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METHODS USED TO CONDUCT A PRELIMINARY CUMULATIVE RISK ASSESSMENT FOR ORGANOPHOSPHATE PESTICIDES

February 7, 2002

[8:30 a.m.]

SHERATON CRYSTAL CITY HOTEL
1800 Jefferson Davis Highway
Arlington, Virginia 22202

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DR. ROBERTS: Good morning and welcome to the February 7 meeting of the FIFRA Scientific Advisory Panel. This is the third day in a consultation between the Panel and the Agency topic of cumulative risk assessment of organophosphate pesticides.

My name is Steve Roberts. It's my pleasure to serve as chair today. Before we the Panel for today's session, I'd to introduce our designated federal official for today's session, Ms. Olga Odiott. Good morning, Olga.

MS. ODIOTT: Good morning, Dr. Roberts. I want to welcome everybody to this important meeting of the of the FIFRA Scientific Advisory Panel. For the benefit of those who are you joining us today for the first time, this meeting is being conducted under the provisions of the Federal Advisory Committee Act. And all background materials and all documents related to these meetings are available from the Office of Pesticides Programs docket. And many of the materials are also available from the EPA web site. Your agenda lists the contact information for both places.

I would like to thank the Panel members for their commitment, for their contributions, and for their willingness to be with us during this process and to provide to the Agency the much appreciated feedback on these issues. And we're looking forward to very good

discussions today. Thank, Dr. Roberts.

DR. ROBERTS: We have a new Panel member with us joining us today and there's possibility that there are some folks in the audience who have not been with us previously. So I think it would be useful for the Panel to introduce themselves. So let me ask the Panel, beginning on my far right, and then proceeding around the table clockwise, and for each member to state their affiliation, and the expertise they bring to today's discussion.

DR. BULL: I'm Dick Bull from Washington State University. My expertise is in toxicology.

DR. DURKIN: I'm Pat Durkin. I'm with Syracuse Environmental Research Associates. I do pesticide risk assessments for the USDA, and I've been involved with the EPA in risk assessment issues.

DR. HARRY: Jean Harry. National Institute of Environmental Health Sciences in North Carolina. My background expertise is in neurotoxicity.

DR. CONOLLY: Rory Conolly CIIT Centers for Health Research in Research Triangle Park, North Carolina. I'm toxicologist with a strong interest in mechanisms of toxicity that underlie the shape of the dose response curve and in the development of computer models

of those mechanisms.

DR. RHOMBERG: I'm Laurez Rhomberg from Gradient Corporation, also, adjunct professor at the Harvard School of Public Health. And I'm interested in several aspects of quantitative modeling and risk assessment.

DR. MCCONNELL: I'm Gene McConnell. I'm veterinary pathologist and toxicologist from Raleigh, North Carolina, Toxpath, Incorporated. My are of expertise, as I said, was in comparative pathology, toxicology, particularly as they relate to bioassays done in experimental animals.

DR. KENDALL: I'm Ron Kendall. I'm a member of the Science Advisory Panel. I'm from Texas Tech University. I'm professor and chairman of the Department of the Environmental Toxicology. And I also direct the Institute of Environmental and Human Health at the university. Area of interest is toxicology and risk assessment.

DR. HATTIS: Hi. I'm Dale Hattis from Clark University. I do a fair amount of pharmacokinetic analysis and I focus on issues of variability and uncertainty in risk analyses in general.

DR. ADGATE: I'm John Adgate from the University of Minnesota School of Public Health. And my area of research interest and expertise is in exposure analysis and risk assessment methodology.

DR. REED: Mu-May Ruby Reed from California Environmental Protection Agency, Department of Pesticide Regulation. I do pesticide risk assessment.

DR. FREEMAN: Natalie Freeman, Robert Wood Johnson Medical School and the Environmental and Occupational Health Sciences Institute in Piscatawy, New Jersey. I look at residential and children's exposure.

DR. MACDONALD: Peter MacDonald from Mathematics and Statistics at McMaster University in Canada. I have a general expertise in applied statistics and model fitting.

DR. HEERINGA: Steve Heeringa from the Institute for Social Research at the University of Michigan. I'm a biostatistican with specialization in epidemiology and population-based studies.

DR. ROBERTS: And I'm Steve Robert. I'm a professor at the University of Florida in the Colleges of Medicine and Veterinary Medicine. I'm also director of the Center for Environmental and Human Toxicology. My research interests are in mechanisms of toxicity, particularly pertaining to the liver and immune system and toxicokinetics. And I have a working interest in risk assessment.

I'm delighted that we have with us for our session again the Director of Office of Pesticide Programs, Ms. Marsha Mulkey.

Good morning, Ms. Mulkey. Welcome. Did you have comments or would you like to address the Panel before we get started today?

MS. MULKEY: I will just a moment in the midst of this marathon -- I feel like I should offer some water bottles to the Panel -- to thank you just in case the latter part of the day doesn't offer that opportunity for this extraordinary session. And, of course, it's a culmination of a number of important and indeed critical sessions. But this is very important to us, to our work, to our credibility, to our service to the American people.

And I think, as many of you have noted, it also lays a groundwork for the work of many others, us and many others, as we go forward trying to understand ways of thinking about sources of exposure that are beyond a single chemical.

So we are very gratified by the value that has already been added. We look forward to today and to your report and to our continuing collaboration and consultation as we go forward. Thank you.

DR. ROBERTS: I would like to add that your input during our discussions over the last couple of days have been very valuable to the Panel. You've been a real asset to our discussions having you here with us.

MS. MULKEY: That's very gracious. I feel it has been modest at best but thank you.

DR. ROBERTS: Margaret Stasikuwski of OPP, welcome this morning. Would you like to introduce the presenters and the scientists you have with us today?

MS. STASIKUWSKI: Yes, this morning's presentation will be made by Jeff Evans. And sitting to go my left is Dr. Randy Perfetti, also from our division, deputy director.

DR. ROBERTS: Dr. Perfetti, did you want to give us a recap? I think was originally on the schedule for the morning.

DR. PERFETTI: Only insofar as to again welcome the Panel and then give our sincere thanks for the previous two days and the sessions and the great advise you've given us. We really appreciate it.

Other than that, as Margaret said, Jeff Evans will be providing the presentation for the residential nonoccupational exposure part of this risk assessment. And this afternoon, Dr. Beth Evans and Dave Miller will provide the presentation for the risk characterization part of this assessment.

Thank you, Dr. Roberts.

DR. ROBERTS: Welcome, Mr. Evans. We'll be delighted to hear your presentation on the residential aspect of the cumulative risk

assessment.

MR. EVANS: Thank you very much. This morning I would like to go over some aspects of the residential assessment. Today we would like to talk about, briefly, how we used our calendar-based model to address the temporal aspects of the OP uses, in particular, for the residential uses.

I should note that this approach is similar to the approach we took to the OP Case Study presented here not that many months ago it seems. And, also, I'd like to talk a little bit about the data we used in our cumulative assessment.

Not all of it, but certain aspects of it that are a little difficult for us to get our thoughts around and to discuss with the Panel use of distributions of our available data and, also, additional ways to incorporate survey data that's recently become available.

And, also, on Tuesday, there was a presentation suggesting the types of survey data that we will be getting in the future. And it's going to be up to us to decide how to use it. And we are really looking forward to your comments with respect to those possibilities.

This is something very new for us, the use of survey data and, also, using distributions to accompany a wide range of exposure variables. So this is our first stab. It is a beginning. As time goes on,

we're going to have to get more sophisticated. So with that in mind, I can proceed to the next slide, please.

Now, just to lay out the use, I think anybody that does risk assessment, and particularly a large one like this, wrapping around all the uses is always difficult. The minute you think you have it, something else shows up. And it was also very difficult with the single chemical assessments still in progress, what was in, what was out, what were people going to support. And it's important for the Panel to know that the DDVP strip use that's presented in this assessment is no longer registered and that's going to change.

The pet uses for DDVP and Tetrachlorvinphos were not included in this preliminary assessment primarily because we're still, I think all of us, are really still working with the difficulty of modeling our relationship with pets, both the receptor and the source are constantly moving. And it's very difficult for us to model, I think, effectively without just having a screen that once loaded into a model would obviously swamp every other use.

So, also, perhaps in our conversations when we talk about the various aspects of exposure to maybe also think about what it would be like to model exposure to a pet wearing a collar or a pet that's been recently treated with a spray or a dip or some sort of top-spot

treatment.

We have home lawns. And the major uses are bensulide, malathion, and trichlorfon. And some of those uses are no doubt going to change as time goes on. Golf course uses. There's nothing like finding out that something isn't registered by someone in a public meeting. And that's certainly been the case for some of our golf-course uses. And we heard you. So if you would limit your comments to other aspects rather than that, we'd appreciate it.

Home gardens. We have in the ornamental sense, we have acephate and disulfoton. And for the vegetables and other edible crops, we still have registrations of malathion.

We also looked at the specific public health sprays for mosquitos, fenthion and malathion. And then also the use of naled for black flies up in areas of Minnesota.

I've been told that your slides have got this very simple equation backwards that we use every day. We know what we're talking about here. And the only point of the slide is to, obviously, point out the fact that we're looking at inhalation exposure, dermal exposure and oral exposure through the mouthing behavior of young children. So that is somewhat separate from than the dietary and drinking water assessments. Now.

For our age groups, we picked what we feel we have the best information with respect to the hand-to-mouth behavior. We have children in one-to-two years old and three to five. And those groups, the one-to-two-year-olds are 12 to 35 months. And the children three to five are 36 to 59. And, again, those are what we feel we have the best information for the hand-to-mouth behavior.

For the adults, we have all the other age groups. And I think that probably the big difference is the body weight surface area of children that has impact on the dermal exposure values. You know, they're shaped a little bit differently than we are. Obviously, their heads a little bit bigger or their trunks, arms may be a little shorter, things like that. And of course, as they get older, they become a little bit more like we are.

Again our focus in terms of having the number of files that went into the model, we focused on those children and adults. But in a sense we feel we really covered everybody.

Just briefly, we've conducted assessments for 12 distinct geographic regions. And we hope that we've reflected climate and pest pressure differences. In California, we just -- one region was put into two residential assessments. We may reevaluate that based on some of the comments we get from the public and regulator

community.

It includes, we believe, are the remaining residential OPs that have significant uses and appropriate exposure data. And, again, I just want to say that we have not, at this point, included the pet products; but we intend to by the time this is all over.

You've all seen this map many, many times over. And I think it really does point out the facts that there are differences where we live and the climate and the climate influences the types of insects that bother us. I think our main goal, really, was to, first of all, keep it simple and also really try and figure out why people were using pesticides. And I'll get into a little bit of that later. And, of course, you've seen this many times over.

Here's an example of the Eastern Uplands. This was the area we used in our pilot. Now this time you get to see some of the pesticides that we addressed there. We really mainly address malathion or trichlorfon.

And on golf courses, acephate, bensulide, fenaminphos, malathion, and trichlorfon. Ornamentals, those three as I mentioned before, the home garden, malathion, and the indoor uses of the DDVP.

Now this matrix, I think, is really important for people to think in terms of the files. Think of each of those as a file for a region.

What the slide does, also, is indicate the time in which something might not applied.

So for each and every one of these there is a AGX file that deals with all of the residue data, all the contact values, the pesticide application schedule, the percent of houses that are treated. All those things are boiled into those AGX files. And it is all those files that are then loaded into the program. And it, also, works with the DEEM.

And it's a lot of data to manage as you can possible imagine. There's a number of people that worked on this, Sheila Piper, Sherry Cenard, Jennifer Tylor, Dave Herd. There's an awful lot of work in managing these kinds of files. Seeing how the model goes, checking out your schedules, making sure things line up, there's obviously some things that we need to go back and fix. And we're in the process of doing that. But it was a lot of work to manage, and we really appreciate their efforts.

And so with those temporal aspects you do then see the efforts. The seasonal aspects in the middle there, the lines, that really is your garden uses, your lawn uses, public health happening in there. There's the use of the strips up there, your food, and this is your drinking water.

So this was really probably the strongest reason to do certainly

something that's, you know, geographically and temporal-based because you really want to be able to line up the possible uses and concurrence.

So with that said, our road map today will talk a little bit about the distribution selected for some of these key scenarios, obviously, lawns and golf courses, public health, and the garden. I'll also go through a little bit of the characterization and our feeling on how we kind of addressed it. And then, also, with a future view towards the consideration of survey data that's going to be coming available to us.

Now for the lawn use information, as I've said many times before, we rely primarily on the National Home and Garden Pesticide Use Survey. It was done a number of years ago, but it still is probably the best data we have available now that is related to the use of pesticides in homes. And we're able to determine the percent of households using a given pesticide. And there are regional distinction.

Treated lawns, there's also regional differences in the percent of the population that hire lawn-care services. So this would be important for chemicals that may be are no longer registered for application by residents but may be applied by the LCOs so that we can address the post-application exposure to those.

And, also, lawn sizes. Having an idea of how large someone's

lawn, which is a variable for assessing applicator exposure is difficult for us to determine, and it's going to continue to be a challenge for us.

And for that we selected a uniform distribution of 500 to 15,000 square feet, a third of an acre, which was the median for homes, you know, throughout the country. But I think it's important to note that that only considers the lot size minus the footprint, and it really doesn't consider other things such as decks and, of course, the fact that there are gardens and other things that we are also assuming people are spraying pesticides on.

But all of this started out with the label. That still is kind of the legal document. And that's where we find our site-pest relationships. This is where we get the application rates. And some of them are more descriptive than others. Sometimes they'll just have a list of thousands of sites and thousands of pests and not all pests get on all sites. So it's really important to find out what is going on in the various regions.

And a very good place to go is the State Cooperative Extension Services. A lot of really great stuff on line, a lot of information about the timing, when to look for pests, when to spray, also recommendations on the number of applications, when to look, when to scout. Also, sort of the landscape as far as what they're

recommending. And obviously this ties into what people may use, what kind of information they'll get at garden centers.

And, of course, timing of applications is very important with respect to all the other aspects of potential exposures from other sources.

And I also looked at efficacy data that is also broken down into regions. Certain pests just don't occur in other areas. And that was an important consideration.

Now, for applicator exposure data, we have some pretty robust data from Outdoor Residential Exposure Task Force. This is addressing two major lawn application methods. Obviously, the push-type rotary spreader for granular formulations. That would be for bensulide and trichlorfon.

