

**U.S. ENVIRONMENTAL PROTECTION AGENCY**

**EPA SCIENCE ADVISORY BOARD**

**CLEAN AIR SCIENTIFIC ADVISORY COMMITTEE (CASAC)**

**PARTICULATE MATTER REVIEW PANEL**

**July 19, 2002**

**DR. HOPKE:** Good morning, and welcome to the Clean Air Scientific Advisory Committee. Today, we want to start focusing more specifically on the Criteria Document.

We have limited amounts of time, so what we want to try to do to get as much done as we can today is we want to start off the morning discussing a follow-up to what we heard yesterday and see if we can work out a game plan for getting a better handle on these statistical problems and the results and where that goes with Chapter 8, particularly how that focuses, then, into Chapter 9, and then, we will move into the reviews of the individual chapters.

What we want to try and do there is to come as close to closure or potentially closure, if everybody accepts that, to get those as finished up as we can. Again, we would like to free up Les' resources, not to keep redoing these earlier chapters which may be in reasonable shape.

In most cases, there are going to be things that need to be fixed, and we all have our sets of comments on the document, but, you know, the question is, is it close enough that we can basically say go away, fix these things up, and we'll only have to take, at most, a very cursory look at it

again when we come back to look at Chapters 8, 9, and the executive summary.

So, that is where we want to try and go this morning, and I think our best start here would be to ask Les if he can give us some idea as to how he envisions trying to pull together, you know, where we are with pulling together information about the epidemiological studies and how he would suggest proceeding from here.

**DR. GRANT:** Well, I think one place to start is to know that, certainly over the last couple of months, is these statistical issues have surfaced, and we have had interactions with different people over time. It is just that about each interaction, we learn something new. Even yesterday, I think we all heard some things for the first time off and on as far as new information.

So, I think it leaves us in a situation, you know, to come away from the meeting having heard these presentations plus some of the discussion that we hope you will have in the next hour or two and have a chance to think through what that all means and then to sort out what may be the next steps.

I think, in some general terms, one of the things we are going to need to do is to sort out and prioritize what studies are very important ones that we think are most pertinent to the standard setting under here and to focus attention on in terms of helping to facilitate, stimulate, whatever terminology we want to use to get an appropriate

reanalysis done and then, also, to see what are the appropriate steps to accomplish sufficient or adequate peer review on whatever, you know, comes out of these reanalyses.

I went through the table that we had attached to my handout to everybody yesterday, and I think there are at least some studies that you could very quickly center in on and want to be sure that we would have some reanalyses or categories of study.

Just going back to the '96 document, as we talked about yesterday, there are really very few of these, comparatively speaking, that use the GAM procedures, and from among them is, I think, clearly, the Schwartz, et al '96 study which we talked about, I think, yesterday, you know, the time-series analyses. That is certainly one that we definitely want to have, you know, well-established reanalysis and so forth available for that.

Again, part of the reason for that is that if it was a very key study in terms of looking at  $PM_{10}$ ,  $PM_{10-2.5}$ , and  $PM_{2.5}$  and comparisons across this.

There may be one or two others there. The Pope and Kalkstein study might be another one. Although it was  $PM_{10}$ , that was one that used a different approach for, you know, to control for some of the weather variables was, you know, very important last time. We have to think through what is the advisability of that.

When you go to the other studies, then, that have

been published since '96 and the large number of studies now cited in this draft document, we could go through and fairly quickly note several that seem to be or categories of study that would seem to us to be of importance. First, PM<sub>1</sub> 0 studies that are involved with multi-city analyses of the sort of the NMMAPS study that we heard about yesterday. Obviously, there are ones that are important.

Probably the APHENA study in Europe, multi-city ones, Canadian ones as well. There are a lot of important studies in that category.

I think ones that compare PM coarse versus fine fraction, PM<sub>2.5</sub> versus PM<sub>10-2.5</sub>, is another category of very important studies. If we are likely to...you know, I'd like to see them in there.

Probably just about any of the studies or at least North American studies dealing with PM<sub>2.5</sub> would also, I think, would be of some reasonably high priority for us.

**DR. HOPKE:** Okay.

**DR. MILLER:** Before you keep going on, Les, I think it is important to find out what the process would be, because I think you can spend a lot of time going through different studies, but it is not clear to me what process you and your staff, if you are relying on the original investigators, if these are reanalyses that your staff are going to be charged to conduct and do they have access to the data and the resources or what, because I think

we could spend...that might also dictate how we would recommend prioritization.

