FIFRA SCIENTIFIC ADVISORY PANEL (SAP)

OPEN MEETING

SELECTED ISSUES ASSOCIATED WITH THE RISK ASSESSMENT PROCESS FOR PESTICIDES WITH PERSISTENT, BIOACCUMULATIVE AND TOXIC CHARACTERISTICS

U.S. ENVIRONMENTAL PROTECTION AGENCY

CONFERENCE CENTER- LOBBY LEVEL

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FIFRA SCIENTIFIC ADVISORY PANEL

MEETING

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MS. CHRISTIAN: Okay, good morning, everyone. We are about to start, please.

Again, my name is Myrta Christian. I am the Designated Federal Official for this meeting, and I would like to welcome everyone and to thank...to thank you for participating in today's meeting to continue the Revision of Selected Issues associated with the Risk Assessment Process for Pesticides with Persistent, Bioaccumulative, and Toxic Characteristics.

I would like to remind everyone that the presentations for this meeting are now available on the EPA docket and that public comments will be available either this afternoon or tomorrow morning.

Now, I would like to introduce Dr. Steve Heeringa, Chair for the FIFRA Scientific Advisory Panel.

DR. HEERINGA: Good morning, again, everyone, and welcome back to the third day of our...our meeting with the FIFRA Science Advisory Panel on the topic of Selected Issues associated with Risk Assessment Process for Pesticides with Persistent, Bioaccumulative, and Toxic Characteristics.

I said yesterday morning I wouldn't have individuals introduce themselves again. I think I'll hold to that. We've had two introductions of the panel, and if you have any questions about who someone is, I think you can ask, but so, we'll...we'll move right ahead this morning.

Yesterday, we had moved into the responses to the charge questions, and we're still in the process of completing our discussion of charge question 3. Before we do that, as we generally do first thing in the morning, is offer the EPA scientific staff a chance to introduce any comments or clarifications from the previous day's meeting, and talking to Dr. Brady, Dr. Faruque Khan, I believe, has one clarification that he wants to introduce this morning.

Dr. Khan?

DR. KHAN: Thank you, Chairman. This is sort of that topic where Dr. Stewart Cohen raised an issue that he could not reproduce our data. What's happened is in my input tables, there's two input data were wrong. It's just a typo.

This is the actual revised one, but the calculation was correct. The calculation doesn't have anything to do with the data, because I actually used the right number which I already put it in there right now in the table.

Anything else?

DR. HEERINGA: In other words, you used the right inputs, just...

DR. KHAN: Right.

DR. HEERINGA: ...reported input that Dr. Cohen then used were that were typos.

DR. KHAN: That's correct.

DR. HEERINGA: Okay, I'm glad we...I'm glad that we have that. I think that Dr. Cohen had indicated that he may submit a written public comment today, too, for members of the panel, too, but I'm sure it was...very much appreciate tracking this down.

DR. KHAN: Thank you.

DR. HEERINGA: Very helpful.

At this point in time, I think that, again, talking with Dr. Brady, there will be some questions of clarification on EPA and EFED regarding our response to question 3, but since we're not complete with our response to question 3, we don't want to anticipate uncertainties, so we'll continue with comments from the panel members.

I think we've had a...an opportunity to hear from the lead and associate discussants, and they're welcome to offer additional comments if they'd like, but at this point in time, I'd like to open it up generally to members of the panel, both assigned this question and others who would like to comment on question number 3.

And, again, I think it would be very useful in terms of the three parts of this question to focus both on sort of short-term emphasis and longer-term aims for improvements or additions, and then, also, I think as Dr. Parker emphasized at the end of yesterday's meeting, to focus on the sort tiered screening structure that is routinely employed in the risk assessments.

So, additional comments on charge question number 3? Dr. DeLorme?

DR. DELORME: All straggling back this morning. Again, I want to emphasize I come at this from...from a...a risk assessment practitioner's point of view, not restricted to incorporating the science and the policy and understanding how things work, how the process works within an agency such as EPA or, up in Canada, EPM. All right? I just want to emphasize that we have to recognize the fact that the pond really isn't a pond. Okay?

What I mean by that is it's representing a variety of water bodies, water body types, that, in generally...in general, based on available information, track results from monitoring of high-end concentrations. It's a regulatory reality that we can't have 100 different scenarios to do for a given chemical. It just doesn't work. There's just not enough time to do it.

There's no doubt that we need to incorporate burial in some way, shape, or form. I think the real question is how and to what extent.

Based on the presentations that I saw by EPA and...and Dr. Frank Gobas at the meeting, the existing models and the resulting EECs, whether you use AGRO or whether you use PRZM/EXAMS, are sensitive to burial and burial rate.

The white paper presented results for burial based on a high burial rate or a high sediment load going into the pond, and I'm not sure if that's the optimal approach or not, certainly not conservative.

I think you need to consider getting a better understanding of sedimentation and burial rates for various types of water bodies or a scenario for situations. I mean, certainly, it was evident from the information presented in the white paper that, you know, a turf situation doesn't result in much sediment coming...or soil coming off. Therefore, sediment rates would be lower.

So, you might want to consider the situations, then decide which scenario or scenarios may be appropriate to bottled based on the problem formulation. What is it...what's it going to be used for? Is it going to be used for a row crop in Mississippi? Well, then, maybe, in a farm pond at least, or a...a static or semi-static water body, you know, a high burial rate is...is justified, but in a flowing water system, it may not be.

I think the ultimate goal is to characterize the risk. Okay? Currently, you kind of have a one-size-fits-all type scenario, and as Dr. Thibodeaux pointed out yesterday, I think it's time, probably, to develop additional scenarios that you can provide your risk managers with a range of potential outcomes from these characterizations.

DR. HEERINGA: Comments from other panel members? Dr. Thibodeaux?

DR. THIBODEAUX: Phil, I...I may have misunderstood you. Did you say that you didn't think there was any need to go to other aquatic systems like a stream or an estuary?

DR. DELORME: No, it...no, I didn't. What I said is that, you know, they need to be considered.

DR. THIBODEAUX: Thanks. I'm not quite woke up yet. Sorry.

The...which charge question was the solubility issue under?

DR. HEERINGA: If that's a test, I'm failing it, but we'll figure it out. I believe it would fall, in part, under...I don't believe there was a...there's no charge question on solubility. Okay. So, I think it might be an appropriate time to introduce it if you have some comments, Dr. Thibodeaux.

DR. THIBODEAUX: So...so, it didn't end up as a charge question?

DR. HEERINGA: There's...that's correct.

DR. THIBODEAUX: So, would you like comments on it?

DR. HEERINGA: Sure. I think Dr. DeLorme suggests it's number 2, but you can go ahead and do it right now. It's an appropriate time, so, please.

DR. THIBODEAUX: Okay. I...of course, if you guys would have read my second edition of The Environmental Chemodynamics, I wouldn't have had to explain this. And I'm a little at fault as well. I didn't bring a copy, so I can't refer you to page number. And it has to do something with Don Mackay's comment about the precip...precipitate solid phase of pure material.

In fact, I think it would be an easy short-term fix for both EXAMS and, possibly, PRZM, to go to a hockey stick isotherm. And what I mean by a hockey stick isotherm is with the input a partition coefficient, or you calculate it from epi-SUITE or whatever, but you calculate a particular system once you have FOC, once you have identified the chemical, once you get a KOW, but we...somewhere in the process, you end up with a KD. And that is used in the mass balance model.

You have no constraints on the range of those concentrations in the water and on the particles, and the rub comes...and I think now the rubs we saw when the particles from the...from the PRZM were diverted, but the chemical is left out, meaning you have more chemical in.

So, what happens is you get a very high concentration on the particle, and if you use the equilib...the coefficient coefficient, it demands a higher than solubility limit.

So, what I'm saying is that the partition coefficient is not an appropriate equilibrium isotherm for the model. The isotherm should be hockey stick shaped. You understand what I mean by a hockey stick?

DR. HETRICK: I assume you're talking about a non-linear isotherm?

DR. THIBODEAUX: Right, yeah, it...it's like...

DR. HETRICK: Right.

DR. THIBODEAUX: The concentration on one axis, it should go up and then level out

DR. HETRICK: Right, right, right.

DR. THIBODEAUX: Now, follow that in isotherms. The partition coefficient is linear all the way up, and that's where you get into problems.

DR. HETRICK: Right, exactly. I guess one of the questions I have for you on that, just for a little clarification, is that, you know, with that type of isotherm, we're...we're making some assumptions that...well, I guess it may not make a difference. I don't know if you...if you form a precipitate like AGRO does versus having that...

DR. THIBODEAUX: You don't have to do, I think, if you put it in as an isotherm.

DR. HETRICK: Okay, okay.

DR. THIBODEAUX: I think that would correct it.

DR. HETRICK: You think that would correct...that would do essentially...

DR. THIBODEAUX: I think it would correct it. I understand what Don's doing. I know the way he thinks. We're both chemical engineers. He's using an off-site compartment that he--, which are...which needs a little programing, but I think the software in your models needs to be...

DR. HETRICK: Doctor, could you just pull the mike a little closer.

DR. THIBODEAUX: All right.

DR. HETRICK: You turned away for a minute.

DR. THIBODEAUX: I think I know what Don is up to, and...but...but I think the existing model, particular EXAMS and PRZM, can be corrected by toying with that isotherm.

DR. HETRICK: Well, the...there's a focused model, actually, that...that has a non-linear isotherm in it, and...which would...we could probably modify that to...to...to...and that focus is PRZM/EXAMS. Now, I'm not sure if the PRZM aspect of that has the non-linear, but I believe the EXAMS does.

DR. THIBODEAUX: Well, you see, the catch comes and is that the partition coefficient is not an isotherm.

DR. HETRICK: I understand that.

DR. THIBODEAUX: Good, but we assume it is in the model.

DR. HETRICK: Yeah.

DR. THIBODEAUX: And that's where you run into the problem. Thank you.

DR. HEERINGA: Thank you, Dr. Thibodeaux.

DR. HETRICK: But I guess my question is, is that, you know, you've got different processes here. You have an adsorption/desorption process as well as a precipitation and dissolution process, and they're not the same.

DR. THIBODEAUX: Well, yes, good point. Partition coefficient going on to the portal-- is what you need, as opposed to a partition coefficient which you have a lot of contaminated data that's been...but that's not your problem when you're...when you're regulating pesticides, is it? I mean, you open...it's short-term. You're just putting it on the soil. Then it goes to the stream.

So, why don't the absorption...why can't you just get by by using those? I mean, us who work in the contaminated sediment area have to worry about resorption pollutant issues, because the...both the chemical and the organic matter in the soils have been cooking together for the last 50 years, and it's clear that they're not the same. There's an immobile fraction that this measure comes off.

Is that what you're alluding to?

DR. HETRICK: Well, that's part of it. I mean, that's...that's another complexity to that. No, I'm alluding to the fact that if you get a solid base precipitate as what's proposed in AGRO, that's a whole different process than what...

DR. THIBODEAUX: Yes.

DR. HETRICK: ...absorption and desorption is, and...and I believe that modeling the two, although you could probably get through with a hockey stick, I'm not sure, mechanistically, you can say that they're the same. That's all.

DR. THIBODEAUX: Well, as clever as Don is, I...I suspect the answer is pretty close to the same, but I...I think, theoretically, the hockey stick would be better, theoretically.

DR. HICKIE: And I'd like one comment on that. We...we have done some experimentation in the past with...with a hockey stick approach, and one of the problems we've had in using that in the model is that many pesticide labels will have six applications 14 days apart, and so, if you get new chemical coming on every 14 days, and so, you have to...so you have a different lag time in the...in a hockey stick for...for each time.

So, you almost need to simulate each application as a separate chemical and then add them at the end, not that we couldn't do that, but...but the model typically doesn't allow that.

DR. THIBODEAUX: The model, ideally, should start with the mass of the chemical from the previous application and just add more to it. Seems to me that's the modeling...

DR. HICKIE: That's true, but the new...the new chemical, in terms of...of when the...the actual rate changes, it changes at a certain time after the application. So, each...each hockey stick, you're starting at a different point, and the change...change happens at a different point.

DR. HETRICK: I think there's a...I'm not sure, but I think there's a...are you talking about degradation kinetics, or are you talking about absorption?

DR. HICKIE: Well, I think either.

DR. HETRICK: Well...

DR. THIBODEAUX: My...my comments were solid. I was strict absorption.

DR. HETRICK: Okay.

DR. THIBODEAUX: But there are better people here to answer that question.

DR. LICK: Could I comment on the...

DR. HEERINGA: Let me turn to Dr. Lick, yes.

DR. LICK: I'd like to comment on the linear versus non-linear partitioning, because we did a whole series of experiments with different organic chemicals, and, in particular, we did a lot with PCBs or other very hydrophobic organic chemicals which tend to have low solubility, and in all of those experiments, the partition coefficient was linear, absolutely linear, right up to solubility, and at that point, of course, the experiment was ended.

On the other hand, if we look at partition...I mean, chemicals with relative lower coefficients, they tend to have higher solubility, and there, we did find non-linear isotherms with their non-linear variation of the partition coefficient as we increased the amount of chemical.

If we take all these results, we can...and normalize them, what we found out was that the non-linearity starts when the amount of chemical actually absorbed on the particle starts to become comparable to the amount of organic matter in the particle. That...in other words, that's a hell of a lot of chemical that can be absorbed onto these particles, but for the very hydrophobic chemical, you never get near that point, because it's insoluble.

On the other hand, the other chemicals which are...have higher solubility, then, in essence, you're binding so much chemical to the particle, I think, that you're actually coating your organic matter. You cannot add any more chemical to this, and...and because of that, you get this non-linear behavior, because the adsorption and desorption to the surface is no longer the same as in the case where you have a lot of exposed organic matter.

But with high...high hydrophobic chemicals, the sorption...the partition coefficient was linear. And that's PTBs and hexachlorobenzene and a few other chemicals.

DR. HETRICK: Just to get back to this hockey stick concept, should we set the where you start to get the...the...the...essentially, the...the flat area of that sorption process at the solubility limit?

DR. THIBODEAUX: Dr. Lick is right. You can begin to see a curve right then. There's some data to show that when you get into that region, it begins to...to curve over, and it's not pure hockey stick, but you're talking about...that's a minor thing compared to the other errors we have in this model. So, a 2-line one might get us through 99.99 percent, but where are we trying to go?

DR. HETRICK: I'm...I'm just asking the...the question is, where do you...where do you draw the line on that? I guess you're going to set that at the solubility limits.

DR. LICK: No, the...the...it starts to curve over when the amount of chemical sorbed to the particle tends to become equal to the amount of organic matter on the particle. So...

DR. HETRICK: Okay, so...

DR. LICK: ...we know what the organic content is, and...

DR. HETRICK: So, it's independent of the solubility is what you're saying.

DR. LICK: Well, up to the solubility limit. In other words...

DR. HETRICK: Right, but...

DR. LICK: ...if...if you start to do this and you get the solubility limit, then that's it. You're at the end.

DR. HETRICK: Right, I understand that.

DR. THIBODEAUX: There was another issue with solubility which was...had to do with aquisols, I think. Let me see. I have Keith's. I could work off of Keith's presentation and the list that he had. See if I can find it. Sorry, Mr. Chairman. Can I do this?

DR. HEERINGA: Sure may.

DR. THIBODEAUX: Yeah, Keith, what do you mean by...this is on page 2 of your presentation, what you gave, the summary, conclusions and fast forward, and slide number 4, uncertainty regarding extrapolation of lab-derived solubility values true to the field. Could you explain where you're coming from on that?

MR. SAPPINGTON: Sure. The question there is how representative is a measurement of solubility in a laboratory, under laboratory conditions and using the barium instilled water, how representative is that to field conditions, because both the procedure that we used in the EXAMS model as well as AGRO assume that that solubility measurement applies in the field exactly as what was measured in the laboratory, and there are some...

I...I heard comment over the last couple of days that there may be other factors that would influence the solubility under field conditions, one of which may even be spray drift in formulated product that would come into the pond from spray drift.

And just doing a back of the envelope calculation in...in tox studies, there is a limit of...of how much you're allowed to add in...in a particular study for a co-solvents, and that's 1 l/l. If you were to just mentally do that for a 20 million liter pond, you would need about 2 liters of co...of solvent, some sort of solvent material to enter that pond which is not a tremendous amount.

And so, the presumption would be, then, you might have some sort of solvent effect. I would say that in mesocosm type studies that are much smaller systems where the formulated product is added, you could get some type of...of solvent effect there, and that's just from the formulated product. You have other natural lichens and things that...that could affect solubility as well as temperature and other things.

And so, that question was to say well,

we're anchoring everything on this one measurement. Is that appropriate? Or, at least, give us an indication of the uncertainty around that.

DR. LICK: There's no doubt that co-solvents will modify the solubility, I mean, enormously in some cases, order of magnitude, and we did experiments with that also, but there...there's a paper by Jepson and others, including myself, where all this, including the non-linear partition coefficients is discussed. It's also in my book, so it's all there.

DR. THIBODEAUX: Of course...

DR. HEERINGA: Dr. Thibodeaux? To make sure we get your name in there.

DR. THIBODEAUX: This is Thibodeaux. Various factors...I believe in the solubility, it's pure solution. As long as you get the co-solvents and even particles like DOC, as you go out and sample the water and measure the concentrations, you may get a value higher in the field because of these co-solvents and particles. It would exceed the solubility for a total concentration. Right?

But if you could just between the particles and get back to water, the pure solution base, I think you would still see which value would be solubility. So, you're picking up the extra chemicals by whatever that carrier is from the drift, whatever the VOCs or other kind of particles that are floating in the water, that pinpoints a very high concentration. But that should be accounted for in the model.

MR. SAPPINGTON: Yes, the model accounts for partitioning to DOC and TOC, so we're working with freely dissolved, and I think where the breakdown occurs sometimes is in the...well, there's an issue both for predicted as well as measured values, and a number of the measured values are...are dissolved concentrations measured through filtration which, obviously, you can have other smaller precipitates and co-loyal material in there. And so, the...you know, there is some uncertainty about what is the freely dissolved fraction.

And that's why we have some guidance about centrifugation to even separate down further. But we often are not getting that centrifuge samples when...when we need it in these cases.

DR. HEERINGA: I'd like to go to Dr. Doucette for a comment.

DR. DOUCETTE: Switch comments now, first to the co-solvent issue. There's...obviously, it's been discussed. There's a fair amount of literature looking at the impact of co-solvents on the solubility, and in terms of that being a...an issue, I think you hit it right on the head. In...in order to get a significant enhancement of the concentration in the...the aqueous phase, the...the co-solvent concentration has to be very high, probably unrealistically high.

Now, that said, there may be some cases where the pesticide is applied as a...with a surfactant formulation in addition that you may get some localized artificially high solubility for a short period of time, but generally, once...once it's mixed in the pond, I don't think that that's probably the...the issue at all in terms of, you know, super-enhanced solubility.

Second is regard to the...the hockey stick isotherm and the idea of patching the model that way, and that certainly is a fix just like the AGRO approach is to...to artificially pull that out and call that a precipitate, and neither of them, really, are...are reality. It's a...it's a fix for, from what my understanding is, the fact that we're not accounting for sediment and water continuing to move into that...that body of water. That is really the prob...the problem. The solubility can't be exceeded.

So, I guess I would rather not put on a

fix if I could. I'd rather adapt the model to...to allow for that to actually mimic reality a little bit more, and I think Don's approach it's really not a precipitate, because a precipitate would have kinetics. It's really just a...a way to pull that...that solid out and then immediately set it back in to keep it from exceeding the solubility.

I think that might be a better fix than trying to do a...a hockey stick just because that hockey stick doesn't really reflect the...the true isotherm, and the isotherm shape of the curve is going to depend on the type of soil and the type of...of chemical.

For sediments where it's really hydrophotic, it is fairly linear, but for compounds that are less soluble or soils that have low organic matter, you...you get quite a bit of deviation from linearity in the desorbtion isotherm. So, I'd rather give it the -- typical of the sediment.

DR. THIBODEAUX: The hockey stick mimics the Langmuir. Langmuir is a well-known isotherm. I've got a physical chemist over here who will vouch for it, and that's theoretically based.

DR. DOUCETTE: Gas it not really not a solid.. It's just a convenience.

DR. THIBODEAUX: It's the same...the same...by the way, I think the same technique should be used for KOAs. Sooner or later, you're going to get the same violation of KOAs. You're going to get chemicals, sooner or later, in your analysis in which you're going to exceed...the partial pressure is going to exceed the vapor pressure for the same reason. KOC, KOA is not an isotherm. It's a fine point. They're not isotherms. They're the linear extrapolation and you get the low concentrations.

DR. DOUCETTE: There's no...

DR. THIBODEAUX: It's a compliment I'm going to get exceedances on

DR. LICK: On the basis of experiments, I agree with you.

DR. HEERINGA: Yes, Dr. Lick.

DR. LICK: I'm sorry.

DR. HEERINGA: Make sure to say your name.

DR. LICK: Willie Lick. There's no doubt that hockey stick or non-lin...non-linear isotherms are present as you...as you saturate the system, and that's, basically, what the Langmuir or the theoretical derivation of the Langmuir curve says, and that's what we found in the experiment. And it's consistent.

DR. HEERINGA: Dr. DeLorme and Dr. Gan, and then I'd like to wrap up at least this round. We can return to this if we have extra time, but I want to make sure we maintain sort of appropriate time for the other charge questions, too, today, but Dr. DeLorme and then Dr. Gan.

DR. DELORME: Peter DeLorme. Just a clarification, Keith. Your assumption is with respect to solubility that the bioavailable fraction is the freely dissolved fraction?

MR. SAPPINGTON: Yes.

DR. HEERINGA: Dr. Gan?

DR. GAN: Keith, you mentioned that to get closer to the freely dissolved concentration, centrifugation is a better method than filtration, but centrifugation, still, you cannot separate DON, but question one or comment one, but there are some other techniques, I'm sure you know, that like color plates, microextration, and some other techniques that people are working on. They're especially used to measure freely dissolved concentration.

And, you know, the other thing is the KDOC you mentioned, you know, to get to the freely dissolved concentration, you can...people can use KDOC, but the fact is for those compounds, the KDOC numbers are simply not there, I think. You have KOC but not KDOC. Right?

MR. SAPPINGTON: And, actually, Dr. Burkhart has surveyed information on KO...KDOCs, and as you would expect, there's quite a big range in those values, depending on the type of organic carbon, and so, there is information on KDOC. I believe in the model, KDOC is estimated as a...there's a coefficient applied to KOW in the organic carbon content used to estimate that.

Lawrence, do you want to add anything to the KDOC question?

DR. BURKHART: Could I ask...

DR. HEERINGA: Dr. Burkhart? Microphone.

DR. BURKHART: Your point is well taken, and there's a lot of research going on looking at partitioning the organic...dissolved organic matter. There are correlations. I've developed one. The Europeans have developed some, too.

And what the models are doing are...are using some fraction of the KOW and...and marching forwards, and that's what we do right now.

DR. HEERINGA: Thank you, Dr. Burkhart.

DR. LICK: I just have a...

DR. HEERINGA: Yes, Dr. Lick.

DR. LICK: Willie Lick. How do you define dissolved organic carbon? I mean...and then I have a follow-up question.

DR. BURKHART: This is Lawrence Burkhart. It's operationally defined as something passing some type of filter.

DR. LICK: I know, but what is the filter, 1 micron, 0.1 micron, what?

DR. BURKHART: There's no standard formalized ASTM or OECD cutoff. It's usually something like 0.4, 0.5 micron or 1 micron, depending on who's doing it.

DR. LICK: Okay, then, I'd like to comment further on that, because, again, we did these sorbtion experiments, and we had a lot of trouble with what was dissolved and what was not, and we used real sediments. Of course, there's a distribution of sizes, and there's always a little bit of this stuff below 1 micron, and if you filter out 1 micron, you're automatically putting that in the dissolved state or the...in the...yeah, dissolved state, and you get a totally different depend....now, your partition coefficient suddenly depends on your sediment concentration which doesn't seem reasonable.

So, what you have to do is after you filter...once you filter out a 0.1 micron, then you part...you've essentially taken out most of the dissolved stuff, especially if you're working with high concentrations of sediment, and then your partition coefficient is a constant, whatever it is, but it's now independent of sediment concentration.

So, it's that 0.1 to 1 which is not only important, but it depends on your sediment concentration which is a tough one.

DR. HEERINGA: Thank you, Dr. Lick. Dr. Steenhuis?

DR. STEENHUIS: I...I understand that for the chemical engineers, this absorption and desorption is extremely important. However, for the hydrologist, there's also the resuspension of the sediment and there is more to this model, that is, much more. And it seems that it is more sensitive to...I mean, absolutely, the hockey stick is very important, but it seems also that it's not as important as the sedimentation rate. The resuspension rate is also very important, especially if you have a chemical which has a very short half-life in water and a very long half-life in sediment.

The re...resuspension rate then will completely determine what the fate of the chemical is. So...and maybe we also should talk about what...what model should be long term. I mean the whole model, not only the absorption partition coefficient, but what kind of pond model we should take for tier 1, tier 2, tier 3, and what is long term and what is short term, and I would like to take a stab at it.

Tier 1, I think what is being done is fine if you look for persistent and non-persistent pesticide and you sort on that. Tier 2, I agree with Dr. Thibodeaux that you probably should have...what is being done is fine, but there should be another version too, that also sort for different ponds or different rivers, one which has a high sedimentation rate, a river which has a low sedimentation rate, and...and an estuary where we don't know anything about. So...I have no idea what to do down there.

DR. HEERINGA: That's all of the above.

DR. STEENHUIS: Yeah, probably. And tier 3, I think the main problem with tier 3, and you saw an example of that, plus you can probably simulate anything, depending on what kind of resuspension rate you take and what kind of depth of the mixing zone you take.

Dr. Lick presented some equations which are continuing equations, and they are not that difficult to implement at all. They...they are the same... you can in high...in leaching models, essentially what we're doing is you can assume layer of fine, I guess, and depending on the diffusion coefficient, you assume a certain depth, and you can simulate the effect of dispersive situations very well.

So, we're taking more depth, more layers in the...in the future, not immediately. We're taking more layers and simulating especially with diffusion and dispersion between those layers. I think you can get away from choosing an arbitrary mixing depth.

And then, in tier 4, we never...I mean, I think we can go to the... So, for tier 3, run conventional model, and for tier 4, really, you need to simulate the whole system and...and there was talk about...before about these equations about resuspension in all these rivers.

DR. HEERINGA: Thank you, Dr. Steenhuis. That's val...very valuable to explain. Okay, Dr. Lick, one more comment.