And then hose-end sprayers which are available as a ready to use where the concentrate is already mixed in and the person doesn't have to really handle the concentrate and the proportion is already calibrated.

And there is another one for those that still have the old fashion one where you have to add your own concentrate and make your own settings to determine how many gallons per thousand square feet of lawn area.

The data also address a range of clothing, which include short-sleeved shirts, short pants, up to long-sleeve shirts and long pants.

Just by way of example or just for people to understand what the unit exposure is, it's really the amount of pesticide that gets on an individual as a result of an activity and how much they actually used. And this would be used in our simple algorithm unit, exposure times how much the individual applied and divided by body weight. Sometimes other metrics such as dermal absorption are used. But we had a dermal endpoint for these scenarios, so we didn't make any adjustments.

Now the hose-end sprayer, we have for this go-around anyway, we used uniform distribution. Obviously, there's quite a range there. And we've also done the same thing for the granular applicators.

Now as far as an activity pattern, this is pretty easy to understand. And it's also easy to measure. We selected a uniform distribution that would reflect a range of clothing to be worn because we did see some survey data that suggests clothing worn will change over the season. And the survey data were temporal based on formulation type. And we only have percents with respect to application type.

So even though, normally, we would have -- in our typical screening level assessments we would use the short-sleeve shirt, short pants. And those we've already determined to be log normal. We would use a mean or some other statistic. But in this case, since we have in some case two application types which we may need market data for, we have a sense that as time changes, people are going to shed off a few clothes while they're making those applications.

We had a little bit of difficulty really trying to wrap my mind around that, so I took the flag of convenience of a uniform distribution. And I don't know if it really is going to make that much of a difference in this assessment. I think with a view towards the type of the data that we may be getting where you're going to actually have longitudinal survey information about what people wore while they made that application, then we can probably do a better job of developing distributions for those specific clothing types. But it will take many more files to load that into the model, so we want to make sure it's worth it.

Post-application becomes a little more difficult. It becomes more difficult to identify an activity pattern that is representative. Many years ago before this Panel some of you members may remember, we had an activity pattern or macro activity pattern as we would use in

this case called "Jazzersize" which would be a series of exercises on the floor or on the lawn in which you can roll around and do exercises that put you in pretty good contact with the treated area but for a short period of time.

It was a very reproducible study. It gave you very uniform results. The standard deviation would be less than the mean which was, you know, really great from a person designing a study, but it was really difficult to communicate to people what it really meant.

In the meantime, we decided to look at other studies which were a little more understandable anyway. So we looked at two studies, one with a spray and one with a granular formulation of choreographed activities but more believable kind of activities. They used crawling in one sense to mimic adults that still weed the old-fashioned way and edge or dandelions and things like that but also to perhaps mimic a child crawling, also playing touch football, Frisbee, things like that.

But there were activities like sun bathing on a blanket, which really are not all that intensive but perhaps maybe more representative of a picnic at a park or typical activities with the family on the lawn.

For children we took a look at a study that was done really as someone's dissertation. But it was a very interesting one that they used a nontoxic substance that's used to whiten shirts, other types of

clothing, safe. And you read with a short of a UV technology that measures florescence. And these kids were really nonscripted. They were just given toys and a half hour to just mess around, really, on a treated lawn. And that really seemed like a really valuable thing to also include with the children's transfer co-efficients.

So here they are for addressing post-application exposure. I should, also, add that we use the up to two hours and up to three hours -- well, two hours for adults and up to three and a half hours for children. The two hour value if the Exposure Factors Handbook. And that's actually time on a lawn.

There is a similar value for children, but with concerns about them being other places, other lawns, at the park, at the school, other places, I bumped it up to the three and a half hours so for time outdoors for that age group. But again that was a cumulative distribution based on the statistics and the Exposure Factors Handbook.

The adult transfer co-efficients range from 2,000 to 13,000. We used a uniform distribution. Again, you know, these are representative. Is it really what people do? Is it really something that's deserving of a log normal distribution? I'll leave that to the Panel.

And, also, for the children, you know, we're combining kids transfer co-efficients scaled down from the adults and, also, the inclusion of the nonscripted activities. You know, these may look like small numbers to most people, but they're fairly descent compared to what we've seen.

For the lawns, we have transferable residues. Often these studies are done in a number of locations. In this particular assessment, some we have a number of sites that are appropriate for the geographic regions. So we did a range of the distributions, uniform distributions, for values for each day that could include as soon as dry up to 8 hours, 12 hours after the application is made.

It, also, includes such factors as watering-in or not watering-in. And it also includes days that there's also the potential for rainfall.

And nondietary ingestion is even harder. Again, applying, that's pretty easy to measure. That's pretty easy to understand. What do we do on lawns? That becomes a little more difficult. And then what do kids do while on they're on lawns, hand-to-mouth behavior, it becomes even more elusive and difficult for us to address. It's very important pathway, obviously.

So we looked at a number of things. We looked at, first of all, frequency, which is based on observational data. But that really

doesn't tell us very much about how much gets on their hands. So we had to think about how much gets on hands by looking at some data that was done on behalf of ORD for this particular aspect. Also, how much comes off once it's on the hands.

Now for the hand-to-mouth frequency of events we continue to rely on Reed. And this includes 20 kids in day-care and 10 at home. I selected a uniform distribution of .4. I guess one can obviously say 1 to 26 would be a little bit better. But in that study, the mean was nine and a half; median was eight and a half; and the 90th percentile was 20.

Some issues for consideration is the differences in hand-to-mouth behavior that may happen when we're indoors or outdoors and, also, the differences between active and quite play. I know this Panel has touched on this before. And just to go even further into discussion, some recent information that Dr. Freeman has looked at. Again, a small subset of children, but there's differences between the indoor and outdoor frequencies of hand-to-mouth events.

Now, if their mouthing, the hands are wet. So we wanted to make sure that we accounted for perhaps the increased transfer to the hands if the hands are wet. There was a comparison of wet-hand efficiency and dry-hand efficiency with three surrogate compounds.

And it was very helpful that these data had a very similar transfer efficiency as the available data that we have.

The turf-transferral residue data that we have measurements of. The range there was .9 to 3 percent for two chemicals. And we noticed that the chlorpyrifos was much, but it showed the same percent transfer.

So we would take the turf-transferable residue and increase it one and a half to three times higher to account for the hand-to-mouth behavior.

Now once the hand goes in, how much comes off. And that I think that's also fairly difficult to look at. One study by David Camann showed 50-percent removal by saliva-wetted sponges. And this struck us a sort of a vigorous wiping method. So we used that as our high value.

There was, also, another study in which people grabbed test tubes that were spiked with a know concentration and then a more passive sort of removal technique of hand wash with ethanol and with water was also used and they recovered 20 to 40 percent of that which is spiked on the hands.

And then, also, since outdoor play may also include, you know, residues and grass stains and smashing into the soil, you're going to

have kind of gamish of soil and residues. And so took a look at soil-removal data in which people had a certain amount of the soil on their hands and they measured how much was removed from various mouthings events, thumb sucking and the like. So that's kind of the basis of the removal efficiency for the hand-to-mouth.

Getting into golf, that's a little bit easier. But for the percent of individuals, we looked at a study that has statistics on the percent of people that play golf also the number of hours playing golf. I mean I pretty much left it for four, unless there was some indication that only greens were treated and then two to four hours. I didn't really mess around with that too much.

The percent of golf courses that were actually applying those pesticides is available, you know, in proprietary-type data available in Doane very recent. And this is also an activity pattern that is pretty to understand. You can just put people in dosimeters and go out and measure after they played golf on a treated golf course. That's a lot more easier to understand than what kids do and adults do when they're playing on lawns.

Although with it being that easy, you'd think there'd be a little more data. But we were able to get round 10 transfer co-efficients that addressed the playing golf, walking around, using a cart. There

really wasn't that much difference. Typically, fairways and the greens are treated. So if I guess if you're a duffer, you have less exposure if that helps anyone when they're having a bad day on the course. Again, we use chemical-specific turf-residue data.

Public health gets back into the difficult. And that is, you know, how much gets on the lawn from these applications. In the single-chemical assessments, the reviewers relied on information for how much actually deposits on to a lawn as a percent of the application rate. And that ranges considerably, depending on ground equipment, whether or not it's being applied by aircraft, you know, nozzle size, all those kinds of things, how much is evaporating. So we used that just to get a concentration to the lawns.

And once we had our deposition on the lawns, then we pretty much addressed it the same way we would a lawn chemical with the same transfer co-efficients, same hand-to-mouth values that we used and I just discussed previously.

To determine the number of population, we looked at statistics suggested how many people have lawns. When these things are applied, we spoke to people responsible for making these applications. And, obviously, part of the comment period we are certainly expecting a lot more information: Where, when, how, and why these things are

being used.

Now garden, again, this is pretty easy to understand. Application, and we have a number of studies to address the uses. We have a chemical-specific. For disulfoton we used a shaker can and this is just a systemic insecticide so you apply it to soil, rake it in, and it's great for roses and those types of things. We also have used the garden duster for vegetable gardens and also small tank sprayers for gardens and spraying trees and those types of things.

It has the same issues with the types of clothing. You start with long-sleeve shirt and long pants and as the season begins. And as summer progresses, you find yourself wearing less and less. But, again, to address that, we simply left it with the uniform distribution for this time.

The area treated for gardens, this was a fairly difficult to determine. So we simply used a median home area and assumed a certain perimeter. But in this case, we made sure that whatever the area that was treated, everything was treated. We didn't really make any distinctions there.

Vegetable gardens there was data suggesting it was log normal. There was a survey conducted by the Outdoor Residential Exposure Task Force with the Gallup Survey people. Vegetable gardens are a

little bit easier for people to understand, how big it is versus their lawns which is obviously complicated by the structures and green spaces and shrubs and trees and those sorts of things. And we went ahead and used a log normal for this statistic of garden sizes.

Now post-application dermal exposure, that, again is a pretty easy thing for us to understand in the agriculture region anyway. Someone is going to pick apples all day; that's great. The problem is when you get into home garden there's a certain number of crops that people have. There's a number -- they'll have trees. They'll have strawberries. They have grapes.

So, you know, with that, knowing there's so many difficulties, we just simply selected a uniform distribution that would represent a number of activities. And it includes hoeing and weeding, harvesting, staking tomatoes, picking apples, those kinds of things.

The duration of garden activities, survey data suggested five minutes to an hour, a couple days a week. But we went ahead and set it for every day.

And we also have a chemical- and regional-specific residue data which would most importantly impact the dissipation and how long it's actually in someone's garden.

For inhalation, for the indoor use of DDVP, we have standard

work horse, unit exposure from the pesticides handlers exposure data base. We just simply used the uniform range there.

For post-application inhalation exposure for adults and children, we had the pest strip data. But then, again, that use is no long registered. Crack and crevice from Gold. These aren't the most recent studies in the world, but they are what we have available to do this assessment with.

The duration of time spent indoors and breathing rates, we used readily available statistics in the Exposure Factors Handbook, obviously, up to 24 hours. And we used rest to moderate breathing rates.

Just simply, we discuss the majority of the data that we used for the major uses in this assessment. For example, we have the lawn residue data for all the compounds, and we made regional adjustments where feasible. We addressed a wide varieties of activity patterns. Some are more straight forward. Application, that's pretty easy. But it gets more difficult as you get into post-application in lawns, and the hand-to-mouth is still proved to be difficult for us to address.

And if it wasn't clear in my presentation, I'll simply say now that we tended to use uniform distributions our flag of convenience when we were presented with scenarios that had a lot of confounding

variables and it was a little bit difficult for us to address.

Now to characterize, again, for us the hose-end data, there's a lot of replicates. And we have the mix-your-own and ready-to-use. So, you know, we think that's pretty realistic with some further thought, you know, on developing distributions of the types of clothing that we have indicated by the survey or, you know, some other way to really handle that. You know, perhaps determine what percent of people are applying understand a certain clothing scenario and develop distributions for that.

For the push granular, 30 replicates of, again, high confidence. And these studies were performed by people that, you know, they don't work for chemical companies. These are just regular people that belong to garden clubs. So those type of people are recruited and they just went and did what they did without any coaching.

The lawn size, you know, is fairly reasonable considering the equipment used. It might be a slight underestimate in areas that have larger lawns. You really would be a deal breaker wouldn't have a huge impact on the assessment to make that variable larger.

For post-application on lawns, we do have activities that are representative. But, you know, the distributions may really reflect the study design rather than the actual activities. We are really more

interested in if we had a realm of activities that are representative or that can at least cover some of the other things, say, if you're just walking across the lawn. We were fairly confident that these cover things that are less than that. And, again, it seems like a reasonable suite of activities that people might be doing.

For the children, again, we have a combination of scripted activities. And then also there are unscripted activities, just kids being kids hanging out on the lawn. So we feel pretty good about that.

We have turf-transferrable residues. And it reflects a range of high values immediately after. But it also, you know, in the real world, it does rain and that's also a possibility on the second or third day or so after application.

The turf-residue hand-to-mouth, it's based on surrogate data; so there is some uncertainty there. It would really be a whole lot nicer to have chemical-specific data on that.

The frequency is, you know, it may be an overestimate; it may not. But, again, these are based on kids indoors, so there may be differences with kids outside.

Duration on lawn, for kids, again, we bumped up the value to beyond the times they spent on lawn. If the lawn was treated, you were reentering. So that's an aspect of this assessment.

For public health, it's a distribution of -- the uniform distribution of aerial ground equipment values. The percent of applications made by ground equipment and aerial. The population exposed to the public health we limited it to those having lawns and, you know, those having kids.

For the home gardens, you know the applicators, again, high confidence. Again real people making applications. The same deal with the home gardener and the granular application as well.

The garden, that area treated was pretty descent. We thought a pretty decent survey data. And, also, an outfit that's been collecting this kind of data for a long time.

Vegetables, you know, certainly a well-studied variable for individual crops. It gets a little complicated when you realize that in gardens people don't just have one thing. And it's a pretty high available exposure scenario.

Frequency applications. For frequency for the applications, again, you know, we used survey data. That's based on generic insecticides and it's not chemical-specific.

The post-application in the garden. We're assuming all the plants are treated. What it would also be reasonable to assume that you're only going to treat certain crops, certain types of year, certain

pests, that sort of thing.

The residues, we're pretty confident with those. Again, they're regional chemical-specific.

The indoor air is chemical-specific.

The duration, breathing rates, those sorts of things are pretty well-established factors in the Exposure Factors Handbook.