I may be getting into another part of the discussion here that you are actually articulating now. I really don't understand how this is going to happen.

**DR. GRANT:** One thing, for sure, my staff and, you know, myself, whatever, we do not have the resources to go through and contemplate us taking on...bringing the data sets and doing the reanalyses, so it is going to have to be done through the original investigators.

And that is probably most appropriate in any event. It's their analyses, they have published them, they have a certain responsibility to do the appropriate reanalyses, given that the new information has come forth that may indicate for some of them that they need to be done.

I think one of the things about this, as we go through and hear presentations of the sort yesterday, that becomes obvious is well, is that different study that used the GAM procedures and whatever different software, they have been variously affected, and that is, I think, you know, as we listen closely to what was said yesterday, the more complex the analyses, the more the different, different types of variables that were in the models, the more sophisticated the models in a lot of ways, the higher the stretch, shall we say, you know, computational stretch, and the greater the likelihood that there may have been misapplication, if you will, of some of the key parameters.

So, I think it is even going to take us a little bit further here to take a little further look and some discussions, further discussions, with some of the investigators. We have indicated our intention to a number of them or several of them to have discussions on some of these key studies that I sort of noted and the type of them to see what they did do.

So, there is probably going to have to be some further selection process in the way, even along that line, as to which are really in urgent need, let's put it that way, given the complexity of analyses or whatever that, you know, need to be undertaken as far as reanalysis.

So, first off, it is going to be the original investigators primarily doing the reanalyses. It is not going to be us stepping in and doing reanalyses.

Second, to identify a set of things here, I sort of outlined at least some of our initial thinking as to the types of studies that we think should be accorded high priority for reanalyses.

I think, thirdly, then, we are going to all have to come to a point of trying to sort out what is going to be sufficient in the way of whatever, additional peer review and so forth and mechanisms for that.

Yeah, I think it will be useful to hear the committee's thinking about that as well, and then for us to go away, taking into account, indeed, the comments and sorting out afterwards as to the specifics as to how to approach

doing it.

We have had some discussion, including with Phil and some other folks. Note being taken that, at times, when somebody does the reanalyses and simply submits it to a journal, you know, to an editor or whatever, there may be varying policies on the part of the journals as far as the peer review. Many still haven't published them, though. Perhaps some others may, you know, require peer review and so on.

So, that is a nuance of it here that I think we are going to have to sort through.

And, again, I don't know. It may be different if there is a very small or minor change coming out of the reanalyses from what was originally published, maybe that is different than something where, you know, with the sort of things we heard yesterday on the NMMAPS and the changes, you know, some very major changes in certain ways, you know, in the outcome may require...

**DR. HOPKE:** Well, let's take that step by step. First, to me, it sounds like you are not yet in a position to really come up with a prioritized list of the studies that you would see as the most critical. You have got some general categories, but you need to go back and see which ones you want to pull out and put up to the top of the list. How long would you see it taking you to put that together?

**DR. GRANT:** Well, I think we are going to

be certainly looking at it, working on it, in the next week or two to get that completed.

**DR. HOPKE:** In other words, what I might suggest is that, you know, we ask Les to come up with his top 20 hit list or, you know, whatever it takes, with some idea as to why these studies would, you know...now, we don't need another Criteria Document, but, you know, what the basic criteria were for why these were chosen relative to the rest, and then, I think, we could have a teleconference in which we would then provide our advice back to Les as to whether, you know, he has missed ones that, you know, people think should be moved up, things that people think should be moved down.

Then, you know, in that time, I think it would also be useful to try and tap those which are at the top of the list and get some feeling for the willingness of the participants to do it and what kind of time frame it is going to take to get those done.

Again, you know, the clock is ticking. We would like to come to a conclusion on this document. On the other hand, we don't want to have major scientific issues hanging fire.

**DR. SPEIZER:** I think you have to add the question of the resources that are going to be required.

**DR. HOPKE:** Right, that was the next one.  
Thanks, Frank.

You know, one of the questions with regards to

getting it done in a timely manner is, you know, might there be some resources available for some of these groups who need to divert people from currently funded projects to redoing what...I guess authors have a responsibility to make sure that their work is properly done, but in many cases, that also could produce some significant financial difficulties, and, you know, a little bit of sugar makes the medicine go down.

