the same surface again. Unless I misunderstood the paper which is --

DR. HEERINGA: I believe Dr. Dang will response.

DR. DANG: Yes, they did clean the hand before the next wipe. Between each 20 wipes.

DR. LEBOW: I didn't get that from the paper. I'm sorry.

DR. DANG: It's from the ACC study.

DR. LEBOW: Yeah. I know which one you're referring to.

DR. DANG: Right.

DR. LEBOW: It didn't explain that in the methodology. But if you're certain about that, then I certainly stand corrected. I apologize.

DR. DANG: Thank you.

DR. HEERINGA: Dr. Lebow, just for clarification, the issue you're getting at here is not he maximum dermal loading but what happens when another child comes along after a previous child has taken the hit.

DR. LEBOW: Touches the same surface area.

DR. HEERINGA: Touches the same surface.

DR. LEBOW: Dr. Solo-Gabriele mentioned yesterday she shows for three replications only of the same surface and there's a reduction of about 33 percent from the first to the third wipe. So about 66 percent it looked like. The third hand only got one-third the amount as the first hand. Now, eventually, it would level off at some concentration I'd imagine. I'm not sure if the -- I wasn't clear how the RTI study handled that.

DR. HEERINGA: I'd like to go wrap up fairly soon, Dr. Stilwell.

DR. STILWELL: I gave some similar data at the EPA 2001 SAP meeting on multiple wipes on the same surface. And with a new board, I got pretty much the same results as Dr. Solo-Gabriele's work, it goes down a lot. But then with older boards, you a rejuvenation and then it just goes to some steady state. So it never made it into the paper the I just published. But that's an avenue the should be looked at on playgrounds to see like a buffing and the sort of thing,

DR. HEERINGA: Dr. Stilwell, are you aware of any data on replenishment rates, if a child wipes it at Time T how much later would we see that same concentration restored to the surface of the wood?

DR. STILWELL: No. I actually only revisited the surface after maybe a month or two. So there is like some steady state value the may occur. And then there has to be some sort of time for it to actually go up and down where the wood might have to undergo weathering phenomenon. So it's a good point, but one the we don't really know the answer to right now.

DR. HEERINGA: Thank you very much. Dr. Hattis.

DR. HATTIS: On that same issue, I was reassured by the fact that they were taking boards from actual playgrounds which do reflect something like a whatever degree of contact, repeated contact, you know, exists for those playgrounds grounds. Now then we have to get into the actual details of did the ACC folks or RTI folks take the samples from places that were likely to have been in contact. And if they did, then I think it's reasonable to

use those data as reflecting reasonably real-world conditions at least at the time that the boards were sampled.

DR. HEERINGA: Okay. Dr. Matsumura.

DR. MATSUMURA: Regarding the information gap, I would like to suggest the metabolism as Dr. Styblo has been mentioning. I was impressed by the data that Dr. Solo-Gabriele presented and the microbial degradation could affect of the entire fate of the transfer. I'm quite sure that the arsenite formed is likely due to microbial action and of course the sealants could affect those microbial actions as well.

I moved from Michigan to California. And in Michigan, how bad those decks become in a few years. And I tried my sealants, but it went down pretty fast. And the surface becomes very slick. And I'm sure that those places are lots of arsenite and more forms from the separate from the regional, those complex that the Dr. Laurie was mentioning. And I'm quite sure the original months and that's mobile.

But, yes, humidity indeed affects those decks. There's no question. And that the mobility from the surface to the human skins may be altered by those kinds of conditions. And if my deck in Michigan was a good example, it becomes slimy after awhile and you can't avoid those fungi affecting. And I need a little help from Dr. Styblo.

But the humidity information of the metabolic fate affecting those exposures has not been really addressed in this document. A big difference from California to Michigan, I can tell you that.

DR. HEERINGA: Dr. Portier.

DR. PORTIER: I promise this is a small one. Since Dr. Hattis added an exposure environment in the chips, I think we really should look at the unloading as well. Right now in the model, you only have bathing, hand washing, and mouthing as an unloading process. But we heard that touching, wiping on your clothes, or other processes. And I think the model right now probably if a child visits a deck three or four days in a row, they

probably maximize. And if they don't take a shower -- even if the do take a shower, they probably hit the maximum in the model; and allowing some temporal unloading might actually keep these kids from hitting the maximum in the model as often as you experience it.

DR. HEERINGA: Okay. Dr. MacIntosh.

DR. MACINTOSH: Thank you. A general comment to follow up on Dr. Portier and also one from Dr. Hattis earlier. And it also related to earlier, Issue 4, it talked about what I see is the importance of describing the purpose of the uncertainty analysis. And I think it's also important for the variability in the overall assessment.

In my experience, it's common to see in a risk assessment some description of the objective is to be like a screening level assessment or a conservative assessment or a realistic assessment. And I'm not sure that there's much description of that or characterization of the assessment that was done and the context in the report.

And it's possible even that some of the analyses

or inputs to the model are intended to be realistic and others are intended to be conservative. But, again, I think that's important because it would help with the interpretation of the results, much like the stratification that was discussed down here earlier would help with interpretation. I think characterization is -- we think this is a conservative or realistic, et cetera, assessment would be helpful.

DR. HEERINGA: Thank you very much to everybody who participated in this discussion. We got one more. Dr. Kissel.

DR. KISSEL: The prior discussion something popped into my brain. I haven't really figured out how you've created those maximum dermal load numbers, the cap, the accumulation. But if they're based upon a straight forward use of numbers from wipe tests or rinse tests of hands, then they may underestimate true loadings. It's a classic can problem in industrial hygiene or in environmental health is that rinsing and wiping of hands does not remove the entire load.

We have two choices: You can use a dosimeter which probably over estimates what's on the hand because it sucks up stuff that the wouldn't; or you can do a rinse or a wipe which will give you something less than the total load because you won't actually extract everything from the skin crevasses. So if you haven't done some type of a correction for efficiency of removal by whatever that technique was, then those numbers are an underestimate of what the actual hand loading was.

DR. HEERINGA: Thank you very much Dr. Kissel. At this point in time --

DR. HATTIS: I believe that's in the model.

DR. HEERINGA: Clarification as to whether there is in the model, exposure model, some allowance for essentially underestimation due to the quantification technique that's been used for the data. Efficiency of removal.

DR. HATTIS: I believe that there is a removal process from the skin. There is not a removal process for multiple touches as I understand it. Correct me if I'm

wrong. But there is removal, some finite degree of removal for each washing event if I'm understanding the model. So you don't get all of the stuff off when the hands are washed in the model. Right?

DR. KISSEL: That wasn't the point. I was talking about the -- they have a maximum level for what could be on the skin at any time which is based upon some empirical measurements made somewhere else. And if recovery of removal from those empirical measurements was not included, then those measurements are an underestimate of what the true loading on the skin was in the CPSC and ACC.

DR. HATTIS: It goes to the inputs to the maximal --

DR. KISSEL: I'm not talking about what's going on in the model. I'm talking about What's going on in the data set that they're using as caps.

DR. HATTIS: I didn't understand. Thank you.

DR. HEERINGA: Sort of a calibration of the original measurement issue I think. Dr. Zartarian.

DR. ZARTARIAN: Yes. The way that we are using -- the maximum determine loading in the model comes from the experiment data. We divided the hand-wipe data by the wood-block data, and we do not correct for the type of wipe, the extraction from the hand. So your point is well taken that the way that we've done it may underestimate the maximum dermal loading. And perhaps that helps address the issue of the negative dermal transfer coefficient on some occasions.

I guess I would, again, ask the Panel, if that's not a sufficient correction factor for the removal processes, to advise on how we may consider that negative dermal transfer coefficient as I'm interpreting these removal as processes. Or how to come up with a correction factor for the maximum dermal loading directly as well as a negative transfer coefficient.

DR. HEERINGA: Thank you very much.

At this point, I think we'll have a chance for some general review. This has been a very broad question, and I'm glad that it was included at the end of the

session on the exposure report because it's a dangerous thing to ask academics if they have ideas about what other people should do. But I think it's also been very productive here. And many of our comments, I'm sure from this session, will be probably if not reflected in the response to this question, integrated with the other responses and in the general introductory response. Dr. Ozkaynak.

DR. OZKAYNAK: Yes. Since this is the end of the exposure questions, I want to take this opportunity to thank the Panel. Also on behalf of my colleagues from both ORD and OPP for the time that you have taken to go through the material and the discussions among yourselves as well as in this forum With regards to some of the challenging issues that we have tackled and wanted to seek your advice.

And you have done exactly what we have been looking forward to during the course of these two days. Again, we're grateful for your insight and comments. And we'll seriously consider everything that we have heard and

discussed and hopefully do a good job in incorporating that in the next version of the model. Thank you, Dr. Ozkaynak, and also to everyone on the EPA staff and their consultants who contributed to the preparation of this exposure assessment report.

And I think what I'd to do at this point is adjourn briefly for a break, a 15-minute break. Let's return here at 11:05. And my aim is, if possible, to cover Questions 8 and 9 prior to our noon-hour break leaving Questions 10 through 12 for the afternoon.

(Break taken at 10:50 a.m.;
session resumed at 11:07 a.m.)

DR. HEERINGA: Let's reconvene to continue with our responses as a Panel to the questions.

Actually, I think I'm jumping the gun because it appears that a few key members of our panel probably our checking out of their rooms.

VOICE: All the risk people have left.

DR. HEERINGA: We're still missing a few key members of the panel. Okay. I believe that we've reached

a quorum. I'd like to ask Paul Lewis if he has any administrative comments to make.

MR. LEWIS: Members of the Panel, we know we've given you a vast amount of papers in the past several of days. To make your travel easier, if you want us to ship any materials back to your home office, please approach myself or members of the SAP staff and we'll have those materials sent back to you. You'll probably have them when you arrive back on Monday. Thank you.

DR. HEERINGA: I think the most convenient way to do that is, in the break-out room, if you were just leave your materials with a slip with your mailing address on the top of it, we'll handle it that way.

In addition for the record, the Panel has received three additional documents. The first one appears to be an advertisement for a conference in Orlando, Florida, sponsored by the Florida Agricultural Mechanical University and University of Miami. FYI.

The second is a series of distributions that I believe we requested yesterday from the EPA staff on the

annual distribution of exposure time and days, contact days, and also exposure events on playgrounds. This is presented for the warm climate data. There are four charts here that will again be part of the public docket.

And in addition, there's a packet containing the PowerPoint slides for the extra question slides that the EPA staff referred to periodically in our discusses over the last two days. So those are also available to the Panel now and will part of the public docket.

At this point in time, I'd like to continue with the series of questions directed to the Panel.

Mr. Jordan, should we go directly to Dr. Dang.

MR. JORDAN: Dr. Dang will read the questions, and he'll provide clarifications if there are any questions about our questions.

DR. HEERINGA: Thank you very much.

DR. DANG: My name is Winston Dang. I'm going to read the Question No. 8.

Issue 8: In the study by Nico et al. (2003), X-ray absorption spectroscopy (XAS) was used to determine

the chemical and structural state of arsenic and chromium molecules in CCA-treated wood residue samples. Based on the results of their analysis, Nico et al. (2003) determined that arsenic and chromium formed a "chemical complex bonded to the wood structure." Based on this study, the dominant oxidation state of the two elements is arsenic 5 and chromium 3, and the local chemical environment of the two elements is best represented as a stable chromium arsenic cluster consisting of a chromium dimer bridged by an arsenic 5 oxygen ion. Nico et al. (2003) also maintained that this chemical complex was quite resistant to leaching.

Question A: The Panel is requested to comment on the Nico et al. (2003) study and particularly on the arsenic and chromium chemical complex from CCA-treated wood surface residue, and whether the Panel believes that the chemical complex is formed during the fixation process. What is the meaning of this complex cluster formation to the current risk assessment?

DR. HEERINGA: Thank you, Dr. Dang. And Dr.

Wauchope will be the lad discussant in our response to this question.

DR. WAUCHOPE: Thank you. Can you hear me? This was a lot of fun. I didn't know any of the other discussants. And that's Drs. Bates, Francis, Styblo, and Stilwell and myself. And with enough food and drink, we've managed to consense, I think, closely. I won't say that. They keep bringing me more notes. I'm going to read, this is Draft 3 of this response. And then I will ask each of these other discussant if we've more or less represented the discussions adequately or not.

This Issue 8 is really three questions, so we've reformulated the questions a little bit. The first questions is the complex formed during the fixation process. Second is this is the complex identified by Nico et al. The second question is the complex identity certain. The third question is what is the relevance of the complex identity to the risk assessment process.

So is the complex formed during the fixation process. There is little doubt that chemical reactions

occur between arsenic and chromium during fixation and that these reactions greatly diminish the solubility of arsenic in CCA-treated wood. The Nico et al. study does not attempt to address the mechanism of formation of the complex. However, given the complex is almost complete dominance of the species present in the CCA-treated wood, new and aged, and in the American Chemistry Council's residue preparation samples, we will call that ACCR from henceforth, it is likely that the complex is the major product formed during wood treatment.

There's a been a process here in which this material which was prepared by the American Chemistry Council and distributed to several researchers has been referred to as residue and that's a rather generic term. So we've decided to acronymize it and call it ACCR because this is a special material prepared under a specific set of circumstances and the issue is whether that material is representative of dislodgeable residues in general as utilized by the risk assessment.

Second question, is the complex identity

certain. The specific complex described by Nico et al. is consistent with the spectral data. But a requested review of the manuscript by an expert in X-ray absorption spectroscopy elicited the following comment: "The author should clearly indicate that their proposed cluster structure is just one possible example of longer range structure second coordination sphere, and the real structure is probably much more polydispersed than this suggests. I would agree" -- this is the reviewer -- "that the cluster structure proposed is not a unique solution to the X-ray absorption's fitting and that other potential cluster structures" -- actually it's X-ray absorption fine structure fitting -- "and that other potential clusters should be considered and used for fitting to give the reader a feeling about the uniqueness or lack therefore of these longer range interactions."

Continuing the quote, "The most comment mistake made when analyzing XAS data is the failure to realize that molecular models that provide good fits to defined structure may be only one of a number of models that

provide equally good fits. That is the uniqueness of given simulation can almost never be proven. The other important realization is that XAS always provides an average environment and cannot be used to uniquely identify structural components of a mixed population. Often missing this key fact causes authors to propose homogenous structural environments when a heterogeneous sample is analyzed.

This expert reviewer also noted that, There is an apparent consistent fluctuation of chromium arsenic rations between lower and higher density wood areas suggesting some variation in speciation between the areas. It's likely there are additional fixation products, at least for chromium, given the reactivity of chromium and the range of possible reactive sites within the wood structure.

Studies are also in general agreement that when the fixation reactions are complete, less than 1 percent of the chromium in the wood is hexavalent. There have been fewer studies confirming the valent state of arsenic.

And the Nico study is important in this regard. For the purposes of this SAP, the exact nature of the chromium arsenic fixation product may not be critical. However, further work in characterizing the chemical nature of the arsenic chromium complex, particularly in dislodgeable residues, would contribute to the risk assessment process.

Anybody want to comment on that so far? Okay.

What is the meaning of this complex cluster formation whatever it's precise structure to the current risk assessment.

The Nico study is an important advance in understanding the nature of the speciation or structure of fixed chromium and arsenic in CCA wood. The point is that the arsenic in CCA-treated wood has low solubility, the arsenic is primarily pentavalent, availability, and the chromium is trivalent.

The Panel agrees that this complex regardless of minor variations of structure, which is bound to the wood structure, is liable to be of limited bioavailability compared to arsenic in solution. This conclusion is

strengthened by the near identical spectra in new and aged wood samples and in the ACCR.

This indicates that the complex is quite stable at least while it's incorporated in the wood structure. It must be remembered that ACCR appears to be mostly a dried suspension of fine CCA wood particles. And we refer to the Battelle study which was circulated very shortly before this meeting. Thus ACCR would not be expected to exhibit significantly different speciation in an X-ray absorption study.

There is some evidence, see the Casteel studies in Issue 9, that a significant fraction of the arsenic in that preparation can be solubilized in the GI tract. That's the 27 percent figure.