DR. LICK: I...I agree with you. I think there should be a lot of emphasis on this tier 3 taking...essentially, you're taking EXAMS and improving it to make AGRO, and then you're improving it again to separate that lower benthic layer into three or maybe five layers where you could talk about the details of the sediment/water interactions and...and get a good model.

You're right, then you don't have to worry about defining a thickness which is somewhat arbitrary. You can also, as you do this, include fine adsorption rates in the overlying water as you...as the particles precipitate out.

There is one thing that you should do, and that is the top layer is...the bottom layers are...are fixed. The top layer has to be variable to take into account erosion deposition, and once you do that, I think you have a nice model where you can investigate ponds, streams, or different conditions in ponds.

DR. HEERINGA: Two more questions. Dr. Norstrom, comments?

DR. NORSTROM: Very quick one. I just wonder whether people are aware that there has been an application in EXAMS to an estuary. I just ran into this paper by McCarthy, et. al. called Modeling Pesticide Fate in a Small Tidal Estuary, and, apparently, it works rather well.

DR. HICKIE: We are. We actually funded that study through a U.S. Geological survey a few years ago. We have the results. We haven't finalized the estuary modeling system for the Division, but we are aware of that.

DR. HEERINGA: Dr. Biddleman?

DR. BIDLEMAN: Well, I...I applaud that, because I think estuaries are really quite important, because there's a lot of agricultural land that...that...that is in coastal regions, and you get drainoff and...and sometimes fish kills in estuaries. So, I...I think if...if we're putting an over-emphaisis on farm ponds, I...I think, really, the...the impacts are more likely to be in estuaries. So, I would...I would applaud any...any further work to try to understand pesticide fate in these regions.

DR. HEERINGA: At this point, what I would like to do is...we've had a lot of discussion, a lot of information presented and a lot of comment on this issue, and I'd like to turn to...to Dr. Parker. I think you've been nominated, I believe, by Dr. Brady to, I think, come back at the panel with any questions of clarification that you've had. You've heard a lot of information. Is there some framework that you're still looking for? Are there pieces of information that you'd like to hear about or questions you'd like to have answered?

DR. PARKER: Yeah, there are...there are a few questions. I might also ask some of my colleagues to...to chime in here as well.

In terms of the long-term and short-term question, we have explored the estuary issue. We have explored the flowing water issue and have not implemented those at...at this point, but we are headed in that direction.

We will all go home on Friday and...but next Monday, we will be sitting in our office doing new exposure assessments for new and...and older chemicals. And so, one question that we would have is what can we do in the short term that sort of allows us to...to move ahead in a scientifically valid manner. I have...I have a couple sort of sub-questions under that...under that heading.

We have discussed the...the PR Benthic issue in which EXAMS takes all of the material that is sorbed in the field and automatically puts half of that into the water column and half of it into the...into the benthic layer. Options would be continuing to use it as it is with a...a...putting half of it each place. Another option would be, I suppose, automatically tying the percent benthic to a KOC or a KE value so that something that is more sorbed would automatically go to the...to the benthic layer. I believe Dr. Lick yesterday said it's all going there anyway on the first day or...no?

Anyway, so we could...

DR. LICK: For hydrophobic.

DR. PARKER: For hydrophobic, right, or hydroophobic...hydrophobic, yeah. So, options would be using it as it is, eliminating it completely, tying it to...this is for hydrophobic chemicals...tying it to some sorption value. Does anyone have a...

DR. HEERINGA: Yeah, let's turn to the panel on that specific question. We have a fixed parameter that, right now, is set into this program at 0.5, and that, obviously, has some major implications for how much of this sorts out fairly quickly into sediment or water.

Dr. Lick, what would you do?

DR. LICK: There's...there's a dimensionalist parameter that governs that. It's the time for desorption as compared with time for settling of the particle out of the pond, and so, if the time of desorption is KOW...and I've written that up, actually, in the notes...is KOW times the settling speed divided by the depth of the pond.

It's a dimensionalist number, and if you...if you plot so and so as a function of that, you get from 1 to 1, and as for any chemical, you can say as a first approximation, this parameter is so and so, and, therefore, this is so and so. Okay? It will be a simple plot.

DR. PARKER: So, using that plot versus setting the...the...that value...

DR. LICK: Right.

DR. PARKER: ...as the specific default.

DR. LICK: Highly hydrophobic chemicals would be 1. For low, for hydrophobic chemicals, it would be zero, and in between, you'll get some variation.

DR. PARKER: Okay. Is it actually needed? I mean, will that happen without PR bend just as a function of the KD of...

DR. LICK: No.

DR. PARKER: It won't. So, that...

DR. LICK: In other words, if you take your model and run PR bend between 0 and 1, you'll get different results.

DR. PARKER: Yeah, okay.

DR. HEERINGA: Dr. Doucette, you had

a...

DR. DOUCETTE: A follow-up point to that, I guess. You actually have...or do you use the desorption data that you receive in any way?

DR. HETRICK: No, we're using adsorption.

DR. DOUCETTE: Right.

DR. HETRICK: So, the desorption coefficients are not being used in the...

DR. DOUCETTE: But they're available?

DR. HETRICK: They are available.

DR. DOUCETTE: Could they be used in conjunction with Willie's suggestion?

DR. HETRICK: Yes, that's one possibility, and...and as Dr. Parker said, the other possibility is to...and...and I believe it was presented in the white paper where for a...for the current estimate of...there's a...there's a relationship there showing the PR bend as a function of KOC and how that changes, and we were thinking that if we could just take that relationship and modify it so that, in essence, those compounds that have lower KOCs would have a lower PR bend, and those with higher KOCs would have a higher PR bend.

DR. DOUCETTE: But if you actually have the data to support that...

DR. HETRICK: Oh, I agree with you. No, I agree with you.

DR. HEERINGA: Dr. Thibodeaux?

DR. THIBODEAUX: I'm sorry, I...I think I got blindsided by this PRN thing. As I understand it, this is from the PRZM?

DR. PARKER: From EXAMS.

DR. THIBODEAUX: From EXAMS?

DR. PARKER: Just from EXAMS for the water body model.

DR. THIBODEAUX: When you enter the chemical into EXAMS...right...dissolved chemical and spray drift are automatically partitioned based on the...the KOC, but chemical that is sorbed in PRZM that comes off the fields pre-sorbed is automatically routed half of it to the water column and half of it to the...to the benthic layer at this point, and you're wondering what's the best way of using that parameter might be, whether it's to keep it as it is, to eliminate it, or to vary it depending on chemical properties.

In the pond...right...you would know the mass of particles, sediment and solids, and you would know the mass of water, certainly. The present technique is to assume that that is used...you're just using--

DR. PARKER: Yes.

DR. THIBODEAUX: Okay. Half of the mass by each...half of the mass of the chemical for each rainfall event in which there's runoff, half of that mass is instantaneously dissolved in the water column, and the other half of the mass is instantaneously dissolved and completely mixed in the 5 cm benthic layer.

Now, that's the total mass of chemical leaving the watershed or just that on the solids?

DR. PARKER: Just that on the solids.

DR. THIBODEAUX: They're simulated separately, and the spray drift, then, comes in on the day of the application.

DR. PARKER: Yes.

DR. THIBODEAUX: So, you've got three entries. You've got spray drift, you've got from the watershed as a fluid, as water...

DR. PARKER: Correct.

DR. THIBODEAUX: ...and you've got entering the watershed as particles.

DR. PARKER: Correct. Particles are, obviously, entrained in the runoff water as it...as it comes off the watershed.

DR. THIBODEAUX: Right, I understand the problem. Thank you. Let me think on it.

DR. HEERINGA: Dr. Parker, additionally, I think you had a...another follow-up question or sub-question you had indicated?

DR. PARKER: Yeah, one...one more. We are using the static pond as a representative of flowing and, actually, estuaries as well. The difference in settling rates and resuspension rates between static...our static pond and any sort of flowing water with any velocity at all would be quite different in terms of burial.

Burial for a static...for our static pond with no flow, everything that comes in, obviously, accumulates in the pond.

In a flowing stream, that chemical would be temporarily buried by during times of low flow, but as you have larger storms come through, each larger storm digs up that old chemical and resuspends it and moves it on...on downstream. So, the burial would be substantially lower in flowing water.

So, for these hydrophobic chemicals, does our static...does our static pond continue to be a...an adequate representative for the flowing water which we now assume it is?

DR. HEERINGA: And by adequate, you mean conservative with respect to exposure?

DR. PARKER: Well, does it...does it...I mean, is it too conservative, possibly, is...is the question. Obviously, it is conservative if you're keeping all of the...all of the sediment and all of the chemical there, but is it...is it overly conservative considering that we do represent all flowing water also with the...with the static pond?

DR. HEERINGA: Dr. Thibodeaux?

DR. THIBODEAUX: Right, well, as you brought that up, I...the first tier, I...I agree with you. Burial is very important, and I think you need to...to have it right as far as streams, ponds, estuaries.

I'm using as my model here, the soil model which I call Universal Soil Loss Equation, and I think it came up last time, and I'm using that as sort of a general context to propose that to handle the different situations, that...that we use...and I call this...it's a ruse-based model. That's the way I define Universal Soil Loss. It's got a lot of theory in it, but you...you really can derive it from scratch. It's...

DR. PARKER: It's data based.

DR. THIBODEAUX: Data based, yes. The two primary parameters on selecting...it's important to select deposition and resuspension which is based on erosion. As erosion rates...I'd have to defer to Dr. Will...Lick, but erosion rates are the most difficult, I suspect.

DR. PARKER: Erosion rate in the field.

DR. THIBODEAUX: In the field, yes. Now, what about coming up with a matrix in which you have, on the Y axis, something about flow. Ponds have low flow, mostly stirred by the winds. Estuaries fluctuate flow, but they're on the low side. On the high side, you would have streams. So, on the Y axis, you've got flow. On the X axis, you have something about soil type, starting with clay, getting bigger into silt, and then you get into sand particles.

So, right there, you've got a 9 by 9 matrix. Now, if you could get Dr. Wick...Dr. Lick to...to...to put you in an erosion rate for each one of those boxes, then there's the model I'm using for the soil loss equation. That way, you would have a template, you know, when you decide, you know, if you've got a pond, you've got particle size. So, you've got a little better...at least the next tier.

So, my...my question is, to Dr. Lick is, you know, could...could...is that possible, that you could...erosion rates like cm/hour for these type particles, could you fill that box with reasonable values? No formulating now. You'd have to...

DR. LICK: Well, we do have an algebraic formula for how erosion rate changes as a function of sheer stress, but we do not have any formula for relating erosion rate and this type of sediment to this type of sediment and so on.

On the other hand, we've done enough experiments so that we have guidelines with some idea of how things do change from this box to that box and this box and yeah, we could give you approximate numbers for a box or matrix of that type.

But...are you through? I mean, I'd like...I have some more comments.

DR. HEERINGA: Dr. Lick, I'm going to...if you would give your comments, and then I'm going to wrap up on this question, because we...we've been on it for almost two and a half hours, and I want to make sure we...

DR. LICK: Yeah, but it's interesting one.

DR. HEERINGA: It is. Hands down, this is the most interesting topic I have been on for at least three months, and I've learned a lot, and there's a lot of expertise, and that's why it's gone on for three hours. We appreciate it. We certainly appreciate it.

DR. LICK: But back to your question of whether the pond is representative or conservative enough, I am familiar with some of the major problems of contaminated sediments. For instance, is it a safe a river. The question there is you've dumped PCBs into the river and into the sediments for a long period of time, and so, you literally have meters of contaminated sediments, but recent sediments are fairly clean, and so, the...the top layer is clean.

Now, the question is what do you...do you leave them there, or do you try to dredge them, or what do you do? The fear is that if you have a big storm, you're going to erode those clean sediments which may be only centimeters or maybe tens of centimeters, and it's certainly possible, in many cases, but if that happens, now you have contaminated sediments all of a sudden which then diffuse or get resuspended into the overlying water.

That is the problem on these complex things, and I don't know how to answer your question, but I'm trying to give you an example of a more complex situation and the more complex question. Certainly, you could try to imitate that by a one-dimensional box model if, you know, with little thought about what was happening by eroding that...taking that top layer and throwing it away and seeing what was happening.

DR. HEERINGA: Okay, thank you very much, Dr. Lick and Dr. Thibodeaux and all of the other contributors. Dr. Mehta?

DR. MEHTA: I have a comment.

DR. HEERINGA: You haven't spoken yet, so you might...please weigh in. We're going to be...

DR. MEHTA: You know, I think there was a suggestion. The next step from the box model is as we said the 1-D vertical model, and the...that model gives you concentration as a function of height, and it...if you can import current, a weak current, not a strong current, or a wave, and you put in some parameters for the erosion which, as you pointed out, there is...as Dr. Lick pointed out, there is a way to characterize those within some broad boundaries which you are not doing and which if you did do it, that would be...that would be an advancement in technology as far as collection process is concerned.

And the other important part is

velocities, and as was pointed out, the erosion in the field is very difficult to measure, but certain velocities are easier to measure, because you can use indices to apparatus to image and improve devices.

So, quite often, what we do is you...you measure the concentration in suspension, and you measure the settling velocity, and then you run this model and adjust the erosion rate until you get a balance...well, if there is a balance. So...and even settling velocities can be put in the 9 by 9 matrix box for different kinds of sediments and so on.

And also, of course, nowadays, there are equations available that allow you to...to, you know, somebody said about...you said about settling in a pond versus settling under flow. The flow can be a different type, and there are new equations available that allow you to actually determine the settling velocity not only as a function of the settling silt, sand or place but also the type of flow you've got.

So, again, there is a...a characterization possibility very much exists, and I think that that would be...that, as you said, it could be done fairly quickly, although it still would be approximate. It would be much better than pulling out these numbers from air.

DR. PARKER: It sounds like that one-dimensional settling code is available and has been used. Maybe after the meeting, we can discuss if that could be something that we might be able to use.

DR. HEERINGA: Certainly, and I think if there's specific references, as Dr. Mehta says, either equations or already model modules, definitely mention them in our report, but if you want to get to that quicker, I'm sure just a conversation would do it.

At this point in time, I want to thank everybody who's contributed on this. This was a...probably one of the more complex questions and, obviously, one that has a lot of impact in terms of immediate modeling and risk assessment, and I hope that we covered everything that's important and that we have a concise and clear set of recommendations coming forward.

I would, at this point, like to move on to charge question 4, and, of course, for those discussants who still have some points on 3, if we have time at the end, we will get back to that, definitely.

Dr. Brady, could you read charge question 4 into the record?

DR. BRADY: Yes, thank you. Charge question 4: Aquatic bioaccumuation methods.

Traditionally, LPP's assessment of pesticide bioaccumulation potential in aquatic organisms has relied extensively on the use of bioconcentration factors. BCFs consider direct chemical uptake through aqueous exposure routes only.

For organic chemicals with PBT characteristics, bioaccumulation from non-aqueous exposure routes can be substantial. For these chemicals, risk assessments and other Agency programs have used the combination of laboratory, field, and model-based methods for incorporating bioaccumulation via multiple exposure routes.

In the pesticides program, a similar integrative approach is being considered for assessing the bioaccumulation potential of organic pesticides with PBT characteristics. This approach considers the type and quantity of data typically available for pesticide ecological risk assessment, relative strengths and limitations of each bioaccumulation assessment method, and uncertainty associated with bioaccumulation predictions using each method.

Please comment on the need to consider alternatives for the BCF method for assessment the bioaccumulation potential of organic pesticides with PBT characteristics.

Please comment on the applicability of the Agency's approach of using multiple methods for assessing bioaccumulation potential of organic pesticides as illustrated in the white paper.

DR. HEERINGA: Thank you very much. Dr. Hickie is our lead discussant on question 4.

DR. HICKIE: I have a presentation. Would you load it, please?

I'd just like to start by acknowledging my co-discussants. We had some very lively discussions on this topic. James Oris, Jim Meador, Kirby Donnelly, and...and Daniel Schlenk, and I'm sure they'll weigh in with some comments.

Next slide.

To make the answer to question 1 very short, it's a...almost a one-liner, and that...that is that the BCF method is clearly inadequate for assessing organic PBT pesticides, and we can elaborate on...on that, mostly under question 2.

Next slide.

Just...just briefly on this question, some of the alternative approaches that we gave some thought to, obviously, we need to address accumulation from multiple pathways, water, diet, and sediment, trophic transfer or biomagnification when and where it occurs, and biotransformation is an ongoing headache in this realm.

And some of the other issues that...that we'd like to address that particularly tie into modeling work is borrowing Dr. DeLorme's comment he made to me yesterday, is we need greater ecological reality. And that...that encompasses a number of things, many of which have been addressed in...in the white paper.

We'd include temporal variability and chemical exposure, the need to address bioaccumulation as...as a non-steady state process, and greater environmental variability incorporated into probably the EXAMS model and...and the bioaccumulation models. And one example of that is that temperature is an important driver of things like metabolic rates in organisms, and that has a large influence on...on chemical kinetics.

More comprehensive view on the aquatic food web, and in the discussion over the last few days, there...there are several suggestions. Dr. Simonich brought up the point of amphibians. She beat me to the...that question.

And, of course, fish-eating birds and mammals are...are discussed in a limited way in the...the white paper, and I think we need a more comprehensive approach to dealing with them. And in the white paper, they...they really just use one sort of generic food web in...in the area of plankton and fish, and we had some discussion as to whether that was perhaps adequate, given the geographical range that we're dealing with.

And that's...that's the extent of comments I have for question 1. I think we get into a lot of the details in...in question number 2.

DR. HEERINGA: Question number 2, you mean the second part of question 4?

DR. HICKIE: Yes.

DR. HEERINGA: Why don't you ugo ahead and present...

DR. HICKIE: Okay.

DR. HEERINGA: ...those, and then we'll have a...

DR. HICKIE: Okay.

DR. HEERINGA: ...your associates' comments.

DR. HICKIE: So, on...on the second question, it asked us to comment on the Agency's approach of using multiple methods, and just summarized here the...the different approaches, and maybe I put some of these in my own language as opposed to taking them direct from the...the white paper.

But there's essentially five of them, lab studies to measure BCFs, and other lab studies which can...was a mix of things ranging from microcosms, biosediment accumulation factors. There's perhaps several other tests that I...aren't coming into my mind at the moment.

Number 3 is...is controlled field studies such as mesocosm. Number 4 is open field studies using natural food webs, and...and the point was brought up that that's not all that applicable for new chemicals. And number 5 is bioaccumulation modeling.

The strategy that I...I see going forward...and it's...it's...it's really in the white paper, but it's maybe not explicitly stated as such...is that at the core of this is and should be bioaccumulation modeling and...and that lab studies, in particular, should be focused on providing information to...to verify or refine inputs to these models.

And this is the desirable approach for a number of reasons, relatively low demand on time and resources. That was mentioned. And the modeling approach gives the potential to deal with a range of issues in...in a holistic manner. And I think a good...another good thing is...is that there's a variety of existing models that...that, at a minimum, provide a good starting point, if not take us well down the road to doing this. And...and I could add one more point, that it will keep modelers such as myself perhaps busy for the...the remainder of my career.

Next slide, please.

So, in this strategy, the idea of the lab studies is that they...they provide data for validating the assumptions of the model by...by looking at the data compared to predicted values for...for things like gill uptake and elimination rate constants, and if they agree, then it gives you some confidence as you move forward, and if...if they don't, it gives the amount that you would need to refine model parameter values on a chemical-specific basis. And...and we actually saw efforts to do that, primarily with chemical 4, in the white paper.

Next slide.

Any time you use models, you...you...you have to use them wisely, and you need...for that, you need a sound knowledge of their limitations, or you can use them where you shouldn't be using them or where you should use them with caution.

And, for example, pretty well all the bioaccumulation models I've worked with or see don't work particularly well with polar or ionic compounds. I don't think anyone's managed to...to get a model that...that works consistently for them.

And, of course, you need to understand the uncertainties both in the model structure and those associated with the...the inputs and the outputs of the model.

Next slide.

Just now going into some of the particular issues that I thought of and had some discussions with...with my colleagues, question of...of KOW, very important input parameter of the model, but it...it also provides guidance of...of when bioaccumulation modeling is required. And if you go through a model like the Arno & Gobas model and...and work through it, it would suggest that you really need to start paying attention to dietary accumulation for the plankton and fish food web somewhere around log KOW 4.5 and upward.

If you bring in modeling for birds and mammals, that start point is at a...a lower log KOW, and I'm suggesting somewhere about 3.5. I could probably refine that number with a little bit of thought.

And...and there's a number of reasons for this. First off, there...there aren't...they're breathing organisms, they're warm-blooded, and...and by breathing air, they're...they're...the respiratory elimination pathway is...is not as important in general.

Another point I'd like to make that...is that many bioaccumulation models, particularly with...with aquatic organisms, are really faced with the challenge of...of calibration for what I refer to as super-hydrophobic chemicals in that there simply isn't very good data or an abundance of it to calibrate certain...some of the values, again, such...such as gill uptake and elimination rate constants, and that becomes a problem somewhere in the range of log KOW 7 to 7.5.

And the last point I'd like to make with KOWs is...is...and we all face it...is finding reliable values of KOW to work with. This has been discussed for many years, and it's particularly problematic when you get to very hydrophobic chemicals. So, in any process, you...you need a means of...of vetting or...or looking carefully at the available values and trying to pick the best one as opposed to just picking the...the average of them.

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There was quite a bit of discussion at various points about the utility of bioconcentration factors, and in thinking about that, bioconcentration factor tests, even with very hydrophobic chemicals, can still provide very useful information if they are done properly.

An important aspect of that is...is when you look at an aquatic food web, the single largest step increase in...in concentrations in an aquatic food web is that initial partition from water into the small organisms, phytoplankton or...or zooplankton, and bioconcentration factors are...are the best thing to describe that process.

Out of the bioconcentration factor tests, you can get information on bioavailability, uptake, elimination kinetics across respiratory surfaces. You can get some idea of...you can either verify the time to steady state, or you can get some idea of...of how long it might take if...if it's a kinetically-derived BCF.

The utility of these tests is...is increased considerably if additional information is reported. Fish size, growth rate, lipid content are...are important things. The reason for that is...is with that kind of information, you can scale the bioconcentration factor to other sizes or...of fish or ones with different lipid contents, and...and you can tease out the effect of growth rate on...on uptake/elimination rate constants.

And bioconcentration factors can also provide some information on whether a...a chemical is subject to biotransformation, simply if the BCF is substantially lower than...we've got an echo back there...if the bio...if the bioceontration factor is substantially lower than you might predict from KOW or KOW-based partition.

Of course, there was a lot of discussion about the...the caveats of using BCFs, and...and we've...we've included, of course, discussion about exceeding water solubility, the use of co-solvents, and whether, indeed, some BCF tests give sufficient time for...for the chemical to reach steady state. And I think a problem there is that some standard protocols may need to be revisited to allow time to steady state or to simply accept that...that BCFs would have to be derived from ratios of uptake and elimination rate constants.

Next slide.

The thinking about the food web model, then, first off, I...I think that a model like...such as Arno & Gobas has developed is...is fundamentally sound in...in concept, and the equations are fine, and there may be some challenges in...in calibration and, as I mentioned, its application for very hydrophobic chemicals, and it could be a bit of a problem.

But there's a num...a number of other issues that...that we think could potentially get worked into food web model. Refining food web structures to reflect dynamic modeling, I...I brought up the point that in the version that...that Frank was presenting, his 1 kg fish modeled over 30 years was the same 1 kg fish, but it still had a growth rate.

And...and the way to address that is you have to introduce each classes which...which makes it...makes the model more complex and...and so, you have a constant turnover of...of...of the 1 kg fish as...as you progress through...through the simulation, and that adds a fair bit of effort, but I...I know Frank Gobas has a different version of the model where...where he has done that.

Another very important point in any of these models is...is to...and perhaps, particularly, in the pond model...is the percent benthos represented.

In the diet in the generic food web that all the simulations used, several species had 50 percent of their diet from...from the sediments, and I don't quite know where that's coming from as to whether it's a best guess, but it...it's something that definitely needs to be considered carefully, particularly for high KOW chemicals.

Water temperature is...is an example of an environmental characteristic that...that probably needs to be better incorporated, and I think Dr. Gobas' simulations and...and, I believe, the ones in the white paper used a...a constant water temperature. And several good papers, one of which was just out last year by Andrea Buchman, et. al., that...that shows that water temperature is...is a major driver of elimination rate constants for PBT chemicals. She was principally working with...with PCBs.

And the background to that is...is...is that these are cold-blooded animals, so water temperature is a major driver of...of the bioenergetic aspects of these models, driving respiration rates, feeding rates.

And, additionally, growth of...of fish is...is a temperature-dependent function, and, I believe, in the Arno & Gobas model, they...they plug in a...a set growth rate that...that doesn't reflect temperature, and, for that matter, it's also not connected to the feeding rate that they plug in, and as we all know, if you eat more, you tend to grow.

One aspect that is not addressed by these food web models is...is the fact that, particularly at the base of food webs, is...is that biological production is a significant source of organic carbon in many systems, and in a place like an aquatic pond that's receiving a lot of nutrient input along with the pesticide runoff, there can be sub...substantial algal or macrophyte production, and this, perhaps, needs to be addressed in some way in...in the concept of...of it has the potential to bio-dilute the concentration of chemicals in the system.

And bringing in additional species, there's a number of issues here. If...if...and it depends on...on the...the detail you want to get into with the biology of the animal and...and their particular life history. Amphibians, for example, go through egg, tadpole, adult stages, and amphibians are also partly aquatic and...and terrestrial at times, and that creates a...is an example of a significant problem with the aquatic/terrestrial overlap in food webs.

And birds and mammals are...are a particular problem, again, because their biology and life history may be kind of difficult to incorporate into the type of model that...that...such as the Arno & Gobas model, and I talk about that on the next slide.

Just start by making the point that the treatment of birds and mammals in the aquatic bioaccumulation chapter of the white paper is...is in stark contrast to where we've gone with the sort of plankton to...to fish modeling where we've gone to really quite elegant dynamic model that tracks temporal changes in concentrations all the way through the food web, and...and yet...and with that, there's a really wonderful thing that now you can take different time averaged concentrations to...to calculate acute and chronic risk quotients based on the 1 in 10-year peak exposures and things of that.

And when...when we get to bird and mammal approaches, we take information from...from the primarily fish data and really just plug it in and calculate sort of a single point estimate of exposure in terms of sort of daily dietary intake, and there's no consideration of...of time to steady state for birds and mammals, which may be substantially longer than many of the lower trophic level organisms.

And so...so, that brings up, you know, the...the challenge of the need for dynamic modeling of birds and mammals and how do we incorporate that into a tiered approach.