**DR. GRANT:** Right.

**DR. MCCLELLAN:** I think, in terms of looking at this, there is a piece that perhaps you haven' t mentioned that is implicit, but I'll make it actually explicit here on the table. I think part of the guidance in terms of that prioritization really goes to the linkage to the staff position paper and, from there, on to the setting of the standard. It seems to me the guidance, to state the obvious, is to what extent do these studies inform the decisions on the four basic elements of the NAAQS, the indicator, the level, the averaging time, and the statistical form.

Those, to me, become the paramount consideration in terms of prioritization of the studies for critical review within the Criteria Document, and, ultimately, those are going to be the studies that are going to appear in the staff position paper.

**DR. HOPKE:** And are applicable to the population of the United States.

**DR. MCCLELLAN:** Right.

**DR. HOPKE:** Because, you know, again, there may be some things there that are political. So, yeah, I mean, I think that is a good point.

Yeah, Jon?

**DR. SAMET:** To get the possible suggestions to Les and his crew, it may be appropriate to hold a workshop and bring together those investigators to identify PM, and I think we all know that there's enough sensitivity and subtleties of the modeling that it might be useful to try and explore strategies in advance, but in some of the other circumstances, it is probably unnecessary and can sometimes cloud interpretation for some of these studies to be addressed, but it might help you and clarify the document.

**DR. HOPKE:** The question, then, is again one of timing. Is that going to, you know...are at least a number of these issues sufficiently well understood that useful reanalyses could be done, you know, starting right away, or do we need a workshop to clarify the issues enough to be sure as to just what needs to be done?

**DR. SAMET:** I think that some of the work that has been done points to sort of a major aspect of reanalyses that, basically, give you change in the alphabet. I think somewhere along the way, though, I think it would be useful if a group were convened maybe somewhere along the

start of the third or halfway point. It would probably help.

**DR. HOPKE:** Sure, okay.

**DR. SPEIZER:** Can you remind us what the deadline dates are, what the drop dead date is?

**DR. HOPKE:** Today. Today, a new standard should have been promulgated. So, at least...there should have been a message from the Administrator with a decision. So, we are now in violation of the law. We see Jon Bachmann smile just before he heads off to Leavenworth.

**MR. BACHMANN:** Hey, wait a minute.

**DR. SPEIZER:** I mean, there is an issue of science here, and...

**DR. HOPKE:** Well, absolutely.

**DR. SPEIZER:** And, you know, the law may not view...we may not be able to provide the science for the law.

**DR. HOPKE:** The question is, can we pull enough together that is useful to make sensible decisions? There is a significant number of these studies which are not contaminated by these problems. The bulk of the studies prior to the last CD are not subject to these problems. Case crossover studies do not seem to be subject to these studies. Cohort data do not seem to be.

So, there is a whole body of the epidemiology which isn't directly related to some of the difficulties. Some of the large and important studies are. The question is, can we

get enough information to be useful in a time frame that is sensible that we can, you know, take a step back for some period of time...as yet, I don' t think we can fully define that but not an enormously long period of time...and get a much more scientifically valid and defensible document which can then be used for rational decision making?

**DR. SPEIZER:** Yes, but, you know, HEI and Samet and Schwartz, et cetera, have embarked on the process of doing their rethinking, and, indeed, those, presumably, will be done quite soon. Everybody else is either going to have to do this or not have to do this, and if we have to go through a process for Les to come up with a list, it is going to take some time.

Why not start with those and assume, with the body of information that we have, plus the NMMAPS information, that that is it? That is what we have got for the science on this round, and let's finish. Let's go as far as we can with that.

**DR. HOPKE:** Warren?

**DR. LIPPMANN:** It' s all been...I think people have addressed the issues very well. Phil raised the process issues, and Les talked about some of the difficulties of dealing with the process.

There is one way, it seems to me, that we could move this process along in a credible and timely way with many, maybe even most, of the studies that Les is able to

identify, and that would be to build on what HEI has already done. As has been noted, the HEI-supported research will be going...will be reanalyzed using a common procedure. That is part of the base, but, clearly, EPA and NIH studies, there is not necessarily going to be a uniform approach to reanalysis.

Then, the problem, of course, is getting them appropriately peer endorsed, because, as was stated, we don't know what the different journals where the papers appeared would do to make it reasonably and effectively uniform.