An important question which we consider to be unanswered at present, is whether the ACCR preparation adequately represents those chemical species that are leached from CCA wood to soil; or more importantly, those chemical species that adhere to skin, the most significant route of exposure to arsenic. The reason for this concern

is that leaching studies of CCA-treated wood consistently report that a higher proportion of arsenic than 2 moles of chromium per mole of arsenic is released from the wood. During weathering, UV degradation and leaching may release forms of arsenic that are more soluble while releasing less chromium.

The result is the soluble part of the residue has a lower chromium-to-arsenic ratio than residue particles or bulk wood. This hypothesis is strengthened by the ACC wipe study. Residue obtained by the block wipe and coupon wipe method had a higher chromium to arsenic ration than the obtained by gentler hand wiping suggesting that the more aggressive stirring wiping methods remove more wood particles thereby raising the overall chromium arsenic ratio.

Running that by you and reading it to you is a little tough because we had a good deal of arm wrangling trying to get this to make -- the bottom line is: Is that CCA wood has a 2 to 1 chromium to arsenic ratio basically based on the X-ray data, based on most analytical work.

Material leached from arsenic from rainfall, for instance, typically has a much higher arsenic level. In other words -- please jump in here if I'm not saying this correctly -- arsenic is the most leachable of the element, is the more leachable of the two elements; and, therefore, it's most likely that what kids are exposed to has a higher fraction of soluble arsenic than there is in this complex.

The chromium arsenic mole ratio of 2 predicted by Nico's dimer model is consistent with the 2.2 reported in aged, treated wood and somewhat consistent with the 1.7 in ACCR residue. Stilwell reported an average mole ratio of about 2.2 in dislodged residues, and the ratio was 1.7 in residues analyzed by the RTI study. However, the ratio found on hand residues in the ACC hand wipe studies was only 1.3, suggesting the hand contact with wood surfaces dislodges fewer wood particles containing this insoluble arsenic chromium complex and more of an unbound fraction of arsenic, probably an arsenic that is more available.

Thus it is possible that some arsenate detaches from the chromium dimer where it's preferentially leached

from the wood. The driving force behind the disassociation of the dimer could be UV radiation and acidic rain water. In Nico et al. the potential for reaction with acid rain was mentioned.

Some examples showing that the chromium arsenic mole ratio is less than 2 can be found in a review of leaching by King et al. And this is a review of arsenic leaching and arsenic leaching materials. I won't give you all the numbers. But it can range all the way down to just a very small fraction of chromium.

In a paper by Lebow et al. in '99, the long-term release rate of copper, chromium and arsenic was given. Computed chromium arsenic mole ratios from Table 7 in this work are .16, .48, and .23 as opposed to 2 to 1 in the complex.

Lebow also measured leaching of new wood under simulated rainfall conditions 2003. In this case, the chromium arsenic mole ratio was .34. In soils, the chromium arsenic mole ratio after background correction for chromium and arsenic was .5 in studies by Stilwell and

Gorney. While the mole ratio was .7 in a report by Segury et al.

The bottom line is the arsenic that you find away from the wood particles is very high in arsenic and very low in chromium compared to the material that's found in the ACC residue. Therefore, the erosion material represented by ACC residue may not adequately represent the longer terms affects of rain water, sunlight, UV, and diffusional components as pointed out by Nico et al. As pointed out by Nico et al., Stilwell has proposed a model to explain a rejuvenation effect noted on the wood surface, a slow replacement of dislodgeable residues after removal by leaching. This model evokes erosion, diffusion, and rain water affects.

Any residue description would have to account for the observed preferential release of arsenic in the leachate in the soils. One explanation for the discrepancy between the mole ratios is that the actual surface layer when exposed to environmental conditions could contain both soluble and relatively insoluble

arsenic fractions.

In summary, the Panel concludes that the Nico study, while important in the understanding of the nature of chromium and arsenic fixation in CCA wood is of little utility in the arsenic or chromium risk assessment.

DR. HEERINGA: Thank you, Dr. Wauchope and associate discussant. Any comments from the associate discussants either in support or extension of the presentation? Dr. Lebow.

DR. LEBOW: That was an excellent summary. After hearing it spoken, I think there is some value. I'm not sure how it would be used in risk assessment. I certainly think this does help us establish the valence states in the wood itself and if the wood compose the majority of the residue, whatever fraction of that residue is wood fiber is going to be insoluble arsenic.

DR. HEERINGA: Thank you. Very much for that clarification. Dr. Hattis.

DR. HATTIS: I'd like to try to induce you to draw the implications a little bit more for the use of the

arsenic bioavailability study in the pigs which I gather was done with the same wood residue material. And so it's -- but also degree of contamination measured in the ACC study because both are being used here in the analysis.

I had earlier thought that it was, you know, we really should be taking the 27 percent bioavailability as good an estimate of reality as like is to be the case. But, clearly, if you think that that doesn't material doesn't actually represent to some extent the available stuff, then there's two different kinds of corrections that could be made. One is the available stuff is a minority of the stuff that's measured on the surface, but also the available stuff is more available than we thought it was from the pig expert.

DR. WAUCHOPE: The fraction, the relative bioavailability fraction of 27 percent is more or less addressed in Issue 8. Issue 9. We address that a good deal. Because the bottom line here is this residue preparation by the American Chemistry Council is -- what I'm saying is going to go into the record? I guess it

will. We think that it may be pretty much artifactual in that it's apparently a good representation of finally ground CCA wood.

And the question is: Is the material that we we've been calling dislodgeable residue, which is whatever gets on skin, hands, is that the same material. And we don't think it's very representative.

And that also, of course, raises the issue with the monkey study because this same material was taped to the abdomen of monkeys. And when we get to the discussion in 9, I think the issue is there's probably a fraction of dislodgeable residue generally speaking that is soluble. And that's the fraction that gets into the soil and it's the fraction that probably gets through the skin. And it's probably the fraction that is ingested from the fingers when you put the fingers in the mouth. And this ACC residue preparation may very well have missed the soluble residue, the soluble part of the dislodgeable residue.

DR. HATTIS: So my interpretation of the bottom

line to some extent here is that we should have somewhat greater uncertainty due to the possible representativeness of this stuff for the actual bioavailable arsenic that's really on the surface.

There are two different possible corrections. There's less than we thought. But it's more available than we thought. And I don't know which way the net effect goes.

DR. WAUCHOPE: We sort of agreed amongst ourselves we wouldn't come up with a different number unless we were pressed. The 27 percent probably is low. But that's probably not 100 percent either. Obviously only a fraction of any of the studies is going to be soluble. The .01 percent we really have a question. I think -- well, we've not discussed that amongst movements ourselves. But I certainly think that the .01 percent based on the powered ACCR residue is probably very problematic.

DR. HEERINGA: I think we'll have a chance to pick up the bioavailability issue in Question 9. Dr.

Francis.

DR. FRANCIS: Just a little clarification. And your absolutely right. Most of it will be discussed in the next question. I think what people were thinking is that if in the residue, the ACC-prepared residue, everything was a complex. Well, then everything would be totally insoluble and it would just go through the body. Well, clearly, the pig study shows the something is happening in the digestive tract. So even if this residue, this complex, is in the residue outside in the environment, that doesn't necessarily indicate what's happening in the body.

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

DR. CHOU: I agree with the assessment of this team. But with regard to the meaning of the risk assessment, I guess it depends on what are we talking about. Are we looking at the risk of children's exposure to material transferred through their hand upon contact? Or are we talking about children mouthing the wood? If we're talking about children mouthing the wood, maybe the

chopped up wood would be a good complex, would be a good estimate that could be used for that kind of risk assessment. Maybe in the future when they incorporate mouthing the wood as additional route of exposure.

But as far as for what we were talking at hand, touching, hand touching, I agree totally that this material is not representative of, I would say, what's actually transferred to the hand upon contact.

DR. HEERINGA: Dr. Matsumura.

DR. MATSUMURA: Yeah, I certainly agree with the analysis. Pretty good job. There's no question that if you use the leaching as a good indicator, there's no question that they leach out, soil residues and increase the arsenic content.

I was trying to think why there was such a big difference between the residue provided from the one that they are rarely touching the surface. I felt probably water may be a one of the mediums that we have to consider. Ionic forms indeed penetrate and indeed accumulate in the human skin and that's shown by the

Wester's '93 paper. So there is affinity and probably this ionic forms which will help them to transfer.

So again, I may go back to the question that maybe one of the factors and we were thinking like those fishing on the fishing boat and the outdoor activities and teenagers like fishing, how many wet butts that touch. And if water is the medium through which these ionic forms are transferred to human skin, then we should not neglect that. We still have to resolve why a difference between the monkey studies with those residues, so-called residues. And probably you are right that the when you grind them up and you scrub so hard, you may get residue from inside which is intact. Where the ones on the surface may represent really truly a soluble form coming up or down, whatever the direction. So I agree with Dr. Stilwell's assessment that the ratio show change is a really good indicator. So I agree with you.

DR. HEERINGA: At this point, if the Panel agrees and has no further comments, we have the opportunity I think to move onto Question 9 on

bioavailability. And I think that's a logical successor to the discussion we've just heard on Question 8. So, Dr. Dang, would you, please, read the question.

DR. DANG: Issue 9: Casteel et al (2003) reported that the relative bioavailability (RBA) of dislodgeable wood residue is 27 percent. This value is significantly lower than the default value of 100 percent that is usually employed when reliable site-specific data are lacking and also lower than the RBA value recommended by the SAP 2001. The result of this study indicates that the arsenic in the dislodgeable arsenic material is not as well absorbed as soluble arsenic.

Question A: Does the Panel agree that, in light of the Casteel study and the Nico study discussed in Issue 8, the Agency should use 27 percent for the RBA to estimate the bioavailable dose?

DR. HEERINGA: Dr. Wauchope,

DR. WAUCHOPE: Was it David MacIntosh? I can't read. Who said the short answer is no.

DR. MACINTOSH: I said the short answer is yes.

DR. WAUCHOPE: This is a shorter read you'll be glad to hear,

As stated in Issue 8, there is little doubt that arsenic in CCA-treated wood is less soluble than it would be in a form such as sodium arsenate. The form and solubility of arsenic in the ACCR residue preparation is less clear although the results of Nico et al. suggest that is is similar to that of treated wood.

Casteel et al. measured urinary excretion of arsenic in juvenile swine feed ACCR as compared to soluble arsenic 5 arsenate at similar total arsenic dosage. They reported a urinary excretion factor of 23 percent and a relative bioavailability compared to arsenate. this is 29 plus or minus 3 percent is the correct No. 27. I don't know. I got 29 percent here.

Since ACCR is essentially particulate CCA-treated wood, we would expect the RBA to be small. Other residues from other sources could behave differently. Our concern, again, is that the residue used in both these studies may contain a higher proper

proportion of wood particles than would be obtained by a hand wipe. The residue was generated by brushing the wood with a soft brush and then filtering out the larger material. Comparisons of hand wipe data to that from other forms of wiping, such as the ACC study in 2003, the RTI study, indicate the nonhand wipes are more abrasive. It is possible that residue on a human hand may contain a lower proportion of wood particle than a higher proportion of arsenic.

Other concerns suggest that the ACCR feeding experiment may underestimate CCA wood dislodgeable residues in general. I've got, I think, six of these: 1 to 3 year old deck is not a typical neighborhood deck. One other study suggested longer weathering results and a great leakage of arsenic 3 -- we heard that yesterday from the lady from Miami -- from the CCA material. Older decks may yield results.

Methyl arsenic species standards were not checked as part of the arsenic methods validation for the urine analysis. Do pigs metabolize arsenic to form methyl

arsenous acid or dimethyl arsenous acid or trimethyl arsenine oxide? What is the reverse of the method for these species? For example, trimethyl arsine oxide recovered from urine can be poor when acid digestions are used.

In general, under steady state conditions, urinary excretion patterns of arsenic are representative of GI absorption. Previous studies in swine suggests that the steady state for soluble inorganic arsenic species reached after approximately five days. The metabolic patterns including pharmacokinetics of urinary excretion and tissue distribution for arsenic species in dislodgeable residues or CCA-contaminated soils have never been characterized. The calculation of relative bioavailability in Casteel's report is based on the assumption that steady state was reached for the metabolism of arsenic in all treatment groups, i.e., those fed with arsenic -- I'm sorry.

I'm getting ahead of my mouth. Those fed with arsenate and those feed with various doses of CCA-treated

materials. This assumption is, however, based on a limited number of time points, three for dislodgeable arsenic study and two for the soil study. In fact, the urinary excretion patterns indicate that steady state was not reached in animals treated with the high dose of arsenic contaminated soil. We're talking about both the earlier Casteel study and the CCA residue. And in animals treated with a low dose of arsenic in dislodgeable residues. And I need to change that to ACCR, Figure 4.2 in both papers.

In addition, the steady state was not reached in animals fed with arsenate in the dislodgeable arsenic study as indicated by increasing urinary excretion of arsenic between days 6 and 11. These discrepancies undermine the Offices conclusions and contribute significantly to uncertainties regarding the validity of the calculated RBA values for both dislodgeable arsenic and arsenic from CCA contaminated soil.

Suggestions: The steady state conditions for metabolism of arsenic from dislodgeable residues and

contaminated soil should probably be evaluated before accurate RBA values can be determined. Obviously, examination of absolute bioavailability would provide more valuable information. This may require examination of biliary and fecal excretion and tissue distribution patterns in animals chronically exposed to dislodgeable residues and CCA-contaminated soils.

Problem No. 4, speciation of arsenic in the urine should have been performed to provide basic information about metabolism of both arsenic treatments. For example, higher urinary levels of arsenic would indicate that methylation is suppressed and consequently greater amounts of arsenic of species are retained in tissues.

Problem 5, The Panel was unable to ascertain from the information given the relationship between the concentrations of metals in the ACCR preparation and the surface area the boards extracted.

Let me insert my own comment. Maybe it's out there. Maybe in reports filed by somebody there was an

analysis where they reported, for instance, the volume of water used to extract all the boards and the mass of material that they got from that volume of water. But that information is not available anywhere that we can find it. And this means we have no way of relating the arsenic concentration in the ACCR material to the original surface concentrations that were extracted. This means we have no way of relating the dosages in any of these experiments to dosages that might be acquired from a hand-wiped dislodgeable residue. Thus we have no idea how to relate the dosage to use to the risk assessment scenario.

And finally, No. 6, if there were soluble metal species present in the original board wash water, could it have formed a thin film on rotary evaporation and could it have been left behind when the particulate material was collected? Was the rotary evaporator flasks rinsed and the rinsate checked? If arsenate was released and arsenate turns out to be the molecule, the species that is causing all of the exposure and toxicology, then that may

be a very small fraction of the ACC residue. It may be a very small fraction of what you get in the leachate test. But if it was left behind in the rotary flask, then that check was not done, then this preparation ACCR may simply have left behind the important fraction.

The Panel concludes that the 27 percent figure may be approximately correct for ACCR, the residue material, except for the uncertainties given above. But this represents a lower bound on CCA wood dislodgeable residues in general. The issue is whether the 27 percent figure applies to actual dislodgeable residues on the hand, and the answer is unknown.

Any comments from the other discussants?

DR. HEERINGA: Thank you, Dr. Wauchope? Other associate discussants? Yes, Dr. Chou.

DR. CHOU: I would at this point try to point out the distinction between the so-called ACCR and what we consider as presumably leachable soluble arsenic on the wood surface.

DR. HEERINGA: Thank you. Dr. Styblo.

DR. STYBLO: Just jumping to what my colleague just said. In evaluating Casteel's work, it was actually useful to look at both papers; although we were asked only about the dislodgeable material. But if you compare data from soil and from dislodgeable material, ACCR, if you compare data from soil, and I mean the relative bioavailability, it's much greater in soil based on this data whatever problems with these data may be, which would suggest that, again, whatever leaks from the wood is much more bioavailable than whatever is in the wood.

DR. HEERINGA: Thank you.

DR. STYBLO: And one more comment. I would like to put more stress on it. I believe in 2003 and any time later any studies that has metabolic components regarding the arsenic should include a speciation of arsenic. I mean especially if you deal with compounds that are basically unidentified or components for which metabolism is unknown. It would give us a much better idea about what's happening from the animal,

DR. HEERINGA: Thank you very much. A question

for the Panel to help me think through. This particular parameter, the relative bioavailability, I assume this is oral ingestion? It's really a linear scaling factor in the exposure analysis, is it not? So if it were off by a factor of 2, it would change the overall exposure assessment by a factor of 2?