The population exposed, for the pest strips we based it on the use of all pests strips including those sort of hideous sticky strips that just catch flies. And the use patterns for all scenarios were based on the percent of households that were actually using that particular pesticide.

So, you know, now we're going to get into survey data. And that, also, presents, you know, a number of possibilities. So we're going to, first of all, look at how, you know, how we put people together in our assessment. And then, also, just by way of example, what one might do with survey data. And also to discuss a little bit about the upcoming pest use survey data that was discussed just this past Tuesday.

So survey data, you know, primarily to look at what they would like to call "human activity patterns." And these are macro activity patterns. This is, very simply, in the garden. Obviously, that's a

macro activity pattern. And the types of transfer co-efficients are macro activity based. You know, driving to work, time at school, those sorts of things, you can track an individual during the day.

But our basic approach for this assessment was kind of an independence/dependence. First of all, we identified households based on their reported use of an OP for a given scenario and relied pretty heavily on the National Home and Garden Pesticide Use Survey. For example, 6 percent of households in Region 5 used lawn chemical A.

Then we identify, from the Exposure Factors Handbook, how much times do people spend on lawns. And those values were taken from surveys such as the National Human Activity Pattern Survey, a pretty large cohort survey. Not necessarily addressing the use of pesticides. I think it was primarily designed for addressing secondhand smoke. But, again, it was useful as far as where people spend their time.

So in our simple step-wise process, you have your food exposure calculated from DEEM. And then you would select the residential treatments for an individual on a given day; and this, of course, is regional-specific. You know, where the pesticides applied are in or around the home, and if so, what are the treatments, what are the frequencies.

So that's why it was really important that we had that early matrix be the windows of exposure possibilities. So for each day, as it works its way through the year for each individual, it is going to go does this house, a certain percent of houses are using a pesticide. And so it will pick statistics from those libraries that have all those exposure values for that scenario. And you'll just keep repeating this step until you've addressed all the uses that are available, again, going back to that large matrix.

So for this assessment, co-occurrence is driven just by random probabilities. So, again, largely the percent of the houses being treated. So 6-percent lawn use, 10-percent crack use will give you a certain percent that has both. And, again, we just want to stress, whatever household is selected, the probability of -- you know, you're going on that lawn and you are in that house. So we don't really mess round with, at this point anyway, of looking at the people who responded that they didn't go on the lawn. But there is data that suggests that people just don't exactly go running right out there. But for this assessment, if you have a lawn and if you have a lawn chemical applied to your house, you're going out there.

So now this very nice new web site that's available to us all, the Consolidated Human Activity Data Base. There's a lot of survey data

that's suddenly available to us all. And it's a compilation of lot of human activity pattern surveys. So you can look at the questionnaires and you can look at the responses. So there's now the possibility that you can develop a daily activity patterns for individuals. You can kind of track their life in a given day.

But, again, these surveys are mostly cross-sectional and they're not longitudinal. We do expect a pesticide use longitudinal survey one of these days from the regulated community.

And with all apologies to Drs. Zartarian, Xue, and Ozkaynak, I just pinched a couple of their slides that suggest, just by way of discussion, a strawman, if you will, and how one could approach using survey data.

And this would be that you could get individuals and track their time. So you could actually identify how much time they spent in a given room. And this may be important for the crack and crevice uses. It could be important for other uses of pest strips if it's simply being used in a garage or something like that. You know, how much time did they spend on the lawn. Those sorts of things. So you have an accounting for all the time they spent in the day.

And then possibly you could assemble diaries that would simulate a person. You could use a number of surveys to address what

they might do seasonally, what they might do on the weekends. And I would imagine that we would have to also somehow tie it to the type of person that we also selected from the CSFII. So, again, this is just the kind of thing that's going to be available for us to address perhaps this assessment, perhaps more likely future assessments.

You know, finally, the Residential Exposure Joint Venture is collecting data longitudinal in nature that actually address the application of pesticides in and around the household. We're going to have information on when and where the applications of specific active ingredients are made. We're going find out whether or not multiple applications are made.

In our scenario, it might be very likely that, based on the application treatment type, you could treat your garden and your ornamentals in one day. It would be nice to have survey data that suggested that that is exactly what people did.

I think what's really important is we also have what they wore while they were making those applications. So it would make our management of those log normal distributions of clothing scenarios a little more of a fit for the seasonal aspects. And it's also going to discuss the demographic information. Do they have children? A lot of people who garden are a little bit older, the kids are gone, and they

need something to do, so that isn't necessarily figured into this assessment. But that might be something that may be of importance in future assessments.

So with that, I'll conclude my presentation and would be happy to answer any questions of clarification.

DR. ROBERTS: Thank you, Mr. Evans. Are there any questions from Panel members clarifying from your presentation or your methodology?

DR. BULL: This is probably in here, but I was not able to find it nor did I catch it out of your presentation.

You got these transfer co-efficients in turf-transferable residues. Transfer efficiencies is kind of different unities that you go after this. But I didn't see -- is, say, dermal absorption included in one of those? I saw no mention of the absorption rates.

MR. EVANS: Yeah, a lot of times we do, obviously. But in this case, our endpoint is from a dermal study; so we have made no adjustment.

DR. BULL: But how do you relate that to the amount that's absorbed from the area that's exposed?

MR. EVANS: Do I have that data?

DR. BULL: That's what I'm trying to ask.

MR. EVANS: Well, the endpoint or the effect is based on a dermal application to the laboratory animals.

DR. BULL: I see. Okay.

MR. EVANS: But a lot of times we have endpoints from oral studies that we do.

DR. BULL: So it's purely empirical.

DR. ROBERTS: Dr. McConnell.

DR. MCCONNELL: Yeah, a quick question. Are these different procedures you're described to us today written out in SOP form, and are they available?

MR. EVANS: The --

DR. MCCONNELL: How you --

MR. EVANS: How do we calculate all those things? Those are, first of all, our standard operating procedures for residential exposure.

DR. MCCONNELL: For how you collect this material, are those in form of a standard operating procedure?

MR. EVANS: We have a standard operating procedure for how to make the calculations. And we also have guidelines on how to conduct those studies to get those --

DR. MCCONNELL: That's what I'm more interested in.

MR. EVANS: Yeah, very much so.

DR. MCCONNELL: Okay.

MR. EVANS: I believe some members of this Panel actually may have been on a guideline-related subject.

DR. MCCONNELL: I recall the guidelines for post-application.

MR. EVANS: Yes.

DR. MCCONNELL: But that's the only one I recall. There are guidelines for other things.

MR. EVANS: Right. Not this Panel, but previous panels have addressed the application aspects as well.

DR. ROBERTS: Dr. Durkin then Dr. MacDonald.

DR. DURKIN: I see that you cover the public health use of chemicals in that sort of indirect sorts of exposure. What I didn't see -- and I may have missed it -- did you address pesticide exposures to populations that live close to or adjacent to agricultural areas? You know, cotton fields, tobacco --

MR. EVANS: No, we did not.

DR. DURKIN: Okay.

DR. MCCONNELL: Isn't that your spray drift?

DR. ROBERTS: I'm sorry. Dr. McConnell.

MR. EVANS: I believe you're referring to spray drift.

DR. DURKIN: Drift from agriculture.

MR. EVANS: Right.

DR. MCCONNELL: Excuse me for interrupting, but they have guidelines on how to measure spray drift.

DR. DURKIN: No, I'm not talking about how you measure drift; I'm talking about those populations who their residence is close to an agricultural area where pesticides may be applied over the course of the season, so folks living next to tobacco fields, cotton fields. I know they have methods to get at the drift. I wanted to find out was that drift factored into the risk assessment.

MR. EVANS: No.

DR. ROBERTS: Before we get to Dr. MacDonald's question, let me remind the Panel that our proceedings are being audiotaped; and it will be very use for someone listening to the tape if they can sort of make sense in terms of who's commenting. So if I haven't just called on you or it's not otherwise obvious who's making the comment, I'd appreciate if you could just briefly state your name before we dive in. And that way, we'll be able to sort it out later on.

Dr. MacDonald then Dr. Bull.

DR. MACDONALD: Just a couple of questions. Very clear presentation. But 4-19, Lawn Applicator Exposure Data, you said you selected a uniform distribution. It's not clear what this is a uniform

distribution for. What's the variable being considered there?

MR. EVANS: You unit exposure is the metric that describes how much gets on you on a per AI basis on the amount of AI used.

DR. MACDONALD: And, also, considering that you've accounted for the amount of clothing worn, but do you also consider what happens to the clothing afterwards? They'll come into the house. They'll sit on furniture. It will be handle by someone doing the laundry. So I don't think wearing clothing is necessarily the end of it.

MR. EVANS: Yeah, I mean, that's true. There's a number of -- I mean pesticides migrate. That we do know. But how do we actually model that is really difficult. We're really focusing right now on what we sort of think of as "big ticket items," the actual handling of the concentrate. That's certainly one aspect.

Probably over the course of -- at least my experience in this is that, you know, our guidelines are not -- you know, they're conditional. So we've always had a sort of step-wise view of things. The old days of agricultural applicators were okay, you know, in even probably home garden people were. But as time goes on, we get more sophisticated; we ask more questions.

For the residential, we're beginning to become comfortable with the application or beginning to come a little more uncomfortable with

post-application. But some of the more elusive and arguably smaller concentrations of pesticides that's still on the horizon for us to consider.

DR. ROBERTS: Dr. Bull, do you have a questions Mr. Evans?

DR. BULL: Just a quick. The past question about public health spraying brought up a question in my mind. That at least in some geographical areas lawns would not be sprayed for that purpose. I don't know how wide sprayed it is that you spray residential areas in other parts of the country. But where I am, it's most likely the guy that's got his kids on the boat running up and down the Yakima River that's going to be exposed rather than someone being exposed on the lawn.

I'm a little bit worried about the issue of identifying lawns as the major determinate of exposure for public health spraying. It actually might be drinking water exposure in some cases because that's the drinking water source, too. so I'm questioning that a little.

MR. EVANS: Right. Again, just thinking how we approach some of these things. There's an infinite number of exposure scenarios. But if it is applied to one's lawn and then goes out and performs activities, that's a pretty good hit. I think a random flyby is, you know, in my view, a little less of a potential.

DR. BULL: No, it's deliberately done in specific areas, not in lawns; that's what I'm worried about. Along the river, for example.

MR. EVANS: Right. I mean you're suggesting more of a refinement of our assumptions.

DR. BULL: Yeah. It may be true for the nation as a whole; but certainly in the area I'm in, it would not be sprayed over residential areas.

MR. EVANS: Right. I think I could say, fortunately, that none of these are used from a public health perspective in Manachi, Yakima area, the Washington area

DR. BULL: Tri-city area, yes.

MR. EVANS: Yeah. At least to my knowledge, these are used more in Florida, East Coast, you know, places like that down in the south. At least these pesticides are used in this respect.

DR. ROBERTS: Dr. McConnell.

DR. MCCONNELL: I just wanted to state that Dick lives in an unusual area. My neighbor, for instance, he subscribes to one of these outfits. And seven times a year, they're putting something on his yard. And, in fact, they put a little sign up to let you know when you've been there so that you don't let your pet run over on their yard. I mean in the neighbor I live, this is about every second or third yard has one

ever these signs in it, seven times a year. So this is not unusual at all.

DR. BULL: Not unusual in North Carolina.

DR. ROBERTS: Dr. Adgate.

DR. ADGATE: I just want to make sure I've got this straight. And as I've been thinking about this, and it's a very good presentation.

The question I have: This model as we look at this and try to fit all the pieces together is essentially cross-sectional. Right? You can -- I'm worrying about you got a bunch of different scenarios and how is it constrained so if you have a lawn you're more or less likely to have a garden, I would assume. And there's certain things fit together and certain things you wouldn't as you look at this. And I'm wondering how the model deals with that particular issue.

MR. EVANS: Yeah. We deal with it totally randomly at this point. So the percent of houses that use this pesticide on the lawn, you know, you're going to have a certain odds there. And just totally independently, you're going to have a garden.

DR. ADGATE: So there's no sort of correlation made --

MR. EVANS: Right. That's why the type of data that's bandied about every once in a while about the longitudinal, what people actually do, that would really be the key to really identify that co-occurrence. Right now, it's just kind of a roll of the dice.

DR. ROBERTS: Any more question before we move to public comment? If not, thank you very much, Mr. Evans, for a very clear presentation.

We have two individuals who've indicated an interest in addressing the Panel on this subject. One is Dr. Jeffrey Driver, from infosciencs.com. Dr. Driver. Welcome. Can you introduce yourself for the record?

DR. DRIVER: Good morning again. I'm Jeffrey Driver with infoscientific.com. I'm making some comments this morning on behalf of the Implementation Working Group, but also beneath that Residential Exposure Joint Venture, the group conducting the survey that Jeff mentioned, the temporal survey; also a group called Sound Science Policy Alliance that represents some of the OP manufactures.

A very good job, Jeff. And I have a theory that some of our hair loss may be associated with this cumulative risk assessment.

The comments that I want to make this morning really reflect my position and I think the position that I think many of us share. If you want to make comments, you should also be part of the solution. So some of the issues and next steps that I'll be suggesting are things that EPA has already recognized, is addressing, and also other stakeholders are addressing.

Some of the issues, I think, also as I'll point out, are work in progress or things that we need to do in the future. But I'll try to distinguish those.

I think, as Jeff's given you an appropriate impression of the complexity of residential exposure analysis. It's truly multi-route, multi-pathway issues of interdependence or dependence versus independence rather, conditional probabilities. There's a lot that we don't understand. We're ostensively trying to simulate human behavior across time. So we're all sort of residential experts in some sense and we all have an appreciation for the dynamic of that.

So you know, again, as Jeff said, we try to keep it simple but with the caveat that all models should be as simple as possible but no simpler. So I think that's kind of the state of the science and the challenge that we face.

What I'm going to do quickly is just give you a quick overview of some of the issues, next steps. First under the rubric model input and output quality assurance review. As Jeff mentioned, some of these issues have already been recognized. So I won't belabor some of it.

Label application rates, just checking our accounting system, making sure things are correct. Product-use scenarios, Jeff mentioned there's kind of an ongoing understanding of what's registered and

what's not. I give an example of a scenario that is not registered as we understand it, but it is included.

Exposure duration corrections at some of the upper percentiles. It appears that we have greater than 24 hours per day for some individuals. That is, they might be spending 24 hours inside the home maybe inhaling DDVP and then they go outside and spend a couple hours on their lawn. That's another quality occurrence check.