So, my suggestion is that EPA approach HEI to handle the organization of studies, not only their own, but those supported by other sponsors to at least some limited extent, that is, if there are available soon some generally recognized ways in which these data can be vetted for the reanalysis as was suggested by what Hopkins has already done, that other authors agree, in advance, if they wish to, to do the reanalysis according to the common model that HEI has or will adopt, and HEI, if this were to go forward, would attest to the fact that the reanalysis by Jones and Smith or whoever were done with the same procedures as their own study and put it into this review committee document that we heard about yesterday that Dr. Vedal is grappling with in a separate section or whatever, because there is a difference between a study that was fully endorsed by HEI and HEI attesting to the fact that the reanalysis used the right procedure.

And, of course, then the documents coming out of HEI are considered peer reviewed. So, this is a way to

expedite the process, and I throw it out as a suggestion that be considered by EPA.

HEI is under no obligation, of course, to accept this assignment, but if they, EPA, were interested in asking them to and they did agree to do so, I think we could wrap this up in a reasonably timely fashion where the reanalyzed data were looked at in a uniform way and in a timely way, because if the authors choose to submit that to HEI, it would have to be by a certain time.

**DR. HOPKE:** Okay, what do people think about...Sverre?

**DR. VEDAL:** I guess I want to support both the comments that Jon Samet made and Mort Lippman made. I think without...well, first of all, Jon Samet' recommendation has merit that you have some sort of standardization here. We know that, you know, with the reanalyses, there is some...there is a fair amount of play in what you can find, depending on your model of choices.

So, I think maybe a workshop is a reasonable thing to do. Without a central mechanism such as Mort Lippmann recommends, I just can't see how this is going to be resolved. The various forms in which the reanalyses would be disseminated, erratas and letters to the editors for some papers and...it just seems to be a mess to me. So, that may be well a solution to that.

And the timing issue is probably...it will expedite it, but it is going to be problematic, I think. With respect

to HEI, we'll probably have to get some comments from them, but in terms of a commentary on NMMAPS, I think that is on a real fast track. I can't see, at this stage, all the other studies being on quite that same track.

There are other complexities here. I mean, what we are talking about is sort of the simple numerical reestimates and such, but there was a lot of not quite a Pandora's box opened but something similar to that yesterday in terms of uncertainty issues.

You know, the pre-GAMs studies are not totally immune from those issues. There is a reason to use GAMs and approaches like that, and that shades a little bit what we can...how we view studies that were done pre-GAMs. This is a complicated phenomenon going on here, and how we model that is critical.

So, in general, I think I support the recommendations of both Jon and Mort.

**DR. KOUTRAKIS:** I agree with everything said here, but I still think that somehow, the authors may have to write the errata, a letter to the corresponding journals. I think if we decide to do the HEI report, I still think that, somehow, a letter has to be even to the corresponding editors.

And, especially, I think that if these are substantial corrections, probably the editors would like to go back to the reviewers. So, I think it is going to be in a process. It is going to take time, and I think we cannot

really accelerate it. You know, things have to happen in their natural way.

Also, I would like to go back to perhaps the suggestion that we really cannot stop the process. I mean, as scientists, always we will find things to improve, and that is the nature of our work. For the regulatory purpose, I think, at X time, we have to make a decision based on the science that is on the table what we can do, and right now, I think that, you know, we have our opinion about this, you know, how important these studies are and, you know, if we have to make our expert judgment.

I am not saying just rush and decide, but I think we do have to be cautious not to procrastinate, and the other thing is we cannot take all the scientists who do research in this field and just get them focused on this specific issue, because is going to delay chronic studies and other research.

So, I think a little way...somehow, we have to settle so we don't make this a big and time-consuming effort, because I think it is no big deal probably.

**DR. HOPKE:** That is why I think it is important that we not have just those studies that were early involved in identifying the problem. We need to make sure that we have identified those studies which we think are important to the standard setting process and try and get as many of those.

We may not be able to get them all, because the people may not be in a position to do the reanalysis in a

timely manner, and those may slide by, but at least let' s...I think it is important to take a little time to try and make sure that we have identified those things which we think are likely to have significant policy implications in the ways that Dr. McClellan laid out and give those people at least a reasonable time to get...and a process by which we can have reasonable certainty that what they have done is appropriate.