Dr. Zartarian.

DR. ZARTARIAN: Yes, I'd like to clarify that in the exposure assessment, we did use a point estimate of 27 percent. We used a beta distribution fit to the pig study data with a mean of 27 percent but intercortal range of 20 percent to 35 percent. And that's all I'll say about that just to clarify.

DR. HEERINGA: Dr. Dang.

DR. DANG: One more thing I'd like to respond to. Dr. Wauchope mentioned about ACC studies. Original studies are 29 percent. Actually, we review it. That slight difference is because we calculate based on the same group. In the ACC study, they used 5 control and 15 test animals. And for the ACCR tests animal is used

difference. So we try to compare the same group of animals. That's why there's the slight difference of 27 percent.

DR. WAUCHOPE: 27 percent.

DR. DANG: 27 percent is what we considered is correct. And another thing, one more think I'd like to mention, the center correction is from a wood use based on the brush bristle-brushed wood from 35 ppm wood, is about one to years old, aged-wood. So basically the same as the dermal absorption one.

DR. HEERINGA: Thank you, Dr. Dang. Dr. Riviere.

DR. RIVIERE: I'd like to make a comment on pigs. Assuming the absorption of this complex in pigs, that pigs probably absorption this better than humans. Based on another panel I'm involved in with FDA on looking at interspecies's bioavailability comparisons to human data, there are two unique aspects about pigs that differ with humans.

One is that, unlike other monogastrics, pigs

have a lot more distal intestinal tract and they are capable of metabolizing cellulose. So the question comes into play that with this CCA complex that essentially is bound to wood, that the bioavailability of a complex like that would be higher in the pig compared to a human.

The reason this was an issue is that a lot of slow-release pharmaceutical preparations in humans are cellulose-based. If you administered those to a pig, you get a rapid release. You don't get a slow release because of metabolism. That's pretty well known.

The second aspect is the gastric empty in time of the pig compared to the human is much longer and especially longer for particular matter. So another situation that if you do have the wood complex. And I agree with the soluble aspect. But even assuming that just from this angle is that there's a lot more potential for acid hydrolysis in the pig stomach with particles than there is in the human.

So this 29 percent, if this is only reflecting bound compounds, is probably higher than what the

bioavailable fraction would be in the human.

And I have a reverse and a statement for this. This has been pretty well worked out and a known situation for looking at particulates compared to other species.

DR. HEERINGA: Thank you, Dr. Riviere. Dr. Styblo.

DR. STYBLO: Just a question. Does this apply also for bioavailability of absorption of the metals? You mentioned cellulose, microflora. How about metals?

DR. RIVIERE: No one has looked at that. But the key is --

DR. STYBLO: What you say is a general feature for absorption in swine compared with human, can you really say that it applies to metals?

DR. RIVIERE: You can say it applies to breaking down the cellulose structure. That then would potentially liberate the free compound.

DR. STYBLO: That may liberate the complex chromium arsenic based on the structure.

DR. WAUCHOPE: That's right. But I guess the

point is that probably what makes this material so insoluble is its linkage to the lignin and the cellulosic structure of the wood. So if the pigs can free the complex from the wood structure, then maybe the stomach is the only else you need.

DR. HEERINGA: Thank you, Dr. Wauchope. Dr. Bates.

DR. BATES: I just like to say that reading the two reports, the Casteel report said both got identical figure 3.1 conceptual model for arsenic toxicokinetics. And it seems to me that there is a fundamental error in it. In the calculation of relative bioavailability, it seems the KU, which is the fraction of absorbed arsenic which is excreted in urine, it assumes that they are identical for both the reference material and the dislodgeable residue. And we've got no reason to believe that's the case. And it's only if that is the case, then, in fact, the conceptual model works. But I don't think it is correct.

DR. HEERINGA: Can you see that Dr. Wauchope has

that?

DR. BATES: Sure.

DR. HEERINGA: Thank you. Dr. Matsumura.

DR. MATSUMURA: I generally agree with what this group has concluded. I wonder whether we could suggest that instead of using that shaved material or scrubbed materials, this committee should really recommend that leached or leachable material from those wood that means the soluble forms which can be washed of out those boards which actually should represent better material as a standard testing for bioavailability.

That means those wood particles would just scrubbed away from the wood is not the one that you are going to transfer to the human skins. And if you used washed materials that may represent a better type of bioavailability sources.

I'm just wondering whether that could be possible. Because we want to simulate both the dermal as well as the oral bioavailability. Right? So we have to start paying attention to that big difference between

those bound really processed fixed materials from actually transferring to human skin potentially at least.

DR. HEERINGA: Dr. Lebow.

DR. LEBOW: If my understanding is how this is working, that would lead to a great over estimation of availability because how the EPA is handling this is on the amount of residue on the hand. Now, some pro portion of that residue may be soluble arsenic. It looks like most of the most of it is probably wood fiber. We don't know if it's 95 percent wood fiber or 85 percent wood fiber. That's what we're getting with this brushing. It's probably still mostly with fiber on the hand, but we don't know what the proportion is relative to brushing.

If you just use soluble arsenic, that would represent a much greater proportion than you would have on residue. So if you're going to use just soluble arsenic, you have figure out what is the proportion of soluble arsenic in the residue on their hand and adjust the dose accordingly. So if the soluble arsenic in the hand is only 1 percent of the -- if the residue is only 1 percent

soluble arsenic, you would have to reduce your dose accordingly.

Do you see what I'm saying? You couldn't apply the same volume of leachate of soluble arsenic, or the same mass, because that would be a higher proportion of soluble arsenic in my opinion.

DR. HEERINGA: Thank you very much. Dr. Wauchope.

DR. WAUCHOPE: I agree with that. Fumio, we don't want don't now want to say that the ACCR residue doesn't represent anything. It probably represents mostly the nonsoluble fraction of dislodgeable residues. That's what we're really trying to say. And to the extent that it does not contain the soluble fraction, then it's not representative of exposure.

DR. HEERINGA: Dr. Lebow.

DR. LEBOW: I think it does contain the soluble fraction. It has just as much soluble arsenic, but it probably has a little more wood. So the proportion of soluble arsenic may be slightly lower than what would be

on a child's hand. That, I think,, is the gist of the residue difference.

DR. HEERINGA: Thank you very, very much to the members of the Panel particularly the specialities represented here. That's very thorough.

Are there any additional points of clarification from the EPA on this question item? There's a lot of new research that's been brought to this issue, and I appreciation the contributions.

Dr. Hattis.

DR. HATTIS: I guess my own casual interpretation of what's been presented in the last half hour is that one should have more uncertainty in this 27 percent parameter than for many of the other parameters. And if we were to offer some quantitative guidance on that, that it doesn't sound implausible that the true number could be three fold difference in either direction.

Would the people who are more expert in this suggest some other factor?

DR. HEERINGA: Dr. Styblo.

DR. STYBLO: Well, I didn't mean to make it formal. We have two papers from Casteel's lab, one dealing with dislodgeable material, whatever you call it; and one dealing with soil contaminated with CCA. There are two numbers for relative, relative -- just remember, these are relative availability. That's pretty important. We have two numbers. One is 27 or 29.

DR. DANG: The other one is 49.

DR. STYBLO: Right. So if we are not sure about the proportional distribution of arsenic between soluble and insoluble part, we can be pretty sure that whatever is in the soil is the soluble arsenic.

Why don't we use these two numbers to derive more certain or average number for bioavailability of arsenic in dislodgeable residues? That's my personal opinion. It wasn't discussed with the Panel I should point that out.

DR. HEERINGA: Dr. Hattis.

DR. HATTIS: I think that that's not at will unreasonable for raising it. It's doesn't quite meet your

full concern about the measurement of bioavailability though because, if steady state has not been fully achieved, then you could possibly have a farther removed from steady state for the residue than for the soluble arsenic because it would take some time perhaps to be digested in the intestine and then absorbed. Right? So that would lead to a greater underestimation of real bioavailability for the residue than would be measured in the direct test.

On the other hand, if the pigs are much more able to digest the residue at the very least than people are, as I think it was pointed out over here, then we have some possible over estimates giving us uncertainty in the other direction. So that's partly why I'm trying to capture that this expands your confidence limits a bit. Three fold perhaps is not out of the question. Combining both of those -- three fold in either direction is not out of the question combining those. The question is whether we have got the right central estimate as well, but also whether the Panel agrees. And by plausible, I really fuzz

the uncertainty description here.

DR. HEERINGA: Since the effect of this particular parameter on the exposure assessment is nearly linear, a three fold increase is 100 percent roughly. and a three fold decrease is about 10 percent. And I think the critical issue is whether or it's 27 percent or zero because that's going to make orders of magnitude difference in the final exposure assessment. Dr. Zartarian.

DR. ZARTARIAN: In light of the this discussion, I thought it would be helpful to remind the Panel of the analysis that we did do, sensitivity analyses that we did on this factor as well as increasing and decreasing by a factor of two as well as the special simulation where we assumed it was a hundred percent.

When we assumed a factor of two, when we increased it from 27 to 54 percent or cut it in half, we saw a difference in the dose of plus or minus 40 percent with the increase or decrease. And when we increased it from the mean, used a point estimate of a hundred percent,

we saw an increase in dose for the children assumed to contact both playsets and decks by 90 percent.

DR. HEERINGA: Thank you. Dr. Chou.

DR. CHOU: I also wanted to point out the uncertainty around the soil. Actually it depends upon the soil type. That's arsenic from CCA leachate from CCA-treated decks coming down to the soil usually stays around underneath less than two feet. It's a very tightly bound. It depends upon the soil as well. I don't know whether tying to use this as an estimate is -- will be introducing more uncertainty.

DR. HEERINGA: Dr. Wauchope.

DR. WAUCHOPE: Well, amongst ourselves, we agreed that the 50 percent perhaps is the central tendency of this number is probably what we would like to recommend. How you distribute that in some kind of distribution function is your business. But it sounds like that's about the best we can do.

DR. HEERINGA: That in combination with the sensitivity analysis that's already been conducted, I

think. Dr. Ozkaynak.

DR. OZKAYNAK: Just a quick clarification. Is that both for residue and soil?

DR. WAUCHOPE: I think the soil was already 50 percent, wasn't it?

DR. OZKAYNAK: Right.

DR. WAUCHOPE: Using 27 percent for the soil as well.

DR. STYBLO: No.

DR. DANG: No, we don't.

DR. OZKAYNAK: I thought it was 49 percent.

DR. WAUCHOPE: Our recommendation involves the dislodgeable residue bioavailability.

DR. HEERINGA: Dr. Francis.

DR. FRANCIS: Yeah. I know we discussed that. I was sort of part of that. And that sort of makes sense. But given I think I might want to change my answer. But I don't know how given what's been said about the pigs. So I think someone needs to kind of figure this out a little more. Maybe you need to go back to the original

researches or whatever and determine what exactly went on or try to make some kind of an estimate based on this research on the pigs. I think that really does need to be considered.

DR. RIVIERE: Concerning the pig stuff, I gave a reference that's a pretty comprehensive review. The problem is that's assuming that everything is the bound complex. Now if you have a soluble component to that, it's going in two directions. I would think 50 is too high if you're going to have to use available data.

Again, you have to do this all the time. Do you take an average between the two of them? If anything, I have a strong feeling that is overestimating at least the absorption from the particulate.

DR. WAUCHOPE: Two things. One is that the soil study gave was about a 50 percent bioavailability. And, in fact, I would expect that to be rather high since arsenate, which is the most soluble form, is quite strongly bound by soils. So something went on there. It's kind of an unknown.

And the other thing. - the comment I was going to make, I just lost track of that. Just a minute. It will come to me.

DR. HEERINGA: Any other comments? And Dr. Wauchope, as issues come up again, we do have an opportunity to bring those back.

Any additional comments on this question? We will have an opportunity at the conclusion for a wrap-up summary. So as your though processes solidify -- Dr. The, Kissel.

DR. KISSEL: Can I just say something by way of background? Dr. Casteel et al. did a bunch of prior studies of lead and arsenic available in mine tailings and things of the type. And undoubtedly, that's why they picked the pig because they were already using the pig for those other things. So I can't say explicitly, but there was a determination made at that time that the pig was a good model for those metals in soils. Perhaps they didn't think about whether that would change when you're dealing with metals in woods in instead of metals in soil.

DR. HEERINGA: Thank you very much for that comment.

At this point in time, we have reached the end of our discussion on Issue No. 9. And we're relatively on our agenda.

DR. WAUCHOPE: Oh, I'm sorry. I'm sorry.

DR. HEERINGA: No. Absolutely, Dr. Wauchope.

DR. WAUCHOPE: My senior moment just clarified.

Let's hypothesize that it's arsenate anion. That is the -- we really don't know, do we? Based on everything I've heard, we have no clue what the chemical species are that go from deck to fingers to mouth to gut. We don't know. We have no clue. Certainly, though, based on all the chemistry we know, arsenate is the most probable species that is getting to the gut. And, therefore, the RBA would be a hundred percent for the species. Are you following me, what I'm saying?

So to argue that the RBA should be low based on the residue studies, again, is arguing on what we know but we don't know that that material is representative or not.

Okay.

DR. HEERINGA: Thank you very much.

At this point in time, I would like to .recommend that we adjourn for a one-hour lunch period. It's 12:10 by my watch. And I'd like to reconvene at 1:10. I think the progress is good, and I want to commend the Panel on their preparation, their level of preparation. This is, I think, getting a good discussion and a good foundation on the initial presentations started. And let's reconvene at 1:10, and we will continue with final three issues, Issues 10, 11, and, 12. Thank you.

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

meeting reconvened at 1:15 p.m.]

DR. HEERINGA: Thank you, everyone. And welcome back to our final afternoon session of this meeting of the FIFRA Science Advisory Panel.

Before we continue with questions 10, 11, and 12, it's come to my attention, and I think that Dr. Dang has concurred, that it would benefit us to have a short

statement, presentation, by individuals involved in the design of some of the bioavailability or at least informed on the design of the bioavailability studies.

And I understand that Dr. John Horton is here to make the presentation. Or Dr. Sharma, if you'd like to make the introduction, you may do that.

DR. SHARMA; Thank you, Mr. Chairman. thank you for allowing us to add a couple of points of clarification which relate to the bioavailability studies and also specifically to how the dislodgeable material was, in fact, collected. And for that, I'm going to hand over to John Horton to describe that.

DR. HEERINGA: Thank you very much.

DR. HORTON: I'm John Horton. I'm with Osmose, one of the CCA registrants. And I know there was a lot of discussion early on about the removal process for collection of the dislodgeable material from the surface of the actual treated wood. And while I'm not the researcher who did the actual dislodgeable process -- that was Dr. Pascal Camden of the Michigan State University --

I do have a of description of the process that may be helpful to further clarify that. And there might be some other possible questions we can field. But we can certainly follow up with more specific information if the Panel feels.

DR. HEERINGA: Would you like to read the description?

DR. HORTON: Yes, I'd like to read a pretty brief description of the process. And also the collection of the wood decks and where they came from.

Basically CCA-treated boards of various commercial dimensions were removed from in-service residential decks. The decks were obtained from two different locations in Michigan, actually the Grand Rapids area, and four locations in Georgia around the greater Atlanta area.

And the decks from Grand Rapids that were removed were actually a Ponderosa pine species, the decks that were removed from the Atlanta, Georgia, area were Southern Pine. So we did try to get to two different

species into the composite sampling mixture.

The decks ranged from 1 to 4 years of age. They all consisted though of CCA-type C, which some of you may have heard before, which is the commercial formulation type that is used today and has been for over a decade for the treatment of this material.

All the structures were selected and were screened based on the criteria that none of the decks could have had any coatings or any treatments applied during the life of the deck. And we did that obviously with a survey with the owners of the decks. And we wanted to make sure that this was just wood that had been exposed out there in service in actually deck usage without any coatings or sealants applied.

Commercial contractors were used to go and dismantle and collect all the boards. And then the boards were shipped to the University of Michigan State for the dislodgeable removal process. All the boards were cut into two-foot sections at Mississippi State. And there was a total when we got done -- actually, we collected

over 11 decks, 5 from Michigan and 6 from Georgia. And a total of about 1,500 boards sections, two- feet board sections, resulted from cutting this material into two-foot sections for the dislodgeable removal process.