The evaluation of the impact of alternatives of uniforms distributions under the guise of sensitivity, you know, as Jeff has requested the Panel's advice in this regard, I think we do have some opportunities to explore distributions other than uniform, which, of course, assumes that every value within that range as an equal likelihood of occurring. Most data sets have some shape and some inferred probability at the upper and lower tails, typically, of occurrence.

So, you know there are some examples that I mention there. The hand-to-mouth, I'm particularly interested in. And I'm hoping Natalie and others can give us some advice there. We mentioned the indoor versus outdoor differences.

The unit exposure distribution as Jeff indicated, we have some fairly good data sets for those. This is getting an applicator exposures

for different methods of application, clothing configurations. I think that's a ripe opportunity there.

We, also, recommend that EPA and other groups for that matter, too, really investigate this temporal product use and single-day co-occurrence prediction. As Jeff mentioned, you know, what we have is a predictive algorithms that allow us to do this. But I very it's very important that we have explicit understanding. I challenge us to do this.

We need to understand how the algorithm is structured and is working. And very importantly, what's the interpretation quality of the underlying data. For example, Jeff mentioned this generic sort of general market share values by scenario. What's the percent of uses versus non-users in the U.S. that use lawn-care products.

But underneath that, there are other conditional probabilities that John Adgate was sort of getting at. For example within, you know, this general market share, what's the relative market share of using one OP versus another. If you have multiple OP products that could be used for the same scenario, say, to treat the lawn, which one do you pick within that group?

There are other examples of conditional probabilities. You know, if you have a lawn, is there an associated likelihood that you

also have a garden, a vegetable garden.

The REJV survey and other survey data I think allow us to get at some of those conditional probabilities that otherwise we have to kind of piece together as a patchwork quilt from various data sets.

Timing and frequency of application by region. I think as Jeff pointed out, why do people use pesticides? That's kind of where we have to start. You know, you're managing pest population dynamics which, of course, can change from year to year. But, again, temporal survey information, I would submit, is what we really need to understand this in a realistic way.

Explanation of the peak exposures observed in graphical outputs. I'm sure you all looked at these three 65-day plots of different percentiles. And, of course, those each day might be a different person. You know, it's a 99.9-, 95-percent person represented at that percentile. And sometimes you'll see peaks and features in these plot schemes.

Well, understanding what's driving those peak exposures, what's the underlying demographic of that individual, their activity pattern, the scenarios involved that are driving their residential assessment; you got to really investigate those peak exposures. Obviously, they have important regulatory implications.

That kind of leads to the next theme of contribution sensitivity and uncertainty analyses. And I think, again, under the guise of sound science, transparency, stakeholder involvement, we have an obligation to pursue this, to give our risk managers the best information and advice we can.

One of the things that concerns us is I think EPA, and we have an obligation as well as others of us who are interested in, evaluating the biological plausibility and statistical representativeness of some of these upper percentile values. Are there people who are spending more than 24 hours in the day? Are they consuming, you know, if you look at the dietary, same issues really apply. Are they consuming plausible amounts of foods? So are the combinations of various input values resulting in simulated people who are understandable and within the realm of reality.

Meaningful drill down. As I implied with the previous slide, contribution analyses. Trying to figure out what's driving these peak values or for any given person or population strata, what chemicals are contributing, sources, scenarios, lawn care, garden, et cetera, even which specific products they're using. Which specific OP product they're presumably using, pathways and routes.

This type of uncertainty contribution sensitivity and uncertainty

analysis, I would submit, is really needed prior to determination of an appropriate percentile regulation. I mean, what confidence do you have at what percentile that you're looking at. I think you've got to establish that before you can really decide on a percentile regulation.

I'd also submit that you need these analyses, again, for meaningful risk management. If you're going to do mitigation, you really have to decide what you're mitigating. You know, what products are involved, what scenarios are involved. Particularly with the residential, you know, again, it's a variety of inputs that create this exposure estimate. So we've got to be able to drill down. We can't just look at methamidophos equivalents. We have to drill down to figure out if mitigation is necessary and what it would be.

An issue that has been raised previously that I think deserves careful consideration is what's the most appropriate exposure metric. We're looking at route-specific exposures right now, external exposures, and comparing them to methamidophos benchmark doses and going through relative potency factors. That's fine.

Another alternative altogether is to look toxic equivalent dose in terms of total absorbed dose. With the current situation, we're looking at route-specific external exposure and comparing it to some bench route specific benchmark dose, should we be looking daily

exposure metrics or should we be looking at some time averaging, moving average metric.

And I think that's if you look at the underlying kinetics and I think the Panel can hopefully give us guidance in this regard, what should we be exploring in that situation. I think there's a relevant opportunity to look at some type of moving average here.

Finally, it's important, you know, for all of us to review and participate in and also review the upcoming revised version of the cumulative risk assessment.

Thank you very much.

DR. ROBERTS: Thank you. Are there any questions for Dr. Driver? I don't see any, so thank you very much.

The second individual who's requested the opportunity to address the panel is Dr. Judith Schreiber from the New York State Office of the Attorney General.

Welcome, Dr. Schreiber, and could you, also, introduce yourself for the record.

DR. SCHREIBER: Certainly. Good morning. Nice to see you again. I'm Dr. Judy Schreiber, senior public health scientist with the New York State Office of the Attorney General.

Again, a very commendable effort by EPA and certainly a very

clear presentation. These are clarifications and questions, observations I had during the presentation. My office will be submitting formal comments to the EPA on the cumulative risks.

The first question I had was with the regard to the pet products. It was mention, I believe, that that has not yet been assess but the intention is that EPA will be assessing exposure from use on pet products. Particularly, I'm concerned about potential children's exposure to hand-to-mouth activities in playing with their pets.

How does the EPA intend to assess this, and will the public have an opportunity to comment on that portion of the assessment prior to the document becoming final? That's one question I have. Should I just continue and --

DR. ROBERTS: Sure. Would you, please.

DR. SCHREIBER: Okay. Thank you.

Another question that came up. And I'm taking these in order of the presentation that the EPA made. What about inhalation exposures during the scenario of children playing on lawns? There was quite a bit of discussion about the rolling around and dermal absorption and clothing contamination that sort of thing. I think that's very good.

But I believe there could certainly be a possibility that the child might, also, inhale some of the material as they're rolling around with

their nose to the dirt in the grass and so for the. So I think that really needs to be assessed, at least a ballpark assessment of whether that's a significant contributor.

Also, ingestion of both soil and grass by young children is a common phenomenon. I know my kids were little they definitely dug around in the soil and often tried to put it in their mouths. Was that assessed with regard to the rolling-on-the-lawn scenario?

Another comment about the golf scenario which I thought was quite interesting. I've read a number of recent reports in the popular press in the popular press about increasing numbers of children playing golf. Tiger Woods has inspired a whole generation of kids to really like golf and go out there. And there's been a lot, I understand from my golfing colleagues, in golfing magazines they're talking about the increasing number of children and, also, the effort to try to include more children in playing golf.

So has there been any effort to assess the percentage of the population of children that might be actually on golf courses and potentially exposed to government treatment chemicals?

One particular area that I didn't hear and maybe I missed. It's possible it was included in another section. School exposures to pesticides, I didn't hear that mentioned at all; and I think that's

potentially a very large area. I know certainly in New York State we now have a pesticide notification regulation where schools that treat their indoor environments and their outdoor fields, soccer fields, football fields and so forth, have to notify parents. There's been a lot of concern from parents about potential exposures in school settings. And I didn't hear anything about that. But I think there probably are some data that are available that talk about the percentage of schools that treat either indoors or outdoors with OPs.

And I think it's a great concern to parents and especially for young children, are they being exposed to OPs in their school environments that could cause them to have undue exposures, especially for young children, but also for sexually maturing teenagers, I think that's probably equally an area of concern. And I didn't hear that discussed.

Two final points. One, although, I certainly understand the need for these mathematical manipulations, they're also a little bit troubling in some regards. For example, it was mentioned that -- and it might have only been an example but let me just carry it through.

For instance, 6 percent of homes and lawns are treated in a particular geographical location in the country. While that may be true and one can figure out what the overall average population

exposure could be if 6 percent of the lawns are treated. But if you are a child playing on that lawn, your exposure probability for that child is a hundred percent. That child is definitely being exposed. And I would like to see an analysis that in terms of the children who actually being exposed, how close is that child's estimated exposure to the point of departure for cholinesterase inhibition? How close is that exposure to the point of departure for neurotoxicity and neurodevelopmental effects. I think that's something that really needs to be looked at.

You know, if we take this room of people and only one of is exposed and we divide by the number of people in this room, well, then that number is very low. But if you're that one person who's exposed, you could be exposed to a very high level that can actually cause health effects. And I think that's a very serious oversight. At least in my reading of the documents, I haven't seen anything looking at that.

And then finally the public health uses. In New York State we have had experience using -- you have to forgive. I forget which chemical it. But for the control of West Nile Virus in New York State where there was quite a bit of public health spraying to control the mosquitos carrying West Nile. And we received a lot of residential complaints about inhalation exposures as well as concern about

exposures of lawns, gardens, and people because the spray would come down in areas where people were located.

And so I think that's a big concern that should be addressed even though it might be sporadic and it is necessary for public health protection, I think that's something that the EPA ought to consider.

Thank you.

DR. ROBERTS: Thank you, Dr. Schreiber. A long list of the questions. I guess, would the Agency like to respond to those?

MS. MULKEY: Well, I think that for most of this, that we will treat these as public comments. And we will be sure that we include them in our docket from these comments as well as from any that the Attorney General's office may subsequently submit.

I would say that if any of the issues give rise to questions in panelist's minds, we would welcome hearing that as you go through.

The only thing of this list that might be useful to spend just a few minutes on, because it comes up in a lot of context and I know that we've done some thinking about, is the school exposure situation. So, Jeff, if you just want to spend a minute on how we've thought through that issue. But beyond that, I think, in short of panelist's questions, we will treat these as public comments for our docket as well.

DR. ROBERTS: Thank you. Mr. Evans, did you want to respond to that one?

MR. EVANS: Right. I think, if I remember correctly and I know you always do a good job of refreshing my memory when it fails me. I think with the schools, we did look into the use of these pesticides, and we pretty much came up empty. Also for lawn uses, again, we stretched the time that someone could be on a treated lawn to include all time outside which, you know, at this point in time is at least a way to address time at school in which a soccer field or something like that may be treated.

You know, when we get a little more sophisticated and move people around in this model, we'll be able to do that. But right now, we just jam up all the time on the lawn to include the time at home and also time in other places.

DR. SCHREIBER: So I guess then you're assuming that the schools -- their use patterns will be similar to what the residential use patterns will be?

DR. ROBERTS: That was a follow-up question by Dr. Schreiber for the record. Go ahead, Mr. Evans.

MR. EVANS: Right. Right now, again, since we're not moving people around, we're just extending their time on a treated lawn to

account for other places.

DR. SCHREIBER: That would be a yes.

MR. EVANS: That would be a yes.

DR. ROBERTS: Let me just ask the Panel members if they have any questions for Dr. Schreiber or for the Agency in view of Dr. Schreiber's questions.

DR. HATTIS: Do you have any sort of documentation about insecticide use in school's day-care centers? I'm thinking of sort of cockroach treatments and things of that sort.

DR. SCHREIBER: I do believe that we could probably generate some. I think in New York State, because of the notification requirements, we probably do have some data that I could try to provide for the EPA. Sure. Thank you, Dale.

DR. ROBERTS: And Dr. MacDonald.

DR. MACDONALD: I'd just like to say the contact I've had with this work it still leaves me wondering why institutional exposure isn't taken more into consideration. I'm thinking back I think it was the Lifeline, for example, which was looking at the residential exposure but not institutional. And it was showing that when children started to spend more time hanging around in malls and schools and places, that their apparent exposure levels dropped. And I really had a

concern. Was that simply because the model wasn't taking into account the exposure they would find in the places they were hanging in.

MS. MULKEY: It may be helpful to remind all of us that many, though not quite all, of the organophosphate have been canceled for these public-setting uses. So the remaining compounds that lawfully used -- or will be at the relatively short time line -- are only those that are identified in this assessment. I need to make absolutely sure about that. But I'm pretty sure about that.

So we don't have a different group of compounds. And the number of compounds involved is now very small. Nevertheless, the rest of the answer was the one Jeff gave, that the attempt to have and, in fact, have home setting be a surrogate for the institutional setting by extending the time.

DR. ROBERTS: Thank you, Ms.Mulkey for that clarification. And thank you, Dr. Schreiber, for your comments.

Let's go ahead and take the first question under this section. Could you pose the question to the Panel, Mr. Evans.

MR. EVANS: I do have to confess. This is a little difficult for me so bear with me. I'll be visiting the eye doctor in two weeks. I'm at the trombone phase of reading large and small print. I'll do my best

here.

Historically, the Agency has relied on means (primarily arithmetic or geometric) from residue and exposure studies for key input variables in exposure assessments. The recent development of calendar-based models and others having features to incorporate distributions of exposure values has presented the Agency an opportunity to consider using all available data points from existing exposure and residue studies.

In the Cumulative Risk Assessment Case study presented to the FIFRA Scientific Advisory Panel in September, 2000, most of the exposure variables were presented as uniform distributions. The exceptions were for variables that are reasonably well established, such as exposure factors taken from the Agency's Exposure Factors Handbook.

The data used in the Case Study and the preliminary CRA are believed to be from well-conducted studies of generally high quality. However, these data sets tend to be small (e.g., n = 10 - 30) and are being used to address wide variety of exposure situations.

The uniform distribution appears to be the most appropriate for these relatively small data sets because it relies on easily established values such as the minimum and maximum and provides the most

conservative estimate of the standard deviation.

Does the Panel have any additional comments or thoughts on the OPP's use of the uniform distribution in general on OPP's selection of the uniform distribution of the specific parameters chosen? What criteria, if any, would SAP recommend for parametric input distributions from available data? Under what circumstances, if any, would it be appropriate to use available data empirically?

Does the Panel have any recommendations on how sensitive analyses could be performed to determine if the assumption of a uniform distribution is responsible for a majority of the risk at the tails of the exposure distribution?

DR. ROBERTS: All right. The first question is, of course, in fact, a lot of questions. Dr. Adgate, would you like to lead off the panel discussion on this.

DR. ADGATE: Fortunately, I have lots of answers or at least attempts at answers.