And I think one...one thought I have on that was that we...we could look at the relatively simple risk quotients and...and where they've played relative to the...the levels of concern, and...and if they're substantially higher than the level of concern, maybe you don't need to go to dynamic modeling to...to evaluate risk, nor do you have to do it if...if the risk quotients, these simple risk quotients, are substantially below the level of concern.

And I...I think the gray zone is where things are hovering around the level of concern and...and perhaps, then, dynamic approach might better answer questions regarding risk for birds and mammals.

I think another very important point of...of better incorporating birds and mammals into these food web models is if it provides estimates of tissue concentrations which very nicely dovetails with the good idea of using critical body residues to estimate toxicity, and I think we'll talk about that a little bit in question 6.

Next slide.

Again, birds and mammals, there are some good models out there that could either be used or...or modified for use, and I've just thrown up a few examples. Ross Norstrom and his former student, Ken Riard, have a very nice ... model. John Nichols with EPA has...has a nice example of one with tree swallows which, as...as an interesting twist, that...that a good part of their diet are emerging insects from ponds.

And the Gobas group...and we'll talk about these in a little bit in...in the next question...has...has models that...that work for mammals...mammals. And my own work is principally on marine mammals, but I'm in the process of turning the marine mammal into a...a mink which...which modelers can do.

And...and I'm not advocating that we could necessarily go and start modeling marine mammals, al...although the question of loading as to estuaries came up, but these models certainly provide a nice starting point in...they all have a sort of similar basic structure.

And it...it makes it relatively simple...I'll never say easy...to adapt them to other species in that there's really four main elements here that...the biology and life history of the organism, bioenergetics, and the need to define the diet which can be quite tricky, and...and the chemical kinetics and so...so, shifting them from one species to another is...is substantial work, but...but you're not starting from scratch.

Next slide. We did discuss the issue of biotransformation, and the consensus seems to be...and the approach taken in the white paper is fundamentally sound, that there's currently no reliable means to predict the rate constant KM that goes into these models, so you have to get it experimentally. And if you don't have that data, I think, starting with the assumption that...that it is value of zero is...is the...the conservative approach.

I'd like to make a couple of points here, is...one is just because you...you have experimentally derived metabolic rate constant for...for producing degradants, you have to be careful in extrapolating it between species. And one example I can give is work that I've done...and...and Ross Norstrom could also comment on this...is if you look at PCB metabolism in seals versus Beluga whales versus polar bears, you see very, very different things.

Beluga whales are not particularly good at metabolizing PCBs. Seals are quite good at degrading many PCB congeners, and...and when you get to polar bears that primarily eat seals, there's perhaps a half dozen congeners that dominate. So, it...you have to be cautious when you...you do that.

Another point in biotransformation is that bioaccumulation models that are out there right now don't really deal with metabolites that's chemical degraded that actually disappears from the model. And if you were to try to apply these models to accumulation or elimination of degradants as...as chemicals out in the environment, just a caution that these models are largely developed for...for neutral organics. So, if the degradants are polar or ionic, you're...you'll...you'd be in trouble.

Next slide.

So, the solubilitiy bioavailbility...bioavailability and bioaccumulation issue that...there was a lot of discussion this morning about solubility, and I...I think the white paper addresses this quite well with respect to bioaccumulation, but one point I would make to...like to just go through again is that our definition of solubility is operationally defined. So, if you use a different method, you get a different outcome, and...and as such, just thinking about this, what we use as dissolved may not be synonymous with bioavailable.

And...and this is something that we've usually assumed that once we calculate what the dissolved should be, we assume that's bioavailable, but, of course, our measure of dissolved really depends on how we calculate it or...or measure it.

And while I'm on being a grammar cop, I'd just like to point out that the term equilibrium and steady state are not synonyms.

And also gave a little bit of thought to long-range transport and...and the bioaccumulation issue, and can't really say much on that yet, because we don't have any...there's no way of addressing the issue of loading into an aquatic ecosystem at this point, and you need that loading before you do any bioaccumulation modeling.

I think that's gone backwards. So, that's it for my comments.

DR. HEERINGA: Thank you very much, Dr. Hickie, for the organization and presentation of your comments.

I'd like to give the associate discussants a chance to add comments to what Brendan has already provided. Dr. Oris?

DR. ORIS: Jim Oris. I think that Dr. Hickie's done an outstanding job of summarizing the discussions that we had on this, and I don't have a tremendous amount to add, but I do want to touch on a few details that...that are critical for me as I see some of these things.

First of all, you need to get this part right, because if you're going to use critical value as it is to toxicity, this part has to be done correctly. So, it's really critical for this part to be done correct.

I'll reiterate some of my comments that I made yesterday about the transparency of the assumptions that you make that need to be put up front in the problem formulation stage so that everybody knows going in what the assumptions are, when they're violated, and the implciations of those violations. As we know, all models are wrong; some are useful.

These models are wrong, but they're very useful, and if you violate the assumptions, then they don't...they lose their utility. So, just be very transparent in...in what the assumptions are.

In terms of methods that are used and...and looking towards a tiered approach for PBT chemicals, the...the laboratory-based BCF methods don't address potential for trophic transfer, and they shouldn't, but if you have a PBT chemical, there is a test guideline for a laboratory-based assessment of trophic transfer, and maybe you should implement that as a...as a tiered step.

There is a need it incorporate growth and metabolism in the model. There's a need to incorporate dealing with solubility issues, and I would encourage you to continue pursuing the use of the AGRO version of the modeling that you're using.

You must look at ranges of dissolved organic and particulate organic matter in your modeling. Currently, just fixing it at one particular value, I don't believe, is sufficient if you're looking at a range of...of ecosystems.

And some of my comments are random, because I'm reading through some bulleted points here, so bear with me if I jump around just a little bit.

In current BCS laboratory methods, there's a strong encouragement to reach some kind of steady state level in the organism, and with PBT chemicals, that may not be possible. In fact, if you have a steady...time to steady state of several hundred days, unless you have a Willie Lick student, you're not going to get there.

Mathematically, it's clear that you can use the ratio of the uptake and elimination rate constants to estimate a pretty decent value for bioconcentration factors, and, in fact, it may be more accurate for PBT chemicals, since you can't get towards that steady state. But a reliance on those rate constants, I'll encourage you to be very careful about how you use those and the assumptions that go into them.

And an example is in Table 5.18 on page 139 in which there's rate constant that's listed from a different kind of a model. So, when you have an uptake rate constant that's less than 1, chances are it was done using a different kind of a model, and there's at least one in there.

If you use a mass-based rate constant which that one is and you try to apply it to the models that you're using, you'll have some significant error. So, be very careful about the kind of model.

There are mass-based models, and there are concentration-based models. You're using a concentration-based model, and you need to make sure the units are correct.

Saying that, if you...you can't assume that a liter of water and a kilogram of organism are equivalent. So, by publishing or reporting units for the rate constant, for, especially, the uptake rate constant of just inverse time, 1 over days, is not appropriate. It must be in liters per kilogram-day, and the same thing with bioconcentration factors. A liter of water does not equal a kilogram of organism.

And when you go to do the calculations for the CDRs if you don't carry those units through, you won't end up with the right calculations. It's just a technical caveat that you really need to be careful about.

You can also use information from the bioconcentration factor test if you do a little bit of extra effort to look for things like metabolism, or when you are interesting in adding extra tiers for the critical body residue, if you can find different compartments in the organism. Again, the model is wrong. You assume that an organism is one compartment, but you can look at the elimination phase for multiple slopes on the elimination constant and determine whether there's more than one compartment.

If there's more than one compartment, perhaps the assumption of the organism either non-metabolizing or multiple compartments for target organisms may not be an appropriate assumption when you go to the next phase. So, it's a potential we can highlight these for further study.

I think that's all I want to add right now. Thank you.

DR. HEERINGA: Thank you very much, Jim. James Meador?

DR. MEADOR: Hi, Jim Meador. I also thought Brendan did an excellent job of summarizing the various points...points in our thoughts. I'll add just a couple of things.

Brendan made a point about pri...primary production in ponds, and what I found in...in my copper work with the microcosm is that algae were actually quite leaky, and they lose a lot of dissolved organic carbon. And, actually, microcosm hit with massive concentrations of copper could actually recover just by the dissolved organic carbon, dissolved organic material when this algae was leaked. So, I think that's an important; point also to consider.

I also had a comment about biomagnification factors. I really don't think you had that as part of...as part of your protocols, and I know you have a trophic transfer test, you know, that really is two trophic levels or more. So, I don't know if you address that through modeling or if you consider...considering actual biomagnification tests or how you're thinking about that.

DR. HEERINGA: Dr. Sappington?

MR. SAPPINGTON: Yes, there's a...a trophic transfer test which is usually a...a feeding study just to get at the transfer between two trophic levels. I think for addressing multiple trophic levels, the approaches would either be modeling or using mesocosm type studies where you actually include several trophic levels in...in the experiment.

DR. MEADOR: Okay. And I also wanted to make a point about this concept of using KOW to determine the importance of water versus dietary exposure. That's based on equilibrium modeling, and rarely in an environment do you have equilibrium. So, you can have an animal that accumulates a fair amount even at a low KOW, a particular compound at low KOW, move out of the area, still have a lot, and be a very important component for the dietary. That low KOW can actually be very important. It's not...it's not just based on KOW.

That pretty much covers my extra points.

DR. HEERINGA: Thank you, Dr. Meador. Dr. Donnelly?

DR. DONNELLY: I really don't have much to add. I...I do think Dr. Hickie did an outstanding job of summarizing our discussions.

And, quickly, I...I think I want to put in a plug for potential alternative field-based methods. We've been doing a study with...in collaboration with Dr. Meador and...and some of the EPA Region X Superfund folks for about five years now up in...in Region X.

And at the request of the EPA last summer, we incorporated a solid phase microextractor to look at bioavailability and bioaccumulation of sediments. And, certainly, we don't have the results from that, but it seems like a pretty nice tool for field-based methods. And given the variability of sediments both within a site and from site to site, it may be an option for...for looking at bioavailability and bioaccumulation.

DR. HEERINGA: Thank you, Dr. Donnelly. Dan Schlenk?

DR. SCHLENK: Last but not least, I'd also like to thank Dr. Hickie for summarization of...of our discussions yesterday and...and previous days.

I just...a couple things to highlight it. I think in a tiered approach, you're...the models that you have seem to be...work pretty well for your...for compounds of about 5.

A log KOW of 5 or less seem to...to be pretty...pretty nice in terms of at least what was presented in the white paper, particularly some of the hybrid models with the AGRO/PRZM/QUASI and the Arno & Gobas 04 model. The dynamic model seemed to coincide pretty well with some of the...the predictions of the empirical data. So, I think that looked pretty good to me anyway.

Unfortunately, I guess, for the compounds that are fairly high that tend to...you have some issues with that, and it's tough to...to model that.

So, in terms of sort of revisions, it...I think Dr. Hickie had brought up, but just a little bit more detail and also to re...reiterate some of Dr. Oris' comments.

I think, from a tiered approach, the kinetics can tell you a lot in terms of whether your not you had inflection points in terms of uptake or elimination. I think those are...are critical in terms of the tiered approach that could drive you towards, you know, a different hypothesis testing in that regard.

One of the things...and, again, it's

interesting, Keith, you brought up the...the solid phase microextraction. We've...in our group, we've been seeing, actually, the potential input of...of oral exposures being fairly significant with compounds log KOWs about 3 to 4. We haven't gotten up to 7 or 8, but it would make a lot of sense, given the discussion of the last question, that you are getting interactions with DOC or forms of DOM, that colloidal material, that, again, how you define this, you know.

We are seeing uptake from oral absorption primary from a...from benthic mass invertebrates as well as...as well as a fish study that we've seen. So, consequently, with an oral exposure, I think metabolism becomes much more important in that regard, particularly the...the hepatic metabolism that you get with some of these compounds. Not all of them.

Obviously, it's...you know, it's not a, you know, one size fits all type of thing, but...but I think one of the things you could explore in terms of refining, perhaps, some of these models with a high/low KOW would be looking at...at that as...as a route.

And I think, you know, size does matter in terms of...of what those particle sizes are. I think the information that we're getting out of animal materials and now particles is demonstrating that, that we are seeing absorption from the aqueous environment and some of these aggregate type compounds that are less than the 1 micron that go into...what are dissolved per se but are actually being absorbed and taken up.

So, consequently, I think that's something that you might want to refine in terms of a near-term sort of recommendation.

From a more futuristic perspective...and then, this sort of deals more with question 6, but I think your...your interactions with...with Duluth in terms of John Nichols and developing some of the more PDPK based approaches, I think I'd highly recommend that. I think you'll see perhaps some differences, and maybe that would, particularly with some of these compounds, we've already seen that you have some barrier issues with these...the gill membrane.

Again, if we incorporate an oral exposure, then I think the multi-compartmental aspects become a little bit more relevant in those sort of situations. So, again, more futuristic, but, you know, something that you might want to look at.

And, again, I think with the data that's coming out of the material range, that would be fairly critical in terms of plugging that in, perhaps, to your particle size model. And I don't know how to do that in terms of the...the AGRO model but something that might be toyed around with in terms of just assuming a, you know, 1 DOC concentration but maybe tweaking that a little bit in terms of, you know, fines and...and even going below the fine concentration, whatever that is, in terms of what the...what the information is showing us.

We're seeing about 800 nm as being pretty critical in terms of the cutoff size in some of our studies anyway, but...so, let's see.

And, again, specific...I think the lipid issue is very important, particular in life stage issues and gender issues, particularly with male versus female spawning animals. I think that can have significant impact in terms of loading, retention in terms of accumulation, too.

I think that's something that...I don't know if that...I couldn't tell from the literature provided whether or not that's incorporated in the Gobas model or not in terms of gender or developmental stage in terms of...of lipid content, but I think that's something else that would be pretty interesting to sort of tweak around and...and play with and may at least reduce some uncertainty in terms of those high

KOW numbers.

So, that's about it.

DR. HEERINGA: Thank you, Dr. Schlenk. We have about ten minutes before we break. Additional comments on either any of the discussants or other members of the panel on this particular...Dr. Hickie?

DR. HICKIE: Just one comment to follow up on the...the lipid issue when we run the Gobas model and...and other similar bioaccumulation models. Lipid content is...is put in as a fixed characteristic of a property. It's a dynamic biological thing, and so, you...I'm actually working on a paper right now where one fish species goes from 1.5 percent lipid in the spring to 9 percent in the fall, and PPD concentrations are constantly chasing towards trying to reach steady state, but they never catch up, because the lipid's always changing.

DR. HEERINGA: Dr. Norstrom?

DR. NORSTROM: Thanks, Brendan for doing a great job too.

I have a few comments here, mostly on...on this super-hydrophobic thing which...but also on the...on the whole use of log KOW. I sort entitled it kinetic considerations.

And for super-hydrophobic compounds, non echoed in kinetics is definitely the rule, and we have to be really careful about using some of these models, I think, and just assuming that we can take these log KOW relationships and use them without any further thought. Too much reliance can be placed on them.

And...and my point, when I talked about this to Dr. Mackay a couple days ago, about the fact that we view log KOWs as ratios of concentrations when, in point of fact...or activities, if you like...they are actually also the ratio of rate constants between...transfer between media.

So, you could have two compounds that have similar log KOWs, but if they're solubility, for example, in... is relatively small, possibly the rate of transfer between the media might be slow in both directions where you get the same log KOW, but you get quite different kinetics or approach towards equilibrium.

And I'd like to sort of submit that we have a...a perfect example of that in...in the case of oxythiodibenzofuran which is not soluble, really, in anything that's non-aromatic, and in that case, you find that it transfers in the environment extremely poorly, essentially stays where it...where it goes, because it just simply doesn't move around very well, from water, even though it has as log KOW which is, I believe, somewhere in the range of 8 to 9.

And that doesn't really model its kinetics in the environment at all. So, I think you have to consider, when you're looking at some of these pesticides, whether the solubility is itself rather small and...and worry about whether...if the kinetics might be affected as a consequence of that.

So, just relying on a constant like the log KOW may be a...a bit dangerous in some cases.

And I'd also like to point out that if you look at the log KOW dependence, for example, the bell curve that was shown yesterday on clearance rates in fish, the reason that those fall off at high log KOWs is because of internal kinetics in the organism. The rate of transfer to the gut and, therefore, partitioning into the gut contents as the mode of...of release is just simply inefficient, because the compound doesn't move from its storage site in the organism to the gut very efficiently, and so, it falls off.

And you have to be concerned, then, about that, too, because, you know, it is not a static situation. You have to consider there's a kinetic or a dynamic one.

And remember, too, that even the fact that you have a log KOW dependence in the first place for a number of these parameters indicates it's a non equilibrium situation.

And I'd just like to sort of use as an example the study by Catalan, et. al. there was a lake in the high mountain in the Pyranees, I believe, and they studied corranamids, terrestrial insects, mollusks, and anabacteria in trout. Used nitrogen stabilizer to determine trophic levels and definie the food web.

And there, they showed that, in this case, organochlorines with log KOW higher than 6 showed lower concentrations in food than expected. So, non equilibrium, and they stated that distribution of compounds didn't reach equilibrium within the lifespan of the food organisms which was approximately a year, and in fish, however, only PCB-180 with a log KOW around 8 showed this kind of...this equilibrium thing.

So, you know, I think you just have to be careful not to sort of assume everything is equilibrium kinetics and...and consider, especially for the high log KOW compounds. Equilibrium is seldom reached in...within or between compartments.

I'd like to just briefly comment, too,

on the example that Brendan used of, I believe, it was the field polar bear comparison. That's a special case, I think, because marine mammals are quite different than terrestrial mammals in their metabolic capability. And it's possible, I think, that within the...in mammals, terrestrial mammals, possibly dividing it taxonomically more into sort of rodents or whatever...and undulates, you would probably find that there are at least similar type of metabolism there going on, if somewhat different rates come under the individual species.

I think that relationships could be developed which might be quite useful for this kind of thing. So, I don't...I think it would be worthwhile exploring, looking to see whether interspecies comparisons for other types of chemicals are...whether this is shown to be reasonably valid or not, and perhaps you can use, for example, lab...lab studies as a surrogate for a rabbit or something in a terrestrial ecosystem without...with reasonable security.

So, I think that's my comment. Thanks.

DR. HEERINGA: Thank you, Dr. Norstrom. Other comments at this point? Dr. DeLorme?

DR. DELORME: Just a...just a couple points that I don't think were...were covered already.

I have others that were already covered.

From a...for the modeling approach, I...I want to start by saying I like the sort of multi looking at several lines of evidence to look at this. I think that adds strength to your case in your...when you're doing this. It also will allow you to look at, you know, maybe when your models aren't working the way they are for a compound 4, you need to tweak them a little bit.

For the modeling approach, though, you could consider a tiered approach with respect to the complexity of the food web and receiving water scenario. For now, an initial tier 1 could be a simple food web like you used, standard farm pond, fixed inputs for certain parameters which allows for relatively quick implementation, you know, in the near term, you know, based on what you guys have already done.

I think you also have to be aware that you need to integrate, as Dr. Oris said, into the model structure any results with respect to resolution of the solubility issue, and also from Dr. Mackay's stuff, we saw that there was an impact of burial as well into the outflow.

So, when those issues are resolved, you

may want to look at...you need to have an integrated approach so that what you're doing in your...your fate modeling is also in your bioaccumulation modeling. Okay? They are all linked.

As...as Dr. Oris pointed out as well, I think you need to consider regular development of additional data through either modification of existing study protocols or perhaps incorporating additional data requirements for PBT chemicals. That's going to help reduce your uncertainty, I think, in the long term.

I think we're really dealing with a new paradigm here. We're moving away from, you know, the paradigm that we've used or the approaches we've used in the past for non-PBT chemicals into something that's a little bit different. We have to look at it a little bit differently.

And in that respect, for chemicals that are subject to long-range transport, I think we need to recognize that there is a shift in risk both temporally and spatially. Okay? If you have something that's subject to long...long-range transport, you don't only have to be concerned about what's going on at the field scale which is sort of the typical thing that we've always done.

I think you have to look at what's going on elsewhere, you know, what's going on far afield and also temporally. I mean, you know that you're not going to see these things right away.

So, maybe what you want to do is, for a farm field assessment of new chemical when field data is not available, consider projecting a steady state future assessment if we can find a mechanism or a model to look at loading.

And you could use a simple approach where you just take your...your simple scenario, put your loading into it, and see what happens there.

DR. HEERINGA: Thank you, Dr. DeLorme. At this point, I guess I'd like to turn to EFED scientists to see if...if you feel this response has been comprehensive or whether there are points of clarification or questions you'd like to ask. Keith Sappington?

MR. SAPPINGTON: Well, I want to thank the panel for all the excellent suggestions. I think they're very insightful, and I appreciate them.

One question I have...and Dr. DeLorme talked about this with the tiered concept...is Dr. Hickie, with the recommendations of the different modifications to the food web models, if there's a way to sort of triage those as ones that may be more important versus others, just because of the mode that we're in, and I...I...I think starting out with a tier 1 and then moving to more complexes is probably something that we're very interested in. So, that's...that's one question.

DR. HICKIE: My main problem on that primarily had to do with adding the complexity of birds and mammals with...with the aquatic food web modeling. I...I think probably a lot of the issue there is...stems from what comes out of the EXAMS model in terms of exposure concentrations fluctuating over time, and I haven't quite wrapped my head around providing you advice right now on...on how to do it, but I can...I can certainly appreciate that keeping it simple on the first pass.

And...and...I think you could probably stick with a...an existing model at that first pass, but it's...it's...and it depends on where you're...you're working the things, you know, an example being water temperature. In some cases, it might be an issue; in some cases, it might not be and might have to deal with...with where the pesticide is being used. Is this...is it in a southern, warm location? Is it in a more northern state, or does it have stronger seasonal fluctuations in temperature?

DR. HEERINGA: Dr. Norstrom, one additional comment?

DR. NORSTROM: It just occurred to me that, you know, if you're looking for something like a...a species that could be representing birds in a pond, you'd be hard pressed to find a better species than a great blue heron, because they're distributed widely everyone, and everybody knows that they even eat goldfish out of your own pond. So, you know, there...that would be fairly straightforward, I think, to sort of include a species like that as kind of a standard thing and would have some ecological realism.

DR. HEERINGA: Dr. Hickie?

DR. HICKIE: One thing you're certainly getting to with birds and mammals is...is the issue of home on the range, and there may be, you know, it's...and it...this also comes into play with the...with the aquatic versus terrestrial mixing. Birds such as a great blue heron might be feeding in multiple ponds and...and some might be predominantly aquaticly based in terms of their...their diet, and...and other ones may be a tremendous mix.

So, I...it...it...it's a difficult issue, and...and the home range issue, I think, is an important one, and I've been addressing that with some mercury studies, looking at mercury in mink versus otters, and the home ranges vary tremendously.

DR. HEERINGA: Home range issues, obviously, come up in other modeling considerations like TIMS with the avian exposures and so, too. Dr. Meador and then Dr. Oris, and then we're going to take a break.

DR. MEADOR: Yeah, I was going to add to that, too. There's some great work by Chuck Henney with osprey from the Columbia River and river systems where you look at concentrations of plots in eggs, and they seem to be quite indicative of certain reaches where we...we seem to have a pretty narrow home range, like within a kilometer or so. Good indicator species.

DR. HEERINGA: Dr. Oris?

DR. ORIS: Yeah, if you're...if you're looking for tiered approaches, you know, it's been mentioned...and maybe I can try and...and summarize how I'm thinking about it. If...if the compound meets PBT requirements, then you might add a day requirement for a trophic transfer test in the laboratory. If that seems significant, then you may want to do more extensive modeling.

If the food web modeling, as...as

Brendan suggests, if you get a hazard quotient that's either well above or well below your level of concern, then maybe you don't need to go too much further with getting out of the actual water, but if it's close, then you might want to start looking at more dynamic models and the terrestrial connections with birds and mammals.

So, there...there's ways to...to go at it more tiered without requiring, over requiring detail.

DR. HEERINGA: Okay, at this point, I'd like to thank everyone for their contributions on...on question number 4, and we'll have a chance again with follow-up. There's questions 5, 6, and others that deal with similar issues.

But at this point in time, I'd like to call a break, and why don't we plan to reconvene at 10 minutes to 11:00.

(WHEREUPON, a brief recess was taken.)

DR. HEERINGA: Okay, if we can get underway, at this point...welcome back, everybody, first, and at this point, we have completed our initial discussions on charge questions 1 through 4, and we're ready to move on to question 5.

Just a little forward thinking in terms

of schedule, it's not clear whether we'll be able to complete the charge questions today, and it's not my intent to rush this along that we do, but I think we're on a pace that we could potentially wrap up the discussion of the charge questions today, but if we need to carry over into the agenda tomorrow morning, of course, we'll do that, but I'll have a better sense of that by 2:00 or 3:00 p.m. this afternoon.

So, let's...let's turn to charge question number 5, and, Dr. Brady, if you would, read that into the record for us, please.

DR. BRADY: Charge question number 5: The Agency currently assesses risks to terrestrial vertebrates that result from direct deposition of pesticides on food items that inhabit the treatment area. In general, this assessment is considered to provide relatively high-end estimates of excute...of acute exposure through the ingestion pathway.

At this time, however, the Agency does not routinely assess pesticide bioaccumulation in terrestrial food webs in sites, in part, because the methods and tools for assessing bioaccumulation in terrestrial food webs are not as developed compared to those for aquatic food webs.

Please comment on factors the Agency can consider to identify when bioaccumulation potential in terrestrial food webs may be important to consider in its pesticide ecological risk assessment. Please comment on the current state of the science underlying existing terrestrial food web bioaccumulation models and their relative strengths and limitations.

DR. HEERINGA: Dr. Hickie is our lead discussant.

DR. HICKIE: And just...just before getting into it, I'd just like to comment that...that the original lead discussant was unable to make it, and...and I was asked at some point last week to take this on, and I...in hindsight, I kind of think I should have said no, since there are other people on the...in the group that I...I think are better suited to taking the lead. So, I'll have quite brief comments, and then I'll defer to them.

My co-discussants are Will Doucette, Randy Maddalena and...and Ross Norstrom, and it's a very nice blend of...Ross and I deal more on...on the sort of animal wildlife side, and Will and Randy are...are really well suited to talking to the...the soil/plant related issues.

To address the...can you move to the next slide, please?

To...to address the first of these questions, yes, KOA and KOW are important things in...in the decision or the formulation process of...of trying to decide when this should be looked at, and I...I started trying to think through, you know, what sort of break point in...in these values you would use for guidance, but I quickly came to the realization, a) that my knowledge was limited, and...and b) it depends on the situation, the...the scenario that you're working with, whether it's a near field, whether it's far field, and...and the mode of...or the input pathway of the pesticide into the system.