To collect the material, each board was placed at about a 45 degree angle over a plastic tub. Each board was then sprayed with approximately 50 millimeters of deionized water. The upper surfaces, weather-exposed surfaces, of the boards were then brushed with a test-tube brush. And I can pass that test-tube brush, the type of brush that was used for this brushing around for you to get a feel that this brush is a very soft, nonabrasive type of brush. So we weren't really trying to remove wood. We were just trying to remove whatever, what we called dislodgeable from the surface of the wood. And if that might be some small particles of wood with it, so be it.

And again we started with 50 milliliters of deionized water on the surface. And then the board was brushed about 10 times, one direction, down towards the

bottom of the slanted area towards the collection tub. All the brushing was performed in the same direction. The wood surface and the brush were then rinsed with approximately 150 milliliters of deionized water.

And then after about five boards were rinsed and brushed, the rinsate and the particulate matter in the tub, whatever that might be, was filtered through a glass wool. The filtrate was collected in two-liter flasks. the glass wool was rinsed a second time to ensure that all the fine particles were removed and any large wood fibers that were taken out were removed from the rinsate from the glass wool. Sometimes you could get little some little larger particles that would come off the surface of the wood that were deemed to be more splinters than just dislodgeable material.

Then the filtrate was concentrated because we had to, in order to get the material ready to feed to the pigs in this case, Dr. Casteel asked that we deliver a fine, dry material. So the material was concentrated by rotary evaporation at about 46 degrees C. Then the

material was taken out in sort of a sludgy, moist, wet mass. And then it was just allowed to air dry at about 22 degrees C and about 65 degrees humidity level.

The dried material resembled a very fine brown colored particulate. The air-dried material was then gamma-radiated. This was to make sure when it was packed into the containers that there wasn't any bacteria in there growing that could ruin the samples. And then the material was shipped overnight courier to University of Missouri Veterinary Medicine Diagnostic Laboratory for use in the swine bioavailability studies.

DR. HEERINGA: Thank you very much, Dr. Horton. Since we've had this presentation of protocol for the collection of the residues... Dr. Wauchope.

DR. WAUCHOPE: That's very helpful. And I appreciate that. And I think if my colleagues, we'll take out the issue about the thin film forming on the rotavap since they removed materials of wet mass and air-dried it in a tray. And that meant the solubles were in the final product.

Now, can you tell me how many square feet of board surface were represent by the experiment and how much mass of material did you acquire? Or could you get us that information?

DR. HORTON: Well, there was approximately 3,000 lineal feet. I think, obviously, this was 2 by 6 material. So that would probably represent around 1,500 total 58 square feet.

Now as far as the total mass of arsenic, we also measured coming off in that, I would have to go get the numbers of the removal and, obviously, get those numbers and calculate that. And we could get back to you on that. But I apologize. I don't have that information at the fingertips.

DR. HEERINGA: We understand. But if you could supply that information to the Panel, that would be useful. Supply it to the docket. It will be part of the docket.

DR. SHARMA: One additional piece of information that would also help in some of the questions that have

come up is that we are, in fact, conducting a study which we have worked with EPA in terms of the protocols, to look at the difference in the nature of the material removed by the brush versus the hand of pressure-treated wood. And as part of that analysis, we will be looking into solubility characteristics of that material as well as looking at ratios for the metals that come off brush versus hand. So the study is ongoing right now, and I think it help, go a long way toward some of the questions that have been asked.

And the final point really is, we appreciate the comments on the Casteel studies. And we certainly would like to respond to those, through Dr. Casteel himself, just to remind the Panel that this really was a study and a model that was agreed at the last panel meeting that we move away from what was presented before which was the hamster model to this model and that the protocols for use for the Casteel were approved by several agencies including EPA, PMRA, et cetera. So I just wanted to remind the Panel of that. But thank you, again.

DR. HEERINGA: Thank you very much. Dr. Portier.

DR. PORTIER: I just had a clarification. All this dried residue was put in one bag. It's all composited. Right? That's the first thing.

The second thing -- so that's an affirmative for the record.

And the second thing is all of this was from a worn surface. You didn't take vertical surfaces. This was the deck flooring. And if there were ends that showed no wearing, you removed those?

DR. HORTON: Well, again, all the decks were at least 1 to 4 years as far as their weathering exposure. And of course these different climates from Grand Rapids to the Atlanta area. We took all the surface decking, benches, railings that were there.

As far as vertical members, there really wasn't a lot of vertical members that we could use for this process simply because most of vertical members at least above the decking were like rounded decorative spindles or

small 2 by 2s. This was a pretty painstaking process in trying to get enough to feed these pigs because they're pigs, you know. We were told we had to deliver a certain concentration of arsenic in order for Casteel to do this study.

And it was a very sizeable, as you can imagine, 3,000 lineal feet of material being taken off. We did not, of course, take vertical members such as deck supports, 4 by 4s, or that. But we wanted to take the material that typically a consumer or even a child playing on the deck would be exposed to, the above weathered where they might sit on the bench or grab a hold of the rail and sit on the deck and push off.

DR. HEERINGA: Dr. Horton, just a point of clarification. We asked about the nature of the material. This was five-quarter decking or was it 2 by 6 decking?

DR. HORTON: The decking material represented some five-quarter material, five-quarter by 6 inch nominal which really comes down to 5.5 inches.

DR. HEERINGA: Thank you very much.

DR. HORTON: It also represented some actual 2 by 6 material as there are still some people that like a little thicker decking material.

DR. HEERINGA: Dr. Styblo.

DR. STYBLO: Just a curious question. Do we have any indication that during the transport fine particles that would be deposited on the horizontal part of the wood would be shaken off during the transport?

DR. HORTON: Well, the material that was taken from the decks were cut, I'd say, into approximately four-feet pieces. And then they were put together edge to edge, and then everything was separated with plastic. And then there was foam put between the plastic to pad the process from each layer. So we will built these layers. And I can't remember how many pallets were shipped. And the whole thing was wrapped and covered, protected from any outside environmental.

DR. STYBLO: Did you try to collect whatever fell off on the plastic? You stayed said it was wrapped in the plastic. There must have been a lot of material on

the plastic when it was delivered. I would assume that was the finer parts.

See, what we are interested in is what is exactly getting stuck on the hands of children. And finer particles are probably the most likely to be on hands. I just wonder if part of the material could be actually lost.

DR. HORTON: I believe that when the material arrived at Michigan State University, when they started removing the materials from the layers, they did inspect the plastic to make sure there wasn't a lot of material on there. But I can't -- I don't think -- I think if I gather what you're asking, I don't believe they vacuumed the plastic in that case to try to deliver any of the dry particles or things the might have been on there. But they did inspect the material to make sure it hadn't been damaged in transit or the surface of the wood hadn't been visibly be scraped or anything where you might expect there was a severe or some type of removal of material from there.

Now, I know that the RTI study, though, also in the material that they're looking at, they got this material from desks locally. And that has been taken very carefully, of taking it right to the lab there. And, again, I would assume -- well, I know the way the work that RTI does. They're very painstaking. Obviously, when they look at this hand-to-wet-brush procedure removal, I will get them to comment on their transport method and see if they looked at this issue that you brought up.

DR. HEERINGA: Dr. Kissel.

DR. KISSEL: We were given a report from Battelle Columbus, Chemical Characteristics and Morphology of Particulate in Dislodgeable Residue, which appears to be discussion of the same material you're talking about. On page 2 it says that the top and bottom faces of boards were processed at different times and particulate water was kept as separate stocks. And there's a citation of Gradient. And if you go in the back, it turns out to be personal communication between Gradient and Battelle. But that suggests that there were two samples and not one

sample. Could you clarify that?

DR. HORTON: Yes. Again, when we did the procedure for removal, we did take off the top. And then after we took off the top, it was decided to go from the unexposed bottom side that didn't get direct weathering. And we did also remove that material as well. And it was also asked that the material for the bioavailability and the characterization of the complex work as well as the Battelle work that all comes from the top weathered surface the humans or animals would inhabit and not underneath because a lot of these desks were two feet off the ground.

And a lot of them where you couldn't get underneath the deck. So we felt like we wanted to have the material that the weather would degrade the wood or whatever the complex on the surface as well as what would have direct exposure to humans that might inhabit or are doing activities on the deck.

DR. KISSEL: That's fine and makes sense. I just wanted to clarify that when you said it's a composite

sample, it's a composite sample from the tops of the boards and not a composite sample of the top and bottom surface.

DR. HORTON: Yes, sir. This sample is a composite sample of only the tops of the boards. We have run solubility studies just in-house of the tops and the bottoms and find the solubilities of the metals. I'm just speaking about water solubility no other extraction to be the same. And the metal complexes, at least from our internal reports, are showing the typically the metals for just the water solubility test is typically 95 insoluble as opposed to 2 to 3 percent or 4 percent soluble.

DR. HEERINGA: Dr. Portier.

DR. PORTIER: You mentioned the CCA-C has been available for about a decade. Do you know exactly when it came in? It's important because the next question we're going to be looking at a study from 1993 and a study from last, and I'm wondering if we're looking at the same thing because it's a commercial product. And we know they change over time.

DR. HORTON: And I've been reminded by one of my colleagues that that's pretty much a too short of a time frame. As a matter of fact, when I came to work with Osmose in 1974, they were already on the Type C concentrate away from what was the Type B at that time. Actually from the mid 70s, you're looking at over 25 years. I apologize for my...

DR. SHARMA: I think the 1993 study is arsenic in soil versus CCA in soil.

DR. HEERINGA: Yes. Thank you, Dr. Sharma.

Any other questions or comments? Thank you very much for the clarification on that protocol, Dr. Sharma. Thank you to Dr. Dang and the EPA staff for allowing that clarification, too, in terms of our meeting protocol.

At this point in time, I'd like to turn to the Issue 10 that have been presented to the panel and ask if Dr. Dang would, please, read the question to the Panel.

DR. DANG: Issue 10: In the 2001 SAP meeting, the Panel cited the research of Wester et al. (1993) as a source of the dermal absorption rate of soluble arsenic in

water and soil. The Panel recommended using a 2 to 3 percent dermal absorption rate for arsenic residue on the surface of wood. Recently, a preliminary study by Wester et al. (2003) has been submitted by the same laboratory compares the dermal absorption of arsenic in CCA-treated wood surface residues with arsenic in water solution.

Although the Agency has not received the complete results of this study, e.g., the recovery of the arsenic in the urine of the animal given IV sodium of arsenic, the preliminary results of this study indicate that the dermal absorption of 0.01 percent from wood surface residue was approximately two orders of magnitude lower than the results in water. The dermal absorption from this study was based on urinary arsenic data following application of arsenic in CCA-treated wood residue that had been weathered by the environment.

Question A: Taking into consideration the Nico et al. study mentioned in Issue 8, the Panel is requested to comment on whether this new study conducted by Wester et al. provides a more appropriate estimate of dermal

absorption from contact with CCA-treated wood surfaces than the earlier 1993 Wester et al. study.

DR. HEERINGA: Dr. Kissel is the lead discussant on this particular question.

DR. KISSEL: And the associate discussants are Jim Riviere and Michael Bates.

The intro to this question has been pretty well covered by the responses to Questions 8 and 9. On initial look, it is certainly plausible that if you have binding to lignin that bioavailability would be reduced. There are some questions about that per the prior discussion about how to interpret the XAS data and what the environmental data suggesting different arsenic and chromium ratios means.

And I would also point out something that wasn't mentioned previously is that yesterday Exponent showed us some data the was sweat extraction of three media, two of which were weathered CCA-treated soils and one of which was this ACCR that was so-designated by the previous discussants. And the sweat extraction actually generated

more arsenic from the ACCR than it did from either of the weathered soils. So whatever binding there is, there's at least some suggestion that it's not absolute and complete and that there is an available fraction there, which could color any interpretation of both oral availability and dermal availability.

And then the final question from the previous discussion was whether the stuff that was brushed off the wood is the same as what would come off on hands and that's been discussed already.

So the question becomes given the it's plausible that there's reduced bioavailability, can the Wester et al. data be used to provide a quantitative estimate of that reduction. Superficially, the results were 2.8 percent absorption as a mean three animals for soluble arsenic in water, in small amounts of water; and the water is distributed on the skin in amounts that wouldn't run off and would either evaporate or be absorbed and nominally zero percent from the CCA-treated wood residue. And it's been cited a couple places, I think both in the

presentation that we got from Exponent and perhaps in EPA's material as well, that the soluble results are basically the same as the prior result of the 1993 study where the low dose and high dose numbers, or high dose and low dose numbers, were 2 and 6.4 percent bioavailability were estimated in that study. And the current number, 2.8 percent, seems to fall in that range.

I would point out that the 2 and 6.4 percent numbers were 24-hour exposure numbers and the 2.8 number, the most recent one, is an 8-hour exposure. So for comparability purposes, that 2.8, the most recent numbers, should be multiplied by three and give something over 8 percent which is still not statistically different than 2 and the 6.4 percent, but it's more at the high end of the previous range rather at the low end of the previous range.

And then reduced bioavailability was observed for wood residue. And the presumption is that the method is the same. And if the soluble results are legitimate, then the wood residue results are also legitimate. There

are potential problems there with respect to experimental technique in general. And I wanted to make sure that I say this in a logical order.

There are three aspects of the experiments that we have some difficulty with. The first I would call generic experimental problems of which there are two. One is that the sample size is very small, N of 3, which gives you very little power to actually detect affects. In fact, I did the straight forward kind of naive statistical analysis, and the variability and the results are such that you can't distinguish even the first day from the background number because the variability over the three monkeys are so high. And with an N of 3, the T-value gets to be quite large. And so doing statistical difference testing becomes quite difficult.

Now I acknowledge that Exponent has done the statistics in a different way. And although we haven't seen the details, they do assert that there is a statistically significant difference. And there might very well be. It still bothers me somewhat that the

straight forward approach doesn't produce statistically significant result for either the water soluble data or the CCA-residue data. And it bothers Jim that it's N of 3 at all on just a sort of a general philosophical grounds. So we have a problem with sample size.

The second at aspect of these experiments which is problematical is that because it was done in primates, it was done in vivo for the reasons that people generally like to do in vivo experiments. But if you do in vivo on primates, you can't sacrifice the animal and so you can't do a mass balance. And in the absence of a mass balance, you don't really know what happened in the experiment. So there are some -- that's just a fundamental weakness of this particular set experiments.

The other two pieces are the contact scenario and pharmacokinetics. The contact scenario -- and this is I feel like sometimes I'm becoming the designated national crank on this particular issue. But this general prejudice and I'm hearing that no one is willing to say this in public, so I'm going to say it in public.

There is a general prejudice among toxicologist that do work in vivo because it avoids the artificiality of in vitro testing; however, dermal application of granular media is very difficult to do in vivo. You can't instruct an animal what to do. So you have to protect the site somehow. You can't allow the animal to lick the site or rub the site or scratch the site. And so you wind up inevitably with an artificial contact scenario.

So you substitute the artificiality of the of the in vivo limitations for the artificiality of the contact scenario. And it's just my personal prejudice that dermal exposure scenarios should be conducted in vivo and in humans where you can tell them what to do and should not be done in vivo in surrogate species because of difficulties.

Now I do acknowledge that the Exponent folks seemed to be at least partially aware of these issues and worked very hard to try to ensure contact of the material with the skin. I think Jim is satisfied that they did a good job. I am mostly satisfied. Although a hundred

square centimeters turns out to be a very language fraction of an abdomen of a monkey. And it's very hard to actually tape things down to create 100 square centimeters on a monkey without involving the pelvic bones and the rib cage, in which case you could potentially get air gaps between material and the skin.

And, generally, when you're doing dermal absorption work or transfer from an external media to skin, there are three real ways that stuff can get out of granular media into the skin. One is direct contact. If the agent is on the material on a surface which is immediately proximate to the skin, then you can have direct transfer from the material to the skin.

One is diffusion in a liquid phase. If there is sweat or water or something in there, then the material can diffuse. The third way is diffusion in the vapor phase. But for compounds which have negligible vapor pressures, that third phase is not actually in affect. So any air gap would be essentially a complete barrier to transfer of inorganic arsenic from material to the skin.