I want to say just in starting out a couple of things. This is a very nice presentation, and I got a much better sense having seen this presentation what this was about than I got if from reading the document. Clearly, there's a lot of things going on since that was written in December.

And I particularly like that table that though sort of lays out all the key assumptions and what you thought about their quality, the uncertainty associated with them. And I think that's an important thing that goes into the document in it's next iteration.

You know, that said, I think one of the things you're going to hear, I think, from a lot of us is problems with -- I mean we're the ones that told you to go and use the uniform distribution. Which brings to mind, the old analogy about when you have a hammer in your hand, everything looks like a nail.

And I think in this case, while the uniform distribution is a good idea, you know, it's the simplest tool you could use. And I think, as a group, we're probably -- I can't speak for everybody, but I suspect for conversations I've had with people that we're all going to sound something along the lines of you need to talk about characterizing the shape of the distribution based on even the sparse data that you have. So that's a quick summary of it.

We recommended the use of uniform distributions in the cases where data were sparse or uncertain. This is distribution which sets the minimum and maxima assumes each value within the range is equally likely and simplest model input. It's use is appropriate if you can -- which you seem to have done and all the values equally likely to

use as an analyst.

To me, a first step in a continuum as you move from a uniform distribution to a well-characterized distribution, in your question you're calling that fully parameterized or something along those lines, a well-characterized distribution based on large unbiased data sets.

As complex distribution, I think the next more complex is the triangular distribution. You can make use of here and make use of certain statistical testing techniques that will tell you something about shape that I think you could incorporate relative easily and that that would make your presentation of this fairly complicated model a little more convincing to me.

Changing from a uniform to a triangular distribution, for example, is one type of sensitivity analysis that you could performed based on residential exposure scenarios. You've taken away my example. I was going to -- now do I understand correctly that the DDVP scenario has pretty much gone away? Because that was the one where it was most obvious that I think the use of the uniform distribution was a bad idea because you had a case where you have decay over time which I think you could come up with a physical explanation for that that would be much more convincing to most of us. So I won't dwell on that.

In terms of criteria for developing what you call parametric input distributions from available data, I think you need to use an iterative process that's familiar to the Agency from a lot of other things, you know, good laboratory practice protocols and SOP and things like that. Things that ensure studies both are done in scientifically defensible manner and are statistically defensibly.

In the first case, I'm talking about things that have to do with performing the study using standard scientific methods, using QC protocols that characterize measurement error and variability. An example of this would be like chemical measurement use of appropriate methods, field lab, and calibration blanks, development and tracking of calibration curves over time, repeat analysis, standard reference materials and things like that.

There's analogous processes for a lot of the survey instruments that you're -- really, I think, is the nut of the problem is longitudinal tracking of behaviors, human behaviors, that really most of us recognize are one of the key uncertainties in this risk assessment, cumulative risk assessment.

Statistically defensible data is not a just question of sample size but of characterizing the important features of the study design that ultimately effect the derivation of data useful for this cumulative risk

assessment. This means using studies that have large enough sample sizes to characterize temporal, spatial, and individual variability.

It also means that the resulting empirical distribution to data are good estimators because they're consistent, they're unbiased, they're robust, and, hopefully, in the end practical.

To get back to your question about sensitivity analysis. I think that what you need to do is along the same lines of what you've done in other analyses that have been presented at this is you need to block either by the scenario or the compound and systematically remove either a chemical or a scenario and see what it does to your outputs. And that with possibly changing distributions or shapes of distributions to see what happens are sort of the standard things you need to do to figure out what's going on and what's driving your analysis at the upper bounds.

In previous Panels, we've recommended, you know, an explicit analysis where variability and uncertainty are treated as separate entities and doing a two-stage probabalistic analysis and there are people here who have more expertise on this that I do on this topic.

But in simple terms, the first would state the variability distributions, i.e., measurement error, while the second would get away from or characterize the uncertainty distributions. And this

would allow you to get to what I think is your ultimate goal is being able to describe the confidence intervals around your final estimate. It's nice to look at those traces over time, but I think what we all really want to know is what's your confidence in those estimates at the end of the day.

Apart from that, I have a couple sort of minor points. I agree to the exclusion of exposures that have been -- registrations that have been removed. And I do, also, think that the process would be a little more transparent if you present all the age groups that you've looked at. A number of people have commented on this. And I just think for purposes of being complete, folks need to see that.

And this whole issue, what I was asking before and couldn't articulate really well about conditional probabilities and co-occurrence. You know, whether or not somebody treats 100 percent of their lawn and then 109 percent of their lawn is 50 percent garden, but 100 percent of the lawn is still treated sort of questions are things that people are going to have questions about over time whether or not it's realistic.

And I, also, agree that this institutional exposure levels, schools, day-care centers and all that, has to be looked at in a systematic way. Although, I agree that there's -- I don't know how

much those right-to know laws are going to be helpful to you because a lot of the data that they generate won't necessarily be useful in this analysis in my experience.

DR. ROBERTS: Okay. Thank you, Dr. Adgate. Dr. Freeman, do you have any comments to add?

DR. FREEMAN: Yeah, a few.

First, I'd like to compliment Jeff and his colleagues on the work they have been doing. This is really an amazing undertaking and very, very challenging. One of the things that I found very interesting was your figure of residential scenario application and use schedules over the seasons for each of the regions.

I think this is an approach to take because it gets away from the idea of treating all of the United States as a single entity, which it isn't. There's enormous diversity in this country in terms of what you're going to use, when you're going to use it, and why you're going to be using it.

I'm not sure that I'm adding much more to what John has already said about the uniform distributions. My concern is that if you rely too heavily on it that it may, in fact, seriously distort the characters of the distributions that exist. The impact of uniform distribution on an exposure estimate will be determined to some extent by the

characteristics of the original distribution and the size of the data that provided it.

With some of the data -- what I do when I have a data set is I go use my Kolmagorov-Smirnoff test to try to find out what sort of distribution it has. And if it says that it's not uniform, I won't use uniform. I'm a very happy to use medians rather than means if it better characterizes shapes of distributions. And as John was saying, triangular sometimes is a really good way to go.

You asked the question about when it is appropriate to use empirical data. As a field person, my counter-question would be when is it not appropriate to use empirical data? I have colleagues who are model people who say, you don't need any data; all you need is physical principles and you can do everything.

The problem with that is it is the data that is drawn from the field in terms of what people do, what their exposes are, what the biomarkers are that actually tells what's happening. So I say use empirical data whenever you can with great comfort.

I would suggest that -- I think in your study you mentioned something like 11 different variables in which you were using uniforms distributions. When you're looking at the average individual, I don't think that's a problem. But if you're look at the 90th or the 99th

percentile, you may be having extreme effects, creating a high-level exposure that's not really there.

And I think for some of the regional things that seemed to be the case, that the residential was driving these exposures. And I think that may be at these high ends because of this multiple magnifications created by using too many uniform distributions at the same time.

And I guess that's what I have.

DR. ROBERTS: Thank you, Dr. Freeman. Dr. Hattis, do you have anything to add?

DR. HATTIS: Yeah. I, unfortunately, have a relatively comment that's going to conflict to some extent with the advice you got in September 2000. So I'm sorry to be inconsistent. But if you ask more than one person and they say the same thing, at least one of them is redundant.

First I want to that the EPA staff is to be commended for what appears to be an initial effort to apply the techniques of distributional analysis to represent the population variability of residential non-occupational exposure to pesticides. Unfortunately, the choice of the uniform distribution for generic application to limited data sets and summary statistics is very ill-advised.

In my experience reviewing probabalistic assessments in the

past several years, I found that the uniform distribution is the single most over used distribution and nearly always significantly distorts available information about the variability or uncertainty to the parameters to which it's applied. It is particularly the case where there are limited directly observed data.

Analysts often give the perceived simplicity of the uniform distribution as an important attraction. Moreover there's often an impression as stated in the text paragraph introducing this question, that quote, "it relies on easily established values such as the minimum and maximum." In fact, it's not to so easy to appropriately establish true minimum and maximum values from observed ranges from limited data sets of empirical observations.

It's completely incorrect in general to assume that the largest and smallest values of a group of 10 to 30 data points or fewer represents the true minimum and maximum values that that parameter can assume. Moreover, there are few cases where the mechanisms that cause measurement or estimates of exposure-related parameters to vary among people to create situations where there is no greater chance of producing a case near the center of a distribution than at extreme ends as would be required for the uniform distribution to be correct.

Much more commonly, factors that cause exposures to differ from one individual to another tend to interact multiplicitively leading, when this factors are numerous, to expectations of a log normal distributions.

Sometimes where categorical factor of two is likely to have a strong influence like wearing short-sleeved shirts versus long-sleeved shirts or short pants versus long pants influencing dermal exposure from hand spraying on page 14, it's good to create mixtures of log normal distributions weighted by their expected frequency to represent the influence of these different known cases.

The uniform distribution is appropriate in cases where, one, it's physically impossible for the parameter to take on values outside the limits; and, two, there's really no greater likelihood of values close to the center of the range than at either end. For example, I have no problem using the uniform distribution to represent the probabilities of when the meteor is likely to hit, which day of the week for example. That's not a problem.

But my experience is that uniform distribution is often selected in cases where there's -- anyhow. The other generic difficulty with the uniform distribution is that it plays into directly into over-confidence bias which is one of the most reliably established phenomenon in the

psychological measurements of people's misconceptions of probabilities.

And that same things applies to the triangular. Then my prejudice would be to say you ought never to assume a defined limit unless you have a reasonable physical basis to impose that limit. Otherwise you should tend to expose unlimited distribution.

I'll get to ways in which you can put in reasonable limits where they we must be there in a couple of paragraphs.

I want to refer briefly to 1994 paragraph of mine that gives a series of rules and examples of mechanisms that give rise to different distributional forms.

Experience and the basic idea that variability is often the results of combined actions of many factors adding multiplicatively indicates that the log normal form is the most often the best choice for exposure-related data where there are limited information. Both normal and log normal distributions have just two parameters, so they're in fact statistically no more complicated than the uniform distribution. And there's, you know, relatively straight forward methods to estimate the parameters of normal and log normal distributions.

The current document doesn't, unfortunately, provide a detailed

description of the data underlying it's various choices of uniforms distribution. Nevertheless, I'd like to make some specific comments on particular cases to which you've applied this distribution.

Page 9, you talk about this distribution of sizes of lawns, and you've applied this uniform distribution from very small value to something that's slightly over the mean that was observed in the cited paper. And I understand why you might want to have the mean of the distribution you select be slightly smaller than that mean there because of the presence, as you said, of stuff that takes up area that's not lawn that isn't included in the calculations that they made.

But I would rather you be faithful to the original data and then have some variable factor for the rest of the thing. As you say, ranging from 10 to 50 percent, you can easily put that in as a second variable factor depending upon what your information is that leads you to believe that it takes up that lawn, those fractions.

Pages 11 and 13 give 14 applications of the uniform distribution. In general, the ends of the ranges provided differ one from to the other by many fold. Sevenfold, for example, in the case for inhalation exposure from a hand-pump sprayer to over 1,800-fold from a hand garden duster. Such large multiplicity ranges are based presumably on data sets with limited number of observations strongly

suggest that you better be selecting something like a log normal skewed distribution.

A modified Poisson distribution can also be used in cases for which there is, in fact, a defined upper limit to a process, for example, the fraction of pesticide in soil on fingers that's removed by inserting a child's fingers into his or her mouth. In this case, the fraction clearly must have an upper limit of one or 100 percent.

I handle cases like that by postulating a log normal distribution of basic transfer rates K among children and then modeling the fraction of soil particles or molecules transferred as the fraction that receive one or more quote "hits" in a Poisson formula. And the formulas in the thing is very simple.

Basically, the fraction absorbed is the 1 minus the fraction of soil particles that get more than one hits which is 1 minus E to the minus K where K is log normally distributed. As K goes to higher values, then you get toward this natural upper limit.

And then I had a comment on of the DDVP that I won't say because you're going to take that out anyhow.

Thank you.

DR. ROBERTS: Thank you, Dr. Hattis. We seem to be of some consensus that too much use of the uniform distribution but some

differences in advice on what to proceed and what to use elsewhere. Dr. Bull, what do you have to add?

DR. BULL: Not much. This is a little outside my area of expertise, and I bow to the folks that went before me because they're much more schooled in this area.

I did notice one other question I'd just like to ask. Did I understand in your presentation that the 1 to 2 year old age group is actually 12 to 35 months?

MR. EVANS: Right.

DR. BULL: So why don't you call it that? Or is it just -- I have real simple questions.

MR. EVANS: I wish I had a simple answer. But we did go around and around on this and those are just the little boxes that we tick in the model. But that's exactly misleading as can be.

Dr. Freeman had that question, and I made sure that I found out how many months that I was. And I'll get that back to the people that outline it that way.

DR. ROBERTS: Let me open it to other members of the Panel for their viewpoints. Dr. MacDonald and then Dr. Durkin.

DR. MACDONALD: Just a few comments on the uniform distributions. I think I'd take a little more pragmatic approach than

Dr. Hattis has suggested. But just have some general principles. If you got especially a small sample and distribution that really has a long right tail, then you fit a uniform distribution using the minimum and maximum, you're going to overestimate the mean and the median. So that's pulling the values up a bit.

But then when you go to generate data, you're precluding getting any generated values higher than what was observed in the small sample. And that sort of pulling your answer down in the other direction, you're going to avoid generating really extreme cases.

I'm assuming that your simulations here are all set up in a way that's fairly easy to tweak because you're expecting a lot of suggestions for tweaking them. It would seem to be fairly straight forward just to replace your uniform random number generators by log normal, gamma, Y-Bole, or for discrete data, negative binomial.

I would think that just fitting these by moments and using mean and variance of your small samples rather than maximum and minimum and just finding the log normal gamma Y-Bole negative binomial that matches and trying that and just see how sensitive the results are to the change. And I think that would be a fairly straight forward exercise even just to try for a few scenarios.

DR. ROBERTS: Thank you, Dr. Durkin.

DR. DURKIN: Well, Peter, really just made my point. Although I didn't understand half of words that he used. But I seriously do want to strongly endorse what Dale has said I think very, very well.

People like to use the uniform because they think it is simple. They think it's conservative. None of the distributions are all that difficult. And the log normal is no more difficult than the uniform. And the uniform, I think, can run the risk -- and I believe I heard Natalie make this point -- of distorting risk a great deal particularly at the tails.