If it's coming in from the air, KOA is a...a...quite an important driver for accumulation into plants directly from air. If the pesticide is applied to the soil, then...then KOA is less important, but it...it's still a significant player, because the KOA defines chemical release back to...back to the air through the leaves.

And another thing there is if you're dealing with sort of off-site issues or...or areas any distance away from the pest...where the pesticide is being used, you also get into having to consider the...these chem properties that...that help you determine whether it's a long-range transport chemical.

So, that includes things like volatility, and, of course, you...the extent to which it's persistent in the air, things of that sort.

That...that's about what I have to say on...on the first question. Maybe I can defer to my colleagues that...that can perhaps...

DR. HEERINGA: Sure.

DR. HICKIE: ...add more.

DR. HEERINGA: Will Doucette is the first associate discussant.

DR. DOUCETTE: With regards to the physical chemical properties, I think...

DR. HEERINGA: Nearer the microphone.

DR. DOUCETTE: With regards to the physical chemical properties, I...I agree that KOA and...and KOW are important. However, it...and my emphasis has been on root uptake, and I think Randy's probably equally suited to deal with the...the air uptake issue.

We had a...a working group meeting on...and I'm going to specifically talk about the plant uptake. I'm going to stay within my...my comfort area on this and...and we...I mentioned yesterday that there were some more sophisticated models or, at least, newer models from the two listed in your table, and I think that's true, and I passed the references on, so you should get those.

Stephan Trapp has got probably three or four iterations of the model that you have since there, and...and his approach now is...is really looking for specific scenarios of exposure, and I think once you guys decide on what an appropriate scenario is for looking at terrestrial fate which is something I think we'll also mention in the second question, then, I think, there will be models that you could actually use, and the input is relatively minor, at least on a...a tier 1 sort of thing.

And there are bioconcentration factors specifically for plants, and there is another parameter called a transpiration stream concentration. But the difference between plants and...and the fish that we talked about is it...it still is driven by the...the movement of the chemical through the root membrane, but it's...it's passively taken up and so that the amount that actually concentrates within the plant is proportional to the amount of water that's transpired by the plant.

So, the longer the exposure, the longer the water...or the more water that the plant transpires over time, the greater the potential concentration buildup within the plant. And I think that's really kind of the state of the art where we know that fairly well.

What we don't know, necessarily, is the...the distribution within the plant. Generally, it...it tends to concentrate in the leaves. So, if you have an organism that is feeding on the leaves, that's where they're going to get the...the biggest dose.

And unlike fish species where, up to a certain level, the more hydrophobic it is, the greater the concentration in the fish, in plants, I think it's often...or it...it's still a little bit up for debate, but in general, it's the opposite, and the more water soluble the compound, the greater it is the chance it's coming from the roots, but the more hydrophobic, the greater the chance it is to come from...from aerial deposition.

And in our working group, we tried to...to simplify it. I had a...a working group on...on plant processes in...in England earlier...or late last year, and we used an arbitrary cutoff of about log KOW of 3.5. Anything greater than 3.5, we thought that atmospheric deposition was probably the most likely mechanism. Anything less than 3.5, we thought that root uptake was probably the...the most significant mechanism.

And for things that were very hydrophobic, we used a log KOW of, roughly, 5. That probably doesn't get into the plant at all from a root point of view unless it is a root crop like a...like a carrot or a potato. And that, you know, that was just trying to simplify things.

And that's really where the state of the art is. There's a couple of...of good models or, at least, good conceptual models that have been...I won't say validated, but at least they've looked at a couple of small data sets to suggest that they have some...some foundation in reality, if you will, and I think those are probably usable.

And that's really all my comments that I have.

DR. HEERINGA: Dr. Maddalena?

DR. MADDALENA: Okay, thank you. I...I agree KOW, KOA, and also reaction mechanisms are important indicators for terrestrial bioaccumulation, and I'll expand...I will expand it beyond my comfort zone here and go beyond education and look at terrestrial systems as a whole, and...and in that case, yeah, they are.

And the main reason is

they're...they...they basically represent the solubilities in surrogates for pretty much the main parts of the environment. Lipids are represented by the octinol or vice versa, and you have water and air. So, these two partition coefficients really represent all three compartments in...in the real world or in the world we're trying to mimic.

So, by air, we're looking at these PBTs with really, really, really low vapor pressures. Well, it...it turns out that all the...you know, although things like the inhalation exposures may be exceedingly low because of low concentrations, the chemical mass in the air is likely to be one of the more dominating and most important processes for...for transport and mixing of these chemicals in the...in the environment. Certainly, movement in water is important as well, but as far as getting into the terrestrial system, the air is probably the biggest integrator of these chemicals. So, it has to be taken into account.

Therefore, that's why we...we recommend this KOA as an important indicator. And I think there are some indications that KOA also provides some understanding of fate inside the body as well inside the organism, but I haven't gone there. It is a simple and useful metric.

I'd like to extend this to a little bit in the recommendation, anyway, is to keep the...just kind of I like...it's important to look at these processes, these transport processes, in individual media and recognize that they...they really can't be decoupled for this particular class of chemicals. So, you can't just look at water, you can't just look at plant, and you can't just look at soil or air in isolation like you can for other chemicals.

So, there...there are important feedback loops that need to be captured, sediment to water to air, soil, biota. I'd even extend that to indoor air in the built environment. I'll say a little bit more about that later.

And this happens over very, very long time frames for this particular class of chemicals. So, it's...it's a different world, and I think I can't emphasize that enough, that...that these particular pollutants, the PB and LRT pollutants, ignoring the toxics for right now, are very different.

So, likewise, the kinetics...the kinetic constraints of mass transfer and transport for these chemicals is also important, because some of the biotic compartments, I think, as we've indicated in the aquatic system, may...their lifetime may not be long enough to achieve any kind of steady state or even approach steady state.

So, the kinetics have to be incorporated into this. So, at least, you have to go to a...a level 3 analysis if you want to use the fugacity type terminology that we talked about yesterday.

So, in short, although I think that the basic partition coefficients and degradation/metabolism rate are good indicators of terrestrial accumulation, I...I think it's important to consider these phys-chem properties in the context of a fully-coupled, multi-media mass balance model early on in the process before your problem formulations. These things are pretty easy to use.

So, recommendation is a tier 1 assessment mainly to learn from the basic phys-chem properties that you're going to have on your table. A screening phase and in some cases, even a fate and exposure tool such as the level 3 mass balance models are...are relatively easy to parameterize, easy to use, and they're reasonably informative for things like developing a plan to move to more sophisticated modeling approaches.

And they're also informative along the way for interpreting things like PB and LRT. So, at a minimum, these sort of so-called uni-world type models can provide insight into the approximate distribution of specific chemicals in the environment and...and, again, a first approximation.

I keep simplifying this, but it's...it's informative, but it's still a first approximation, but of how much of the mass that's applied in a given location, a given scenario, how much of that's going to be contributed to the global site, because different beast. You've got to think global on these chemicals. You can't think field at...at this point. You can start at the field, but you're going to have to go beyond that at some point.

So, that's my comments to 1.

DR. HEERINGA: Okay. Dr. Hickie, my interpretation is that you sort of split this question, or do you think that these comments addressed both parts of the question?

DR. HICKIE: They...they primarily address the...the...

DR. HEERINGA: First part?

DR. HICKIE: A good bit of the first part. I don't know if Dr. Norstrom has anything to add.

DR. HEERINGA: I'm sorry. Dr. Norstrom, I...I cut you off. You are...

DR. NORSTROM: Yeah, I do. As far as the log KOW and log KOA thing, when I...I kind of looked at it from the standpoint of...of the Gobas models where inition through respiration is...is considered an important mechanism for compounds with low log KOA. I'm not sure how often you'll run into that kind of situation in pesticides but...

I'd like to point out that...that there may be some complexities there. We know that for some compounds...first of all, for compounds that have log...low log KOW, it's not always the case that...in terrestrial animals that...that 4 is the cutoff limit. There are numerous examples of compound with slightly lower log KOA than that that do, in fact, accumulate, although usually biomagnification factors are not very high, sometimes around 1 or a bit higher.

But there's...there's one compound that's fairly well studied, and that's beta HCH which, in fact, accumulates to quite high levels. BMS is very.. well quite high and in some mammals as well. And it has a log KOW of around 3.8, I think.

And in this particular case, the...the Gobas modeling tends to show it accumulating simply because the log KOA happens to be rather high. In other words, the respiratory loss for this compound in organisms is...is rather low.

However, I'm concerned a little bit about whether this may, in fact, be a figment of...of metabolism, because most of these models are developed using chlorinated chemicals. So, the upper end in the regression is defined by compounds that basically don't metabolize very well, even in mammals and birds to some extent. You know, a lot of hexachloro and heptachloro PCBs have...basically, their mechanism of loss from higher organisms is by partitioning in the gut contents. Or in eggs or production of one kind or another, not metabolism.

Whereas at the lower end, most of the things probably are metabolized to some significant extent. So, the assumption in these models that the metabolism is not occurring can certainly affect the kind of interpretation that one wants to put on this. So, although I'm not at all ruling out the possibility that...that the interpretation that's put on by Gobas, for example, in 2003 where he did the... combination, Science 22 through 29, he says he derives a relationship with bioaccumulation log KOA for the life and care of a revoked food chain and came up with this interpretation of log KOA, but it assumed no metabolism.

And then, there's the Gobas paper that uses the soil and earthworms through food chain, and in that case, the maximum BMS that they're calculating is around 6 to 7 which is awfully low, I would say. So, I would say that metabolism certainly enters in there so that the...at least the relative importance of log KOA may be less than indicated and over-compensated for by metabolism.

So, some caution should be used, I think, in the end proofing these models before they're taking as gospel as they stand. So, that's one comment.

I'd also like to sort of come back to the...the whole issue of kinetic considerations within organisms in terms of bioaccumulation in...birds and mammals. A student of mine... showed that PCB congeners fell off exponentially approximately a factor of 10 between log KOW 5.7 and 7.8 for PCB congeners, and the 120-day uptake BMS increased by a similar factor but not a fall off in log...at high log KOW like you see in those bell shaped curves that were shown yesterday for fish.

So, I think for mammals and birds, you tend to not have this kind of kinetic decrease at log high KOW simply because they're higher temperature animals with bigger metabolic rates, and their distribution within the organism is therefore much more sort of at equilbrium.

Nonetheless, it's clear that the fact that we have a log KOW kind of shows that these are not equilibrium kinetics. You know, if it was purely active fugacity between the organism and gut contents, it wouldn't make any difference what the log KOW was. So, we have to be somewhat cautious about that.

I'm not aware of...of similar studies on clearance dependence of log KOW in mammals, but I think that, probably, they do exist.

I'd also like to just briefly at this point comment on the fact that you say that...that you're not sure that the methods and tools are developed. I think it's more going back to what Dr. Doucette said, that it's not so much that it's not possible to...to model terrestrial ecosystems. It's just that the mobility of animals and the complexities of their diets means that you have to define a scenario quite carefully in order to be able to do it, because once you do that, it's really not all that any more difficult to model in a terrestrial ecosystem than it is anywhere else.

So, and some of the examples that, for example, that Dr. Gobas has used could be applicable in this particular case.

I have some other comments, but I think they kind of more on...towards the second question.

DR. HEERINGA: Thank you, Dr. Norstrom. Dr. Maddalena?

DR. MADDALENA: Just to follow up on that, thanks. One other point in this phase of the assessment, early on in the assessment where I think this question about phys-chem properties comes in is the idea that often, if we have a simple model, we get the right answer for the wrong reason. And so, that really highlights the need to always incorporate a sensitivity analysis formally into your assessment process with these simple models, so you can understand not just what the model told you but why it told you that, and it will help you construct your assessment down the road.

DR. HEERINGA: Dr. Hickie?

DR. HICKIE: I'd just like to add in, and Dr. Norstrom can perhaps correct me, but since we're co-discussants, with...within a series of chemicals such as the PCBs, you...you can have a correlation between KOW and KOA. So, when you start looking at bioaccumulation, it's...it may be difficult to...to sort out whether it's KOA or KOW that's...that's the main driver.

And...and traditionally, in modeling organisms, we've...we've always thought of it as being KOW.

DR. NORSTROM: Yeah, it's the old cause and effect thing, no question, although, actually, beta HCH does make a rather interesting example, because it falls off with KOW and KOA and happens also to be in a compound that it has a rather high BMS. So, there are enough exceptions to the rule that it may in fact turn out to be true that it...in other words, it's not just a kind of cross-correlation between the two that's causing that.

DR. HEERINGA: Dr. Thibodeaux, comment on this particular point?

DR. THIBODEAUX: Yes, I think my question is to Dr. Maddalena and Dr. Doucette.

On the tier 1 model which I assume is an equilibrium, if I understand you correctly, you said that because of the size of the species, tree or mammal, you're never at equilibrium. So, if you use an equilibrium model, then it's way out of bounds as far as predicting the concentration, even the organism.

Say if it was in air or even in ground water. Is that true?

DR. HEERINGA: Dr. Maddalena?

DR. MADDALENA: I think I would, for this particular class of chemicals, not go below a level 3 which is steady state, in which case you can have systems that don't...you can work in the death of the organism in the equation as far as mass transfer process say, example, from...from the air to the leaf to the soil becomes a mass transfer...or transport process, not necessarily what's accumulated in that leaf. It's what that leaf carries to the soil each year.

So, if your question was whether equilibrium models are appropriate, only as a very first real rough cut to see where things are moving to.

DR. THIBODEAUX: Yeah. So, level 3 would be a steady state, if I remember right. Level...

DR. MADDALENA: Yeah.

DR. THIBODEAUX: ...4 is transit.

DR. MADDALENA: That would be dynamic. Yeah, that's my understanding of it.

DR. THIBODEAUX: In your opinion, what...if you do a steady state, then this begs the question of transport coefficients, air to plants, air to...what's the state of that?

DR. MADDALENA: Development.

DR. THIBODEAUX: It's a loaded question.

DR. MADDALENA: I think they're fairly well evolved now and fairly well developed for this type of chemical. Again, you're talking very large spatial scale where you're averaging over regions. You're not averaging over a few meters in the bottom of a pond. So, you're talking very large deposition averaging over large spatial scales where the deposition may involve volatilization from surfaces, movement down into surfaces.

So, I think if you put it at that scale, it gets a little fuzzy, but the...the sophistication of the equations, I think, match the complexity of the question at this stage.

DR. THIBODEAUX: Can I follow on? What about trees and uptake from plants? Is...what's your perception of that? Kinetics, in other words.

DR. MADDALENA: There's...my perception of that in...based on the literature is that there's still some disagreement whether as tree can even reach steady state with these high KOA pollutants. Some work shows they do; some work shows they don't. So, there's...I don't know how to quite answer that.

I know what equation I would put into the model, and I think those equations are pretty well...pretty readily available, and there's some consensus in the different groups that have looked at plant uptake as to their...

DR. THIBODEAUX: Well, that...that would become the question, and I agree with you, too.... but when you go there, you're going to need these parameters, seems to me, to be real. And I guess that's my question.

DR. MADDALENA: Bill...and Dr. Doucette...I...I get the sense that these parameters are...are...we can arrive at these parameters for a screening model from first principles with molecular weights and relating these various different chemicals in that sense, partition coefficients with...with various predictive models to get to them. So, I...I get the sense that these parameters to get to the transfer pathways and transfer factors are...are available, at least as a first cut.

DR. HEERINGA: Dr. Doucette?

DR. DOUCETTE: Whether to agree or disagree or where to, but I think part of it has to do with the...I'm still getting my...my head around the...the conceptual model. I think from a...a global transport point of view and looking at persistence and...and bioconcentratable type chemicals, I think it's a little bit different issue kinetically than...at least in terms of plant uptake for...for other compounds.

And my understanding...I realize we're supposed to be focused on...on those sorts of chemicals, but at least in terms of the terrestrial risk assessment, I don't think that that's done nearly in the detail that the aquatic risk assessment is done for...for not only the...the PBGs but, you know, just chemicals in general.

And so, I'm still looking at it both ways. I'd like to see a...a scenario for...similar to the pond scenario for a short-range transport and then dealing with the question which I think a...a level 3 model will probably deal with for long-range transport of the...the PBTs.

So, I think it's almost, to me, separate issues based on the...the properties of the chemicals. I think kinetics are really important for more water soluble compounds, and it's a different set of kinetics that are important for the...for the more persistent compounds.

Root uptake is important for...for polar compounds and not really important for really hydrophobic compounds. So, I think, you know, it's a little bit of both.

And I...and I know we're supposed to be emphasizing the...the persistent bio...bioconcentratable sorts of things, the high log KOW stuff, but in terms of the level of complexity of the risk assessment, I don't think the terrestrial risk assessment is anywhere near as...as well developed as the aquatic, and I would think that that would also be of...of interest to have an approach that would deal with...with all classes of...of chemicals over a wide range of hydrophobicities.

I don't know. Maybe I'm wrong there. And it doesn't seem like the...the terrestrial assessment is...is very sophisticated relative to the aquatic assessment for any type of chemical.

DR. THIBODEAUX: All right, I second that. I...and I liked your comment about short range, near the application rather than long range which is, to me, alpine and arctic. Thanks.

DR. HEERINGA: Dr. Norstrom?

DR. NORSTROM: I think, actually, my...my...one of my comments here probably fits in this category. When we're talking about emphysis of KOA and KOW and...and various things like that, basically, we're talking about partitioning in the environment. When we...when we talk about leaves and plants and whatever, that's great, but when you get into the organism, you can't over-emphasize the importance of metabolism.

So, much of this whole area in the aquatic system is...is derived from models that are developed on persistent compounds that, basically, aren't metabolized by anything in the system, and once you get into the terrestrial environment, right away, that completely breaks down, because practically everything is metabolized.

If you look at the kind of taxonomic development of enzyme systems, terrestrial animals, basically, are exposed to a much wider variety of compounds than marine ones. So, as the difference between a whale, for example, and a cow, they're very different in their metabolic capabilities, as one is exposed to very different things than the other.

So, most of the compounds that we're talking about here are likely to be metabolized by terrestrial mammals, and there...it's...so, you...the actual accumulation, the dose and exposure and so on, of course, can be modeled with these types of parameters, but in terms of...of passing them on within a food web or long term kind of whole body concentrations within an organism that's exposed to something directly in the physical environment cannot be done without consideration of metabolism. It simply can't.

So, that's important, I think, to...to remember that there are differences there.

And I mentioned before that I think that there may be some surrogates that could be used. Types of metabolism don't vary that much among taxa.

You can see birds and mammals all metabolize the...the same PCB congeners, roughly, with the same structure activity rules at slightly different rates, but they pretty much all do the same thing. Whether that's true for all chemicals is...is debatable.

But I think with suitable kind of investigations, what's...what is out there in the literature you might be able to come up with some...with some fairly general rules for that so that if you have clearance rates, for example, in a laboratory animal, you might be able to extrapolate that to a wild mammal but...or a bird of some sort as as a first approximation, at least.

And then, for the compounds that are not metabolized, we have, actually, some quite good data now for size-specific clearance and that kind of thing which could be used. One example that I've used is pulling together some literature by Glazier and Connelly where they show that the clearance rates of DDE which is essentially not metabolized in birds is basically cleared as a function of body weight to the minus 0.3. So, those kinds of alimetric relationships can often be used for both exposure as well as clearance.

Thanks.

DR. HEERINGA: Thank you, Dr. Norstrom. Dr. Hickie, I think I'd like to move on to the second part of this. Well, Dr. Biddleman has a...

DR. BIDLEMAN: Before we leave this part, I wanted to address the...feedback...I wanted to address the problem of accumulation in plants and that the higher KOA chemicals only accumulate by atmospheric deposition on...on the leaf surface.

There have been several experiments done that shows that certain plants, the cucumber type, the cucurbits, for one, but other plants as well, take up substantial quantities of hydrophobic chemicals through their roots and translocate them within the plant. The...the papers I'm looking at right now are done by Mary Jane Matina from Connecticut Agricultural Research Station. Shes' been working for many, many years in this area. It's not only cucurbits. It's other plants as well.

And there seems to be specific transport mechanisms that are going on with...within the sap of the plant. They're even an ancio selective. So...so, there's definitely, you know, discrimination pathways that are going on with transport.

One of the chemicals that she was using was chlordane which is a KO...KOW of about 6. So, it's a pretty hydrophobic chemical, and yet, this is translocated throughout the plant.

So, it may be a bit simplistic to think that...that all the accumulation in plants goes on through atmospheric deposition to the leaves. I...I don't know how this relates to other plants that you might find out in the wild like grasses or...or...or trees or something like that. I mean, maybe the only relevance is to the deer eating my garden vegetables, but I think it's something to think about, and I wondered what...what Bill thought about this. Bill, you...

DR. DOUCETTE: And Jason White, too, and we've had lots of discussions, and...and that is an interesting issue to bring up, and they certainly have shown some potential for those compounds to go up. Right now, though, in terms of, you know, how widely applicable that is, it doesn't seem to be very widely applicable other than to, you know, those sorts of...of plant species.

So, you know, I think some of the other generalizations probably still work for...for most plant species, and I don't think even that group truly understands why those compounds go up. And if...if you start looking at the calculations, the mass in the fruit on a dry weight basis, it's still relatively small to...to the potential of...of atmospheric deposition on...on most leaf surfaces.

So, I...you know, it's an interesting issue. It's just really the state of the art in plant uptake through roots is not nearly as well developed as it is for...for fish and...and, you know, mammalian species. So...but it's interesting.

DR. HEERINGA: Dr. Norstrom, one additional comment, and then I do want to move on.

DR. NORSTROM: I had just an additional comment about...about cucurbits, because as far as I know, watermelon, for example, can even be shown to take up viruses. So, the...the water flow through the root system, to some extent, is just gigantic when they're growing, and, possibly, it just gets kind of carried along with it, but that wouldn't be generally applicable for most plants anyway.

DR. HEERINGA: Dr. Hickie, let's move to the second part of the question.

DR. HICKIE: Next slide. You can...this is my only next slide, so you can see I...I spent far more time on preparing the aquatic part of this.

So, this part of the question now goes to comment on the current state of the science, and I...I think the discussion has already gone in that direction to a good extent.

But I think the way we...we saw this issue and...and sort of way of moving forward is...is we really have two distinctly different issues or...or we could consider that the overall model as having two distinctly different sub-units, and one...one being the lower box there, air, soil, plants, and so, as well, in organisms where the inputs into that can either be from the air going into the plants or...or air to...to soil deposition by various means or...or direct applications.

So, that's different input pathways, and as I understand it right now, EPA methods don't...don't have a way of addressing atmospheric inputs in the current modeling approaches other than spray drift.

Within that model, I...I think there would be a need to address different plant species. I think Dr. Doucette can comment on this. There's connections with phyto-remediation where some plants are extraordinarily good at accumulating certain contaminants from soils.

Another important factor is...is, of course, in the...in the connection to herbivores, is herbivores eat different parts of plants. Some would eat the foliage, the fruits, the seeds. So, there...there's also a modeling need to be able to compartmentalize the...the plants to take this into account.

Moving up to the second sub-unit is...is sort of above ground, we get into birds and mammals where you have both herbivores and...and carnivores, and...and a number of things that...to think of here is in some cases, just modeling an individual species such as an herbivore might...might be sufficient, and that might be done on a...on a very simple sort of first pass approach to see if they perhaps are accumulating some significant amount.

If...if they are, then you might want to follow that up with a...a carnivore. So, some degree of flexibility here is...is important.

Generally, aquatic...or terrestrial food chains are...are short in length relative to aquatic systems. Dr. Norstrom touched on this earlier, I believe. But a challenge is...is that their diet can be quite variable, and this...this is a challenge to address.

And it's something that the two example papers from Gobas' group didn't really get into. They have very simple food chain, lichen, caribou, wolf, and in the case of lichen, the lichen really have no interaction with the soil. It's just direct atmospheric uptake into caribou, and...and they also consider that wolves are only eating caribou, and I'm not too sure about the validity of that assumption. I imagine they eat other things. They're awfully opportunistic.

Another real challenge with the issue of birds and mammals beyond just simply choosing example species to work with is trying to come up with generic food chains that...that might be representative of continental United States. I...I...I don't think...or

I certainly couldn't think of, you know, an example that would...that would be widely applicable like...like we have with the...the aquatic models.

Another aspect in there...and I mentioned this earlier...is...is you have this cross-over between terrestrial and aquatic food webs when you're dealing with birds and mammals and...and the issue of home range.

With that, I think I'd like to turn over to my esteemed colleagues.

DR. HEERINGA: Yes, we'll go to Will Doucette first.

DR. HICKIE: Yes.

DR. DOUCETTE: Let's see, where to start. I guess I'm going to stick to what I feel most comfortable with in terms of...of the plant uptake, and I...I think I'll just reiterate my comments before.

There are some more models that...that might be able to be used in a...in a...a screening level sort of assessment. I'm still more comfortable with the idea of...of two levels of models, one of a...a short range and then another long range, almost analogous to what...what's done now for the...the aquatic system.

And I think, right now, in terms of...of plant uptake, there's a lot of different literature, and there's some...some consensus starting to develop, but there are no standard methods for generating plant uptake data, and if you start looking at...at all the literature information on plant uptake, it's...it's very scattered.

And until there's a...and I wrote this in a paper recently...until there's a regulatory driver to...to require the...the development of plant uptake on a...data on a consistent basis, I don't know that the state of the art in terms of predictability is...is going to improve very rapidly.

And so, that, you know, that's just kind of a limitation. There's no big driver to generate plant uptake data. There used to be a lot of plant uptake data from the...the pesticide groups early on, but it wasn't...it wasn't shared, and there's just not a lot of...of good, solid...solid literature data.

But I think Stephan Trapp, some of his initial models would be good screening level, at least for getting it up into the...the plant and deciding if that's actually important, and I think the atmospheric deposition models are probably a little bit more well developed for predicting what concentrations might be on leaf surfaces coming from atmospheric deposition from the more hydrophobic compounds. And you might be able to correct me if...if I'm wrong there.

And I...I guess that's where I'll quit. I...I think it's appropriate to have a short term transport scenario and then the...the long term and then kind of build from there.

And, oh, one other comment. Metabolism is also important in plants. We talked about it in...in terms of mammalian species and fish, but it also happens in plants, and the...then enzyme system very similar. So...and that's something there's not a lot of information on, but it's also a consideration.

DR. HEERINGA: Dr. Maddalena?

DR. MADDALENA: Okay, I'm going to, once again, approach this in just a slightly different...from a little different direction. I'll try and answer the question you asked but in a little different way.

So, if we put this question in the context of overall uncertainty...sorry, I'm just going to kind of read through my notes so I don't get to rambling too far. That's all the rambling I'll do.