Solid phase diffusion is not on my list because it occurs at rates which are much too slow for residence times in these experiments and for real exposures to granular media on skin so it becomes irrelevant.

You have to be very sure that you have not created an artificial air gap between the media and the skin, or else you will essentially have no transfer. And while I would say that they did everything they could to avoid that issue, short of having microfiber cameras under the bandage to see what was going on there, I don't know that you absolutely know that you have avoided such a problem.

Okay. A second issue related to the contact scenario is the notion of monolayer. And I keep having to give this speech also. The standard in dermal absorption world is the expressed stuff is percent absorbed. Now, if you can envision -- and I will tray to do this without any graphics. Coverage of skin by graphical materials occurs in stages and can be complete or incomplete. And if you have a small amount of stuff and a very incomplete

coverage of the surface, you will have some amount of flux associated with that degree of coverage. You would anticipate as surface involvement increases, that flux will increase to some point until you have complete effective coverage.

Now because of lateral diffusion from particles, effective coverage may be short of visual coverage. You may not need complete visual coverage of the skin to have effective complete monolayer coverage of the skin. But there is some transition there from incomplete coverage which gives you low flux or lower flux, top complete coverage which would give you maximal flux.

Then as you go above maximal flux, you pile on more and more material on the skin, the flux does not increase. And so flux, which if you express flux as a percentage of the total amount of material which is the obstensively added, the percent absorption can be decreased artificially by simply piling a lot of stuff on the skin. And that's been in EPA documents for quite a while.

The original '92 dermal document has a correction which is not written in the absolute best way. But it's expressed in a way that people who are cognizant of these issues should no longer be doing experiments that are not monolayer or should no longer be doing experiments from which the results are presented as percent absorbed. They should be presented at flux numbers. Now, if the number is zero, it doesn't matter which of those things you have. To the extent reporting the raw result does not make too much difference. But it does make a difference when you start talking about detect limit.

Now the Wester et al. work was done at 4 milligrams per square centimeter on the basis that from an EPA document that 5.4 milligrams per square centimeter would give you monolayer coverage for a relatively fine soil. There are two things wrong with that argument. The first is that the -- the way EPA estimated those monolayers was not particularly careful. They used an average particle diameter for a given size class rather than a median or perhaps a 25th percentile. When it comes

to skin coverage, it's the small stuff which actually makes the difference and not the big stuff. And you can easily have -- if you had a reasonably wide distribution of particular sizes, you could easily have in 5 milligrams per square centimeter of loading, you could have 1 milligram per square centimeter of stuff which actually provided complete coverage and the other 4.4 milligrams was simply excess material.

The estimates are based upon face-centered spheres which is an idealization. But you can run the numbers yourselves, and the estimating techniques are published. And small particles can cover a fair amount of surface with not much mass because their volumes are quite low

The second piece of that is that there is a density dependence. The mass of the material you have depends on the density of the material. And the EPA estimate is based upon a typical sand density which is used by people that are doing soil work which is 2.65 grams per centimeter cubed. We know from prior testimony

that the material is more likely to be wood than soil, that this ACCR is mostly wood which should have a density much less than soil. And therefore the mass that you would require for the same size particles, the mass that you would have that would b e required for coverage would be much less for woody material than it would be for soil.

So my kind of rough guess at what a monolayer of coverage would be for this experiment would have been more like 1 milligram per square centimeter than 4 milligram per square centimeter. And that there was probably 2 to 4 layers of material on the monkey.

And we actually saw some visual evidence of that in that we saw pictures of the Tegaderm patch peeled back and the Tegaderm patch was covered with material and the skin was still covered with material. So we know there were at least two layers of material, which means that any percent absorption that is reported should be multiplied by at least 2 and perhaps by as much as 4 to get an estimate of what the --

Now in this case, the number that we're

multiplying is zero so we still get zero. But it means that the detection limit is 2 to 4 times larger than would be reported if you didn't make this correction.

And that two-to-four-times correction number to translate to something that looks like the EPA number, you should multiply by 2 to 4 for the layering effect and then multiply by 3 for the fact that the EPA number's a 24-hour number. And these were 8-hour experiments. Basically, whatever the detection limit in these studies was would have to be multiplied by a factor of 10 to give you of a conservative estimate. If you assumed otherwise that everything with these experiments was okay, you have to multiply by about a factor of 10 to get a number that you could then use as a bound that was actually observed.

The final piece of that is the pharmacokinetics. These numbers were like the prior numbers adjusted by the urinary response observed following intravenous injection of soluble arsenic. And we have grave doubts that that is a good indicator of how material which wasn't soluble arsenic to start with and was applied dermally as applied

intravenously, would behave.

There's lots of opportunity for material which is not soluble arsenic to behavior differently if absorbed through the skin and to be transported differently. And we think that the overall adjustment by virtue of intravenous response is simply invalid or unsupported by anything other than wishful thinking. And, therefore, leaves the results to be somewhat uninterpretable.

So the overall conclusion is that we can't get any quantitative estimate of dermal absorption from the Wester at al. study. And, therefore, there's no grounds for adjusting the current EPA number, which, as I noted already, is closer to the low end of apparent availability of soluble arsenic dermally as opposed to the high end.

DR. HEERINGA: Thank you, Dr. Kissel. Any of the associate discussants, would they like an opportunity to either clarify points that Dr. Kissel's made or add to the discussion? Dr. Riviere.

DR. RIVIERE: I pretty much agree. As it's obvious, the loading and the monolayer aspect is

questionable how much was on there. But the problem of expressing everything as percent dose in this line is that if there's more there than is actually biologically available, then whatever number adjusted is over estimating it.

The big concern I had is philosophical and that is using an N of 3 for such an pivotal estimate. There's just too much variability. You already have the problem of it being not human. It's being an animal model. It's a decent animal model for adult human skin. That's been shown. But that's a very, very small number to base any statistics on at all.

And finally, I agree completely on the correction factor goes into the Casteel study on the in vivo pigs also. We don't know what's being absorbed. And if it's another species of arsenic, that's not necessary that that's going to be excreted in the urine which basically invalidates using the urine as the only way to determine absorption.

DR. HEERINGA: Any other comments or additions

from the Panel members on this question?

Dr. Dang, if this was satisfactory in terms of the response.

DR. DANG: Yes, thank you,

DR. HEERINGA: Completeness of the response.

At this point, let's move on to issue No. 11.

Before we read this question, I think that with regard to the biomonitoring study I'll say in advance that if there are questions of fact regarding design of the biomonitoring study, that Dr. Floyd, Dr. Floyd Frost, presented yesterday that Dr. Beck and I think Dr. Sharma are here and could address questions of fact regarding the design of that studies just as we had clarifications previously on the design of the residue extraction.

So with that note, Dr. Dang, if you would, please, read the question.

DR. DANG: Issue 11: In the 2001 SAP meeting, the Panel recommended that a biomonitoring study be performed on children who are normally exposed to CCA-treated playground equipment and decks. The Panel

recommended that the study should be designed according to well-accepted epidemiological principles, including adequate sample size, to resolve the issue of whether there are substantial exposures to children from arsenic residues after playing on decks and playsets.

The Panel indicated data from such a biomonitoring study could be directly used in the risk assessment and could be used to validate the exposure assessment model. Recently, a proposed protocol for a pilot study was submitted to OPP for peer review.

I'd just like to stop for one second to make a qualification here. Yesterday, we have a public comment some comment mentioned about EPA endorse and also cosponsor. EPA wishes to point out that the federal government is not a joint sponsor of the proposed biomonitoring pilot study. Moreover, EPA is not requiring the industry to conduct this study. For EPA has reviewed the protocol from the proposed pilot study and has provided the sponsors of this Prower with preliminary comments.

EPA has not endorsed the proposed protocol or any alternative protocol because EPA sees many significant scientific issues raised by the proposed biomonitoring protocol and because it appear responsive at least in part of the earlier SAP recommendations.

Let me continue on Issue 11.

DR. HEERINGA: Certainly.

DR. DANG: This proposed protocol is an attempt to determine if changes in exposure to arsenic can be assessed by examining changes in the urinary excretion of arsenic. EPA has provided the Panel with a copy of the proposed protocol for the pilot study. In summary, the proposed pilot study will determine whether a significant difference in urinary arsenic can be discerned when a population of children are switched from arsenic-containing tap water to an essentially arsenic-free source of drinking water.

Question A: The Panel is requested to comment on the strengths and limitations of the approach to be employed in the proposed pilot study to help resolve the

issue of whether there are substantial exposures to children from arsenic residues after playing on decks and playsets. In particular, please comment on the feasibility, the potential confounding background sources from the statistical analysis, the sensitivity and accuracy of analytical method for quantitation of arsenic in urine to detect changes, the determination of intraindividual variation and interindividual variation based on the current knowledge of exposure, and any other aspects of the proposed pilot study that might affect its utility.

DR. HEERINGA: Thank you are very much Dr. Dang. And Dr. Ryan is the lead discussant on this particular question.

DR. RYAN: Yes. I'd just like to acknowledge as well my coconspirators if you will in this particular review. Dr. Bates, Dr. Steinberg who has already left for the day, and Dr. Styblo.

Just to put us all on the same page I'd like to take a few sentences just to summarize what this proposal

entails. The proposed pilot study which I will refer to as the pilot study throughout this will investigate the effect of elimination of the intake of arsenic-containing drinking water on the total urinary arsenic concentration in a group of young children. The pilot study will take place in Albuquerque, New Mexico, a location with modestly elevated levels of arsenic in drinking water reported to being approximately 15 micrograms per liter if I remember correctly.

Using an expected intake of about a half a liter per day for these children of municipal water sources, the expected intake of arsenic from drinking water is approximately its potential intake experienced through the contact with CCA-treated wood products given as several micrograms per day. It's hypothesized if the differences in urinary arsenic can be seen in the drinking-water-based approach, then it's feasible that such an approach can be used in assessing CCA-related dose and dose differences experienced in mitigation strategies.

I'm going to now present the critique. Again,

as Dr. MacIntosh pointed out at the beginning of the day where this group is near the end of the set of presentations, so we've had an opportunity to meet several times, iterate through a couple of written iterations of our critique and so on. So we might be a little bit further along in our critique than others might be.

The study as designed offers little insight into the exposure and dose relationships expected for children who come in with CCA-treated wood. And is, therefore, not responsive to the SAP request from 2001. It's not a pilot study,but rather a preliminary investigation in which somewhat relevant data may be collected. Specifically, the effects of mitigating arsenic dose through reduced exposure to CCA-containing materials will be inferred from the reduction of drinking water intake of arsenic.

Arsenic found in drinking water is almost exclusively inorganic arsenic. While arsenic exposure from CCA-treated wood s product and potential contamination associated with such products consist of a complex mixture of CCA, CCA-wood complexes inorganic and

perhaps organic species bound to soil and other forms. It's unlikely that all of the forms discussed above will be equally eliminate via the urinary pathway and it is nearly certain that they will not be eliminated in the same manner and at the same rate as arsenic ingested in drinking water.

Other elimination pathways that might correspond to metabolic loss of arsenic, for example, the biliary pathway, would not be included. The hypothesized decrease in total urinary arsenic after the, quote, "wash out," unquote, period, may well reflect a this component of exposure related to the consumption of arsenic contaminated drinking water.

However, the reason behind focusing on this approach is not clear. For example, with the absence of a decrease in excreted the urinary arsenic suggests that the CCA component of the exposure is more significant than that associated with drinking water.

In an ideal approach, a pilot study that is aimed at examining exposure to arsenic from CCA-treated

wood, would be carried out in populations that are not concomitantly exposed to arsenic from other environment sources. One would strive to control intake of all arsenic containing foods, for example, rice, grapes, and grains, in an effort to assess the impact of reduction of arsenic intake through reduced contact with CCA-containing material.

This might be modeled in the manner suggested in the proposal through the removal of arsenic containing water from the diet. However, this is still artificial in that the arsenic intake through drinking water in no way mimics the intake through contact with CCA-containing wood products.

The discussion above brings into question utility of the study as designed. Consider two similar questions, if the pilot study works, that is a reduction in urinary arsenic levels is measured, what information of use or relevance to the CCA-based exposure would be obtained. It is our belief that little useful knowledge will be gained from this.

On the other hand, if the pilot does not work, which I mean no reduction of urinary arsenic levels can be ascertained, what implications can be made about the CCA-based arsenic exposure. It is our belief that extrapolation of the results CCA-related arsenic exposures in tenuous at best.

Our conclusions and recommendation can be summarized as follows. Our assessment as it stands is not responsive to the SAP 2001 request. It is more appropriately a preliminary study in which data of some potential utility may be gathered but which in no way assesses exposes or doses likely to be experienced by the target group, namely children, coming into contact with CCA-treated wood products.

The study as presented is flawed in many ways. We have listed below a series of major flaws followed by a longer list of minor flaws that should be assessed prior to implementation. We believe that if implemented as planned, results are unlikely to be reliable or meaningful and we question whether it could be carried out

successfully to address the goals mentioned.

It is our recommendation that the pilot slash preliminary study, now I'm combining the two because we now believe this to be more of a preliminary investigation, should be discussed by all potential stakeholders. this includes the public, EPA and industry in refashioned to be more responsive to all needs. After receiving input from these three groups, a new study may be implemented that provides information useful to all parties and reflective of the need to understand exposure through this specific pathway.

We further recommend that funding for both a pilot study and the full study be identified and that a mechanism be developed to solicit proposals for work collecting real data on CCA-related exposures. The willingness of Drs. Sharma, Beck, Peterson, Chassian, and Frost, et al., to entertain outside peer review in this matter is encouraging as each will be involved in various components of the study. With more peer review including involvement of EPA's SHEDS-Wood personnel, a redesigned

biomonitoring study could be an excellent source of information to improve the SHEDS model.

We have a series of more detailed comments here which we divide into sort of major comments associated with the investigation and minor issues. For the record, I will not speak about the minor comments at all. But they will be part of our written comments and should be alluded to in this record, I. Will touch upon briefly the major comments that we made in major more detail comments.

These come under the general headings of design and statistical and quality assurance design, statistical and quality assurance issues, IRB-related issues, confounding factors, and analysis of arsenic itself.

First, the design and statistical and quality assurance issues. We question whether the report or whether the report that would come out of this study would address the feasibility of confirming or producing a main study for this overall report. Secondly, the pilot studies to be done in Albuquerque, New Mexico, accepted by the admission of Dr. Frost is probably not a good choice

for the large scale investigation. We would prefer to see a pilot level investigation in a place where we're likely to see the main study being done.

I have a series of bullet points regarding subject recruitment and sample size, mostly focusing on the numbers of samples to be taken, the 40 children, 5 duplicate-type samples, multiple recruits in the same family and so on. We have some concerns about the details of those issues.

Another design and statistical issue is knowing something about the temporal variability of arsenic in drinking water in Albuquerque. No data were presented on that, yet it was assumed that a single sample of water taken from the tap on the first visit would be sufficient to characterize the arsenic in drinking water at the beginning of the study. It would be more beneficial if we could find out more about the quality assurance samples that should be taken in this investigation, the number of blanks, the number of replicates, and so on that might be necessary.

And a detailed issue but one the is still important is they plan on maintaining records for a period of one year after the end of the pilot level investigation. I don't believe this is adequate, and I believe EPA would require more.

We have a number of different bullets on IRB-related issues. It appears that this is a major problem. And IRB-related issues are becoming more and more of interest in these types of investigations. First off, the present form of informed consent and ethical structure of the pilot is suboptimal. We have a couple of points on that.

Families familiar are being asked to provide a relatively small number of urine samples, four, five, six, something on that order, fill out a questionnaire a few times, and submit to a series of five or so household visits that will likely be less than 30 minutes in duration. The incentive offered for this is relatively and might be reviewed as coercive by some IRBs.

We saw no recognition of HIPA compliance rules.

This is something that's going to have to be addressed. One should consider developing an outside agency or an outside IRB consultant, perhaps somebody from the community or perhaps a community member on the board. For their field technician should be subject to IRB certification and so on. There are several other points under this area.