So while my understanding is not as sophisticated as perhaps others, I don't think it's a very difficult or complicated issue. So I would encourage the committee to basically put in the elegant discussion that Dale has given us.

DR. ROBERTS: Okay. Thank you. Dr. MacDonald.

DR. MACDONALD: Yeah. Since Dr. Durkin commented on my terminology, I'd like to make another comment on terminology. And that's the use of the word "conservative." When we talk -- it's never clear when you use the word conservative in the documentation here whether you're meaning conservatively high or conservatively low. If you want a conservative estimate of exposure, I think you usually

mean we're overestimating just to protect people.

But in the wording of the question here, you're referred to the conservative estimate at the standard deviation. And I'm just not sure whether you mean overestimate or underestimate. So I guess I'm advocating against such general use of the word conservative.

DR. ROBERTS: Dr. Heeringa.

DR. HEERINGA: I'm trying to go back through my recall on some initial sessions on residential uses. And I think what may have occurred here with the use of the uniform distribution is that we offered an alternative as an SAP to a methodology which was using constant values for many of these parameters. Essentially, the suggestion to use uniform or a triangular was in a sense an attempt to move EPA in this particular simulation off the use of a large number of constant values, often with very little empirical basis if any empirical basis, to introduce the sort of any type of uncertainty into the parameterization of this particular piece of the model.

So I think that the suggestion to introduce some distribution to introduce uncertainty into the estimation. Now, maybe that was a poor recommend. But it was really in contrast at the time to the use of fix values and often values without any empirical basis as the basis for the residential route of exposure.

DR. ROBERTS: Okay. Thank you. Any other discussion among Panel members might help sharpen our recommendation? Dr. Adgate.

DR. ADGATE: Just to say that Steve's right. I think that's historically accurate.

DR. ROBERTS: Okay. Then it seems to be, as I pointed out a little earlier, the consensus that it would be good maybe to move beyond the uniform distribution. We have lots of suggestions for how you might do that. Hopefully. Those might be useful. Do you have any questions, clarifications back to the Panel about our comments and recommendations?

MR. EVANS: No, I don't.

DR. ROBERTS: In that case, let's go ahead and take a break now. I'll reconvene in 15 minutes, and we'll take the second question.

[Break.]

DR. ROBERTS: Let's go ahead and begin. Before we tackle Question 2, I believe Ms. Mulkey wanted to make a comment.

MS. MULKEY: Yes. I think it would be a good idea to clarify the regulatory information on DDVP pest strips, as I understand it, perhaps a misimpression we gave you. We wanted to that analysis will, also, have to consider a different scenario.

But, in fact, the regulatory status of the pest strips is that the registrant -- well, first of all, I should say that DDVP is one of a handful of remaining organophosphates where we have not completed the risk assessment and the risk management process for the chemical. So it is still one where are actively working through the issues specific to the individual chemical.

The registrant of that product has asked us on a voluntary basis to remove from their labeling the authorization or the labeling for use of the pest strip in primary living areas such as bedrooms, living rooms, kitchens, any primary living areas as I understand it. But the product would continue to be marketed even during this period for areas such as closets, basements, attics, garages, perhaps. And I'm speaking without absolute precision. I don't have the labeling with me.

I believe this is consistent with the regulatory status of the product in California. But as of now, the registrant has not voluntarily amended its license to prohibit those uses. They have instead voluntarily changed their marketing, that is, their labeling for that period.

So unless and until we complete our regulatory conclusions about the product, I think, and in light of the limitations or the scope

of the voluntary actions by the registrant, we should not leave the impression that the DDVP pest strips are quote "canceled."

And I wanted to say that early enough that if that caused you to be more interested, any of you, in talking about that part of the risk assessment, it does not appear to be moot or irrelevant, those parts of the risk assessment.

DR. ROBERTS: Thank you for that clarification.

Let's go ahead and take Question 2. Could you pose that one to the Panel. You did, by the way, a great job on the first one.

MR. EVANS: The use of calendar based models also allows exposure accessors to consider exposure from a variety of sources from the same or from different chemicals. Longitudinal survey data such as the national Human Activity Pattern Survey (NHAPS) are available for consideration by HED for use in future assessments. In addition, from a practical standpoint, the use of such survey data ensures combinations of exposure do not come from unrealistic random combinations that current models may produce (e.g., activities adding up more than 24 hours in a day).

The use of calendar-based models provides an opportunity to explore the potential for the co-occurrence of multiple sources of exposures from residential pathways. In the cumulative assessment,

OPP used summary statistics from sources such as the Exposure Factors Handbook (EFH) regarding the time spent indoors, time spent on lawns, and time spent at other outdoor locations. In the preliminary assessment, we assumed these activities were stochastically independent.

OPP is currently evaluating data in the EFH such as data from the NHAPS to determine if it can directly incorporate (i.e., empirically) information on an individual's activity patterns over a full day from this database to account for the likelihood and duration that an individual might be exposed to a pesticide through various activities over the course of a day.

Please comment on whether and how OPP might directly incorporate NHAPS or similar time use data into the software to better account for variation in activities across individuals?

DR. ROBERTS: Thank you. Dr. Freeman, any suggestions in that regard?

DR. FREEMAN: Basically, I was trying to think about that. And what I said was, Gee, what you really need is a statistician. But, in fact, I think incorporating NHAPS might be done similarly to the way the dietary data was incorporated for that model.

I love NHAPS. I think it's a great data set, but there are

problems. One of them is that while it is a very rich data set, it is about half the size of the CSFII. It only has about 10,000 cases for the United States. And if you are then breaking it down in terms of children of different age groups, you're beginning to get into small numbers again. Small is relative. We're talking hundreds across the United States.

There is, also, the problem that there are several versions of the NHAPS questionnaire that were used. And trying to integrate results of them, I'm not sure how you do it. That's going to take somebody who really knows how to work with those data sets.

One of things that's really great about NHAPS, which would be very useful for you, is that if you look at the data as a whole, you can see both regional and seasonal differences in activities. Everything from ventilation, whether you have your windows open or not. In the winter, it's very different in Minnesota than it is in Florida. This is very useful in you're looking at infiltration from outdoors or things like that.

If you go back to the children, if you then break it down either by region or season, you're getting into small numbers. And if you break it down by both, then you're really into small numbers. You're getting to where we are with the hand-to-mouth stuff, you know, 10 to

30 in a group. And that's very, very frustrating.

But at the same time, there may be differences that you want to pick up when you're doing this regional analysis. And I'm not sure how you're going to want to play the game. Whether you're going to want to use, for instance, all children between the ages of 12 and 35 months for the nation as representative of kids all over the place so you can look at seasonal differences or whether you want to break it down by regions or forget the seasons. It's going to be a little bit of a challenge there.

One of the other things that you talk about, ask questions about, is whether or not activities are independent. Many activities that people engage in, not only activities but where they engage in them, are not independent either within a day or across days.

For school age children, children of people who work, and for adults who work, both daily and weekly activities time allocated to them when they are done and where they are done are driven by the occupation or for the school-age children by being a school-age child.

You have to keep that in mind when you're going to be drawing from this wonderful rich data set that some of the things for individuals are not independent.

I guess that's all I have to say.

DR. ROBERTS: Okay. Thank you, Dr. Freeman. Dr. Adgate, would you like to add something.

DR. ADGATE: I don't have a whole lot to add to that. I think I said pretty much what I was going to say in response to the first question.

The one additional thought that I have is that -- and I'm not a statistician and they probably ought to be consulted on this -- there are techniques that exist for estimating longitudinal patterns and distributions from what is essentially cross-sectional data. And I think that's a general problem that you have with a number of your analyses. And it might behoove you to put some resources into that general problem in seeing how you can apply it where you need to as a tool in this analysis.

DR. ROBERTS: Thank you, Dr. Adgate. Dr. Hattis.

DR. HATTIS: Yeah. I think, generally, the idea of incorporating the activity pattern data over sequence days is a good idea. And the likelihood is that these things are going to be associated with weights that you can use to adjust your population weights of each individual that was studied in the survey.

I would say that, as we go forward, in general, the approach here should not be a rolling average but a very simple compartmental

model in which the cholinesterase inhibition tends to decay at some rate that can be inferred from one model of the approach to steady state observable in the animal experiments.

And, two, a human-animal adjustment factor to take into account that we big animals tend to metabolize and eliminate things at a slower rate. And the center of that distribution is usually approximately given by a animal body weight to human body weight to the one-quarter power-type formula as Lorenz can testify to.

I basically got -- as to the uncertainty of that translation, I've got some recent work that sort of gives the observed spread of animal-human conversion factors, in this case rat-human conversion factors, based upon the old Frederick data sets and several other sets that have been compiled by Paul Price.

To make a long story short, for the 18 rat-human projections that were available, sort of the geometric mean departure of the human potency from the observed animal toxic potency for these anticancer agents was about .89 with 95th percentile of about, you know, 4.3.

Anyhow, there's some real data that can be used to get the uncertainty and what, at least, a starting animal-human projection factor for the reduced metabolism rate is that can be used for that kind of modeling. And I cite a reference here.

But basically the 7-day window or a 21-day window is possible. It's almost as easy to model the co-expected brain cholinesterase inhibition itself with the adjustment that you should expect the humans to eliminate the inhibition at a lesser rate than the rats do.

Whether that's something that you want to attempt for June or on some longer-term basis, it's up to you.

DR. ROBERTS: Dr. Reed.

DR. REED: I don't have a whole lot to add into what's been said.

I'm really excited about data becoming available. I'm curious about and I'm not a statistician and I'm not ready to make some recommendation or anything. But I'm curious about how the different data bases could be used together in separate sets or how that choice would be. I'm hoping that someone might be able to make some comment about this issue. I think it's very important.

The other one is sort of not directly about this question, but I think it's an important point. It might be a good place to bring it up. It's that the importance of doing a mass balance whether it's been time or location or anything. I think in one of the previous meetings we brought up an issue or the concern about such a situation where, if a certain proportion of the ratio has been taken up from the same

location area or contact surface, then it should be that it's no longer available for the next time series exposure.

So that I would like to see a more clear coverage on that issue.

DR. ROBERTS: Dr. Durkin.

DR. DURKIN: Since I'm kind of at the anchor position here for exposure assessment, I do want encourage, of course, the use of calendar-based models in response to the question that you proposed to us to the extent that we can demonstrate that they lead to plausible results. But there are a few other odds and ends with the exposure assessment that I would like to bring up briefly.

Two of those relates to comments that we heard from the public; one being the transparency, the ability to drill down by chemical. I was thrilled to see the graphics from the drinking water folks who were showing us over time the different individual chemicals. I haven't seen that in food. I think that sort of thing is very important, and I want to encourage that kind of transparency.

The other minor footnote that I will pass on is that, on the issue of inhalation exposures, I think you have addressed extremely well, perhaps not in the document that we are dealing with here but in a document that you referenced. I went and got ahold of it; it's your document on I think it's called "Residential Exposures," rather large

and it's on your web site. And in general, except for things like DDVP, the inhalation exposure, I think, it's relatively well known and documented is going to be extraordinarily small compared to the dermal and oral exposures.

Two other points. One is I am a little concerned that my lap top always goes to sleep when I look at it. Okay, there we go.

The one sort of serious concern that I have about your exposure assessment is the failure to address populations that live adjacent to sites where there might be a lot of agricultural use. To me, conceptually, this is something like the sorts of exposures that you did address with sprays for public health which I think was very appropriate.

But there is a subpopulation, and I don't know how big it is. But they do live adjacent, right up next to things like cotton fields, tobacco fields where there are a lot of chemicals put out over the course of a growing season. And these people do have gardens. They have lawns. The extent to which you want to look upon them as maybe a typical subgroup; I can't really answer that. I don't know. But I just bring it to you for your consideration.

The last point that I'll address again, just briefly, relates to how you do your exposure assessment and then start to segue into risk

characterization. And this is really a follow-up from a question that Dick Bull had.

What you have always done with the pesticides has been to combines different routes of exposure by taking the let's call it a "point of departure" for the route-specific points of departure. So you take an oral study, an inhalation study, and a dermal study; and then you take ratios to the exposures by the same routes. So you're not really doing route-to-route extrapolation; and that's fine.

I'm not critical of it. But I do think the document might benefit from at least addressing why you don't take the other approach, that I think Dick is comfortable with and I am as well, and, in fact, it is one that I tend to use, where you take the multi-route exposures and do your best to convert it to an equivalent oral dose and then you use the oral tox data as your point of departure. The nice thing I can say about that approach, and you ran into this with your analysis, is that, in general, the oral studies are more abundant and they tend to be better. A lot of the dermal and inhalation studies, first of all, there's fewer of those and they often do not have the same quality. And this is particularly true had you look at the longer term effects.

So I'm not trying to proselytize here to get you guys to convert in any way. But I do think it is something worth talking about in the

document because I do think it makes a difference in your ability to characterize risk.

And I would, also, note that taking that route-conversion approach is going to end up very consistent with where I see you going, and we'll talk about this at the very end of the day or tomorrow, where I see you going with PPBK models as you have discussed in your future dates.

So that's all I have. Thank you.

DR. ROBERTS: Thank you. As Chair, I appreciate the interest in panel members in getting in comments before we move away from exposure into risk characterization, that it may be not exactly to the questions being posed.

Let me ask the Panel members, though, as we go through the questions, let's go ahead and focus our comments and feedback on the specific questions. And if we will sort of maintain our discipline in that regard, I will promise the Panel the opportunity this afternoon or at the end of the session to offer whatever comments they might have had that just didn't fit in with the questions or they didn't get the opportunity to raise earlier. And that would apply to any of the aspects of the cumulative risk assessment, hazard and dose response exposure, risk characterization and so forth.

With having said that, are there any comments from other members of the Panel as it specifically relates to the question posed to us here by the Agency?

Let me ask the Agency, would you like some clarification on our response to this question, or is it pretty clear?

MR. EVANS: It's pretty clear.

DR. ROBERTS: Okay. Great. Then if they're no other comments on this question. Let us proceed to risk characterization.

If the Panel will note, and the audience as well, that we are well ahead of schedule. I believe that it is possible for us to complete our discussion of these questions this afternoon. Having said that, I want to assure the members of the Panel that they will have every opportunity discuss the remaining issues as fully as necessary as well as having the opportunity to make these other comments as I indicated just a moment ago.