So, if we just...if we put this question into context of...of really overall uncertainty in the assessment that you're dealing with which, I think, is quite high, and I think most would agree it's still quite high, I would conclude that the existing terrestrial assessment tools are fairly well developed. Certainly, that depends on how much resolution, both temporal and spatial, you want to put into your assessment, but for the chemicals with PBT characteristics, it may be okay to accept a fair amount of less spatial and temporal resolution in exchange for much broader coverage for the assessment, and this particular class of chemicals, I think, warrants a broader coverage in both space and time.

So, let's just assume we believe that...that the tools, algorithms, equations that describe these processes, that it fits as to fate of terrest...the terrestrial fate of chemicals are available, and assume they're adequate for the crops anyway, then the question really shifts to whether or not you've identified the...the best use of these tools for this particular application.

And based on what I saw in the...in the white paper and the presentations on it, I'm not sure that the conceptual model has been fully developed yet for PBT type chemicals, at least in the terrestrial environment. And I'll give a few examples, and then I'll...I'll give you some suggestions, at least, what I think some reasonable suggestions would be.

The first example is with spatial scale. So, the current OPP approach to the terrestrial fate seems to be primarily focused on near-field accumulation of pesticide, exception being this...this screening of long-range transport. But the assumption is that...that this is going to...the way I understand it, the assumption is that will represent a...the highest ecological exposure.

Well, this may be true if...if, in fact, the vulnerable organisms or habitat happen to be near the treatment area, the agricultural region that's treated with whatever pesticide is being registered, but for PB and LRT chemicals, we shouldn't be surprised to find them in places that we didn't use them, and I think that's a lesson that was a hard-learned lesson, and I don't think it should be forgotten, that they do move around even if they just don't seem to have a vapor pressure. They're going to go places.

So, really, you can probably provide adequate spatial scale in your conceptual model, and the assessment that captures these unique...and I quote...hazards, because they're not hazards in the classic toxicology sense, but it...the exposure hazards certainly exist for this particular class of chemicals.

So, a second example would be temporal scale. So, another aspect of the conceptual model is the...the time frame of the assessment, and for this particular...again, this class of chemicals, the scale needs to be quite large. It can't really focus on a growing season necessarily. It's got to focus on a lot longer.

So, although the resolution is also important and should be built into the assessment, I think that, for this particular class of compound, we should first make sure that we use an overall duration that is adequate to capture long-term behavior of the chemicals, both during and after use, in other words, a full life cycle of these...these chemicals.

And this life cycle view of the assessment requires an understanding of the possible use patterns for a given chemical, and I don't know if that goes into your current decision making process, but it...I think it's going to be important for PBTs.

o, in other words, for this group of chemicals...and I keep focusing on this, because you've got a long history of doing it right for other chemicals...I think it's very important to understand not only the recommended application practice, i.e., pounds per acre, things that you classically look at, but also the anticipated aerial coverage. And I tried to bring this question up yesterday. And the primary regions where this stuff is going to be used, because that's going to impact your global contribution to the mass balance.

A third point would be transport processes. So, given a high overall persistence and mobility of these chemicals, it's going to be important that the conceptual model include a characterization of feedback pathways that control the long-term mass balance, not necessarily near field, but long-term mass balance on a larger scale.

And there's a lot of low-hanging fruit, I think, in this area for characterizing transport and transformation processes, at least at the level of detail that is needed for these chemicals. So, from this information and from the presentations yesterday and the conversation this morning, we can go to great detail about mass transfer into a plant from the roots into a cucumber, specific varieties of cucumbers in a specific garden and then try and build this all up, and...and it's really easy to get lost. And I'm not suggesting that.

What I'm suggesting is understanding the...the...the primary pathways. For example, rather than look at plant uptake, we may be satisfied with the moving air mass over a forest canopy and looking at that interaction. So, larger scale stuff.

And understanding primary compartments in the system, air, water, soil, sediment, vegetation, should be a high priority, because I think it then can control the mass balance, and then, the things that contribute to exposure, like uptake into a specific food chain or a plant or an animal, can be plugged into this mass balance at a later point.

And that brings me to the...the endpoint or the receptor that you've got included in your conceptual model. The current model right now, recognizing that OPP is somewhat constrained by these...these classic definitions of ecosystems where plants and animals are the only thing you can look at...and I...I'm not from the regulatory side, so I don't understand the institutional expertise or turf that needs to be respected, but for this particular class of chemicals, I think it's essential that you include human exposures in your assessment, even on the effect side.

I'm not saying take up human health risk assessment, but you've got to include the consideration of humans in your conceptual model. In fact, human exposures may dominate the final outcome of any assessment you do, so that's got to be considered when you're putting together your terrestrial food chain, that you understand what it's feeding into, I think.

So, for example, considering uptake and accumulation into vegetation, understanding exposure concentrations for target plants and terrestrial animals may important and, you know, and likely will be important, but looking at the uptake pathways as a way to get tox into the food chain may be adjusted for.

And the good news is that could simplify your assessment. The detail may be able to be reduced a little bit.

So...so, you've got the approach. Early on or the last question, I said a tier 1 approach might be these mass balance models, simple...relatively simple, uni-world steady state, but once the overall conceptual model is established, it may not be necessary to develop new modeling tools from scratch. I think these models are available and of sufficient detail for the lower tier assessment if not even higher tier assessments.

One example would be a better model...and I can give you a citation...but this, to give you a sense of what the kind of scale I'm thinking about, this particular model provides a continental scale, dynamic, level 3 or level 4, a mass balance model that compose...it's composed of eco-regions. So, you can actually put applications in certain places and see how that contributes to exposures in other places. It's got some eco, very low-level detail, eco and human exposure in there, and it also has some food transport, movement of food products, through out the...the continent.

And another example that I brought up yesterday was this TRIMFATE model, and that could take you to even another level of complexity, because it allows you to construct your polygons in a way that represents a real site and go to as big or small of detail that you want. Again, don't get overwhelmed with complexity there, because I don't think it's necessary.

But, ultimately, one of the biggest concerns that's going to drive these decisions...and it's a hard decision when you deal with these types of chemicals...the biggest concern is how long is it going to take to show up in human tissue? And we're measuring human tissues all the time, and every time a new one shows up, it...it's like well, how did that happen?

So, these decisions being made now are going to be really challenging. So, I think you've got to look at the broader picture on fate and not just a near term or a near...near field like has worked classically for these chemicals.

So, sorry to be so long-winded, but that's...

DR. HEERINGA: Very helpful. Thank you, Dr. Maddalena. Dr. Norstrom, and I won't forget you this time.

DR. NORSTROM: Yes, I'd like to reemphasize that it's not...from the standpoint of...of birds and mammals, it's not so difficult, once you know what the exposure is, to do the rest of it. It's...it's a problem of deter...determining your scenario, so following upon Dr. Maddalena's comments, it really is important to develop some hard and fast kind of scenarios that...that can be, you know, if you need the sort of terrestrial ecosystem that...that's sort of like a standard ponds.

In other words, if you're going to do local term things or if you're going to take it further afield, then the models exist to do that, but you need to define it in some fashion or another so that you can then say okay, you know, bird or mammal X and Y are...are eating this particular thing. Otherwise, it just gets to be hopeless.

So, it's not that it's not possible to do. It just needs to be well defined.

One of the things that...that...that occurred to me while I was just sitting here thinking about it, I was thinking about a colleague...former colleague of mine, Dr. Surei Betat who works on agro ecosystems and...and biodiversity on the borders of agricultural plots.

And it occurs to me that this is something we haven't talked about. I don't know whether it's part of...of what you're pursuing here or not, but the effect not so much on bioaccumulation, but, for example, if you're moving a particular animal from an ecosystem in terms of food supply and the effect of that on...on the predator of that, is that something that EPA is...could, at least theoretically, consider including in this kind of a...of a system?

DR. HEERINGA: Dr. Bradbury?

DR. BRADBURY: The...yes, and we're doing a little bit of reductionism here so that we can kind of focus on the questions we have here which is essentially trying to get a handle on how, with the right temporal and spatial scale, to predict or estimate what the risk could be to chemical...to direct effect of the chemicals on identified species.

And in other parts of our program, we are working on population modeling and taking a look at the community level effects, and we are looking at what we call the indirect effects. You know, a certain part of the habitat is in a different state. What kind of ripple effect may that have on...on different trophic levels.

So, we are working on that. We didn't bring that up in this SAP to try to keep focused on the question at hand.

DR. NORSTROM: Okay, thanks. I have, well I, just, I think, really one other comment here, and that is we know now, from some of the surprising results that have been found, for example, the chlorinated compounds but other...other types of things that I'm more familiar with, for example, persistence of hydroxy PCBs and strange things like that that were not suspected. We have to think outside the box, I think, sometimes when we're dealing with new classes of chemicals in terms of what actually determines persistence. So, it's kind of going back to the KOA/KOW thing.

In the case of chlorinated compounds in

higher organisms, it turns out that probably angio-hepatic circulation is kind of trying to get trapped in that kind of thing. So, they persist, not because they have a high log KOW, but they're mimicking bio acids.

And protein, specific protein binding, for example, is responsible for things like phenolic compounds being caught in plasma and...and liver. So, you have to consider this in addition to kind of traditional type of partitioning mechanisms that...that we've been considering here.

Probably for everybody in this room, the second or third highest foreign chemical circulating in your body is pentachlorphenol. It's extremely persistent, because it binds to thyroid transport protein, and even though levels in the human food chain are rather low, it's actually quite persistent in blood.

So, those kinds of surprises are coming up all the time, and we need to be aware that we can't just look on it as a simple partitioning process, especially for new chemicals, as there could be some big surprises.

Thanks.

DR. HEERINGA: Thank you, Dr. Norstrom.

Additional comments on question number 5 from panel members? Dr. Biddleman?

DR. BIDLEMAN: I...I don't know if this falls within the purview of your...of your panel or sub-panel. It's not really a bioaccumulation mechanism, but I wondered if...if you've considered the...the special exposure of...of birds and other animals picking up the pesticide directly, like ingesting granules, micro-encapsulated pesticides, treated seed, et cetera. Is this...probably a near-field effect, but is it...is it something the bioaccumulation group has been discussing?

MR. ANDERSON: Brian Anderson. We...we do directly evaluate potential risks to birds and mammals that consume granules and...and treated seed.

DR. HEERINGA: The SAP, Dr. Bidleman, has had a number of sessions on models for avian exposure...

DR. BIDLEMAN: Oh, okay, okay.

DR. HEERINGA: ...and risk but an active program there, and, actually, it's part of the most recent carbofuran review. There was a very extensive set of deliberations on the avian exposure part, both on field and near field.

DR. BIDLEMAN: So, it's...it's covered elsewhere. Okay. Thank you.

DR. HEERINGA: In fact, it's very much covered elsewhere. My impression is there's a lot of activity in that area, at least, a lot of focus.

Dr. Oris?

DR. ORIS: For the terrestrial bioaccumulation and, to a certain extent, for higher trophic levels coming out of aquatic ecosystems, for these chemicals, I think you...you need to be prepared to look at multiple compartment modeling, and...and there's two reasons for that.

The first is that, similar to what Dr. Hickie said about selected feeding on...on plants by higher trophic level organisms, carnivores also are selective feeders. So, you might need to know what the dose coming out of the liver is for...from fish into birds or from other mammals, from one mammal to another mammal.

And especially in times when there's seasonal times of over-abundance like during spawning runs for fish. The birds go after the hide. Bears eat the liver and then leave the rest behind. And so, they're targeting specific organs, and so, you really need to be careful about what compartments you're using to estimate dose for transfer.

The other reason to...to do that is to consider storage compartments. These chemicals aren't going to be uniformly distributed throughout the...the organism, and so, if there's a...an organ of storage and those storage compartments change seasonally or temporally or with life stage, then you need to consider what happens as those change.

So, be prepared to need to go more complex with your bioaccumulation models and do multiple compartments or PBPK type model.

DR. HEERINGA: Dr. DeLorme?

DR. DELORME: One of the dangers of sitting around with people at night is you get ideas in your head, and, certainly, Dr. Maddalena last night, we had some discussion, and he brought up the...the human aspect.

You know, terrestrial organisms can potentially be the ultimate recep...receptor, at least maybe from the risk manager's perspective. There is a link between potential bioaccumulation and environment in humans.

I was just wondering, is there anything you can borrow from human health risk assessments to aid in the modeling of your assessment of bioaccumulation in wildlife? Certainly, there's data and studies that we already use.

There may be additional things that we can look up, such as residue trials or metabolism that can help in...in bioaccumulation modeling. You might want to explore if any of their models are useful as well. Can they be adapted to a...to a wildlife situation?

For far afield, long-range transport, things like Dr. Bidleman here keeps on pulling up articles. He did pull up an article by Zibb, et. al. which was published in 2008 in the SAP looking at bioaccumulation in humans in the arctic resulting from long-range transport. You want...might want to take a look at that, because it includes wildlife in it.

And the other thing that occurs to me, is there information with respect to simple terrestrial food web structure or modeling from Superfund assessments that might be adaptable to your...your stuff?

DR. HEERINGA: I'll turn to...to Dr. Ray and Brian Anderson to ask whether you feel the panel has addressed this topic. Do you have any...Khristina?

MS. GARBER: I have no questions.

MR. ANDERSON: We have one right here.

DR. HEERINGA: Dr. Bradbury?

DR. BRADBURY: Switch my hats around. I.. I really enjoyed the...the discussion about spatial scale and temporal scale, and I tried to bring that up in my opening remarks about, you know, the classic scenarios that come up really doesn't have bioaccumulation potential and low use of qualitative words. It tends to be great.

So, quickly and both from a spatial and temporal point of view, you start thinking close to the field, short time frame, and you move into greater persistence, higher bioaccumulation potential, and more and more in the next charge question, too, about long-range transport, it seems to me, at least, that the spatial and temporal scale of the conceptual model starts to change.

So, one thought I had...and maybe it makes sense in charge question 8, I guess, we look at cross-cutting issues, is one place I'm a little confused now is that we were talking about the aquatic conceptual model in a pond. We talked about stream which I was, in my mind, was imagining a stream reach or maybe an estuary which seems to not be at the same spatial scale that we were just talking about in a terrestrial system and maybe not even the same temporal scale as we were talking in terrestrial systems.

And I may be wrong, and maybe I just wasn't listening carefully, but I think we may or may not have a temporal and spatial scale difference in what we were talking about in the aquatic side and the terrestrial side. Not that we have to resolve it now, but maybe when we get to the cross-cutting question, we could finesse that question a bit and come back and revisit that.

DR. HEERINGA: I think...at this point, I think I would like to break for lunch.

And an update on my thinking which won't necessarily govern the actual progress is I...each of these questions has a lot of meat to it, and there's a lot of content that needs to be brought out by the discussants. It's sort of my...my guess at this point that I will not try to rush this through this afternoon and that we will take our time with each of these remaining questions. They're distinct topics. I would expect about as much discussion on each, and I would certainly want to give as much discussion on each.

So, we'll...we'll probably plan to stick fairly close to the original agenda. That's just for those of you who are planning your afternoon and your morning tomorrow morning.

I think that we'll progress at

about...we're about one question ahead of the original agenda, but I...I think that we'll try to stay roughly on that agenda, and I would expect not to try to force this to wrap up this afternoon. It's too important to get all of this information out.

So, let's take a...a lunch break, and we're going to be back here at...let's say we'll start again at 1:10, so have a little bit more than an hour for...for our lunch break.

(WHEREUPON , a luncheon recess was taken.)

DR. HEERINGA: I'd like to welcome everybody back to this afternoon session, I guess of our third day of the meeting of the FIFRA science advisory panel on the topic of the Selected Issues Associated with Risk Assessment Processes for Pesticides with Persistent Biocumulative and Toxic Characteristics.

We are in the process of considering the charge questions and I think we are up to charge question 6. Before we do that, I just want to bring everyone's attention and for the EPA EFED staff, we're getting copies for you, too.

Dr. Cohen was a public presenter yesterday, has submitted some additional written clarifications and comments and so just bring that to the attention of the panel and I think, Dr. Simonich, there's some additional analysis sort of consistent with the line of discussion that you had, there you may want to look that over too.

Okay, let's begin with charge question number 6. Dr. Brady, if you would read that into the record for us, please.

DR. BRADY: Okay, charge number 6. Incorporating multiple exposure routes. There are a number of organic chemicals with PBT profiles, aquatic organism exposure for your non-aqueous groups, can be important relative to direct exposure from water. Most standard and aquatic toxicity test studies submitted to the Agency for pesticide registration do not incorporate realistic chemical exposure through the diet. Therefore toxicity reference values from these studies may underestimate actual environmental effects.

To address this concern other programs within the Agency have proposed using a tissue residue approach for quantifying chemical toxicity. For quantifying toxicity of organic pesticides with PBT characteristics, the Agency is also considering the use of the TRA.

Please comment on the strengths and limitations of the tissue residue approach for addressing pesticides' toxicity from multiple exposure routes and other methods SAP deems appropriate. In the context of the tissue residue approach, please comment on the strengths and limitations of using measured and predicted tissue residue effect relationships that are derived from water only exposures in laboratory toxicity tests.

DR. HEERINGA: Thank you, Dr. Brady. Our lead discussant on this question is Dr. Jim Meador.

DR. MEADOR: I'll go ahead and summarize the feeling of the sub-group here, Dr. Hickie, Dr. Oris, Dr. Schlenk and Dr. Bucher and they can chime in after I go through some things here.

Just first a little prelude. If you look at this section in the White paper you'll notice that it is not real complete on the tissue residue approach, and I wanted to point out that on your CD was this larger document, it's a 60 page document, that address tissue based criteria for bio-cumulative compounds. It has a lot more detail on the tissue residue approach.

And I apologize, on these slides you'll see a lot of acronyms. I'm going to try hard to define those and spell them out when I get to them but please bear with me, to save some space and like any sub-discipline we do throw a lot of acronyms around.

So TRA we're using the tissue residue approach for toxicity assessment basically and also on this particular slide I wanted to point out that it's not intended to replace ambient toxicity metrics but supplement and enhance information about toxic responses. Next slide.

So on the first question, the strengths and limitations of the tissue residue approach, one of the biggest things we see is a huge reduction of variability in the toxic response, orders of magnitude. There are some compounds if you look at like the LC50, you vary, oh, four or five orders of magnitude over a number of species.

When you look at the tissue residue toxicity metrics often that boils down to order of magnitude or less, and in this particular case EC is the effective concentration, could be sediment or water that's your ambient toxicity exposure metric and ER we use R for residue which is tissue residue. P is just your percent or fraction responding, it could be a fifty or ten ER 25, whatever.

Another very important strength is it integrates over exposure routes and that's a really, that's a very large advantage. All exposure models basically incorporate it. Because it accounts for bioavailability and toxicokinetic rates, you eliminate the future variability.

Most of the variability you see among species for like an LC50 is due to toxicokinetic rates and of course when you go to different sites you have large differences in bioavailability. This helps by integrating and getting you right to the tissue and it's sort a gradation from the available compound that was in the animal, that was in the tissue at the target site, which we will get into a little bit later.

Tissue concentration, especially in the field they integrate over time and space. That's also a huge advantage. If you go out and measure water concentration, if you do that several times on any given day, it's going to change. Sediment concentration is very heterogenous. When you're assessing toxicity, having a tissue residue that integrates over time and space gives you a much better feel for what the animal's been exposed to, much better metric.

It's also very advantageous for assessing toxicity in the field. You can go out based on lab studies maybe you had a good feel for what the tissue concentration was telling you as far as toxic response. You can measure that concentration and have a pretty good idea how the organisms are doing. It doesn't work very well for lethal responses, but most of it for sub-lethal responses you might have an idea. It's very good for mixtures but you need a lot more information on mode of mechanism of action and I'll explain this.

Currently mode of action and mechanism of action are defined differently. Often they're used interchangeably but they're not. Mode of action is a general concept like uncoupling oxidative phosphorylation, acetylcholinesterase inhibition, there's a number of modes of action. Those modes of action, you can have a toxic response by many different mechanisms of action. For example, uncoupling oxidative phosphorylation, that can happen with every different mechanism.

Tribunal... are both uncouplers as a mode but they act by very different chemical mechanisms. You think of a mechanism as an actual biochemical event and that becomes very important when you're looking at mixtures and assessing let's say response versus dose standard. A response additive you can do, let's say you have a growth response, which operates maybe by different modes of action. A growth response you can add those together in a mixture.

If you're talking about dose additive compounds, that has to be a mechanism specific. Basically the compounds act as dilutions of each other and you can add them with some of the response and that's a whole another area which we're not going to get into, but I just wanted to point out the difference between mechanism and mode and how you can you use this in the long run for mixtures which is a huge step.

In the current way we do things, it's looking at single compounds, all these toxicity evaluations are based on compound by compound. In the environment we know that doesn't occur. There's lots of compounds out there that really need to be considered.

Additional strengths, it's highly defensible, the TRA, for translating back to water or sediment concentrations or water quality criteria or sediment quality criteria. These can be guidelines to criteria, whatever you want to call them, thresholds. A simple example here is the water concentrations.

If you define a tissue toxicity reference value, and I think it's a little different than the way it was in the White paper. This again, I have to define the definition. A CBR is a critical body residue. That's a general term for, it's a statistical concept of many different responses, toxicity metrics. LR 50 is a CBR, ER 50 is a type of CBR. That is a critical body residue and you can define it many different ways.

In the second line here you can see I talked about looking at these values, if you have a given compound for a number of species, let's say you have an ER10 for a bunch of species, you can do a species sensitivity distribution, that's the SSD, take the fifth percentile and you could call that your tissue toxicity reference value.

So back up above that you see for a tissue TRD, if you divide that by the BCF you can get a water quality guideline. It's basically just a mathematical rearrangement of the equations to solve for tissue or water or whatever you have.

It's great for sediment, nowadays it's sediment quality guidelines are basically looked at and some recordative responses with a bunch of sediment bioassays that really don't address individual compounds. This is one way to get at that by determining the tissue residue effect and looking backwards through a BAF or a BSAF to get to a sediment concentration.

And within these species sensitivity distributions, most people look at the ninety-fifth percentile, basically the fifth percent of the SSD and for that ninety five percent lower confidence interval is the value that would be used.

So for the BCF I mean there's different ways to approach it, this is just one example. You can take the ninety fifth percentile using a cumulative distribution function with all the BCFs and calculate back. You can use a main value or you could use a model value, this is one approach.

This is one way you could translate back for water or sediment. It seems backwards but it's, you know, all fluid, you can go back and forth. But going with the tissue residue with the low variance is actually a very strong way to look at these things.

In general tissue residue toxicity is relatively time independent and I'll get back to this in another slide, but there are studies showing that there is some compounds that exhibit time dependency but that kind of goes away after roughly about four days. So that's also a very important thing. You can actually do shorter term experiments and you get a very similar tissue concentration where an effect occurs, if it's fifty percent lower or twenty five percent lower or whatever and that doesn't change over time.

Another interesting point in a strength

for the tissue residue approach is that you actually may get away with using fewer species to assess toxicity or the TRB.

Because of this much lower variance which we have for these different responses, you really would, could possibly get by with fewer data points, and this works with the new response and I put this up there because a lot of people don't realize if you look at a bunch of say LR 50s for a given species, those values can be normally distributed. It's not always log normally distributed. And that's actually if you think about it what you might expect.

So you could use a mean or standard deviation or standard air removal if you want. If you go to an SSD approach and then you can do the HC05 the hazard concentration, the fifth percentile and say use this ninety five percent lower confidence interval. That's also variance driven, so that also would be a much tighter estimate as compared to an SSD for, just for a bunch of LC50s.

So it's something to consider, I mean there in Europe, in some cases for SSD that it would be one of four species or four different taxa. Here like the water cholera criteria it's basically eight different taxas, so when you think about it, it's a minor point but in the long run you'll start to see if you start looking at a bunch of CBRs they kind of converge around one value or a much narrower range of values. Next slide, please.

Okay, some of the limitations, there are a few to the tissue residue approach. It doesn't work for highly metabolized compounds, but that doesn't preclude other compounds that are metabolized, for example polycyclic aromatic hydrocarbons, it doesn't work very well.

Although we're finding recently that in bile you get like a bile metabolite and you get a very hard core relation between the dose that you give the animals that are left there, so there is a possibility of using that. It's not a tissue, it's a fluid but it's still an internal representation of the dose, surrogate like all these are.

Tributyl-10, actually in some species that's ninety percent metabolite. Tributyl-10 is one of our best examples for the tissue residue approach, it actually exhibits a CBR with a very consistent value of the co-efficient variation of about forty percent of the eleven species that we actually have LR 50s for. You do get increased information required for this, again the toxic action, the mode and mechanism.

It's really nice to know something about that especially if we take it a step further and look at metabolites or mixtures. Rates, which will come up in a bit for PBBK, it's just more information you need, it's not simple as just doing a standard LC50 assay or just a regular bioaccumulation assay, you do often need more information.

Another drawback which may not apply here because you're looking at new compounds and you're having, you know, this one's conduct experiments in general there's very few studies that have actually generated CBRs or tissue residue based toxicity metrics. Many of those are LOERs, lowest observed effect residues. We really like to see a dose response that's the ER or LC, something that's typical regression, you had a lot more information from that.

Very few endpoints have actually been looked at. The standard ones, mortality, growth and reproduction, the big three, there's other endpoints we think are important and there are three basic data bases. The Army Corps of Engineers runs one called ERED, there's George Bennett Inkley data base that actually I think is being merged now a bit with the ERED Army Corps data base and the PCB Lens data base which has moved from EPA which has got a lot of great information in it.

The people are starting to put these things together, but we're still limited with the amount of data that are out there so it's hard to make some generalizations for a lot of compounds. Some compounds you just have absolutely no data. Of course there's confounding factors, lipids, organism held temperature, but these are really the same things you find for your ambient exposure metrics. I mean it's the same sort of thing but they do have to be considered and adjusted for.

And of course you need to consider the toxicity metabolites. Metabolites can actually confound things quite a bit and an assay on the next slide will have some information on that.

Well, that was basically it for number one and at the end here I have some discussion points and a recommendation which will apply to both of these and kind of come back to some of the points I made here so I think maybe I'll just go through question number two now and look at that and then we'll go back and we can talk about all these together.

So question two is the strengths and limitations on the predicted tissue residue effect relationships that are derived from water only exposures live studies. So strengths and limitations for those water exposures. Some strengths, basically water only exposures are acceptable, it doesn't matter you have a tissue concentration, you can get that through a dietary exposure or water exposure.