Under confounding factors, we feel that there has been poor control for confounding factors in this investigation. Other aspects of diet other than seafood are probably important in this particular area. We mention several of these. In particular, we're concerned about the specific diet that might be had by people living in the Albuquerque area. Rice is probably a major component of the diet, and it might be subject to arsenic contamination or high levels of arsenic naturally occurring in the rice. How is this going to be controlled and what affect is this likely to have?

It's also not clear in this confounding factor general picture. It's also not clear that the washout

periods the are alluded to here are sufficient to remove the body burden of arsenic the might already be in an individual. I've done some preliminary calculations that would suggest about two-thirds of the arsenic present initially would be washed out. This could leave a very large amount of arsenic still in the system certainly after the five days especially if a fish meal eaten before that.

Analysis of arsenic, this is a significant part of the investigation; and it bears some more concern. We already mentioned the tap-water-related issue. The specific analysis of arsenic in urine is not completely sufficient. There was general acceptance among the group that a large degree of speciation would be, appropriate. That we'd like to see speciation of the various MMA species and the DMA species and indeed also look at some of the more complicated compounds, the arsenosurgars, arsenocholine and arsenobetain, for instance, to make sure the we are indeed controlling for seafood consumption.

There are several points regarding the use of

the analytical chemistry in the presence of analytical chemists from the beginning of the investigation. We think that's important so that the collection of samples will be done in the most expedient and appropriate manner.

There are a series of minor issues, as I pointed out. We have literally dozens of these small things that we considered to the not actually crucial to the investigation; but it would be better overall if indeed these were followed up as well.

So going back once again to the conclusions that we present here, I just want to reiterate that. We think that the best way to go about doing this would be to develop a panel to put together an RFA for this program, generate the funding in some fashion, and go out there and get some proposals from a number different individuals and see a number of different ideas to go forward with the rest of the investigation. I would ask my associate members on the panel to add their comments at this time.

DR. HEERINGA: Dr. Bates, do you have anything to add?

DR. BATES: Well, Barry has covered it fairly thoroughly. But just a few things that I would like to add.

As he mentioned, we determined at a very early state it wasn't a true pilot study and so we regard it as a preliminary study. And I looked at the specific aims, and the question became after we decided it was a preliminary study as to what utility did this have in terms of the proposed biomonitoring study, the ultimate study. So I looked at the specific aims, sit out on the pilot or preliminary study, just to see how relevant they may be. And I thought I would just run through them quite quickly and just for the record to address them.

The first specific aim was to determine an effective method for recruiting young subjects and their families into a urine biomonitoring study. But as I think I said in an earlier session, when you do a pilot testing of a recruitment process, you need to do it in the actual area because demographic areas vary between different areas. What works in one area may not work in another.

The second specific aim set out was to compare urinary arsenic levels during exposure to tap water containing arsenic, e.g., 15 micrograms per liter, with urinary arsenic levels after exposure to essentially arsenic-free bottled water. It's unclear to us how this could be relevant given that it appears that there is a different arsenic species that young children are exposed to from CCA-treated wood.

The third one, assess the value of arsenic speciation analysis in explaining variability and urinary arsenic levels. It was not really clear how they intended to do that. how would speciation explain variation in urinary arsenic levels. There was no discussion of that that I can recall.

The third one was to assess whether 5-to-10-day period is sufficient to allow for substantial elimination of the body burden of arsenic resulting from chronic low-level exposures. Quite apart from the issue of the different species, there is the question of whether the washout period may in any case be concentration dependent.

And there is some evidence present in the report that in fact elimination is triphasic. And it may also be concentration dependent. And the exposures from the CCA-treated wood are likely to be quite a lot lower than were in Albuquerque.

The fifth one was to develop estimates of interindividual and intraindividual variability in urinary arsenic levels. Use these data to refine power calculations to determine necessary sample size for the main study. Now, given that the levels of exposure in the study are so much different to what we might expect in a proper CCA-biomonitoring study, it's difficult to see how these results could be used for power calculations.

And the sixth specific aim was to determine based on the results of the first five aims, that I've just discussed, whether the main study is feasible; and if so, the optimal study design. And I think given apparent irrelevance of the first five specific aims, it's difficult to say that no relevant judgments can be made from them regarding the sort of biomonitoring study I

think we're looking for.

That's probably about it. Just to mention also, I thought the questionnaire had some problems. And some of the questions seemed to be addressing, asking the parent about their behavior, their exposure rather than the child. But that's more in the nature of one of the minor comments.

DR. HEERINGA: Dr. Styblo.

DR. STYBLO: Well, I think the previous comments were very exhaustive. So I have just one or two short comments.

I'm not sure there's an analytical chemist on the Panel on the team at this moment. Whether we realize it or not, the analytical data are a significant part of information we base our exposure estimates, and consequently risk evaluation on. And we seem to kind of forget this fact. We need good analytical labs and experts being on the team for similar studies from the very beginning, collecting samples, and submitting them to the lab. And then realizing there is a problem, it may be

too late.

Speciation of arsenic today a relatively routine method. However speciation of oxidation states for methylated arsenic species which has a huge toxicological implications is more tricker, trickier, and requires special attention and well established method in labs.

And I guess that's the major comment I had.

DR. HEERINGA: Thank you, Dr. Styblo. Yes, Dr. Wauchope.

DR. WAUCHOPE: I'm probably the least qualified person in this room to ask this question. But I have a little problem with what this issue group is saying in that they're saying there's a poor comparability to between doing a biomonitoring study on inorganic soluble arsenic versus what's in dislodgeable residues. But I think what we've said earlier is that probably this complex has been identified dislodgeable, residues is probably not be active species in uptake. And I still think that the most likely candidate for childhood exposure is inorganic arsenic 5 and possibly 3. So it

seems like we're a little too strong a rejection of arsenic biomonitoring as to its usefulness.

DR. HEERINGA: Dr. Ryan.

DR. RYAN: I don't think there was any statement we made that would suggest that biomonitoring wasn't a good technique. What we were criticizing was using this particular mechanism of trying get at the biomarker for CCA-related exposure using the drinking water target. It just seemed inappropriate to us. We're strongly in favor of a biomonitoring study. We just don't think this is the right one.

DR. HEERINGA: Dr. Portier.

DR. PORTIER: I'd like to address three statistical issues I think that are problems with this and they've been alluded to. One is the power calculation. The proposal references the work of Calderon and Wyatt. And from what I can read, there's probably information in these studies to give you some indication of what expected levels are going to be and what underlying variability might be. So there's no reason for the proposal not to

present at least a preliminary power analysis. That also forces them to say up front what kind effect or what's the magnitude of the affect they're looking at which is something we don't see in the report. So I think there's a possibility for a power analysis.

The second thing is that, as was mentioned by Dr. Bates, one of the objectives is to look at intra- and intravariability. And yet from what I can gather, after the washout period, there's only going to be one if not two measurements of urine arsenic samples taken. And I think that's going to be inadequate to look at interperson variability. They definitely need more samples; otherwise, we have no idea.

And that's a key term we've talked about the last couple of days, the fact the we don't know what happens within a child. We have some information what happens between children, but really very little what happens within. And this would be a kind of a simple way to expand it.

The third issue is kind of an interesting one.

Most study designs, we're looking for an effect that the effect of the treatment is to increase something. In this case, the effect of the treatment is going to be remove arsenic. And as I understand it, arsenic right now, dietary arsenic, leaves these children with probably something like a 10 part per million level in their urine. And we're going to take about half of that out.

So now we're going to be down at 5. And probably the detection level is 1 or 2, depending on whether they have a good chemist. Right? So we're going to be running into no-detect situations on the treatment end, and there's no discussion of how they're going to handled that both in the estimation and in the analysis point of view. It's going to be a big headache on that end and could wipe out all the gains in good design if they don't think about that up front.

DR. HEERINGA: Thank you, Dr. Portier. Dr. Styblo.

DR. STYBLO: Additional comments which is listed in detailed comments for discussion.

I had one suggestion which may or may not be accepted by others. It would be nice to see some kind of approach, some kind of data, on actual exposures. In these terms, I liked the proposal outlined very briefly by Dr. Solo-Gabriele here because that involved at least brief monitoring of CCA residues on palms. I'm not looking for a detailed quantitative monitoring, but simply semiquantitative yes or no for each day would be very useful for data interpretation and evaluation. So the question is how much would be needed; what it would require to have this component included in a reasonable way.

DR. HEERINGA: Thank you. Dr. Ryan.

DR. RYAN: I'd just like to comment on the points brought up by Dr. Portier. In deference to time, we have a 10-page document. I just elected not to read the entire thing. Each of the points that you made there is something in there about that. We're concerned about for instance the 40 sample size. We have no idea where that came from. And essentially, we would like to see

power calculations as well, what kind of difference are you likely to see.

Dr. Reed just asked me what's the limit of detection on this. Essentially, we'd like to find out. And that is an exact point that we have in here. Do we have the possibility of showing the effect that we want to show if we're going to see a reduction of, say, 5 micrograms per liter in the urine. If that's what our expected drop is, do we have the analytical chemistry power and the statistical power to see that. And that's one of the points we've raised in here. So there are several points on the statistical issues that focus on some of the points the have just been brought up.

DR. HEERINGA: Dr. Matsumura.

DR. MATSUMURA: Yeah, would I like to support what Dr. Styblo said. And so long as it's done properly before and after and method, it will give us at least an idea as to how much, at least what those children playing around will be exposed. So initial step can be established. So, of course, you know, that's only three.

But there is already some indication that you can find that's the radius, whatever that you call, really in the wash. So why not start from the beginning, saying do they really get exposed or not.

DR. HEERINGA: Dr. Freeman.

DR. FREEMAN: Yeah. Should you go on with this? There are changes in your questionnaire that are really need. You need to have a proper dietary questionnaire. Just asking these bunch of questions at the bottom of the page isn't really adequate. That means Setting it up, basically going through food and drug administration, whoever it is the does dietary analysis, and really having an understanding of all the sources of dietary arsenic just not the common not the ones, and not the ones that are common to North American diets but perhaps to Hispanic or Mexican American diets.

Another thing. You have a number of questions about whether you have a wood deck or a structure at your house, but you haven't filtered for all the other wood decks and structures these children may be playing on in

municipals or neighborhoods. And if you're going to do part of it, you have to do it thoroughly for all of the potential sources.

I guess that's it.

DR. HEERINGA: Thank you, Dr. Freeman. And, again, I think an additional comment on thoroughness of background and environmental observation.

I'm not seeing anymore comments on this question for this issue. Dr. Hattis.

DR. HATTIS: I just have a minor suggestion to the folks who are designing biomonitoring studies that some consideration be given to biomarkers based on longer averaging times. Recently, there's been a paper publish using toenail arsenic to reportedly to detect decreased repair gene expression in relation to drinking water arsenic that utilizes the toenail as an apparently useful biomarker. Although the exposures that are reported, the drinking water levels that are reported, appear to be in the 10 micrograms per liter range so in the Albuquerque-type range that toenail arsenic appears to

have some, be used in this case. But because this is a compartment with a longer averaging time, it might well be less subject to day-to-day fluctuations than the urinary levels.

DR. HEERINGA: Any questions or comments?

At this point, I guess, Dr. Dang, if we can move on to Part B of Question 11.

DR. DANG: Actually, when I mentioned about OPP peer review their proposed, I have some kind of summary. I'd like the Panel members, if they need it, copies right here can be distributed to everybody.

DR. HEERINGA: So in your earlier comments you mentioned that you had a chance to preliminary review the protocol for this study and you have written comments. If you could share those with the Panel. We'll include them in the docket as well.

DR. DANG: Yes. Sure.

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

DR. DANG: Question B: The Panel is asked to describe approaches for gathering additional data -- e.g.,

data on the efficiency of transfer of surface residues to the skin surface (which has been identified as one of the most critical model inputs based on the uncertainty analysis) -- to improve the estimates of exposure and or the level of confidence in such estimates, and with respect to these approaches, as well as the proposed pilot study, to comment on the cost of data generation the amount of time to generate the data, the degree to which the data will reduce uncertainty about the accuracy of the model estimates.

DR. HEERINGA: And, Dr. Ryan, I believe you're again the lead discussant for the group,

DR. RYAN: Still on the same question; still on the same issue. We essentially elected not to design a new investigation here. We simply did not have the wherewithal to do that. And it is the belief of the panel of discussants that we have addressed some of these questions in the evaluation and critique of the initial proposal. The proposal does not address the uptake of arsenic from CCA-treated wood products, a critical flaw

that should be addressed in a pilot study. But rather than coming up with a design for the complete study, the critical parameters needed, we are for what may be called a roadmap with the negative connotations that it has, of how such a study might be developed.

We believe the most appropriate method for developing a pilot and then a full biomonitoring investigation through the active engagement of the public, EPA, and representatives of the industry in the process. This diverse group should come up with an RFA, RFP type approach for such an investigation and solicit proposals from the general biomonitoring community. in this way, EPA and industry are likely to get much better ideas in the collection of data appropriate for uncertainty reduction and improved parameter estimates for the SHEDS-Wood model and to improve the general understanding of the methods and magnitude of effects on CCA-related exposure.

The cost of completing this investigation may be relatively high. But if properly designed, will reduce uncertainty in the model by a substantial amount.

I ask my colleagues to comment as they see fit as well on this.

DR. HEERINGA: Dr. Bates or Dr. Styblo? Dr. Bates.

DR. BATES: I don't have very much to add. Just perhaps to reinforce the comment that's been made about Dr. Solo-Gabriele's work. And we saw that as the better model for the way forward.

DR. RYAN: That is mentioned in our comments in a couple of places,

DR. HEERINGA: Thank you very much, Dr. Ryan. Other members of the panel comments at this point?

And Mr. Jordan.

MR. JORDAN: A question if I may. My sense from Dr. Ryan's comment is that the Panel views biomonitoring as the most profitable place to pursue additional investigations to reduce uncertainty. There have been over the course of the meeting a number of other ideas about collecting data to address specific limited data sets and so forth. And our hope was in asking this

question that the Panel would be able to offer some sense of priority among those different investigations so that we'd be able to see where, in colloquial expression, we'd get the biggest bang for the buck.

I infer from Dr. Ryan's comments the biomonitoring, even though it might be quite expensive, represents the Panel's highest priority. But I thought I would ask and see if that inference is correct,

DR. HEERINGA: Thank you for that direction. I think that's an important point to the Panel. And I think, Dr. Ryan, if you'd like to respond in regard to the biomonitoring of relative importance.

DR. RYAN: I think the biomonitoring is of relatively high importance. Your statement was the most important. I would say, certainly, a most important, the indefinite rather than the definite article. And would have to do a lot of balancing before I would say this is the thing to get first. It is certainly among the most important things in my estimation and certainly from this.

Comments from my cohort here? And I certainly

can't speak for the entire panel. I'd like to hear what other people think about this as well.

DR. HATTIS: Yeah, if it were successful, the biomonitoring evidence would be salient for the over all analysis. The chance of success, I think, needs to be weighed a little bit because it's quite possible that background fluctuations are going to be a problem here. So I think you have to judge a little bit the high likelihood of success in quantifying a more modest component contributing to the overall uncertainty and likely cheaper study. So that all of that goes into the priority setting mix to some extent.

So that while I can't -- ideally one could do a value of information analysis. But an important input to a value of information analysis would be in terms of how much confidence limit reduction you get per dollar of research cost. An important component of that is the likelihood of producing data that significantly changes one estimates of either overall variability and uncertainty, overall uncertainty, or a specific component

that contributes to uncertainty and... So that likelihood of success as well as the cost issues. It's not easy for me anyhow for me to imagine off the top.

DR. PORTIER: It strikes me that the biomonitoring is probably most important for this particular application of the model in the sense that it provides the best validation of where you are with the model. But if you take the broader picture of what this models is going to mean to the Agency and other applications, some of the childhood activity information, increasing that database seems pretty important. If we move away from arsenic to pesticides and other situations, you're going to want that same information for those other applications.

So there's a synergistic effect that happens in that investment that helps this model to validate components. It may not do as good in terms of convincing everyone that this is the perfect model. And you may need to do both in the short term. But I'm sure Dr. Freeman is going to follow up on this.

DR. HEERINGA: Dr. Freeman and Dr. Styblo.