To alert the audience, I think we're going to finish the program today. We'll stay as long as we need to do that, so we might run a little bit long today. Barring some disaster, and if that takes place, I'll ask the Panel to meet tomorrow morning. The session will be closed today. Meet tomorrow morning at 8:30 to discuss report writing and coordination.

DR. ROBERTS: Dr. Doyle, welcome.

DR. DOYLE: Thank you very much. Dr. Miller is kicking off the presentation. He's coming in just now.

DR. ROBERTS: Okay. Here he comes now.

DR. ROBERTS: Mr. Miller, are you ready to go with risk characterization?

MR. MILLER: Yes.

DR. ROBERTS: Great.

MR. MILLER: If I can just have the first slide and then the next one.

Okay. What I'll do first is just kind of go through the outline of the presentation. Before I go through the outline, I'll just kind of quickly go through kind of what you've before in the sessions here.

On Tuesday you heard from Anna Lowit and Woody Setzer a little bit about BMD10s, that those were 21-day steady state equilibrium cholinesterase inhibitions based on that time period.

Yesterday, we discussed with you some of the mechanics of the analysis options within DEEM and Calendex. Two options were single consecutive day, and the second option was the rolling time frame.

Today this session is concerned with comparing the time frames of exposure, for example, 1, 7, 14, 21 or 28 days which are available

within DEEM Calendex with a time frame of toxicity 21-day BMD10 talked to you before on Tuesday by Anna and Woody.

Just in this outline here, this slide here, we're going to be talking first just a summary of preliminary results and findings. A single slide on that. Then we'll be talking about introduction to key principles for conducting risk characterization. I'll talk a little bit about the hazard and exposure aspects.

I'll talk about what we did in the preliminary cumulative risk characterization assessment. I'll remind you about the time frame considerations and some of the specific comparisons that need to be done between toxicity and exposure.

After that, what we'll do is some example exposure scenarios, and Beth Doyle will be discussing this kind of in a more interactive session with you with overheads. And then finally we go through the questions for the SAP.

Just as kind of a summary of the preliminary results and findings. In general, we found consistent exposure at risk patterns across regions. The major contributors to risk for indoor residential exposures are uses of DDVP. Exposure through food is considered to be national and does not vary by region. We're performing additional analyses on these results, and Bill Smith went through these with you

yesterday.

And then, finally, drinking water and outdoor lawn and garden uses do not appear to be significant contributors to risk.

Some key risk principles for conducting a cumulative risk assessment. One key consideration is the time frame of toxic effect. For example, what is the time to the peak effect and what is the time to recovery.

With respect to time frame of exposure, some key considerations include how often does exposure occur, at what levels do exposure occur, and then what is the exposure duration. And then, finally, what some consider to be the crux of the issue would be how are exposure and toxicity compared; to what degree to the time frames need to match between exposure and toxicity.

In the September 2001 SAP meeting this was considered of how to compare the time component of toxicity endpoints with the time component of exposure. You said the cumulative risk assessment should ideally compare toxicity endpoints and exposure durations of the same time frame and, also, that, to the extent possible, comparison should take into account the pattern of human exposure.

With respect to -- I'll give you a reminder of some of the hazard aspects that you'd heard about from Drs. Lowit and Setzer. The

BMD10 is based on steady state or equilibrium cholinesterase data. That's the point at which continued exposure at the same dose level does not result in further reduction in cholinesterase activity.

The RPFs and PODs are based on studies of 21 days or longer of continued dosing of naive animals, that is, animals not exposed to OPs before the initial dosing period. This represents 21-day steady state or equilibrium conditions for cholinesterase inhibition and believes to be a more stable measure of relative potency factors and points of departure.

And then finally following the insult, recovery of cholinesterase inhibition that may requires days to weeks.

With respect to the exposure aspects, human exposure patterns to multiple OP pesticides may be single day, for example, spike or short-term exposures through food, drinking water, and residential uses, superimposed imposed upon more or less continuous exposures through food. By monitoring data from NHANES, for example, suggests that a sizeable portion of the population have OP metabolites in their urine.

It should be remembered, also, that most animal data available to OPP are developed using laboratory animals that were naive in their exposures to OP; that is, again, they were not exposed previously to

OP pesticides.

Continuous exposures through food might resemble the multi-day dosing used in determining the BMD10.

The preliminary cumulative risk assessment used the BMD10 which reflects continual dosing for a sufficient period to produce equilibrium response. More specifically, the BMD10 used in the preliminary cumulative risk assessment is based on a multi-day animal studies, dosing studies, and reflects that multi-day dose required to achieve a steady state 10-percent inhibition of cholinesterase.

In the PCRA, OPP developed a distribution of single consecutive day exposures, again, not rolling time frame, and compared this to a steady state or equilibrium multi-day BMD10. What we indicated we would do would be consider the patterns of exposures, looking for periods of sustained elevated exposure over a period of time. And we indicated to you, again, yesterday that we recognize that such sustained elevated exposures at high percentiles are unlikely to reflect the same single individual.

DEEM(FCID)/Calendex also permits the rolling time frame approach. This measure exposure to the same individual. They are tracked. The same individual is tracked over the time frame of interest and averaged for that individual over that time frame. The SAP

considered this issue in yesterday's session of this meeting.

While this rolling time frame approach may allow for a better match between selected exposure time frames, for example, seven days or longer and the hazard endpoint, BMD10, OPP is concerned that this may not adequately permit estimates of risk associated with shorter duration exposures, for example, a single day spike or short-term exposures.

While an advantage of the rolling time frame approach is that it better simulates continual non-naive exposures and allows us to better match the time frame associated with the toxicological data, results of this averaging process may obscure one-day spike or elevated time frame short-term exposures.

BMD10 associated with a 21-day steady state response is appropriate for 21 days or more. If an acute, for example, a one-day or short-term, less than 21 day, exposures, if those are of concern, how might OPP evaluate or compare such exposures with toxicity data that is based on a multi-day BMD10. In other words, how does one estimate the effect of different exposure patterns on risk given those two pieces of information?

Some information is available with respect to how multi-day BMD10s compare to one day NOAEL, no observed adverse effects

levels. This information was provided to the Panel in a supplemental submission in January 25, I believe. A rough comparison of the BMD10s with a no observed adverse effect levels based on the cholinesterase estimates data from single-dose studies reveals a good similarity of values based. Keep in mind, though, that it's based on a limited data set and there are some exceptions to that.

This next session it would be by Beth Doyle, in terms it would be an interactive session with transparency acetates. I don't know if you'd like to ask clarifying questions or hold off until after lunch.

DR. ROBERTS: Let me go ahead and ask the Panel if they've got any clarifying questions on what you've presented so far. I don't see any. So let's go ahead then.

DR. DOYLE: As we discussed before, is it better to do this right before the question or after lunch? What would be your preference, Dr. Roberts?

DR. ROBERTS: Now. I'm seeing some people say they want to go ahead and talk about it now.

DR. DOYLE: One of our concerns is that we have a very thorough discussion of the matching of the time frame for the exposure with the appropriate hazard endpoint. And we have tried to frame here for you, in a very loose way, a number of things that we have

considered as issues. We wanted to impress upon you the variety of types of issues that we have to deal with in this assessment and some of the complexities that we see. And we'd like to hear other complexities you think we've misses and also suggestions for how we might best deal with this.

So I'd like to graph out for you some of the issues to frame-up the discussion. One of the concerns we have is that we have a variety of different potential exposure patterns. If you bear with me, let me draw the first. Unfortunately, our markers are dead.

But the first exposure pattern with which we have concern is one in which there is a very low background and there is a spike above a very low background.

This is about a 40, roughly 42-, 45-day time frame. We have a potential that we have an exposure that looks something like this. Okay. In this case you have a very low background exposure, essentially, no exposure at all. And that will run along for a series of days and then very abruptly a peak of exposure occurs, followed by a rapid decline and then another very low exposure.

Now, you might argue in a case like, if this is our 21-day BMD10, that is not an appropriate endpoint for consideration there because, in fact, you have essentially a true acute exposure. It might

be argued that this would be more appropriately reflected by an acute NOAEL of some sort.

However, if the acute NOAEL is up here, you can see it makes quite a difference. Now, that depends to some extent, though, on how you express your exposure because there's been a discussion of rolling time frame. So we're further faced with the issue that if we do a 7-day rolling time frame, we get something like this. And that sort of shifts our type of concern that we're dealing with quite a bit because you maximum exposure has fallen tremendously. But you have a very wide period of exposure to consider.

So by looking at the manner in which we do the calculation of exposure, we have changed the question, and perhaps artificially; but we certainly have changed the nature of the question. And you could continue to widen and lower that peak based by using a longer averaging time.

Now, we have an alternative possibility which we may be dealing with. We don't know. It looks something like this. This is a higher background level. If you recall, we had a BMD10 that looks something like this. And in this case, your background -- okay. In this case we have a BMD10, which is very close to our background level, so we're running at an exposed individual, they're already

inhibited. Suddenly they incur this peak exposure.

Now this is a little bit of a different situation that you have with our tox data for our acute exposure assessments. You don't have a naive, if you will, person being expose to a sudden pulse. You have a person who already has a substantial potential degree of inhibition. It's not unsafe yet at background. But when you hit this peak, you're rising not from zero anymore but from previous exposure.

So, again, then it becomes a little more problematic about what would be the appropriate toxicity scenario to use for comparison. And if we do a rolling 7 day, then you get a different picture much like before. Looks something like this. And, again, I'm sorry for the drawing. I'm very poor at this. You get something like this, which spreads out the exposure. Well, it comes down. But it does spread out the exposure and, again, widen that peak substantially.

Again, the question, I think, is different now, what the appropriate toxicity comparison is, because you're not starting at zero. You have a substantially exposed population that's now receiving an insult. So that's a different sort of issue.

And then we come into the situation where we have a series of spikes. And regardless of what your background is, it raises another question for us. and we have to deal with this one as well. And, say,

for instance, it's going like this and you have a spike; and then maybe a week later or a few days later you get another spike and so forth.

Now, this is a daily series. And, again, here's our BMD10; and here's our acute. Well, certainly there would be a certain simplicity in being able to say these are three acute values. And that would be very easy to do.

Except that if you look at a rolling average, you get something that starts to ooze together. You start to get something that sort of like this. And then it goes down after. But, in fact, your exposure with decline included, may never truly go back down to even your background. You may have a sustained elevation. And it's a little less apparent.

Again, these are certainly three independent exposures now because they're too close together. And we haven't even gotten into discussing recovery at this point. We're just looking at exposure.

And last but not least is what we're afraid we probably have, and some of our scenarios suggest that we do have, is a mixed situation where you're going along at background and all of a sudden you have an elevation of some sort. Maybe you've been working in your lawn that day. And then after a while it goes back. And all of a sudden you get a peak from some other use and another peak and so

forth.

Well, you can argue very effectively, I think, that for this portion in here, that BMD10 is probably appropriate for this section if, in fact, this is an individual exposure and you're seeing the sustained elevation. That certainly is a subchronic exposure and that would make sense.

But if you go to each separate peak, it's less clear that those are actually acute exposures because depending on how you look at your averaging time for presentation, you're actually doing something akin to this. And then it goes back up here a little more. I'm sorry.

At any rate, you have something then that remains elevated for a substantial period of time. And I think that we have these issues with regard to exposure scenarios. But we have, also, issues with regard to, as I said before, recovery of cholinesterase inhibition. Dave mention that in his presentation. You could argue a person never recovers in this scenario between exposures.

The same is true here. And then you have to allow for the distinction of what your starting point is. What is your baseline condition of your exposed individual? Are they truly what we're referring to as naive, that is, never previously exposed. Or are they previously exposed that are now incurring a separate additional insult.

So we just wanted to frame this up a little that these are the variety of types of issues that we'd like to see you think about. We have no single answer, necessarily, that's the right one that we're looking for. We would be happy to see a variety. We are open to any suggestions. And I'd like to thank you for your comments in advance.

DR. ROBERTS: Thank you, Dr. Doyle. Are there any other aspects of the presentation? Let me, then, open it to the panel for questions of clarification. Let's try and avoid getting into the comments, but certainly clarifications on these issues are fair game. Dr. Bull and then Dr. Conolly.

DR. BULL: Mine was part of the comments.

DR. ROBERTS: Okay. Dr. Conolly.

DR. CONOLLY: Yeah. I just wanted to be absolutely clear. I think it was pretty clear that the graphs you were drawing were graphs of exposure. And so really the question you're asking is what's the linkage, what's the appropriate linkage, between the exposure and cholinesterase level.

DR. DOYLE: That's correct. And, again, the averaging time for the exposure will affect that. All of those things combine to give us a very complex question.

DR. CONOLLY: Right. Thank you.

DR. ROBERTS: Any other questions from members of the Panel? If not, I believe we have some public commentors that are interested in making a presentation. Mr. Jack Zabik from Dow AgroSciences. Is Mr. Zabik here?

MR. MCCALLISTER: Jack Zabik's not here. I'm taking his place.

DR. ROBERTS: Okay. Welcome. And could you introduce yourself for the Panel, please.

MR. MCCALLISTER: My name is Ray McCallister. I'm with the Croplife America here representing the FQPA Implementation Working Group.

Comments are fairly limited, and they're not going to address all the issues that EPA has just raised. But I wanted to say that the IWG strongly supports the multi-day rolling exposure calculation to match the toxic endpoints which is also based on a 21-day or longer exposure test animals. In the risk assessment the exposure and toxicology scenarios must match as the panel has previously advised the panel and repeated during these sessions.

The Agency has raised questions in sessions yesterday about the use of the available food consumption data to approximate a moving dietary exposure average. Some of those questions raised would tend

to make the risk calculation more conservative; some less conservative. And Panel members raised additional issues that need to be taken into account.

For example, I feel that the list of foods and commodities that would influence the leftover issue, that is, what foods might be more likely to be consumed on subsequent days, is probably fairly limited and can be fairly easily defined.

EPA has in hand now data from industry and from USDA that directly address the homogeneity or variability of residues within a bag of apples or oranges or potatoes to determine how variable those residues would be, how likely the residues of fruit consumed from that bag tomorrow are going to be similar to those consumed today.

The EPA can and should call on the expertise of USDA's Food Surveys Research Group in addressing these issues of estimating longitudinal dietary consumption. These are the folks that conduct the CSFII study. They may not have solved all the problems that were raised by EPA and by the Panel members, but they have considered them analytically for years and will have valuable insights to offer.

The CARES software model is designed to specifically address some of the issues raised by Panel members. For example, it assembles a pool of demographically similar individuals for use in approximating

a rolling average of dietary consumption.