Some things to keep in mind though is you do need sufficient time for internal redistribution of the contaminant It's basically a different route whether it's taken up by the gill or the gut and enter the circulatory system differently so some of these very hydrophobic things just need some time to redistribute and get to the target site and that's just going to be a best professional judgment I think on how long that will take. It really depends on the compound.

And of course another strength is the route of uptake is really less important looking at tissue residue approach so to answer the question basically BCF tests I think would be just fine for generating tissue residue values to be used. Next slide, please.

Some limitations. One important point is the toxicity of bioaccumulation based values may not, for some compounds may not be amenable to QUASAR. I've seen at least one example where it really doesn't match.

Tributyl-10 is one although it's a ionizable polar hydrosorbic organic metallic, it's an odd compound but you're talking about new compounds in an lot of your assessments that you're doing that have characteristics you're not too sure about so in some cases some of those may not be amenable to QUASAR, standard QUASAR modeling, so it's just something to keep in mind. So in that case measured values would actually be preferred.

The next one is actually probably more of a recommendation but there is a bit of a limitation because often not many doses are used so several doses really should be tested because we've found in some compounds and you can see this for pHs, PCBs, Tributyl-10, others, you have multiple modes and mechanisms of action that are dependent on dose and actually time, which really is a huge confounding factor that has to be considered so just because you're testing a relatively high concentration and get an effect doesn't mean there's some, not something going on at a lower concentration.

TBT is a great example. Just recently we found that fish were responding at concentrations as low as the snails are to get eco effects, which are extremely low. Before it was just growth and mortality and some other reproductive effects but down at a couple of nanograms per liter, parts per trillion in water fish respond, but nobody really ever tested those concentrations before.

So obviously you need a huge range in dosing and that's also the best professional judgment what those doses are, but you need to capture those different responses with different modes and mechanisms and of course sufficient time for exposure is needed. The time, the compounds that, like Peter Landon has found, that are time dependent have a very strong time dependency for the first four days.

After that, it's really almost negligible and of course there's other compounds that may exhibit longer time traces when you plot them out, but for most of the chemicals we've looked at where we have CBRs, over time, they really don't change much after four days, it was a hundred hours in Peter's case, the compound he looked at so again, that's sort of, of course, doing long term experiments. Next slide, please.

So these points to consider kind of relate to both of the questions and the kind of overarching thing. Metabolites is something that was mentioned. They may be more or less or equally toxic.

In general they're often less toxic when you metabolize these things or hydrophobicity changes conjugated the sequestration on some that really makes it less toxic especially for specific mechanism of action.

If it's nonspecific those compounds still may be able to contribute to the membrane disruption. I'm not using narcosis any, well, narcosis is kind of an odd term because it's based on a behavior. It's really nonspecific which as a mode of action it's not specific. It's baseline or nonspecific, it's basically a membrane disruption and that's the mortality response you can get with chemicals that occurs at around two to eight micromoles per gram or fifty micromoles per gram of lipid.

So in general we find, you know, you have a parent compound in an animal, it's probably going to change. It could actually be more toxic, I mean we have reactive compounds. We basically have nonspecific, specific active compounds or reactive. Reactive is something like binding the DNA or a mollusk ion is activated to an oxon forage, universally binds with acetlycholinesterase and reactive compound, and also reactive compound you can't really do much with for the tissue residue approach although some people are starting to model it. We think there is a way to model that.

So definitely keep in mind the toxicity of the parent compound through looking at these things in tissue. It's probably not safe to assume that they're equally toxic unless you're pretty sure you may have a nonspecific narcosis type mode of action and it may contribute to the overall response. In many cases we really don't know what the mechanism of action is for these compounds.

A few we do, most of them we don't. We know general modes which is great. You can start if you look at McCarty and Mackay's 1993 paper they have a whole bunch of mode of actions and we see about a six order of magnitude range in response from baseline toxicity all the way to dioxin toxicity and lots of things in between there, and couplers, you get them, irritants, the polar compounds, the pseudocholinesterase inhibitors which are the general modes, and as I think I mentioned earlier, multiple modes and mechanisms for given compounds make things very confusing.

pHs, PCB, they also, all have multiple modes of mechanisms that are often dose and time dependent, so I'm not sure how you deal with that, that's kind of a tough one. If it comes up you have to, you know, learn to recognize that there's a possibility, especially time dependent. I mean, an animal might die from an excess dose as a baseline toxicant and then later on you know, it might die from an immuno compromised response. All we have is a dead animal so we really don't know what killed it, so it's definitely something to consider when you're looking at long term experiments. Thank you.

Some recommendations that I'm looking at tissues, most of the data we have now is for whole body animals. Most of it's obviously aquatic. People look at invertebrates and fish but there's other species to consider obviously. For small species, whole body's fine. You get into fish, you might want to consider different organs. Definitely in larger animals you have to consider organs or even plasma.

Egg works for birds in a lot of cases and then you know, this is something, kind of a future thing which we probably wouldn't get into now since the, a simple thing is doing whole body.

In the future you might want to consider the tissues and with that the PBBK modeling, we have rates and all that 'cause these compounds actually have a target and it's often organ specific not always but often it is and that's just another step closer to reducing the variability and characterizing response, but using whole body is actually fine for now because most of the compounds we looked at, there's a pretty good proportionality between what's in the whole body and what's at the target, but that's not always going to be the case, so it's something to keep in mind.

Again, consider long term exposure is more than ten days, and sublethal effects really are what are protecting chronic effects in the field. Consider additional responses, that means behavior, olfaction, inhibition of olfaction, immuno-compromise, all these could lead to mortality, population level effects.

And also I'd like to make a pitch for hormesis, which could be considered an adverse effect. We've seen cases where a compound, there's a new class of compounds called abusagens. Thiolate, Tributyl-10, they're all being used to make animals bigger. I've seen it in fish.

The controls for the, the lotus fish are thirty percent larger than the controls. And it may seem like a good thing, but it's really not because these fish are really finely tuned on their cycles. For salmon in particular, the larger juveniles come back early, they come back in two years instead of four years so the fitness is really affected for the population so it's not always a good thing, it actually could be an adverse effect. So it's, I'm just throwing that out, another response to consider.

Next slide please. Define and clearly state your assumptions, limitations for the tissue residue approach and that's something I think Jim Oris will probably bring up again. He did earlier yesterday. Use specific data for the acute to chronic ratio, and here I want to make a distinction, acute and chronic.

Acute is a time thing, it's exposure's acute or chronic, long term or short term and the response is basically lethal or sub-lethal, it's not really a chronic response or an acute response, so I know you have short term and long term mortality, sublethal so in some cases there's an ACR that's developed or more appropriately for some responses a lethal to sub-lethal ratio.

I know a lot of people have done reviews in literature and they've come up with a value of about ten as an average but if you look at the range in this data, were huge, a lot of pesticides we find a thousand-fold difference between lethal and sub-lethal responses and just because you have an acute or a lethal response, dividing by ten doesn't really get you to a protective concentration.

Determine taxa's, specific TRVs, obviously it doesn't work when you lump invertebrates and fish together in some cases. Documents like toxicity is one sleeve's another example, EPA document from 2004, was basically fish reproductive effects so really it's important to pay attention to the taxier putting in here future sensitivity distributions, and it really should be endpoint specific if you have the data. If you have growth for a bunch of species, and specifically like an ER 25 or ER 50, you start mixing endpoints and you get a lot more variability and that sort of defeats the purpose.

And in general we recommend the tissue residue approach for toxicity assessment for all bioaccumulative compounds. It's not just the very hydrophobic compounds, it works for compounds of KOWs two or three, anything that's bioaccumulative is amenable to this approach and of course I don't have to say this but you know, develop toxicity testing framework to acquire high quality data which goes back to the first point here, defining and clearly stating assumption and limitations through the approach in how you're collecting your data, and I think that's all I have. Yeah.

DR. HEERINGA: Thank you, Dr. Meader. Organized presentation. Dr. Hickie is the first of the associate discussants.

DR. HICKIE: Thank you, Dr. Meader, for a very thorough overview and I only have a couple of things to add to that and it, I guess the main thing is thinking in terms of using this approach for chronic toxicity and one thing I'd like to bring up is that if you look at tissue residue in an individual animal over its lifetime, and the concentrations can vary considerably even if they have a vaccine exposure concentration throughout the lifetime and there's a number of factors that come into play, biological factors largely.

For a mammal it could be offloading the contaminant in utero, thinking about the milk. That can be followed by a growth dilution effect. Changes in fat stores over the lifetime results in increase or decrease in concentrations in throat and body. Reproductive losses by females can be considerable and if at some point in life there is, you reach a threshold where you get induction of metabolite or biotransformation, it can start bringing things down and with some of the work I've been doing, I just went through and looked at some data.

But this can, in an individual, modeled individual at least, we end up with almost an order of magnitude range of concentration over the lifetime of I'm using marine mammal as an example here but I wouldn't be surprised if it would be similar in other species, and this makes it quite challenging because you now have a temporal tissue concentration if you're, and you're trying to connect that somehow with the chronic effect and that causes a few problems. If you then have to rely on modeling these tissue concentrations, your uncertainty expands that range even further sort of making it a little bit trickier to draw connections.

And looking at the Armitage-Gobas shrew earthworm paper, if you look at their figures where they've looked at observed versus predicted concentrations, the predicted concentrations ninety five percent confidence limits are several orders of magnitude and substantially larger than measured ones, so I think this is a distinct problem to be aware of if we're going to use tissue concentrations in, to address chronic toxicity.

One of those aspects is the aspect of a temporal disconnect between the tissue concentration you have and if you, your chronic effect only shows up later, you really don't know how those two connect.

I think just one other comment I'd like to make, and following up on your points about PAHs and that they're metabolized and they don't really bioconcentrate, I played around with this a little while ago and it's one of the things to publish, but you can model that sort of thing and rather than focusing on tissue concentrations you can focus on the movement of the PAH into the organism and it being processed, and perhaps there's some sort of dose metric to draw to that in terms of exposure.

Beyond that I worked on this area for acute toxicity to neutral narcotics to fish as part of my Ph.D. work and I think it works very well for, certainly for acute things and I think we're on a learning curve for how it works for chronic.

DR. HEERINGA: Thank you, Dr. Hickie. Dr. Oris.

DR. ORIS: Thanks. I don't have a whole lot more to add. The only thing that I would say is sort of pile on on the concerns about working on chronic issues, especially related to being able to apply these to population level effects and that's I think going to be the real challenge.

DR. HEERINGA: Dr. Schlenk?

DR. SCHLENK: I also, great job, Jim, on presenting that. I think you presented pretty much everything we had discussed. A couple of things I just wanted to highlight and I've been saying this I think in some of the question and answer periods and again with Keith's prior life in terms of selenium I think you probably, it's like preaching to the choir.

I think in terms of this approach so I think that I totally agree in the strengths in terms of for these, for all bioaccumulative compounds for that regard. I think it's definitely the logical way to go. I think it incorporates all the exposures that we're interested in and especially the oral exposures which again for the tradivores I think it's huge and particularly in a modeling system I think that needs to be addressed, the oral exposure to tradivores, particularly with the size class issues with VOC and the compound in the aqueous medium anyway.

And since Jim hit all the strengths so hard I'm going to just kind of hit a few of the weaknesses a bit and again, we kind of talked about this earlier but I think it's really important to try to compartmentalize things as much as you can, I know it's difficult particularly for the inverts to do that.

Again John Nichols' work with the fish I think is instrumental in this regard in terms of the compartmentalization, particularly with the lipid storage component.

This was brought up I think by Jim with the terrestrial thing, but it is hugely important in fish as a compartmental component to that. In fact if you had to just pick one compartment and split it into two, that would be one in a tiered approach if you want it all so that's the one I would sort of hammer on would be a lipid component in that.

Biotransformation of course, particularly with these compounds already kind of discussed that a bit as another component to that compartmentalization perhaps. And again let me just reiterate Jim's comment on determining the target organ I think is critical, I mean selenium is a great example in that regard. I mean we're pretty fortunate that, you know, you've got that you can target the gonad, the eggs and actually get a nice, you know, critical residue that corresponds to a developmental effect.

And I think the real fear I have and again this kind of goes back to my comments yesterday, it's just, you know, assuming that you have acute toxicity and I'm, again I know this is probably going to fall on deaf ears to a certain degree but I think the whole narcosis aspect is a little bit, I think we need to move on beyond that in terms of assuming narcosis is a mode of action for everything.

It worked, you know, ten, fifteen years ago, but now I think we're seeing that, I mean ethanol is a great example mechanistically. We used to think that its mode of action was, you know, membrane disruption, it's not, there's specific receptors that ethanol interacts with.

pH is a great example, Johnny Cordona's work at NOAH has indicated that you have different mechanisms of action with three, four, five ring compounds that don't correspond to a narcosis based reaction and I think that has dramatic effects on your assumptions of additivity as well as assumptions in terms of accumulation and how they interact at different levels of the ecosystem so I guess those would be things that I would caution against, you know, similarities in structure do not equate to similarities in toxicity and again, I'm sure you guys are probably aware of that so just take that into account.

Let's see, anything else here. Oh, just one other thing. Again we, I'm sure you're aware of the model that's being proposed in terms of focusing on mode of action deriving hypoth...

Don was in the meeting the other day actually as far which was presented by Vicky Delarco, I guess, where again, you sort of set a model if you will or a mode of action hypothesis and then that drives your testing,

And I think if you do that instead of, you know, rely on twenty different studies that you'll actually can refine the testing into specific questions that allow you to really get the good models that will allow you to not only evaluate single compounds of PBTs but even mixtures because if you think about it, again in the human health realm, pharmacists base, you know, common geriatric patient takes nine medications and that's a mixture situation and the way that the risk is evaluated on that is by mode of action.

And I think we really need to pursue that in terms of the Agency's approach in a mixture setting.

So again, reiterate mode of action approach, mechanism of action approach and I think that is already being done but I just want to, you know, emphasize that so it's not just lost in the human health folks but specifically in the eco side I think we really need to pursue that and I think this is a good first step in moving that direction but I wouldn't stop there, likewise I think narcosis was a good first step but I don't think we need to stop there, we definitely need to specify and reduce uncertainty in that regard so...

DR. HEERINGA: Thank you very much for the assigned discussants, turn to the panel or to any of you. Yes, Dr. Meador?

DR. MEADOR: There is one more discussant.

DR. HEERINGA: I'm sorry, Bucher?

DR. MEADOR: John Bucher.

DR. HEERINGA: John Bucher actually had to leave he, I think this being all day it took him away, so figuratively. Dr. Norstrom.

DR. NORSTROM: If I can make some sense out of my hen scratches here. I'll start with commenting on Dr. Schlenk's comment. I wonder whether we should be focusing again for some of these near chemicals on lipid compartments.

This pesticide four, for example, I think it might be quite intriguing given the fact that there seem to be some inconsistencies to see exactly how it is distributed.

Also the whole question of metabolites.

There are some peculiarities out there, for example, again going back to organo-halogens, alga-corto-benzo-dioxin for some peculiar reason in fish seems to be excreted in bile as an unchanged compound.

Mass balance studies shown, for example, in the Baltic that they couldn't account for it unless they list it as kind of lost so those kinds of things don't always work and we should be again thinking outside the box I think for a lot of these types of compounds unless they truly aren't metabolized.

The question of concentration dependence, I have in front of me here a paper by, who is it, Simon and Hermans on concentration dependence of lethal body burdens over time and they make some fairly interesting comparisons here that, for example, over a one day exposure and four day exposure that there's sort of variation of the lethal body burdens.

Some fish died in one and some died in the other, and I'm wondering whether this is something that the one even for acute exposure shouldn't be a little bit cautious about. I'd have to go into some more detail, and I don't really want to go in and describe what they're actually doing here but it is not entirely true in all cases apparently according to this paper that one could just sort of assume that lethal body burdens are not time dependent even in acute exposures. So it may be something to consider.

Biomarkers, I wonder whether a biomarker is something that anybody considered in the panel. Cholinesterase, for example, as opposed to an actual body burden because in some cases these things you're not going to see but you might have a biomarker that's there which is dependent on the exposure and you can correlate exposure to the biomarker response, and it's quite specific.

There are a lot that I think are useless. For example, I know that I don't believe personally that things like EROD activity is all that useful as a metric for anything more than sort of an order of magnitude type differences in exposure but nevertheless there are some that are fairly well developed.

What else did I have here? Oh, my comment on the usefulness of bird eggs. I don't think actually they're very useful at all unless it is a microfilic compound. Most polar compounds don't make it into an egg, they're formed over very quick length of time and the constituents are packaged in the liver and even for organo-halogens probably about fifty percent of the lipid that ends up in a bird egg is actually coming directly from the diet, it is not an equilibrium addressed in the body so it's not necessarily a very good tissue to be using for birds.

And I think that was it, thanks.

DR. HEERINGA: Thank you, Dr. Norstrom. Just mention, too, that I did speak to Dr. Bucher and he said that in your working group discussions that he felt he supported and didn't have anything to add really to what was being discussed at large in the group. Dr. Meador?

DR. MEADOR: Jim Meador, I'll just respond to Dr. Norstrom's point about biomarkers. We are considering biliary effect of the polycyclic aromatic hydrocarbons and did a dose response feeding study with fish and got a correlation of .86 between the dose, micrograms per gram fish per day and the ancillary fat in bile. So in my mind we're actually starting to use this data.

To my mind you can use that as a surrogate for term dose, go out in the field and measure the fat of the animals and know what kind of exposure they had, so the biomarkers do work in some cases and that's just one example, there may be others, just have to look.

DR. HEERINGA: Additional comments from the panel on question number six? Peter.

DR. DELORME: Just a couple of practical comments as per usual for me, I'm probably going to sound like a broken record but in the short term I think you're going to be hampered by the lack of available data, okay, and you're not going to have actual measured concentrations until you actually make changes to the study protocol or have different kinds of studies made.

So I mean that's going to leave you relying on conversion of existing data, there is uncertainty there. You need to understand that uncertainty, you need to understand the variability especially with respect to species sensitivity. I was actually glad to see the FSB stuff, I mean that's not new to EFED, it's not new to PMRE.

There should be some consideration of that in trying to get some sort of assessment of the performance of the conversions to understand the variability and the uncertainty around it. I think you can get that through mining of existing data to a certain extent again.

But I think until protocols are changed to actually require tissue residues be measured for, you know, PBT type substances, you know, there's going to be a little bit of a gap there and along with that I mean the other practical thing is the registrants are going to want some sort of criteria to guide them as to when they might want to do that.

DR. HEERINGA: Turn to Brian and Christina, Keith, any follow up questions?

MR. SAPPINGTON: Yes, Keith Sappington. I have on the note of protocol development, I think that's one area that will be very useful to us to look to your recommendations on changes. These are, the cycle which these are revised varies but it does take quite a long time and even when you think they're just about out the door, they're never really out the door.

With the issue of measurement of tissue residues and this gets back to even the concept of using a PBBK type model is ultimately you have to relate it, if you're going to predict the concentration in a specific tissue then you need to actually have that aligned with your effects data as well, or at least be able to extrapolate that in some way.

Right now the protocol for avian reproduction tests has a loose recommendation in it above log KOW of three, it's recommended that at least one tissue be selected and have compounds measured in that, so we don't obviously always get those types of measurements but again thinking about if, I don't know if this would always have to occur within the context of the guidelines themselves, ultimately we want them there.

But even outside of that if we could give recommendations as to measurement of those tissues and it was brought up earlier that, wow, it would be nice to have measurements over time and not just at the end of the study as well so I just put a plug into that, that yeah, we are living with the guidelines we have right now but we can always look back to your report if you consider that and prospectively we might be able to make some useful changes or incorporate that as we ask for additional data in that specific assessment.

I have one other clarifying question. And it gets to the notion of well, I'm not convinced it's just time dependent, I think it's many aspects, it could be mode of action, mechanism of action, dependence, but the notion of acute versus chronic in the context of tissue residue values, even back in McCarty and Mackay's paper they split out the CBRs for sort of acute versus chronic.

And I just, my sense is that we would

follow a similar path partly in that in the absence of information we may not be having the same mode of action or mechanism of action from a very sort of high dose or high concentration short term exposure versus what's going on in the long term even with different life stages so I'm just sort of we begin to get some feedback on the notion of at least stratifying tissue residue type measurements unless you have data otherwise by sort of acute versus chronic.

DR. ANDERSON: One more said on a little bit what Keith was saying, the term earlier the acute chronic ratio that was discussed for general narcosis the, I guess I would just ask to just for consideration of, if other methods you believe are useful in estimating chronic toxicity from the acute values.

The presentation that was given for chemical four by then public comment there was methodology to extrapolate to a chronic value from an acute value like in LC01 or something like that but I guess I would just also seek some comment on utility of other methods to extrapolate the chronic effects.

DR. HEERINGA: Panel members, any response on those particular questions, the extrapolation conversion from acute values to chronic values. Dr. Meador, do you have....

DR. MEADOR: Well, I sure can't think of any methods, I mean actually measuring it, having real data is the only way to go. It does seem to work for baseline toxicity. The factor of ten is actually not too bad for some of the, especially if you've been going from lethal to say like a growth response.

Often it's the same mode of action, the baseline. When you get into specific mechanisms of action, it's all over the map and I don't think there's any way to predict that with any QUASAR modeling or anything like that.

DR. HEERINGA: Dr. Schlenk?

DR. SCHLENK: Yeah, I just would say getting back into your first comments as far as if you had a tissue to pull, you know, and I think it even relates to the chronic endpoints, you know, obviously if you've got gonadal material, highly lipoidous material, I think if I had a place to start that's where I would go in terms of that and relate that to, you know, development, reproductive development.

It kind of gets to what Jim was talking about, I think that's going to be your best approach in terms of a population level effect in that regard.

If I had to do number two, I'd obviously do liver as another site, and I don't know those are kind of, you've got a non-spawning animal it's hard to get a gonad but or a hepatopancreas for example in an invert would be another sort of tissue based approach if highly lipoidous tissue for that, and those by and large tend to.

I mean I don't know exact numbers but if I had to take a guess, my best expert, whatever that means, opinion it would be your, as far as reproduction is concerned those would be the tissues you'd try to tie it to in terms of body burden concentration and time dependent concentrations in those particular tissues. I mean at least for now anyway.

DR. HEERINGA: Dr. Hickie?

DR. HICKIE: I'd agree with Dr. Schlenk's comment that either lipid stores or liver would be the preferred choices and maybe you can refresh me, did you mention in measuring residues from a particular treatment, did you specify a specific one they should measure it from?

MR. SAPPINGTON: The tissue is not specified and I don't recall if it's even specific enough to say which treatments or it's being measured. I have to go back and check and obviously we'd like to have a residue response relationship because if you happen to measure a contaminant in a tissue that's not correlated to, you know, well and you're just doing that at one treatment level, it's nice to have the proof of residue response in a study like that.

DR. HICKIE: I would want to see another replicate to do that type of work, and it might, it would be useful to know ahead of time to require that rather than to be always in the position of having to estimate the residue. You can always have them collect the tissues to do that so it's there waiting to go and then I would suggest that most observed effect concentration or dose that they derive from the test and if you could do two it would be the lowest and the no observed treatments.

DR. HEERINGA: Dr. Norstrom?

DR. NORSTROM: Just a question, what's wrong with whole body, if it's a fairly small organism, is that not something that could be done? Why do you need to do a tissue specific resonance?

MR. SAPPINGTON: I was specifically raising that in the context of the avian reproduction test where we, where the guideline at least is forward thinking enough to say, look, you have a highly hydrophobic compound, in this case defined log KOW three or higher, then it's recommended you measure the compound in at least one tissue but it doesn't specific the tissue and I'm not sure for Dr. Hickie's question whether it specifies a treatment level or not but I can check it out, so it was picking up on the recommendation that for larger organisms whole body may not be the right metric but for something like a five or eight centimeter fish, it can be pretty challenging to dissect out ovaries and things like that.

DR. NORSTROM: I would agree if it's for bird that liver would probably be the thing you would choose for almost everything.

DR. HEERINGA: Not seeing any additional comments at this point in time, I think that hopefully that we have addressed these questions, last follow up, I think was very useful, at least to my interpretation. I appreciate the contributions. At this point I think I would like to move on to charge question number seven, on long range transport potential. Dr. Brady, if you could read that into the record, please.

DR. BRADY: Okay, charge question number seven. Screening for long range transport potential. For some pesticides with PBT characteristics, long range transport has been well documented. Currently OPPs ecological risk assessment process relies heavily on monitoring data for assessing long range transport concerns. However, this process does not a priori screen for long range transport potential prior to pesticide release in the environment.

Difficulties in linking local use patterns of pesticides to far field deposition and exposure in a modeling framework is considered a major challenge in screening and assessing long range transport potential. Please comment on the strengths and limitations of available tools for screening long range transport potential of pesticides.

DR. HEERINGA: Before we turn to Dr. Bidleman, just a note I mentioned after the lunch break, Dr. Cohen who was a public presenter yesterday has submitted additional written comment during the period of our deliberations and so that may be considered as you choose of course during your commentaries and with that I'll turn to Dr. Bidleman, who is the lead discussant.

DR. BIDLEMAN: Well, thank you, Dr. Brady, for reading this out for us. These are the deliberations of our sub-panel, myself, Staci Simonich, Louis Thibodeaux, Jay Gan, and Tammo Steenhuis, and you can read a summary of the charge to the panel below. Let it be noted at this point that the long range transport can include both air transport, which is mostly what we'll be talking about, but it also can include water transport or both.

So the first thing we had to wrap our heads around when we thought about this was what do you mean when you say long range?

I was at a workshop in the Netherlands a few years ago where we discussed this topic and one of the European colleagues told me in all seriousness that he considered long range to be anything over fifty kilometers. I said oh gee, I drive that far to work every day so I think we first need to say something about what we mean by long range transport here. Can you flip to the next one please?

In the case of air there's a number of documented cases where we can consider long range or meso scale transport. Considering the US for example as a source, it's been quite well documented that the southern end of the US can contribute contaminants to the Great lakes and this may be a transport of a few hundred kilometers. Going farther afield we can move chemicals up to Canada and the Arctic and it's even possible to transport contaminants across the ocean to Europe.

On the other hand if we want to be protective of ecosystems, we don't necessarily have to move chemicals very far to have them show up where they're not wanted. A good example is simply moving chemicals from urban and agricultural areas to high elevation ecosystems in which case we're talking about a fairly short range transport but nonetheless a transport that results in chemical getting to a remote ecosystem.

On the recipient side, the phenomenon of trans-Pacific, that is from Asia to the US, has been documented. Canada sends contaminants down to the US, Glacier National Park and contaminants in the Great Lakes are some examples. It's possible to move those from Mexico up to the US and the actual, the first long range transport studies in the literature for pesticides were on the tradewinds from Africa to the southeastern United States and the Caribbean back in the late 1960s so here we have a very wide range of transport distances which we could consider long range but some not so long range.