DR. FREEMAN: I love the idea of biomonitoring. But you have to remember to put this in the context of who it is you are biomonitoring which are 1 to 6 year olds. The 3 to 6 years old, it's not too much of a problem. Below that age, you're dealing with kids who are not toilet trained which means you're going into either diaper inserts or gauze pads inside the diaper or trying to develop a chemical analysis for these, wonderful modern diapers they have that don't leak which means it's almost impossible to extract whatever goes into them out of them once it's there.

And I know that RTI and Battelle have been working on these activities. But it's a challenging. Then you have to ask the questions: If you're doing all these chemical treatments of the artificial diaper in order to get out the urine, what are you adding to the urine that you maybe don't want to be adding when you're doing the analysis of what you're interested in.

Hand wipes are a lot easier to collect from

kids. The issue there is you have to put it within a context which is what are they doing and what have they been doing over the time period that that hand wipe or rinse represents. Which means that the studies have to be sort of carefully crafted. It's almost like doing a bench study or a laboratory study except you're doing it outside.

Dr. Kissel has also played these games. And he has an understanding of the challenges.

DR. STYBLO: I think once you realize that although we will call a viable project, it will be a costly event even in the small frame. There will be something the needs to be clarified before this pilot project starts. And I will talked about one I am closely familiar with which is the speciation analysis of arsenic in urine. It would be too late to find out that our analytical methods are not capable of proper speciation analysis at these low levels of exposures. So one thing to clarify before this project even starts is do we have appropriate analytical methods that would reflect our

requirements.

Talking about analytical approaches, you know, although there have been great advances during the last 5, 10 years; there's been more done around the world. And we are kind of behind now. Strangely, we're behind in the United States. There are laboratories in Europe that are laughing about our atomic -- and spectrometry approach for arsenic speciation using the current atomic force and detection.

There are developments going on right at this time in European labs, and I can name some of them, that improved instrumentation that means a greater order of magnitude greater sensitivity of high generation approach for atomic absorption or for atomic fluorescence. And that's something that needs to be considered.

Personally, we have somebody recently a small Fogerty Grant, with a lab in my homeland, Czech Republic, that is developing this kind of instrumentation. I'm not pushing the idea that this has to be the lab that could be involved. But there are ideas how to improve

instrumentation and methodology that would mean greater increase in the sensitivity of the speciation methods for arsenic.

DR. HEERINGA: Yes, Dr. MacIntosh.

DR. MACINTOSH: I'd like to ask a two-sided question that may be kind of naive because I'm not that experience in design of biomonitoring studies and their interpretation. But I wanted -- I think it might be useful to think about how the results of a biomonitoring study would relate to evaluating the performance of the model. And a biomonitoring study, we're going to get concentrations of arsenic, hopefully, in urine. Maybe that's going to be expressed as simply a concentration or maybe an excretion rate. But the model predicts absorbed doses of arsenic. It doesn't predict excreted arsenic. So in some sense, there's a fundamental mismatch in the experimental data with the model data.

And so my two-sided question is: What does it mean if the molar amounts of urinary arsenic are less than the SHEDS absorbed doses of arsenic and what does it mean

in the reserve?

DR. HEERINGA: That's an open question. I'm not sure anybody is going to answer.

DR. HATTIS: To properly interpret the data, you would need some kind of a pharmacokinetic treatment of absorption and excretion of arsenic. But such treatments are not unknown in the literature.

DR. Macintosh: So at that point we introduce another layer of --

DR. HATTIS: Yes.

DR. MACINTOSH: -- modeling that we haven't even considered yet.

DR. HATTIS: Yes, indeed.

DR. HEERINGA: Dr. Chen.

DR. CHEN: At this moment, if we are talking about arsenic in water and there are human in vivo study. And it seems like arsenic once it goes into the body, then you excrete for a very short period of time the show urine. And whether it's in it's original form or in it's metabolite. I think this is a main reason that they are

using the arsenic in urine as an indicator. But when we were talking about arsenic in the CCA-treated wood, after it goes through the discussion. And I think we don't know. But I think that's the main reason that they design arsenic in the urine because of inorganic arsenic in the water studies.

DR. CHOU: Actually, one of the references cited by Caldron et al., Actually in there, there's a correlation between arsenic in drinking water and urinary arsenic. This is done in the United States. I think that is one of the references listed in the study. I don't know whether it's sensitive enough to detect low level increment of urinary arsenic in children. But in theory, it's a sound assumption that it should work.

DR. MACINTOSH: I am somewhat familiar with that literature and those relationships in some of the studies by Calderon and her colleagues. But I'm still not sure that that addresses this mismatch in the type of data produced by the model versus what would be collected in a biomonitoring study.

It seems to me if we wanted to know about absorption, that we would be better served to design an absorption study. All right. And that would get more directly at the parameters of the model that we seem not to know much about.

DR. HEERINGA: Dr. Ozkaynak.

DR. OZKAYNAK: Just pursuing that discussion. I think it's an important discussion. Another way of trying to sort of eliminate or reduce the mismatch is to consider a PBPK model be incorporated with the SHEDS model.

DR. HEERINGA: Any response?

DR. MACINTOSH: I agree.

DR. HEERINGA: Dr. MacIntosh, you agree.

DR. MACINTOSH: I agree.

DR. HEERINGA: Any other comments on the extension of the sort of proposed concept for the biomonitoring study as having as an endpoint urinary levels of arsenic? Yes, Dr. Wauchope.

DR. WAUCHOPE: I guess I'm addressing the question up there, not so much as the biomonitoring. It's

asking for any kinds of approaches.

DR. HEERINGA: Yes.

DR. WAUCHOPE: This question my be more a function of not having been able to go through the six inches of paper. When I tried to mechanistically make the connections between contact and then adherence and then, you know, hand-to-mouth and then ingestion, I have a good deal of trouble figuring out exactly how the parameters all fit together. I'd like to be able to do a back-of-the-envelope calculation of all the means, for instance, and see if that works for me.

So some way of perhaps -- I don't how to tell you. It's easy to criticize. Hard to come up with something creative. But some way of linking all of these parameters so that the mechanism is clear to perhaps a list for someone who doesn't do this work all the time.

What would be wrong with doing an experiment where you simply -- I'm starting to sound like a single-note singer. What would be wrong with doing some kind of experiment where you simply look at the most

soluble fraction in the surface of the wood. And there ought to be a mechanical way to measure how much of that gets from wood surface to gut. The ought to be possible do mechanically without some sort of in vitro experiment. We simply look at transfer.

Maybe that's already been done. Maybe it's obvious from your data that it's there. But that number would relate directly to all of the well drinking water studies that people have done. I don't know. Maybe it's obvious that that's been done. But I just would like to ask and get a response to that.

DR. HEERINGA: Are there any additional comments on this point?

Excuse me a moment. I want to confer with.

At this point, we have an opportunity. And I think that we'll honor that in the interest of sort of the maximizing the accuracy of our information to have Dr. Beck come forward just to clarify a few points on the proposed monitoring study as discussed. Dr. Dang, is that agreeable?

DR. DANG: Yes. Fine. I agree with everything here.

DR. BECK: First of all, thank you for your comments. I just have some points of clarification. First of all, I think we want to emphasize that our aim is not to extrapolate from this proposed study which the more I think about it, you are Dr. Bates is correct. It's really more of a feasibility study.

We do not aim to extrapolate from this to what might be the impact of CCA mitigation but to inform us as to considering what magnitude of impact the model predicts as far as say a mean population, exposure of CCA-treated wood, what can we detect in the urine. We may find out, for example, that the effect is too modest to be detectable in urine considering the inter- and intravariability in urine arsenic levels.

So I wanted to emphasize that our aim isn't to extrapolate directly from this to any CCA exposures. But to use this to inform the analysis more appropriately.

We probably could have provided you with more

information on QAQC. We have been work being with Dr. Calman at the University of Washington as the analytical chemist. He certainly is very expert and experienced in urine arsenic measurement, including speciation. I don't recall what the detection limits are, but we're really talking on the order of a part per billion or so. We will be using a sensitive method.

And as part of one of the aims of the study is that Dr. Calman intends to use this study to develop improved methods for improving the analytical detection of the methods of arsenic.

I believe -- were those the key points?

There was discussion regarding power calculations. We've done some limited power calculations. The difficulty with that is that, in order to do it, you need to have a good estimate of variability of urine arsenic in children. And the data are really quite limited. And you can get quite a range in power calculations in terms of number of children you would need to, say, detect 2, 3, 5 micrograms arsenic per liter

urine.

We got very wide ranges in the number of individuals that one would need depending on which underlying urine arsenic study we used for children. So our aim was to use this study itself to develop the power calculations for what would be a fuller study.

And I just wanted to end by saying that as far as the full study, we've been talking about biomonitoring. It's not clear to us that urine arsenic is not necessarily the best measure. It may turn out that it may be more useful thinking of some of the points that Dale Hattis raised, to do video tapes and to do hand wipe analysis at different times of children engaged in play activities.

This is our start. We don't have a final protocol. But certainly our aim is to do some of this discussion of the Solo-Gabriele method. I mean certainly we would want to do something along those lines. But we want to be sure that we've designed it to the best of our capabilities before we get to the point.

DR. SHARMA: I think Dr. Beck captured it. To get to Dr. MacIntosh's point. I think there are many endpoints that you can get other than just urine arsenic which can feed into the model. So I think, when thinking about a main biomonitoring study, I think we should think in addition to those points. A lot of those are uncertainties within the model as we've heard over the last two days, particularly the hand-to-mouth pathway. And, you know, we do want to design the best study. And I know you saw a study yesterday which just had 10 children and didn't seem to have appropriate controls even. But we are trying to do the best science possible in developing this study.

DR. HEERINGA: Thank you very much, Dr. Beck and Dr. Sharma for those qualifications.

At this point in time, we have one remaining question. And I'd like to suggest the we take a 10 minute break, 10 minutes only, and reconvene 2:55. And we're due back here at exactly 10 minutes.

[Break taken at 2:43 p.m.; meeting

reconvened at 2:55 p.m.]

DR. HEERINGA: Let's reconvene to Issue No. 12.

Dr. Dang, I believe we're up to issue No. 12. And if you would be willing to read the introduction and the first question.

DR. DANG: Sure. Issue No. 12, Prior to the availability of probabilistic models, such as SHEDS, OPP estimated the lifetime average daily dose (LADD) and corresponding cancer risk to pesticides via a deterministic approach using central tendency input parameters (median or mean values). Probabilistic models now allow OPP to express input parameters as distributions and subsequently generate a distribution of LADDs and corresponding pesticide cancer risks. In other words, the deterministic approach results in a single cancer risk value and the probabilistic approach results in a distribution of cancer risks values.

Question A: The Panel is requested to comment on whether in this probabilistic approach of using the upper bound arsenic cancer slope factor combined with

using high-end LADDs would result in a significant overestimation of risk for the more highly exposed percentiles of the population? If this is an overestimate, what other values would the Panel recommend using as replacements, or in addition to the values that were used that would minimized the overestimation of risk without substantially underestimating the risk for such percentiles.

DR. HEERINGA: We have presented Question A, and Dr. Hattis is the lead discussant for this issue.

DR. HATTIS: I guess the version of the question that I have in my document refers -- makes a reference that I don't understand. What I have -- I was hoping that you would clarify it. Essentially, in this assessment, the estimated risks are considered approximations because inaccuracies may occur when exposes to some of the cross roots at the cortile level especially in the upper percentile.

And I couldn't identify where that had been done in this risk analysis or this exposure analysis. And

maybe that's left over from some earlier draft of the questions or something.

DR. OZKAYNAK: I don't believe it's done in the exposure or dose assessment.

DR. HATTIS: I didn't see it.

DR. OZKAYNAK: I think maybe it's in the risk assessment.

DR. DANG: Actually, it's in this. Based on the exposure parts. And we would calculate the risk is try to sum altogether. But in the upper percentile, we tried route to route. And we tried to distinguish between the residue and the soil source. So the reason we say when we -- maybe I better present the slides I have.

DR. HEERINGA: Dr. Dang, these are slides to clarify the question.

DR. HATTIS: I don't think that was done here.

DR. HEERINGA: Dr. Portier, do you have a comment while we're waiting?

DR. PORTIER: Isn't it the fact that the SHEDS model does the integration of this exposure for us across

the -- so in a additional approach where you might be looking at sources, you may be take up the quartiles and then summing them across to multiply. The SHEDS model does that integration does in a much more elegant way I would say.

DR. OZKAYNAK: Correct.

DR. HATTIS: The summation is in terms of estimated absorbed dose. So that's appropriate, I think,

DR. DANG: Yes. A slight difference. It's not the -- but we try to show you the slide what I mean in the next one. It's the cancer risk.

In here, we don't have detailed data from exposure, so we use the quartile to sum it all together. We try to say it's in upper percentile is what we say could be inaccurate compared in exposure based on the Monte Carlo distribution. This is one question we tried to ask the panel is: Is the Panel -- should I read the next Question B since we are talking about this issue?

DR. HEERINGA: That actually occurred to me that you could read Question B because I think we have a more

specific answer to that one which might evolve --

DR. HATTIS: I have a much more specific answer to Question B.

DR. HEERINGA: Please, Dr. Dang, why don't you go ahead and read Part B. And then we will keep in mind the discussions of Part A simultaneously.

DR. DANG: Sure.

Question B: The Panel is requested to comment on the range of the percentiles, if any, at which there is a significant decrease in the reliability of the estimates of risk.

DR. HEERINGA: Dr. Hattis.

DR. HATTIS: The technical aspects of this question are best addressed by multiple parallel simulation runs. The differences in percentile estimates among runs give the stability of the calculated values directly. Parallel runs should be standard in our view, my view anyhow, of this kind of modeling. Uncertainties analysis -- two dimensional uncertainty analyses composed of 180 uncertainty runs of 480 simulated people each

clearly in this kind of case, because you're only dealing with 480 people, it's likely that you will find the 99th percentile level would be rather unstable because it would only be based on five people per run. But in any case, the actual quantitative stability is much easier for you folks to calculate then for me to imagine.

Now the second -- however I thought I read into your question a bit of a policy aspect of the question. And there's an underlying policy question, the calculation and the publication --that the calculation of the publication specific percentiles of variability and uncertainty distributions. higher percentiles are generally of interest, for more of interest, for variability than for uncertainty. And I've got a reference on that to a paper and why that is.

As it's reflected in SHEDS in a greater number of variability versus uncertainty iterations in the current approach. However, this group as technical specialists should not comment to overtly on exactly which information for points on the variability and uncertainty

distributions are most salient for particular kinds of decisions under the Agency's legislative...

And maybe you didn't ask me that overtly. I thought I saw in the subtext of the question from previous discussions of the dietary issues whether the 99.9th percentile is of interest. And to some extent, the response to that is you guys are in a better position to understand your legislative mandates than we are.

DR. PORTIER: A quick summary. Basically, what we're saying is that if you pick an upper percentile from a regulatory viewpoint, you can run enough simulations to get that as accurate as you want to get it. You're just going to have to run your simulations over and over again. You may have to increase the number of individuals to get that value as accurate as you need it. It's not something that's statistically derived beforehand. It's an output of how much how much effort you put into the simulation process. So we're kicking it back to you on this one.

DR. HATTIS: Now I could go back to A if you like because we've already sort of made some comments to

some extent on the A part.

PANEL MEMBER: Maybe other people should comment on B.

DR. HEERINGA: I'd like to add a comment to, I think, Dr. Hattis and Dr. Portier have said too. And that is through repeated simulations and increased sample sizes, conditional on the performance of your model and your inputs, you can fully assess the variability and uncertainty over those range of inputs. In other words, there's a bigger issue of do you represent their uncertainty in departure of any inputs in the model algorithm and mechanisms from the real world. We all know that that's the bigger issue.

So with regard to the stability of the percentile distributions conditional on your model and the established inputs, you can, in fact, run large enough and enough simulations to eliminate, I think, essentially quantify the uncertainty at that point.

Dr. Macdonald, please.

DR. MACDONALD: I wish I understood the question

a bit better. But from the wording of Part A, I see at least one of the issues is: Is it okay to do a number of different things, get a high-end estimate from each one and then combine all the high-end estimates. That's what I think you're asking in Part A. And the answer I would give is, no, it's not a good idea. You should always be going back to the complete distributions and somehow combining all the distributions and then get the upper percentiles of the resulting estimates the you want.