The issue of the spikes and exposure rates today must be addressed by combining consideration acute tox values as well as the chronic tox values.

Finally, the IWG has benefited considerably by the EPA's presentations and the SAP discussions of the cumulative risk assessment issues. We will be providing detailed comments to the Agency during the public comment period on the new issues that have been raised by during these sessions.

DR. ROBERTS: Thank you. Are there any questions? Clarification? Thank you very much for your comments.

Let me see. We one other individual that has indicated an interest in addressing the Panel. Dr. Christine Chasen if I pronounced that correctly.

Okay. Could you please identify yourself for the record.

DR. CHASEN: You were close. It's Chris Chasen, and I'm with the Lifeline group. And we've had the pleasure of presenting Lifeline to this Panel before. We will be presenting some written comments to you. But I just wanted to point out a couple of issues for your consideration.

There's been intermittently discussion about the dilemma that

we always face when we're trying to fit cross-sectional data into what basically are longitudinal questions. And there are two components to that. I just wanted to point this out.

One, of course, is that we've all saluted the problem that there are not adequate longitudinal data sets that are in any of these and so about it. So we have to do the best we can with the cross-sectional for the moment. I was very pleased to hear the Panel endorse the idea that you can, however, use cross-sectional data if you take a look at some of the relationships that are referred from other data bases. And so there is still a lot of improvement that we can all make in how we use the cross-sectional.

However, I didn't hear very much conversation about how the models use the cross-sectional data. And this is really important. Because even with completely cross-sectional information, how the models handle it is really going to be important. I'll give you just one of this; but there are many, many, many places in these models where this becomes important.

One example would be that you got to keep the individual in the same house from Day 1 to Day 2 to Day 3 to Day 4 until they move. And that has to be an abrupt difference. So when you talk about modeling a person across some X amount of time, it's not -- the model,

in fact, can take the concept data that we have about mobility characteristics in the United States and whatever, and at least hold that person in a house that is consistent from day to day.

The same would be true. There are socioeconomics. You can't get rich one and go poor the next one, although that seems to be happening. We have to adjust the model accordingly. And, also, hold these people in an urban or rural setting so they don't bounce back from Iowa to New York City. There is, in fact, a significant use of pesticides in urban situations, and we're considering residential treatments here.

A second. I'm just going to go briefly through a couple of these points but we'll be elaborating on that.

Another one is I think we need to take a look at seasonality just a bit more because I think we may be overlooking one important thing. I will concur that in the United States there is not much difference in the intake of foods from one season to another. That seems to be even true with water. And that may be a function of air conditioning or something. But we do have -- now there are exceptions to that, of course, in our food supply. And I think most those are obvious, and we would know that.

However, there is a difference seasonally from residues, on the

residues on the foods. So I don't care whether it's an apple or an orange or orange juice, whatever, the source of that food changes in the United States seasonally. And even though it's nationally distributed, the source of the national distribution changes radically.

And obviously, if you're changing the source, you're changing the pest pressures; and obviously, then, you're changing the patterns of usage. So it's not surprising that if you superimpose on the model one usage profile in the calendar base, you're going to end up with an answer that says there's not much difference from season to season. But, in fact, you need to be able to take a look at the source.

If you don't take a look at the source, you also can't account for import versus export situations. Now we may know an awful lot about usage profiles in the United States. But how much do you now about the other usage profiles from where our increasing percentage of foods are coming.

I know that the PDP data set does look at imports, but there are other ways where we can account for the what we don't know of pesticide usage from the food imports. And that wasn't discussed.

Another thing that was not discussed was how the models use the water intakes, the consumptions of water, particularly for kids. We're going to put in just some basic information if you want about

the water intake distributions in CSFII '94, '96, '98 for the Panel from kids in different age groups, including infants. When we were working with Lifeline, we went through exactly these issues. And we'll share the background information that we have on that and the subsets of information out of those data sets.

Lastly, as you heard, Lifeline will be running this. I just wanted to emphasize that the results of that effort will yield three things. We will certainly have a final report with new manuals. Secondly, we will have a disk with the inputs and the results from the analysis. And thirdly, a free copy to anyone who wants it of the complete version of Lifeline that was used to run those risk assessments. So you'll be able to put the data in, play with it however you want, take a look at the drivers or whatever else is of interest.

As part of this, you know that Lifeline has shown you those situations where it likes like there's less exposure to certain age groups when in fact -- but what we have suggested -- I can't proof this. But what we've suggested is what we're really seeing is there are places in the model where we have the least information about activity levels or the model's most vulnerable, if you will, to underestimating exposure.

There are ways that we can look at and can play with some

sensitivity analysis to know whether or not what you're suffering is a lack of data or whether or not you can compensation for it by things such as increasing the time of the day that you're spent on another field. That does not solve, however, the issue how much time as part of your life are the exposure opportunities changing.

As part of this whole thing, I think that the EPA certainly has done a wonderful job in incorporating a lot of these. And I'm very pleased to hear the comments from the Panel because you zeroed in on many of the issues.

My last comment about Beth's presentation, and I'll make a suggestion for how you can deal with some of the points she brought up. If you take an assessment of all of the -- what she showed you was a situation for a person. Let's say you have a thousand people across your simulated population. Each of those thousand people have a different scenario. Some will be naive with one peak; some will be naive with two, three, six peaks; some not be not native with no peaks. Same situation.

Well, you can't, I presume, regulate person by person in the United States. You're going to go and look at across population. And there are methods for doing that presently available.

What you can do is take and look at the peak values, the

maximum values, across all the people in the population. And then, also, take the averages, you can do that even one day at a time or across rolling windows whatever, and the difference between those two distributions gives you an indication of the frequency in which peaks happen.

If you have 90 days for example, if you have 80 of those days with peaks, the average of that scenario in the population is going to look a lot more like the peak, the maximum of the peaks. As these two things converge, what you have is a frequency of events within that time period. The farther apart they are, it insinuates that you have very rare events, rare peaks happening in the group.

Now, that just gives some guidance, I think, to the regulator as to whether or not you really should be looking at applications of acute metrics or applications that may be long-term exposure scenarios. You can do this across -- and we've done this frequently -- 1 day, 7 day -- this is rolling window -- 30 days, 90 days, and 365 days; and then just compare just for the exposures. Be dammed the toxicology now.

Just for the exposure to see how similar these numbers are because that gives you an indication of whether you're looking at peaks across frequencies that are daily events, weekly events, monthly

events, seasonal situations, or annual situations. And the differences between these distributions at least opens up an idea as to whether you're dealing frequently occurring scenarios for exposure or not.

And I would recommend that that approach be taken at least to take a look at to give you some confidence that you're using the correct toxicology metrics. There are techniques such as this that are available, and I think they will be hopefully a point of discussion in the future.

So we'll put this down in writing very, very quickly and try to get it to you. Maybe it will be helpful. Thank you.

DR. ROBERTS: Thanks, Dr. Chasen. Could you give us an idea on the time frame for completion of your Lifeline analysis? You mentioned that you will have that available.

DR. CHASEN: Well, we're just going sort of going to go as fast as we can. But it certainly will be available between now and June.

DR. ROBERTS: All right. Thank you. Other questions? Dr. McConnell.

DR. MCCONNELL: Yeah, I have a question. I was intrigued by your last comment where you said you'd have some data for one day, seven. What sort of magnitude difference was there in those values for exposure if you look at a 365 day versus a 7 day? Were

they significantly different?

DR. CHASEN: Are you talking about for the OPs?

DR. MCCONNELL: Yeah.

DR. CHASEN: I haven't done it for the OPs yet.

DR. MCCONNELL: Well, whatever.

DR. CHASEN: I didn't get that far.

DR. MCCONNELL: Well, whatever chemical.

DR. CHASEN: Well, it depends on the use scenario and the chemical you're talking about.

In cases where you have a pattern that is seasonally or dependent upon seasonal activities, you're going to suddenly see a break in the 1 year and one day won't look like the 90 day. And maybe the 30 daily will look like the 1 day. And then all of a sudden there'll be a big difference between the distribution of the peak values between the distribution described by a 30-day rolling window versus a 90-day rolling window.

Now, there is no such thing as frequency data, per se. But this infers frequency. I get nervous with all these statisticians sitting, and I say things like that. It's only meant as a tool to give you an idea of whether or not you're looking at frequently occurring scenarios where you have a lot of people seeing frequent peaks or a few people seeing

frequent peaks or a lot of people seeing some kind of seasonal peaks or something like that.

So the models can give you more than just a risk assessment. What they can do is provide ways to play with profiling. Okay. And then from there maybe you go back and take a look at the toxicology metrics that may be most appropriate to deal with this. And you can look at that across populations or subpopulations.

And I will, also, point out to you that here's another dilemma. Those relationships change with age. That shouldn't be a surprise. Think about how the time you spend in your day, change your exposure opportunities, and if you're a 6-year-old, that's going to look very different than if you're 35 or if you're 56. And so those relationships -- I don't know what -- I mean I think this -- I don't want to confound this too much, but I do think it's important to look at these things at different time and groups to see, in fact, where are we seeing those kinds of shifts.

DR. MCCONNELL: Thank you.

DR. ROBERTS: Any other questions for Dr. Chasen? If not, thanks very much for your comments.

DR. CHASEN: Thank you.

DR. ROBERTS: Is there anyone else in the audience that would

like to address the Panel on this subject. Oh, I see someone in the back.

Welcome. Could you please identify yourself for the Panel.

MR. GRAY: Sure. My name is Ed Gray. I work at McDermott, Will & Emery. I'm really not here on behalf of anyone else, although I do a lot of work with the IWG.

I just wanted to raise one question that just occurred to me as this thing came up. And that is it seems like in almost every hazard or risk assessment that anyone does they have a series of different kinds of assessment the do. They do an acute. The do a subchronic. They do a chronic. And they do that because there recognize there are differences in the exposures as well as the toxicity endpoints. But here we seem to be trying to make different things into one thing. And I can't figure out why we can't just do two.

That's my question. I don't have any profound back up on that, but it seems to be a question that ought to be raised. Thanks.

DR. ROBERTS: Dr. McConnell wants to know what are the two?

DR. MCCONNELL: Yeah. Are you talking acute and chronic when you're say two?

MR. GREY: Yes.

DR. ROBERTS: Any other comments or responses to that from the Panel? All right. Anyone else in the audience? The last opportunity for public comment.

Dr. Sass, could you identify yourself for the record, please.

DR. SASS: Jennifer Sass with the National Resources Defense Council.

This is an idea not a comment. It appears to me that possibly one thing that might be on the table for consideration in looking at the rolling windows -- and I'm calling them in my notes the rolling window averages -- is that it might go to tackle some of the problems including possibly seasonality which I think we all recognize is a serious omission is to do a rolling window.

And I like Chris's idea of doing different time periods as a first trial, time permitting and energy permitting. But, also, keeping the having the diets the way they are which is two diets alternating throughout the year but keeping the tolerances constant for that rolling window period. So if you chose a seven-day rolling window period, you'd have the diet as is already -- sorry -- residues -- hold the residues constant for the period of seven days so that it would tackle the problem of the leftover food in the fridge; or the realistic scenario where people buy their groceries once a week or four days if you want

to do that kind of window; and then eat whatever's in that market basket so to speak in your refrigerator for those four days so that whatever the residues are in those grapes or those apples that's what you're getting for X number of days.

So holding those residues constant. It would also tackle in some way possibly the seasonality if you use that approach to try and get at the fact that you eat a lot of peaches for a long time when peach season is here and not so much at other times, and you might be able to extend that.

I think it might, also, tackle some of the Beth's diagrams, which I thought were excellent and really clear, in the sense that those peaks would be muted out; but they would, also, be extended and they might be more easier to detect. So that when we look over a period of a year and see what looks to me like something you might get off a radial, like this, then, actually, some of those larger peaks would be extended for a period of seven days rather than one which might be a more realistic -- well, I think it is a more realistic scenario at least in some eating patterns. And certainly I think we recognize in children who don't have a varied diet but a pretty constant diet often high in fruits. Fruits anyway; I don't know about vegetables. And so those peaks might be extended and more recognizable and in a way more realistic

and capture that.

DR. ROBERTS: Okay. Any responses or comments from the Panel? I think we have another public commentor. Dr. Schreiber.

DR. SCHREIBER: Dr. Schreiber, from the Attorney General's Office.

I didn't realize this was our last opportunity to comment today. So I just wanted to raise a couple of issues I didn't actually hear discussed, but I wanted to just be on the record of bring them up. And, again, we will be providing more formal comments.

I didn't hear any discussion of how endocrine disruption effects are included or addressed in the OP cumulative risk assessment other than I know, in some of the materials I've read, it will be taken up at some point. Can you give us an idea of when it will be taken up and how we will know about it before the final cumulative risk assessment is completed? That's one question.

Along the same lines, at what point is the FQPA Safety Factor considered in this assessment? I haven't heard anything about the FQPA features of this assessment.

And then, finally, and perhaps most importantly, what does EPA and the Science Advisory Panel consider an appropriate MOE for OPs for the cumulative risk assessment? I think that's the million-dollar

question here. We see these, you know, graphics that show that the cumulative risks, at least on a few of those slides that I can recall, are somewhere in the range to 10 to 100 for the cumulative chronic risks. That seems to be over EPA's goal of 100 as a minimum MOE and that's without even considering this FQPA Safety Factor and endocrine disruption risks.

So I guess my question is a combination of when will the endocrine disruption risks be considered, when with the FQPA Safety Factor be considered, and what is an appropriate margin of exposure in terms of cumulative risks and when will you let us know?

DR. ROBERTS: Okay. Thank you, Dr. Schreiber, for offering those questions.

I don't know if there's any Panel members want to do any follow up or not. If not, we'll certainly take those into consideration as we get into our discussion a little bit later on.

DR. SCHREIBER: Thank you.

DR. ROBERTS: As Dr. Schreiber pointed out, and I would like to point out, that this is the last opportunity for public comment before we move into our discussions. Actually, it is the final opportunity for public comment on this topic. So with that in mind, last call for public commentors. Okay. With that, then we'll close the

public comment session.

I'm reluctant to go ahead and tackle the first question because it's a meaty one. And I'm not sure. I think if we go into it we might go very late before we get to lunch. So let's take a lunch break now, let everybody ready to go, their thoughts lined up. Let's reconvene at 1:30 fresh and ready to go.

[Lunch recess.]

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