When you look at the empirical evidence the best example, of course, are organo chlorine pesticides the classic pops like HCHs and DDT and chlordane, toxifene, et cetera and there's many studies that show that these things are truly global pollutants with transport all the way from the Great Lakes to the Arctic and the Antarctic and all points in between.

There's also been documentation of currently used pesticides. This CUPS is a Canadian acronym for current use pesticides in ambient air and deposition in temperate North America and Europe and there have been a number of studies on these that go back a while.

More recently the occurrence of both currently used pesticides and organo chlorines in air and deposition from North American mountains in particular the Sierras and the Rockies that have been several papers, some of them quite recent.

Going farther afield, currently used pesticides have been identified in the Arctic in the air, snow, ice, sea water, lakes in a number of different studies and transpacific transport of both currently used pesticides and organo chlorines has been documented.

In the case of long range transport by the oceans there are far, far, fewer data but this is now being considered a viable mechanism although on a much slower time scale if you have a chemical which is persistent in water and it becomes deposited in the ocean either by river rain input or by atmospheric deposition followed by ocean transport, if the chemical doesn't degrade, it can go a long way although it may take a decade or more to get from the temperate latitudes up to the Arctic.

This has been documented for hexachlorocyclohexanes in particular transport through the Pacific Ocean to the Beaufort Sea. Currently used pesticides have been found in the water of the eastern Canadian Archipelago. At this point we don't know whether that is direct ocean transport or direct atmospheric deposition to the water in the Archipelago.

There are other chemicals that are suspected to be transported by ocean currents, fluorochemicals being one of them so this is a rather new kid on the block, this concept of ocean transport but it is growing especially for persistent chemicals.

How to make the assessment of long range transport? Well, the easiest way is to certainly go by the two day degradation half life that is used now in most international regulations that identify persistent chemicals and the CTAC multi-media partitioning working group noted that at a windspeed of about four and a half meters per second if you keep this up for two days, you can move the chemical or half the chemical almost eight hundred kilometers.

This of course is a very crude way to assess long range transport because there's several things that happen between here and there and there's been a number of fugacity based models which consider transport through the air as well as ocean currents. Air soil and air water exchange especially for volatile chemicals. Particle deposition both by dry deposition and by precipitation and degradations in air, soil and water.

The next step in complexity would be the meteorologically based models. These would be Valerian or La Grange and air transport models which use real time meteorology. These are quite sophisticated. They require much more user sophistication and often much more computer time so I won't be dealing with these today. I'll simply be talking about the fugacity based type models and the outputs of these fugacity based models are characteristic transport distance or characteristic travel distance. This is a distance over which the air concentration drops by sixty-three percent, so you go through one CTD, you have thirty-seven percent of the chemical left.

Overall persistence is simply a steady state residence time with respect to degradation and transfer efficiency which is the ratio of the deposition flux from the air to the surface media in the target region divided by the continuous emission flux in the source region.

Frank Vonya's group has been very active in popularizing another output, and that is the Arctic contamination potential or similarly a mountain contamination potential from global pop. And the arctic contamination potential is simply the mass of chemical in the Arctic divided by either the mass or emission in the global environment. So these are all metrics that are outputs of these models that can be used to assess long range transport.

Here is an Arctic contamination potential map from two recent papers, one is by Chub, et al and the other's by Brown and Vonya, both are very recent ES&T papers and they simply show the partitioning space defined by two PKM properties, log KAW which is the air water partition co-efficient and log KOA which is the octanal air partition co-efficient and they show how within this chemical space, you can place chemicals that have...that are known Arctic contaminants and that's these little group of white dots in here and the closer your new chemical would come to where these other dots are would be an indication that at least has the right PKM properties to reach the Arctic.

You can also use this type of chemical partitioning space to classify chemicals by where they end up in a multi-media model and how they get there. For example, this again is a LOG KO, KAW, the air water partition co-efficient on the Y axis and the octanal air partition coefficient here on the X axis so chemicals going down this way like to partition into the water, chemicals going this way like to partition, oh, you can't see what I'm doing with the arrows, I'm sorry. I'm too used to driving this...I've been pointing to things and...

DR. HEERINGA: I did the same thing with my students the other night so don't feel bad. I actually wrote on the screen of a computer with a magic marker.

DR. BIDLEMAN: Okay, air water partition co-efficient and chemicals going down this way like to partition into the water more favorably. KOA is the octanal air partition co-efficient and chemicals going in this direction have an increasing affininity for the octanal phase or for the lipid phase or a decreasing potential to go into the water phase if you will.

So the chemicals that are up here in this corner tend to end up in the atmosphere, the chemicals that are down in this quadrant would end up in sea water and fresh water, they're the water lovers. The chemicals over here would like to end up in the soil and sediments and the chemicals here in green are, we call them multi-media chemicals. Those are the ones that are the most fun because they partition between the different media.

So in terms of how they get there, how they move around, they have been classified into flyers, swimmers and hoppers. The flyers are transported through the atmosphere, they're fairly volatile chemicals, they don't like to deposit, they mostly just stay in the air.

The swimmers have a high affinity for water and so you might expect river rain transport, ocean current transport to be important for these chemicals and then the rest of them are hoppers but they're classified into multi-hoppers and single hoppers. The single hoppers are mainly chemicals that have a high KOA or a low Henry's law constant or both. They tend to be on particles. So they will get suspended into the air by dust, by particle emissions, and they'll be transported as particles and when they come down they're not likely to come back up again.

The multiple hoppers are the ones that we call the grass-hoppering chemicals that undergo cycles of deposition, re-volitilization deposition, re-volitilization on their way from here to there, so the nice thing about these chemical maps is that they show you at least roughly where the chemical's likely to end up at least in a multi media partitioning system and how they're going to get there.

The CTAC working group on Multimedia Partitioning and Overall Persistence and Transport Potential, that's a long name for a working group, put out or is putting out a book chapter which compares several of these multimedia fugacity modeling techniques and they've actually referenced a number of other papers which have already done the comparisons. One of the ones is Cotrin Finner et al, in ES&T 2005, there have been other ones before that and more recent than that.

Finner actually compared nine multimedia models for over 3000 hypothetical chemicals. They picked the hypothetical chemicals because they wanted to cover a wide range of physicochemical properties and it was easier just to make them up than to actually find chemicals with those properties.

So they went through this exercise and they compared the nine multimedia models for predicting characteristic transport distances and overall persistence.

And they noted that there were absolute

differences among the models, in some cases quite large absolute differences, but the multimedia models tended to rank the chemicals in the same way so if model number one would rank the chemicals A, B, C, D, E, then model three would also rank the chemicals A, B,C, D and E even though the absolute values of CTD and overall persistence would vary depending on the particular model.

They noticed that there was a difference between models that were mainly transport oriented. That is they...their main outputs were these two param...this particular property and target oriented, for example, ones like global pop or Arctic contamination potential which the main output is the amount of material deposited in a particular location.

They also noticed that there was a difference in general between global pop and the other eight models, and those differences were largely because global pop is a non-steady state model, it has variable OH radical concentrations, it has variable temperature, it has variable precipitation, whereas all the other models were steady state, they had a fixed OH concentration, fixed temperature, fixed rainfall rate, et cetera.

The conclusion of the paper, and I think it's an important conclusion, is that all nine models when used in the correct context provide credible and useful descriptions of the complex interactions between the environment and chemical pollutants. The key phrase of course is when used in the correct context.

The other studies that were summarized by the CTAC working group came up with similar results and the conclusion are that multimedia box models are appropriate tools to rank chemicals and their persistence on long range transport potential, that is to rank the chemicals, not necessarily provide accurate numbers for CTD but to rank the chemicals according to their potential.

They also made the comment that on the time scale of days to weeks, the air flow used in the models leads to transport of chemicals along trajectories that are faster than the long term average of the mixing implied in the box models.

I'm still having a hard time figuring out what they're saying here, but I think what they're saying is that you can get event transported, that you can get event transported, transport events which can be quite significant which might not necessarily be picked up by the models and this is one reason why if you go to additional levels of sophistication is that using a meteorologically driven model to capture event transport might be worthwhile.

With that very, very long introduction, we were tasked with saying something about the OECD screening tool. This is a level three fugacity model, it's a steady state, the outputs are characteristic transport distance, overall persistence and the percent transfer efficiency.

The compartments in the model are fixed, we have a hundred meters of ocean surface water, seventy percent of the globe, you have soil at ten centimeters depth for thirty percent of the globe and you have a six thousand meter column of air. There's no fresh water and no ground water and no sediment in the model.

The input parameters are octanal water partition coefficient and octanal and air water partition coefficient and three first order degradation rate half lives for soil, water and air. Now these are fixed inputs, although you can change their values, they are fixed during the transport modeling and it's run at a constant temperature of twenty-five degrees and rainfall is continuous so I mean, it's, you can see it's unrealistic but it might be useful for ranking chemicals, right, which is what it's supposed to do.

The people who developed this tool have a couple recommendations and one is that you perform a Monte Carlo analysis of model results which will give you a measure of the uncertainty due to the uncertainties in the chemical property's data and the degradation rates that you put into it and the other is that you don't interpret the results on an absolute scale but use it to rank chemicals.

So we're getting, we're getting the message here from the CTAC working group, from Cotrin Finner and from the people who develop the OECD screening tool, but what we're using these models for is not to really say chemical X is going five thousand kilometers but to say chemical X is going twice as far as chemical Y.

Okay, how about the real world, what is, what are all the monitoring data telling us about long range transport and can we relate it to CTD?

One of the earlier data sets that was used for this purpose was a set of passive air samplers that was deployed from Costa Rica up to the Canadian Arctic by Frank Vonya's group in 2000-2001, they were XAB columns that were exposed for a year so they integrated the air concentration over a full year, you know, one sample, one measurement, and that represents the year's exposure for that particular site and from the gradients of air concentrations they were able to extract empirical estimates of characteristic transport distance.

Quite interestingly the rankings of those CTDs agreed quite well with three long range transport model results, and the absolute values of the CTD is different from the models in some cases, and they were close in some other cases but the rankings agreed well with the output of the transport models.

A somewhat similar study was done by Derrick Muir and coworkers, published in Environmental Toxicology and Chemistry, where they collected water samples from lakes running from upstate New York up in through southern Ontario and up into the Canadian Arctic, and in this case they were interested in current use pesticides and again they extracted characteristic transport distances from the gradients and concentrations in these lakes and they noted that there were some differences, in some cases substantial differences, between the CTDs that were empirical and the CTDs that were predicted by essentially the same models that were used up here.

But they got better agreement, on an absolute scale they got better agreement if they allowed the model to vary the OH radical concentration because as you go northward, the concentration of OH radicals decreases and so your atmospheric lifetime due to OH degradation becomes longer and they introduce intermittent precipitation. It didn't rain all the time. I can only think that these normal models must be really, really dreary because they operate under conditions of a constant drizzle.

If you introduce intermediate precipitation, they got better agreement so this is an indication that in order to make models more realistic in an absolute sense we need to allow the environmental parameters to vary according to geography.

There was some measuring and modeling of PBDEs and PCBs in lake sediments, again going from northern New York to the Canadian Arctic. Most models overestimated the mobility and from this information Newt Revick and coworkers determined that there were key processes which needed to be included into the models. The forced filter effect, the effect that when you move a chemical cloud over the Boreal Forest you get scavenging by the forest filter effect and that's a function of the physical properties of the chemical.

Intermittent rain, particle deposition needs to be improved, the paramaterization of particle deposition needs to be improved and the photolysis of the chemical in the sorbed state, which is likely to occur they felt for PBDEs.

Now these models in general consider that once the chemical is onto a particle, it is there, it does not degrade and we know that for some chemicals that's simply not true.

So there's clues here by looking at the outputs of the models and the real world estimates of how we might be able to improve the models in the future and this is really the beauty of environmental measurements used in synergy with modeling. The two just work hand in hand.

Okay, there's some things that we know about currently used pesticides that are different from the classic pops and we should be including them into the models. One is the particle gas partitioning. We know that for organo-chlorine pesticides and PCBs this partitioning between the particle and the gas phase is well described by either KOA or by vapor pressure. This is just not true for most currently used pesticides.

There has been a number of studies now that show that the CUPs are more strongly sorbed to mineral matter, they're more affected by aerosol water content, and that the simple Yona Pankow model or the KOA model in general just does not work.

There's something new on the horizon. It's referred to as ppLFERS, or polyparameter linear free energy relationships which take into account not only hydrophobic interactions with the particle which you would get with the pops but also things that would be more important for the polar pesticides like hydrogen bonding and electron donor acceptor interactions and by using these types of descriptors we can get a more accurate picture of the particle gas partitioning of currently used pesticides than by using the older models.

Many, many more data sets are becoming available for which we can test models. There are Arctic sampling campaigns which are simultaneously measuring contaminants in source regions and at all the circumpolar Arctic sites, this is a so called NCPA program that's part of the international polar year.

There are passive air sampling campaigns being conducted on a continental scale, on a global scale. For example, the global atmospheric passive sampling campaign so that within the next few years we're going to see an explosion of data.

We've already seen some of it coming

out, for example, these two papers in ES&T for which we will have a lot more empirical data against which to test these characteristic transport distance models so I'm hoping that someone will pick up the ball in the future and use this as a wonderful opportunity to compare the measured and model CTDs, improve the models and give us a better indication of where new chemicals are going to go.

So we have some recommendations on persistence and long range transport. The first recommendation is that we employ a tiered approach for assessing long range transport potential. Tier one is simply to look and see if your predicted or measured atmospheric degradation half life is greater than two days. If it's greater than two days, then use something simple like the OECD screening tool and compare the outputs to the chemicals we already know are undergoing long range transport.

If the answer here comes out yes, then go to more sophisticated models to assess long range transport. So I think using these three in a tiered approach. This potential for long range transport should be proactively assessed during registration. We don't want to let a chemical out the door and have to wait for ten years to find out if it's going to show up in the Arctic and this potential for long range transport should be included in the overall risk characterization of pesticides and other new chemicals.

We need improvements in the long range transport model parameters to accommodate the special requirements of currently used pesticides which are by and large more polar than the classic pops. Particle gas partitioning is not simply described by the older models, we should consider new ways of looking at that partitioning in our models.

We need investigations of the degradation of currently used pesticides once they're sorbed to particles. Let's not assume that they just sit there on the particles and are not affected, they very well may not be and we need to recognize that the atmospheric oxidation potential program works well for PCBs and for PAHs but it may not be accurate for complex molecules like CUPs, and we need more experimental measurements of the OH radical reaction rates. This doesn't come directly from us, this comes from Roger Atkinson, arguably the God of OH radical reactions.

And finally, measurements and modeling need to be improved to assess the long range transport potential of pesticides via ocean currents. This whole area is just in its infancy right now. And lest you thought we were done and you think we might be considered over-achievers, there was another issue that was on the agenda. It wasn't specifically framed as a question, but it was this statement here. The difficulties of linking local use patterns to far field deposition exposure is considered a major challenge.

So we decided to say something about this as well. Linking the exposure from long range transport implied to us that we need to go beyond the simple ranking of chemicals but we need to come to a point where we can make quantitative estimates of pesticide emissions and source regions and connect those to long range transport. So that's a step beyond simply ranking them according to their transport potential.

Next one please, there we are. So how do we get chemicals off a site? Well, there's spray drift during application, there's precipitation which can deliver the runoff into a pond or a stream or an estuary from which it could either stay there or volatilize. There's direct volatilization from the soil during and after applications, during and after rainstorms and during dry periods you can get soil dust which is entrained and carried long distances.

Next one, please. The volatilization is a very important process for moving a volatile pesticide. This could be a fumaGEN or it could be even something like DDT which is sufficiently volatile to undergo this process.

It depends on the properties of the chemical, it depends on the formulation, how it's applied, whether it's a foliar spray, whether it's applied to the soil surface, whether it dips into the soil. The soil characteristics, how much you mix up that soil, either by earthworm mixing or by going and plowing it twice a year, and it depends very much on the micro-meteorology of the specific situation.

Next one, please. So we have to recognize that long range transport really begins at the source. All transport models rely on estimates of source emissions. There's a number of ways that the models get those source emissions. Some estimate them from the quantity of pesticides applied.

You don't necessarily need to know the absolute source emission amount to rank the chemicals for long range transport potential but if you want to actually say how much of a chemical is undergoing transport and how much of it is going to deposit, then you need to know the mass of chemical mobilized or transported. You need to know the emission factor.

For our LRT models these are sometimes estimated from usage data as I stated above or they can simply be generic. You stick into the model at a hundred tons per year as being used. Some long range transport models use actual soil to air emissions data either mod...you know, which is usually modeled on regional scales. Here's two La Grangian transport models which have done that.

A key step in getting accurate emissions data is to consider what happens when the pesticide is in the soil, undergoes volatilization and mixes up into the air boundary layer which is on the order of a couple of meters or so above the soil. Once you get it up here, now you start your long range transport but you've got to get it to this point first.

There have been quite a few models that have been developed to do this, of various complexities, some of these are indeed very complex models. Some of them you need to dry with real meteorology because that affects how this flux varies during the day.

We need to improve those models by revisiting some of the underlying theories in the mass transport correlations that get the pesticides out of the soil and into the air boundary layer so that we can transport them. This used to be a popular thing to do. Back in the 1970s through the early 1990s there were many experiments done to actually measure pesticide fluxes from fields. Most of these were done with organo chorines but some were done with currently used pesticides also.

A few of these experiments have actually been modeled but not many, but those that have been modeled generally show pretty good agreement between the emission models and the actual measured fluxes. We are suggesting that it might be possible to go back to some of these old flux measurements and mine the data and model them and improve the modeling capability and the confidence in the models for predicting pesticide emissions from treated soils.

If we could do that, then we might be able to extend those soil air models to regional scales using GIS land cover and pesticide use data to generalize emissions so that we could extend these transport models to predicting actual quantities which are mobilized and moved to remote areas. So, thank you.

DR. HEERINGA: Thank you very much, Dr. Bidleman, a very comprehensive review. On the last issue I know that the SAP has actually looked at some of those flux measurements with local meteorological modeling in relation to fumigants and particularly in the Central Valley so that's...

DR. BIDLEMAN: I know a lot of work has been done with fumigants and that's great, but they are in general different from most of the pesticides.

DR. HEERINGA: Sure, okay, well, we have other associate discussants on this, and I guess I'm sure everybody contributed to this presentation but have the chance to contribute additional information or comments, Dr. Simonich?

DR. SIMONICH: I have nothing to add to Dr. Bidleman's excellent summary.

DR. HEERINGA: Dr. Thibodeaux?

DR. THIBODEAUX: Thibodeaux. That was too easy. We got our act together, but I do have a question. How do you do it now? In other words localize to start the emissions that Terry was talking about in your current scheme and I was looking back through some of the papers and data, does PRZM have a reposition compound?

DR. HEERINGA: Dr. Hetrick?

DR. HETRICK: Yes, PRZM can estimate volatilization flux and what's nice about that is you can actually look at that flux as a function of different management practices so soil incorporation would be included, things of that nature.

DR. HEERINGA: Good, thank you. Dr. Gan?

DR. GAN: Very good job, Terry. As a chemist I just tend to think, you know, what's the trigger for the LRP definition? With advancement in chemistry, you know, the likelihood of us finding these chemicals at very low levels in, it doesn't matter where it is, will increase and you know, if you see something at a very low level will that qualify for that chemical to be called LRP compound? Just something to think about I think.

DR. BIDLEMAN: This was actually a question that was raised in the CTAC workshop by somebody who didn't phrase it as nicely as you, he said you know, you analytical chemists are pretty smart, you guys can look for nothing in everything. What does it mean when you find a nanogram in water of the Arctic and it's a good point.

Does a simple detection of a chemical in a remote region trigger an outcry? Do you somehow have to connect it with potential toxicity? It's a question that everybody has an opinion but nobody really has a definitive answer. I'm not sure there is a definitive answer.

It's, I would say one of the key points is to note where that chemical's increasing or remaining constant or decreasing. If a chemical is present at a low level but over the years it's increasing, to me that would send a red flag that we need to start thinking about why. But you're right, it's something that we're not going to answer here but I think needs some more discussion.

DR. HEERINGA: Dr. Steenhuis also an associate discussant with this group.

DR. STEENHUIS: I only would like to point out the total distances are important, well, play a role in this equation, too. I think, coming from the Netherlands, that fifty kilometers is a long way. It's half across the country. Moreover, it drizzles always down there, it is a dreary country so I have nothing....

DR. BIDLEMAN: I said the workshop was in the Netherlands, I didn't say that the person was in the Netherlands.

DR. HEERINGA: Yes, Dr. Thibodeaux.

DR. THIBODEAUX: Thibodeaux. So the emissions, I'm talking about air from the PRZM, is that used in any way in looking at ecological risk in the near field like around the farm plot?

DR. HETRICK: Currently we're not using that aspect of the PRZM model. It's something we're exploring and, but we're not using that currently in our exposure assessments.

DR. THIBODEAUX: It seems strange to me, I was talking to Willie Lick at the break and he says, there he is, sitting in his office at his house and here comes this helicopter, spraying on the avocados and when I go to my mom's old place where there's a rice farm, right after the rice is planted there are planes all in the air.

DR. HETRICK: Let me try to elaborate a little bit more on this. I'm getting my colleagues here throwing stuff at me, but the bottom line is that we do look at spray drift so we do consider that.

But as far as, and we are going to probably evaluate the PRZM model a little more extensively for volatilization in an upcoming SAP that we're going to do on volatilization so that may actually take us into a little more of a quantitative assessment as to what's going on there but currently the volatilization sub routines in PRZM are not used in a routine manner in our exposure assessments.

DR. HEERINGA: Dr. Portier.

DR. PORTIER: I bet you thought I was sleeping, right? One of the things we haven't talked about here is somewhere in between near field which is in, measured in meters or tenths of meters and hundreds of kilometers, that there's that Ag to urban or Ag to suburban transformation that most people are really interested in.

What happens in that rice field shows up in my living room carpet and I'm wondering where does long range transport... I'm probably crossing disciplines here because there's probably a bunch of chemists who look hundreds of kilometers and EPA looks the field and next to the field and I don't know who's looking at that other kind of, maybe our USDA person could answer that.

DR. HEERINGA: Linda.

DR. ABBOTT: Linda Abbott. Actually I was going to say this in response to the question eight but we can get it out of the way now. USDA is looking at that issue, and I wanted to alert the Agency to a program that's being conducted by USDA and that conservation evaluate....the conservation effects assessment program where we're trying to link together models to look at short and long range transport, not specifically of pesticides but of sediments and in some of the watersheds we are looking at pesticides. Now I think that's all I'm going to say at this moment because this comment actually fits better with question eight. I don't want to open that up.

DR. HEERINGA: Thank you. We'll get back to that. I think we'll have opportunity certainly on Ken's question too in relation to question...charge questions nine and ten. Dr. Hickie, you look anticipatory. Did you have...

DR. HICKIE: This is a question for Terry, number one is, I was typing away, did you mention back trajectory analysis and how it might be used?

DR. BIDLEMAN: I did not mention back trajectory analysis because it really wasn't part of a modeling, it was part of the evaluation of monitoring data, but certainly this is something that virtually everybody is doing anymore, they're either looking for a single event air samples, they're looking at back trajectories for those event air samplers or for passive samplers which sit out there for a week or so, they're developing air shed maps which basically tell you where the....what the probability was of the air coming from a certain region and those can be even further extended into something called source area impact factors. Is that right, Staci? Source area impact factor?

DR. SIMONICH: Source region impact factor.

DR. BIDLEMAN: Source region, yes. So there's a way of, yes, of evaluating this. In the case of pesticides which have aerial sources A-E-R-I-A-L, not arial up there, but aerial like spread over a wide area. You don't have a point source, your chemical could be emitted anywhere from where the trajectories started out to where they actually ended up.

And I used to show a very nice example of a very high toxifene measurement we made when I was in South Carolina and the air parcel went straight back to Alberta, and I used to tell people it was a perfect example of Canada sending toxifene down to the southern United States. Of course it wasn't.

It was all of the land, you know, over which the trajectory passed on its way down there that probably picked up toxifene emissions so I think they have to be used with cautions but in the case of trying to say what general region the air passed over there, they are quite valuable.

DR. HEERINGA: Dr. Hickie.

DR. HICKIE: Second unrelated question, but I just wonder you mentioned the ppLFERS, do you know if anybody's using those to look at water to particle partitioning?

DR. BIDLEMAN: Yes, actually Kye Goss's group, Martin Sherringer's group, the whole group in Switzerland has been using these. They have used polyparameter linear free energy relationships to look at sorption to particles of all kinds, they've looked at sorption to hemic acid, sediments, et cetera, yeah, they're generally applicable.

DR. HEERINGA: Dr. Mehta has a comment.

DR. MEHTA: Right, you, I'm not sure if you...you mentioned oceans but did you also mention estuaries or...

DR. BIDLEMAN: We did not mention estuaries, although obviously to get the chemical out of the river into the open ocean you need to cross an estuary. The descriptions of ocean transport over a long distance are not that sophisticated.

In fact the whole treatment of the oceans and the ocean currents for moving chemicals over long distances is not all that well described and it's being evaluated more now but there's a question for chemicals that are primarily moved through the atmosphere whether the riverine input is all that important or whether it's mainly atmospheric deposition into the open ocean followed by transport.

While the, you know, there might be significant loadings in the rivers, there's a whole huge area of ocean available for atmospheric deposition and maybe a situation like the Great Lakes where, you know, PCB input was assessed and it was found that the atmospheric deposition greatly outweighed the riverine input.

DR. MEHTA: The reason why I was asking is that you do have sorbed chemicals on fine particles then the, I'm speaking about the process of aggregation of particles in water and there are three mechanisms. One is ground in motion which is not that important but, and the essential settling where, you know, where you have flat water then particles fall, they hit each other and there can be aggregation.

But the most important one is aggregation of the sheer and there's been a fairly good advancement in science as far as modeling individual particles that grow up and break up under turbulent flows.

The problem comes in is that those specific models when you connect them to regular estuarine transport models, the time required for a concentration purposes becomes so large that it's practically impossible to run them right now, but even then if you do use lump parameter approaches to simplify those equations and some of the work in fact is going on in San Francisco Bay and other places for tracking contamination from the packing estuaries.

DR. HEERINGA: Dr. Simonich?

DR. SIMONICH: I did think of one thing I wanted to stress was that the generic conceptual models should include atmospheric deposition to large surface area water bodies, for example, the Great Lakes and oceans.

DR. HEERINGA: I'd like to turn to Dr. Brady. I think this question has had good coverage but I'll ask you if you have any questions to follow up with the panel.