DR. HATTIS: And in the case that you have some uncertainty on the tox value that's not fully analyzed yet, the ideal situations would be in fact to go make whatever to make a -- an uncertainty distribution for the tox values and combine that with the uncertainty distribution and variability distribution for the exposures.

In this connection. I think it would be much better for you in the document not to characterize the current 3.7 or whatever it is microgram per risk number as an upper confidence limit because, first of all, it's not

a Q1-Star; it's not an upper confidence limit from the Morales analysis. It's a central estimate from the projection from the Morales analysis.

Second, it seems to me important that you mention that -- you do mention the NCR study. But you don't mention, and I think it's reasonable for you to mention, that the NRC risk estimate would tend to raise that. It's not also out of the question to mention Dr. Beck's point that there are claims anyhow that the NRC estimate is inconsistent with the Utah data.

Now it may well be that in the NRC report, which I have not fully read, there is a treatment of that issue. And I would look in there for that issue. And they may have reasons for not being worried about that.

But there are much more -- obviously, there's a much more sophisticated body of folks who have looked at that than I can muster at this stage.

But nevertheless, I think it would be -- the principle is that even if you for regulatory decision-making elect to use a number other than the NRC

estimate, it's fair to the reader to disclose that there is this other estimate and that the effect would be to somewhat increase -- well, actually, rather considerably increase the reported risks.

I think it's also fair to the reader, since this is the EPA, part of the EPA, and another part of the EPA has proposed an adjustment to the cancer potency factors, to mention that.

Now the response that was given during the discussion earlier was that the childhood risks are included in the Taiwan and Chile populations that were studied. And that's quite right. But, certainly, the pattern of exposures that was represented in the epidemiological population is quite different than the one that's being modeled here; in that generally you have lifetime exposures and the doses in those epi studies are calculated on a lifetime basis, or at least on a lifetime-to-cancer development basis. Whereas or lifetime to some 10 years or something before in some cases perhaps.

But the doses that are being modeled here or the exposures that are being modeled here are solely those to young children. Okay. So it's not at all clear that the presence of the children as part of the exposures is represented in the average lifetime cancer risk that's calculated from the epi studies.

I would suggest that in fact some multiplicative adjustment is still likely to be required if you consider that arsenic is in the mutagenic carcinogen category, and there's discussions of that one way or the other. Suffice it to say that by inhibiting DNA repair processes which is relatively well documented, you can show the modeling that if that's a competitive inhibition that's just like the dose response form that you expect from a directly mutagenic carcinogen. If it's a direct competitive inhibitor, that's going to be linear at low doses. If it's an inhibitor that is secondary to some toxic process, that's an entirely different matter and you could have any kind of dose response shape the you like.

If on the other hand arsenic is acting by

changing methylation patterns and that happens nonlinearly as a function of dose then, again, that's a different category of dose response projection. We obviously can't resolve that here. But it seems to me that some paragraph or to mention of those possibilities is fair to include in the summary discussion of the cancer risk conclusions.

DR. PORTIER: I just wanted to point out, Dr. Chou wanted to mention that in the Exposure Factors Handbook the cancer slope factor term is still at 1.5. Right? So if you go by your official published, that's the number that you should be using and that number probably needs to be changed.

DR. HATTIS: That's also based upon the skin cancer. And you might also mention that in fact there are some risk of skin cancers that should be considered to be likely in the light of the large body of human epidemiology available for that site.

DR. HEERINGA: Just for clarification, Dr. Hattis, there are published cancer slope factors for liver, bladder cancer and a separate slope factor for skin

cancer. And these are treated as additive or...

DR. HATTIS: Well, the risks -- to my knowledge, there's no reason to suspect that getting skin cancer would preclude you from getting one of the others. I think if you get lung cancer, the experience is that you're not available to get other cancers.

DR. HEERINGA: They are separate. Thank you. If I could go back. Dr. Portier.

DR. PORTIER: I was going to say the other thing is Dr. baits wasn't here and he asked to mention a little more strongly than Dr. Hattis the fact of integrating over 70 years. He would much prefer to see you integrate over a much shorter time period because of the nature of dealing with children and the fact the their cancers are not necessarily going to be expressed at 65. They may be expressed at 19 or earlier in this situation.

DR. HEERINGA: This is the issue of the 75 year basis for the calculation of LADD.

I'd like to return in terms of response from the Panel to Part A. I read the question, part a, as Dr.

Macdonald did. And just to be clear, Peter, I think you've stated that if we have two values from independent processes or semi-independent data sets that establish upper percentiles at some product multiplication of those is not by any means an upper bound for their joint distribution. And I would agree. We're hampered in much of this analysis by not understanding the covariance structure between so many of these parameters.

If we knew that, obviously, then the simulation models themselves would produce the correct estimates and with the appropriate sample sizes and repetitions, estimates of stability or reliability. We do not know what these covariances are. But most of the world doesn't have, certainly, perfect covariance particularly at the upper percentiles at least partially independent observations.

So taking the extremes of those two, if we could view those as extreme or extreme values in terms of assumptions about the distribution and just taking the product, I think, is probably likely to exceed any real

world simulation of those same individual percentiles. There tends to be a regression toward the mean because of lack of perfect covariance between many of these observations even in things which we feel are correlated highly say at .4 or .5 in this world. The regression toward the mean compared to just -- multiplication extreme values.

Comments from Dr. Macdonald, Dr. Portier, or Dr. Hattis on that.

DR. HATTIS: I certainly agree. And I also think that, you know, one is well over due in making some distributional treatment of the tox values in general. And in this case, there's much more uncertainty that results from the transport -- to some extent from the dose response relationships for arsenic. Although there we have also some considerable amount of data. But also there is uncertainty related to the transport of observations from Taiwan and Chile to the U.S. because we have very different background cancer rates. And that's one of the things the NRC addresses in some detail I

believe.

But even so, one could use at least, some estimates of uncertainty derived from their analysis, I think, separately for Chile and Taiwan or combined to get some sense of the plausible range of cancer potency values.

DR. RIVIERE: I have one question. The word skin cancer came up. I didn't think you were looking at skin cancer rates on this study.

DR. CHEN: Well, the reason that we are looking to the lung and bladder cancer is starting from 1999 NRC report, in the report they find out the lung and bladder cancer can most represent the arsenic kind of exposure or something. And they suggest to do this kind of risk assessment based on do they individually then combined.

DR. RIVIERE: That's what I thought. Because if you were going to do skin cancer, your absorbed doses probably are irrelevant. You need to look at the dose that's in the skin. And, therefore, we haven't discussed any of that --

DR. HATTIS: It's not from skin exposures. It's from drinking water exposures. the quantification of the skin cancer always has been from the drinking water not a direct skin pathway.

DR. HEERINGA: Good. I didn't mean to confuse that issue before. But since the factor of 1.25 had come up, I think, it was associated with skin cancer.

DR. CHEN: And 1.25, and we did some kind of comparisons in our document. And we do know that there's some uncertainty. And once we have the final kind of cancer potency factor decided, I think we need to have some clear kind of explanation why we choose that number. And we will try to prepare a document.

DR. HEERINGA: Dr. Dang, a question on behalf of the Panel to you and the EPA. The final -- we've seen a preliminary risk assessment report, which is based on a cancer slope factor of 3.67. We understand that separate from these meetings that the Agency is reviewing cancer slope factors for arsenic exposures. If and when the Agency makes that decision, would you expect to revise

this probabilistic risk assessment in light of the Agency decision?

MR. JORDAN: The answer is, yes, we would.

DR. HEERINGA: And then I think as Dr. Chen pointed out the actual mechanism by which you derive that, I assume that will be explained by the Agency. And if you modify it for this application, it would be explained as well.

DR. JORDAN: That's correct.

DR. HEERINGA: Thank you very much.

At this point, seeing no other comments on Question 12, I'd like to, before we wrap up, offer members of the panel an opportunity to make a comment on any other aspect of the preliminary exposure or the probability risk assessment documents or processes. We've covered quite a bit. But if there's anything you feel has been left out or that you want to be sure that you state in open forum, I think this is the chance.

DR. FREEMAN: This basically to thank these guys, Dr. Zartarian and her colleagues, for doing just an

amazing amount of work in a fairly short period of time and responding to all the questions that have been had.

DR. ZARTARIAN: Thank you from me and my colleagues.

DR. HEERINGA: Dr. Kissel.

DR. KISSEL: I just wanted to emphasize. I don't know if this came across or not. But one of the industrial commentors the other day gave a sort of impassioned speech not to make regulatory decisions on the basis of this existing model which is not something we were directly charged with. But just, I guess, to reinforce any protection against abuse in that direction, I'd like to say that the current uncertainty analysis doesn't allow you to go to that stage, that a more complete uncertainty analysis would be necessary in order to evaluate percentiles at which you might want to make decisions. And I would hope that no inference of license to go that way would be derived from this panel.

And if anybody want's to disagree with me is okay because I can't really speak for the whole panel.

Just to get it on the record, I don't think that we have turned you loose to regulate using this model even though we have addressed particular issues here and said that individual parts of this model were either okay or not okay.

DR. HEERINGA: Dr. Kissel said it. I think the objective of our panel is to present a scientific report on these observations. And your decision is going to be implicit in that. We're an advisory panel.

DR. HATTIS: I think that I would disagree in part. That I think that there is significant uncertainties, but this is a fuller analysis. And to combine with the sensitivity analysis that have been done which covers some of the key points that have been raised here provides some information that a decision-maker might want to refer to. And it certainly is much more extensive than I have seen done for most cases where regulatory decisions have been reached. So I don't think that you would discard these data if you were making a regulatory choice which they're not.

DR. KISSEL: Perhaps I should explain just a little. I was speaking more in terms of using probabilistic models directly in the regulatory process which is -- we're kind of on the cusp of moving to that stage. And in the absence of a full uncertainty analysis, I don't think we've actually there. In some ways this is a very sophisticated deterministic analysis. So I guess I would just caution that I haven't seen here what I would like to see prior to implementation of a truly probabilistic approach to regulation.

DR. HEERINGA: Thank you, Dr. Kissel. Dr. Macdonald.

DR. MACDONALD: Yeah, I'd just like to pick up on an idea the Dr. Kissel has given out. That is in the various distributions in describing this as a sophisticated deterministic model, there's some confusion in the various distributions that go into the variabilities and the processes to which ones are variable because we don't know the answer and which ones are variable because there's an natural variability.

And it would be a little bit more satisfying and more elegant if those two concepts were separated, natural variability from ignorance.

DR. WAUCHOPE: I served on a working group about 15 years ago when we began talking about doing probabilistic modeling. And you've made great progress. I congratulate you. I look forward to seeing the toxicology part.

But certainly from my point of view, maybe as a chemist, I understand the improbabilities of the uncertainties in the exposure part better than the tox anyway. Of course, it's horrifying when you discover how bad the uncertainty is. Regulating on something where you've got a 6 order of magnitude spread in some of your distribution functions is kind of scary and I don't know how you do that. I guess that's policy.

When all is said and done, and I'm speaking now perhaps as a lay person, it seems to me that the bottom line is your regulating on a hypothetical arsenic transmission mechanism that's totally unproven at this

point. You don't know much about to many of the fractions that are involved in the mechanism of getting arsenic from the deck surface into the GI tract of these children. Maybe you know a lot more than is obvious to me. But I would certainly like to see some more discussion or some more consideration of how you get some actual measurements that validate something, validate some of these parts of the processes that you're hypothesizing.

DR. HEERINGA: I also think to follow up on Dr. Kissel's comments and those by Dr. Macdonald also. One of the toughest things we face in research and particularly anything that involves stochastic analyses or stochastic presentations is that if we can do thing right with stochastic inputs to reflect uncertainty. And when the results are published, the world chops off the uncertainty and works with the point values.

One of the first things that I learned in data publication is that you can present measures of uncertainty, but the people who read and write on those papers, particularly addressing public media, will tend to

lop off the uncertainty. So we have a big education function there. So a lot of effort has gone into producing results that incorporate and reflect uncertainty and variability. But we now also have to education the users of those data as to how to interpret those measures in their own decision-making because they've been trained to make decisions on point values.

DR. HATTIS: I make the concluding observation to a degree that all uncertainty analyses are incomplete because there's all sorts of model uncertainties, systematic errors that are never or very many seldom addressed and very difficult to address. So I think the best one can do in this state of the art so to do the best you can, describe the uncertainties you think you've captured, and fairly communicate it as best you can to the audience. And that has got to be good enough in some sense.

I think Dr. Macdonald's point, the authors have tried to separate variability and uncertainty. They haven't completely done it because, for example, there's

no effort to remove the effects of measurement error from the estimates of variability. That's a big subject. Techniques for practically doing that have not been developed, I mean, in lots of cases. There's lots of cases if you're measuring things that are well measured, it doesn't matter to much. The measurement error is small and you can neglect it. But nevertheless, it hasn't been done and it's rarely the case that people have done model analyses of that kind.

But nevertheless, you have to go forward. The decision-making process needs to go forward both among users and among public decision-makers based on reasonable application of the efforts of the limited number of analysts that there are.

DR. HEERINGA: Well, again, I think we're ready to conclude. Mr. Jordan.

DR. JORDAN: Thank you, Dr. Heeringa. I don't want to truncate the conversation. But I have a sense that it may be drawing to an end. I'm sure everyone is in some measure pleased at that. I know we certainly at EPA

are very pleased to have had as much wonderful advice.

And this last conversation has been for me, as a policy nerd, particularly useful and interesting. I know that the line between policy and science is sometimes a little blurry. And today I've gotten the sense that we've walked up to that policy line a couple of times, and I'm glad that we noticed and we're watching for that and in my view at least try to get into things and stuck with the science.

But the science is immensely valuable to informing and understanding the policy choices that face the regulatory decision makers and the people who give advice to the American public. And I have the feeling that all of us at EPA would agree that we have come away with a much better understanding on the science side and consensus about what we can and what we can't and what we should and shouldn't do. And that represents a very successful piece of work by the SAP. And for that, we're grateful.

DR. HEERINGA: yes. And on behalf of the Panel

itself and the SAP, I would like to thank all of the staff of the EPA represented here by Dr. Ozkaynak and Dr. Zartarian, Dr. Chen and Dr. Dang as well as the other representatives of the EPA for the presentation and the results. Obviously, the materials that have been assembled.

I would also like to thank all of the other participants in this process over the past three days. there's been tremendous exchange of information a lot of which is going to being shipped back to my office. We appreciate this. I think there hasn't been to much held back here in terms of presentation of results. Some things almost right up to the last few days. And I think that's informed the process and helped us to proceed.

And to panel members who have agreed to serve on the panel for the past three days, my thanks to you. I've been a member of many of these ad hoc panels and have observed these processes. And I think in particular with regard to presentation of responses to questions that this group was particularly well prepared and well organized in

their thinking. And I think that allowed us to remain on schedule and focused on the task. So thank you to all of you.

And at this point, I'll ask Paul Lewis if he has any additional closing comments.

MR. LEWIS: Thank you, Dr. Heeringa.

Let me just again express our thanks to Dr. Heeringa for serving as our session chair for this meeting over the past three days. This is, I believe, your second meeting, and you did a wonderful job keeping us on time and focused and moving forward on the issues and deliberations we had in the past three days.

And thanks also to the Panel for your very helpful insight and analysis and all of this will be helpful for our colleagues at EPA in terms of reviewing your remarks.

Members of the panel, again, let me remind you that if you have any written comments, to share them with the report coordinator, that is Dr. Macdonald, and also the lead discussant on the particular questions that you

were assigned to. And I'll be working with you as we move hard forward in preparing our final report.

Again I want to thank my colleagues in the SAP staff sitting over here to my right for all their help in organizing this meeting with me and making this meeting a success.

Thank you, Dr. Heeringa.

DR. HEERINGA: Thank you very much, Paul.

And I guess with that I'd like to call this meet to go a close with my thanks to everybody and save travels for those of you returning home.

[Session was adjourned at 3:45 p.m.]

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I, Jane F. Hoffman, Stenotype Reporter, do hereby certify that the foregoing proceedings were reported by me in stenotypy, transcribed under my direction and are a verbatim record of the proceedings had.

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JANE F. HOFFMAN

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