DR. BRADY: I think Dr. Khan has one or two quick, one comment and one question I believe.

DR. HEERINGA: Sure.

DR. KHAN: That's correct. First I'd like to comment on Dr. Portier's earlier comments about that, whether we ignore the far fields. That's not true either. In a case by case as the chairman already alluded to that in the fumigant we did address far fields. And in other model we used, which is the AG disc Dawson extension to look at far fields, and those two models we do use some far field approach.

And my question is that in the two we have seen that the exercise I did for the validity too, I used very similar a structure we used for PRZM EXAM for input parameters, which we used the 90th percentile because of the large variability between the vertical values and what's the recommendation to use, because it's such a large variable I mean, what do you recommend to approach that?

DR. BIDLEMAN: Sorry, Faruque, I didn't understand the question. Are you asking about the choice of PKM properties?

DR. KHAN: Not PKM properties, but the soil, you know, like aerobic metabolism studies or we get those studies from the registrant and generally they have a large variable sometimes, like Jim Hetrick was talking about it yesterday, like a fifty to five hundred days.

DR. BIDLEMAN: Right, so which one of those do you put in the model? Well, the screening tool does allow you to do a Monte Carlo analysis in sensitivity and you could also just do it manually by you know, plugging in fifty days or plugging in five hundred days and seeing what difference it makes, and I'd say, you know, without knowing a whole lot more about how to choose a particular half life, that may be the best way to do it.

DR. KHAN: Thank you, and thank you, panel members, for the in depth discussion for the long range transfer.

DR. HEERINGA: Thank you, Dr. Khan. At this point we are at an appropriate place to take a break and move on certainly to question number eight following the agenda, and I haven't yet decided whether we finished with question eight whether to move on to nine, and I'll make that decision jointly with you, the members of the panel when the time arrives, so but, let's take a fifteen minute break and reconvene at 3:30 and we'll move on to charge question number eight.

(WHEREUPON, a brief recess was taken.)

DR. HEERINGA: Okay, welcome back, everyone. We've completed our discussion, initial discussion of charge question seven on long range transport.

Thank you to Dr. Bidleman and the team of associate discussants on that, and we're set to move on to charge question number eight, and I think tentatively decided that what I would like to do today is to consider charge question eight and leave nine and ten for first thing tomorrow morning, and that gives our working group a little chance to think on their own and to maybe deliberate a little bit together as a working group and we'll resume again tomorrow morning at 8:30.

We would be here anyway and I think rather than split those questions up, I think we'll consider them both together tomorrow morning but we will have ample time for question number eight, so Dr. Brady, if you could please read it into the record for us?

DR. BRADY: Number eight, in the White paper, the Agency describes a number of issues it has encountered when assessing persistence, bioaccumulation, toxicity, and long range transport in its aquatic and terrestrial ecological risk assessments involving pesticides with PBT profiles.

In addition the Agency has identified various methods and approaches that it is considering for refining its ecological risk assessment process specifically to address these PBT and LRT related issues.

Please comment on the extent to which the Agency has identified and characterized the unique or problematic issues associated with assessing ecological risks of pesticides with PBT characteristics and the need for the Agency to incorporate refinements in the tools and methods it uses to assess ecological risks of these compounds.

DR. HEERINGA: Our lead discussant is Dr. Maddalena.

DR. MADDALENA: Okay, thank you, the co-discussants on this question, Dr. Abbott, Dr. Delorme and Dr. Oris will jump in after I run over, run through a quick series of bullets that kind of came out of conversation over the last few days, have some higher level issues identified I think that will be drilled down into in the next two questions. Nine and ten seem to go in series so next slide, please.

I think that was it, a duplicate, if you can go to the next one again. Thank you. So anyways I think the first thing we want to do is commend the Agency for bringing this to the panelists. This is a big and very diverse panel and I think you probably knew you were going to get hit from every direction and as far as identifying some of the unique problems associated with this particular class of chemicals, we generally thought you did a good job of that, finding those unique challenges.

Characterizing these challenges, although there's obviously a lot of good work that's been done there, there's some very big steps that remain that could be quite a challenge to characterize some of these very unique properties and behaviors in the environment for persisting and bioaccumulative and long range transport type chemicals not to mention the toxic part.

So what I'd like to kind of present or bring forward is that the challenge here in assessing PBTs is likely going to require a big frame shift in the way the OPP thinks about and frames the problem.

What I'm talking about is developing your conceptual model, I think there's a ways to go there and not that you have to just throw out your initial conceptual model, but there is some I think good rationale from what we've heard around the table that to step back and reevaluate what this conceptual model should look like and what the key endpoints or processes are going to be included.

Sure, that's a lot of work, but the encouraging thing or at least what I'd like to personally encourage the Agency to think about is that this probably isn't the first time you're going to come across nor the last time you're going to come across these things that are different and a good example which may not be too far in the future are the engineered mammal materials going into the pest management stream and there's really not a lot of confidence as to whether you can drop those down into the current paradigm and get a good answer out the bottom that you could count on.

So in doing this, you can think a little bit broader than just dealing with PBTs and think about okay, how do we just, how do we adapt to an emerging field of chemicals in the first place and look at that as well so you can gain a little bit of bang for your buck.

So the next slide, I think the point is that in moving forward, the Agency is going to have to rely heavily on either new or modified models and so it's important to look at this as, almost as a model development or selection model, selection model evaluation and model application process that's pretty well described in a number of places and the most recent one, that in fact the EPA put out.

And I referred to it earlier, screen shot here of the guidance document, really lays out a lot. And it's a very simple, short, well written document that really lays out some of the challenges and some guidelines or suggestions on how to move forward in a way that you can learn from your efforts, something that Dr. Gobas had in one of his final slides. Talked about developing a model, calibrating the model, using it, learning from it and improving on it, and that's a whole cyclic process that really doesn't end. 'Cause models, I think if you step back and realize that models are really not meant to be truth generating machines, they're tools that you can use, that it gives you another sense of how you're going to use these things as you move forward. So next slide, please.

So that was kind of my only comments really on question one, do we want to go right through question two first or...

DR. HEERINGA: Why don't you go ahead?

DR. MADDALENA: Okay, I'll finish my comments anyway so question two asks about the need for the Agency to incorporate refinements in the tools and methods to use ecological risk assessments.

The next slide, I think the take home at least from sitting here and it would probably be even more frightening sitting where you guys are sitting is that the suggestions and comments that you receive for refinements, yes, there are a lot of possible refinements that can be made but these suggestions have gone the whole gamut of complexity.

From the conversation, a good contrast is the conversation on sediment dynamics at the end of the day yesterday compared to the conversation on long range transport. The details that go into these models are phenomenally different, they go a wide range of complexities, so it's going to be a real challenge to try and figure out how to deal with incorporating this information into your overall process.

Some of the later charge questions, nine and ten in particular, will attempt to really answer the question as far as prioritizing some of these ideas and some of the recommendations on what to deal with first, but again, just to highlight the fact that one of the important lessons here is that this assessment with the PBTs and LRT chemicals is really going to depend on models, and models depend on no known's, and one way to look at it is, you know, a value, a process, and you know how to parameterize it.

There's also known unknowns so you know the value of the process, you really don't know how to parameterize it but you can put a statistical distribution around it and do a pretty good job of estimating it.

But the challenge is always for these is going to be the unknowns unknowns, so things you don't know that you don't know in other words, are going to surprise you and they're surprising us all the time and that's what is exciting for model developers is because when your model is wrong, you can move forward, but it's probably not nearly as exciting for you guys. You want the model to be right and done.

So just a few of these issues, the inputs, the process knowledge and models and then some strategies that might move forward and again I lifted from that document I showed earlier if you want to slip the next slide.

I lifted kind of a nice visual that helps you, I think helps me explain what I mean by capturing all these different levels of complexity and trying to balance the system, the ultimate, you know, the final approach that you guys decide to use really needs to take into account model complexity in terms of as you get a simple, simple model, you end up with something that really doesn't represent reality as much. It's easier to understand, easier to use, faster to use, and sometimes it's easier to refute, you know, to prove that it's wrong.

But as you move over to a more complex

model, you get to a point where your understanding of the system doesn't quite keep up with your complexity of your model and so uncertainty is in your data and your inputs to the model might overwhelm what you gain on more resolution in your system and so these kinds of, this whole paradigm or this whole idea of building a model that balances complexities and usefulness, I guess I could say, it's going to be a challenge, you know, and to move into that area is probably my biggest recommendation for number eight and that's pretty much it. So I'll turn it over to the co-discussants on this now for a little more detail.

DR. HEERINGA: Thank you very much and Dr. Abbott is our first associate discussant.

DR. ABBOTT: Well, these chemicals because they are going to be persisting for long periods of time are probably going to create some challenges for the Agency in considering both spatial and temporal scales of exposure.

I briefly have two comments. First, in the White paper there is a discussion about the need for potentially looking at the exposure due to multiple applications, there are applications for many different fields within say a watershed because these chemicals are persistent, more than just looking at the simple pond scenario you have, you might have input from lots of different fields and over different times.

So it seems as though you might need another technique to try to assess what the exposure might be from multiple applications to multiple fields over different time periods, maybe not all within the same year but within the period in which these pesticides are going to persist.

I really have no solution to that problem for you, I'm sorry to say, but I do want to alert you to some data and some modeling techniques that might help you in the long term, not the short term as you try to frame how you're going to address looking at multiple applications for many different fields within a watershed.

The Department of Agriculture about five years ago embarked on a project to try to examine the impact of implementing conservation practices within watersheds. The conservation effects assessment program and this is the question that I started to answer in response to Dr. Portier's question to me earlier.

But, I realized it had nothing to do with aerial transport but the Department has expended a lot of resources from many different agencies, the

Agricultural Research Service, the Natural Resources Conservation Service, Cooperative States Research, Education and Extension Service and the Economic Research Service just to name a few, there are other parts of USDA that are also participating in this program.

But where I think it might be able to help you is USDA identified over ten watersheds where we had a long term monitoring data base and we had been trying to develop models and link together or we're linking together existing models and trying to develop new modeling techniques to try to estimate the effect of installing conservation practices on water quality, air quality and soil quality.

And as part of that project, many of the models that you discussed in section, I think it was four in the White paper, are being tested in the field. In some of the watersheds, the ecological stressors include pesticides.

One watershed I can think of in particular that might be of interest to you is the one that's being worked on in Tifton, Georgia. There, they're trying to look at the effect of spatial and temporal scale on the ability of a whole range of models to predict concentrations of pesticides.

I'm thinking that maybe Tim Strickland or Richard Lorenz might be good contacts for you to talk to about their implementation of not just PRZM but I think they're also using EXAMS and some of the other models that you've mentioned here in section four, SWAT and AGNIPs.

And I'd also like to point out that I believe it's in the Mississippi watershed there's an effort to look at bank erosion and the transport of sediments from streams that are undergoing bank erosion and although I don't believe in Mississippi in that watershed they're actually looking at pesticides, just the long term transport of the sediments might be of use to you.

So my first comment is just that USDA is actively investigating a range of different models and looking at them over different spatial scales and different temporal scales trying to determine how well they can be used to look at sediment input into water and pesticide. They're also looking at nutrients, that may not be of much concern to you but that might be a data source or a source of collaboration.

Now my second comment might be more useful to you immediately. In reading the White paper and listening to the presentations here for the last three days, I've been trying to think as a risk assessment practitioner, what would I want to do if I had on my desk a pile of risk assessments that had to be done say by the end of the year, maybe the end of the month, and I wanted to maximize the chance that I didn't miss an exposure that I could possibly address right now.

So with that in mind, I wonder whether or not looking at current agricultural practices, not just the two exposure scenarios that I was able to identify in the White paper, but looking at a range of agricultural practices might lead you to look at areas where you might be having an accumulation of these pesticides that might not be captured by the scenarios that are discussed in the White paper.

Now I'm going to assume, and I know that you probably have other scenarios that aren't in the White paper but just from my reading of the White paper there appeared to be two exposure scenarios that you look at, the one that has to, that's associated with the agricultural pond where you have the ten hector field that has runoff transported directly into a one hector, is it a one hector pond and then there also seems to be a scenario from the terrestrial side where you might be looking at accumulation of residues in the treated field.

I'm thinking that there might be some agricultural practices that range between those two scenarios that might present a challenge that...well, they might present an opportunity for an accumulation of pesticide in an area that's not captured by the scenarios you're already looking at.

Now I'm assuming that with the agricultural pond that that ten hector field is all one cover type and all one soil and it flows directly into the agricultural pond.

I'm also thinking that maybe if you, the practice that comes to mind immediately that might have a different, that might not be captured by what you're already looking at is if you have a buffer or an untreated, not untreated, a non-agricultural area that's in between the field and the pond and I'm thinking specifically of a situation where the soil type in the non Ag area is of a different type and the cover is different than that of the adjacent field.

I wonder if there might be an opportunity for looking at that scenario to see whether or not you might have an accumulation of pesticide in the soil that is radically different than what's in the field like maybe a wet area or a marshy area.

DR. PARKER: It's actually easier to look at that accumulation in the water than it is the field itself. The field does have not only dissipation but leaching into the vadozone and the ground water plus runoff plus volatilization from the field so that the field isn't a static area with no sink, like a water body is.

So, as someone pointed out if you continuously put something into a water body and you have no place for it to go then it does accumulate essentially forever so it's the half lives that will determine whether something accumulates or not, but we do and that's part of the reason that we've looked at, that we're looking at these four example chemicals is because they do tend to accumulate in our static pond and sort of looking at how do we deal with the impact of that.

DR. ABBOTT: Well, I guess I'm thinking of the, this untreated area not only from the standpoint of the aquatic assessment but also perhaps the terrestrial assessment. I don't know whether or not in the terrestrial assessment you look at ingestion of soil.

But, I'm thinking that if there's a different soil type, perhaps more organic matter or something that might change the accumulation and the persistence of these chemicals in that area that maybe that would be a different type of exposure that you could look at right now.

Now I don't know if this has merit. I mean, maybe other members of the panel might want to opine on whether or not it would be worthwhile for the EPA to try to capture something in between the treated field and the pond that might be a completely different type of soil and cover that might have different types of wildlife than you would find on the field but that was one area that I thought might be something you could look at right now.

The other AG practice that I wonder if it's captured in the scenarios that I saw in the White paper would be irrigation and return flow from drainage from a field.

I don't know whether or not that would be radically different than what you're looking at as coming off of the treated field into the pond. It almost seems as though return flow from irrigation, if you have a large irrigation event and you're moving a lot of water through the field, you might be adding more organic matter or more sediment than you would just from a series of runoff events and I was thinking that that might be another issue that you could address right now without having to wait to develop more complicated models, and those are my comments.

DR. HEERINGA: Thank you, Dr. Abbott. Dr. DeLorme.

DR. DELORME: I'll try and keep it short and sweet. With respect to the first question the extent to which the Agency is identifying and characterizing unique or problematic issues, I think you guys have done a pretty good job. You've identified I would say probably ninety-five percent of the issues. There are a couple of things, however, that I didn't see there.

One is the issue of bound residues and the implication for determination of persistence of bioavailability. We do have a NAFTA project with you guys on that one. I think it is a consideration in this case. We do have to consider. I'm not quite sure how we're going to do it but we do have to look at that issue and there's probably science out there that can help us with respect to Superfund sites or other things but it is something that we need to consider.

The shift in risk. There is a shift in the risk, there's a shift in the risk spatially, okay, from maybe a field level to a far field. And temporally, I mean there is risk obviously at the time of application but with these persistent chemicals and bioaccumulative nature especially when they're subject to LRT, I think we have to take a look and say what's the risk in twenty years.

We were sitting around the other night and we all said we would hate to be sitting there ten years from now and saying oh geez there's chemical four, and on the front page of The Washington Post. How did we get it wrong again? You know, and that's not what we want to do, you know, so I think we need to make sure that our assessments are good enough or our characterizations are good so that the risk management decision is good.

And in these cases, you know, the risk is shifting from being at the time of application to being later on, although it does exist at the time of application too, so in your model frameworks and whatnot or in your conceptual models that needs to be taken into consideration. I think it's there, but it wasn't explicitly stated.

And again, that leads to the next one which is the aerial scale of use is an important factor to be considered. We are obviously here using these kinds of chemicals on cotton or on corn or on wheat, you know, on big crops like that there are implications.

If you're using it on smaller, for registered over smaller areas, well, you'll, you're going to have a different outcome, okay, but it does play into it, you know, and I think if we look at the chemicals that we had problems with in the past, part of the issue has been how much they're used.

The other thing I'd like to point out and it's not necessarily with the assessment but in risk management, and it's too bad Steve's not here but there's also a temporal separation between the benefit and the risk because of the persistent and bioaccumulative nature of these things. The benefit is going to be accrued at the time of application or shortly thereafter in terms of protecting crops or whatnot.

But the risks, although they occur at the time of application, they also are going to occur in the future. I think you have to be careful about, you know, making sure that that is characterized so that the risk managers understand that. And that's all I had to say on question one.

With respect to the need to incorporate refinements in the tools and methods, my interpretation of this question is the need to incorporate new tools and refinements from where you are now with your sort of standard risk assessment.

I don't think we'd be sitting here if we all didn't think that we needed to do that, but I think the short answer to that is yes, definitely to the extent of refinement differs depending on the particular issue to be addressed but I think, I have a minor in evolution, I think what we see here is a case of punctuated equilibrium, it's a real leap forward.

For those of us who understand what a standard pesticide risk assessment has been for the last ten or fifteen years, you know, in, in the past five years with the addition of probabilistic now with the potential addition of additional methods for considering PBT chemicals, we're really looking at a, quite a step forward in our thinking in how we do these. So, you know, my only other comment there is you know, the refinements proposed should be based on science to the extent possible.

You know, we do science based risk assessment, that's what our job is. In some cases you know, we may not be able to use the best science, you know, because of the pressures we're under with respect to time and resources, but I think to the extent possible what I've seen is based on science and you're to be commended.

DR. HEERINGA: Thank you, Dr. DeLorme. Dr. Oris?

DR. ORIS: Thank you. I'd like to start off by saying I think you did a very nice job of summarizing most of the scientific aspects of the issues here.

With regard to the things that Peter was just talking about, and he and I did talk about this a little bit at one of the breaks, there is a social aspect here that I think that you need to be explicitly aware of and deal with and that's that because the risk and the benefit are so separated in time and space and that if one thing we've seen especially in the last few weeks is that humans are really, really good at accepting instant gratification and at the risk of delayed impact.

That there's a social dimension here that you need to be very careful about and history repeats itself. We're looking at chemicals now that we weren't able to deal with in the past and that weren't being used that extensively when we developed the risk assessment method, so we're back where we started again.

And so these kinds of chemicals personally scare me so I think that socially there's some things that need to be dealt with. As far as the second part, yeah, obviously there's refinements that need to be made. For a few examples, chronic toxicity is still an issue in my mind, but I think with refinements we can deal with that.

Critters are not going to be dropping dead, so you're not going to know when you have an immediate problem so that they're going to have, you're going to have feminization, you're going to have changes in sex ratios, you're going to have decreased reproduction, you're going to have changes in behavior, how do you deal with these subtle effects with the effects of other multiple stressors or longer term change? So climate change and changing temperatures over time and how that might affect, so there's some evolutionary aspects that are of concern and need to be at least considered in these kinds of things.

We need more clear links between aquatic and terrestrial systems, than there's some presence, but I think we need to do a better job of doing that and we need, because of that we need to explore additional receptors, I think in the risk assessment. So for example, birds, spiders, aquatic insects that emerge, amphibians, anadromous fish.

These are things and benthos and epi benthic in organisms that move around and deal with things that adsorb to colloidal material. These are things that I don't think we do, we're dealing with now and you typically don't need to deal with the impacts of ocean going fish accumulating persistent chemicals from a pesticide long range transport and then bringing it back into another place continentally in a fresh water system.

So those are things that you're going to have to deal with and so the receptors that you're looking at I think are going to have to be expanded depending on the type of risk assessment you're doing.

We need, and I'll beat on this again, we need to address multi-compartment issues so, in larger organisms where these things may partition, those, these, we can't go with a simple single compartment organism and we also need to address some of the temporal issues, how long it takes for these things to accumulate and move from place to place and get around.

So those are sort of my summary comments on question eight. There's a lot of overlap in my mind between or among eight, nine and ten and so I'll come back to some of these tomorrow when we get to those.

DR. HEERINGA: Thank you, Dr. Oris. You cite some social aspect of this as well. Other comments from members of the panel on this particular, yes, Dr. Norstrom?

DR. NORSTROM: Going back to thinking outside the box again, I think it's important we talked about metabolism and solubility being important for bioaccumulation but we should also be considering metabolites I think.

It's not just a question of whether these things partition or whatever, it's a question of whether some of the metabolites might also be persistent and that may not be something to do with its lack of phobicity or its hydrophobicity either.

So some of the examples that I gave earlier are ones that I think need to be considered and we need to take a very exhaustive kind of view of what, how will this thing break down if you have the metabolites identified, then look at them and say well, they possibly may also be as or perhaps more persistent. Sometimes that happens, than, than the starting compound.

Just looking at this Parabola model, for example, I can see that thing splitting off to produce something that looks very much like thyroid hormone.

If I looked at that myself I would say I wonder if this thing is acting like a, if that metabolite is present or some version of it, it could possibly be bound to TTR.

If you start looking at it in fat you're not going to find it so you wouldn't even know it was there and those kinds of surprises are around all the time so I think you really have to be very broad looking at each of these chemicals in terms of not just looking at it as a partitioning phenomenon in the animal.

DR. HEERINGA: Next, Dr. Meador.

DR. MEADOR: I just wanted to add to what Dr. Oris said. An example, long range transport, actually with some on it, say you go out into the open ocean and 90...oh, at least 99 percent of the PCBs that accumulate are from the ocean, you come back in some of our most pristine water sheds are actually contaminated by PCBs as they die and respond to a huge biomass.

DR. HEERINGA: Let me ask one question of my own interest. I know from as a liaison to the Science Advisory Board that the Office of Research and Development is looking into nanotechnology and its use. In OPP and in the Environmental Fate and Effects Division, are you thinking in terms of nano particles and how they might be used in pesticides or are you seeing... maybe it's, I don't need to ask that question but is it something that's clearly on your mind and that you're thinking about at this point?

DR. TORTON: Dr. Heeringa, I"m Bill Torton with the Office of Pesticide Programs, and I might be able to provide a little bit of background and answer that question.

We have within the Office of Pesticide Programs formed a team to study the field of nanotechnology and to anticipate the scientific and regulatory issues that will confront us when we receive some applications for registrations of products for uses, pesticides that are based on nanotechnology or that incorporate nano materials.

So far we have not received any applications, although I will note as some of you may already be aware, that there are in the marketplace products that claim to use nanotechnology that make pesticidal claims. There are gym socks that supposedly have nano particles in them that keep the socks and maybe even your feet from smelling bad and there are air fresheners and other products that supposedly operate with a pesticidal mode of efficacy.

We are working with the nanotechnology

industry to remind them of their responsibilities to get registrations if they are in fact selling products with pesticidal claims regardless of whether or not they make, whether they actually use nanotechnology. As I said we haven't received any such applications, but we've been working with our colleagues in the Office of Pollution Prevention and Toxics where they have seen a number of products in nanotechnology.

And we're working with our sister agencies, the FDA and other parts of HHS and I just found out that Dr. Abbott is heading up a similar program or part of a similar program at USDA and was happy to make that connection.

The team of people includes folks from the Environmental Fate and Effects Division, from our Health Effects Division, from our Biological and Economic Analysis Division to help us with exposure and use patterns, as well as lawyers and folks like me who do policy work so we think we're trying to get ahead of it, but the more we work on it, the more we discover, to use a phrase that just happened earlier, that there are a lot of unknown unknowns.

DR. HEERINGA: As I understand and you correct me, too, that in the registration process now the guidelines have been clarified so that if carriers or other secondary components of the compound including nano particles, those are reported to you by size categories?

DR. TORTON: We are hoping to clarify that. We expect that with our current version of our regulations and guidelines that information will be part of the description of the statement of the formula, the products that applicants provide to us with their products but we're, as I say, working to clarify that as well.

DR. HEERINGA: Very good, thank you Dr. Torton. Other comments on this particular question or is everybody ready to take a break for the evening? I'd like to thank everybody today, oh, first of all before I get ahead of myself, I'll turn to Dr. Brady, Dr. Parker, Andrea, any questions of clarification on this last, on question eight?

DR. BRADY: I just want to, this is to go back to Dr. Abbott's discussion about looking at pesticide residues in terrestrial ecosystems.

We included an analysis of that accumulation in the White paper as an illustration to show what the capabilities of PRZM are, that we could get that information from PRZM.

We normally don't use that information

in our terrestrial risk assessments and that's, we feel that there's some useful information in there when we, we can model accumulation in the soil of the environment, we might be able to take that further and look at that in our terrestrial risk assessment. That's...

DR. HEERINGA: Well, if there are no other comments this afternoon, I think with question eight there will be ample opportunity in the context of questions nine and ten to introduce your thoughts tomorrow, and I would like to I think adjourn for today and give everybody a chance for a break, it's been a very productive session.

I always learn something here, I should be learning something, I don't know much to start with, and I appreciate everything that everyone has contributed today.

And so let's call it a day and we will reconvene tomorrow morning at 8:30 to pick up charge questions nine and ten and my intent is that we will cover these within the three hours that the agenda has provided us.

So if we could sort of set that in our mind and I think that's ample time for these two issues, an hour and a half or a little over an hour and twenty minutes each with a break should be able to do that, so Myrta, do you have any comments? Nothing from the DFO so we'll say good afternoon, good evening to everybody and see you tomorrow morning at 8:30.

(WHEREUPON, the **MEETING** concluded at 4:12 p.m.)

CAPTION

The foregoing matter was taken on the date, and at the time and place set out on the Title page hereof.

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Further, as relates to depositions, it was agreed by and between counsel and the parties that the reading and signing of the transcript, be and the same is hereby waived.

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AT LARGE:

I do hereby certify that the witness in the foregoing transcript was taken on the date, and at the time and place set out on the Title page hereof by me after first being duly sworn to testify the truth, the whole truth, and nothing but the truth; and that the said matter was recorded stenographically and mechanically by me and then reduced to typewritten form under my direction, and constitutes a true record of the transcript as taken, all to the best of my skill and ability.

I further certify that the inspection, reading and signing of said deposition were waived by counsel for the respective parties and by the witness.

I certify that I am not a relative or employee of either counsel, and that I am in no way interested financially, directly or indirectly, in this action.

MARK REIF, COURT REPORTER / NOTARY

SUBMITTED ON OCTOBER 30, 2008

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