Paul?

**DR. LIOY:** I don' t like to disagree with my colleague, Mort Lippmann, but in this case, I have to. I think I agree with Frank Speizer' s approach. I think it is much more appropriate for the situation that we have at hand. It is going to be very difficult, I think, to arrange to have funding put together for HEI to ensure that we find these other...we have an added guest today...to have these other studies put into some kind of framework for analysis in a timely manner.

I am not sure as workshop will be effective in accelerating the process. Maybe after the reanalyses are done and people can evaluate what people have done for each project, it would be reasonable to have a workshop, but I just don't see this becoming accelerated. I think it is going to be decelerated if we have more and more steps.

And in some ways, I feel that we are putting the onus on the reviewers at HEI to, in a sense, now start taking some of our responsibility to decide what is going to be the best studies to include in the Criteria Document.

And I think that the investigator is responsible for his data or her data, and at some point, they have to send their manuscripts back to the journal. In fact, they should be sending in letters now indicating that there is a problem and that there is at least going to be an erratum, and, in fact, that there may have to be a withdrawal and a resubmission. I mean, this is serious business, and I am not sure that this committee should take on the task of redoing a whole host of studies. I think I agree with Frank.

**DR. MILLER:** Well, I don't like to disagree with Dr. Liroy, but this is one where I will have to disagree. I heard from Sverre yesterday there is no gold standard for these models and analyses, and despite the Hopkins group and others saying we now have a road map, I clearly heard that there has to be an aspect of sensitivity analyses for perturbing the different models to see the magnitude.

And the bigger thing that comes to me from hearing the presentation of Dr. Moolgavkar and looking at the iteration, I, as a member of this group am now at the position of saying we can establish statistical significance, but I question some of the biological significance aspects. So, if we just simply go by what is in there now, we could be providing the inappropriate advice.

So, I feel that these reanalyses, at least some of them, have to be done, and they have to be put in the context of not just one approach, because others are going to perturb

those models.

And when I see the regional heterogeneity aspects, I would think whatever approach is used, you would also explore, in some limited number of studies, what could perturb you by looking at different ways that you are doing a B-spline, a natural spline, or, you know, ad nauseam, if we are going to get into checklists, but when I see values going from 0.4 down to 0.12, depending upon...and Rick Burnett didn't disagree with me that this looks like it is becoming an art form...you have to really step up to the plate and say, what are the criteria and what is the reasonableness of it?

And right now, I, quite frankly, am confused as to how much I could endorse on some of these studies that there are effects there that have been previously stated. And yes, they are statistically significant, but they are getting down in the range where I wouldn't want to live on the difference biologically.

**DR. LIOY:** I don't think I disagree with you on anything you said.

**DR. MILLER:** Okay, well...

**DR. LIOY:** Maybe it is process we are both thinking about.

**DR. MILLER:** Okay.

**DR. HOPKE:** Ron?

**MR. WHITE:** I mean, I think, on the one hand, I don't agree with Frank and Paul that I think we just

sort of stop the process right here and move forward. I think there is a problem that has been identified with some of the key studies for the standard setting process, and I think I have to agree with Roger. I think, you know, the emphasis really needs to be focused on those studies that the Agency and this committee feel are the key studies that relate to the standard setting process.

I would hope that that is something that the Agency could develop and bring to this committee very, very quickly, and then we could have some review and response back to the Agency to give them our views on whether we agree their selection or we have other advice.

I think what has happened is a first step. I mean, the Agency, I think, needs to set out a schedule, a reasonable time frame to allow for some key studies to be relooked at, and I guess, yeah, I would agree, again, with Fred in that we really need to leave it to the investigators to decide, you know, what approach to take to do the reanalysis, because it doesn't sound like there is a...I mean, I don't know, Sverre, if you feel there is a way that we can standardize this process, but I thought I heard you say yesterday also that that can't be done in terms of having a specific paradigm for everybody to follow.

**DR. VEDAL:** No, I don't think we want to totally standardize it, but I think to sensitize people to the issues as to what play there is in the options of modeling.

**MR. WHITE:** I agree, but I think that that would need to happen very, very quickly so that the reanalysis work can proceed quickly. I do think, while the investigators have a responsibility to address the issues in terms of the problems with their previous studies, reality is that there are a lot of other competing issues where they have got funding to do other things, and it is in the Agency's interest and the public's interest to have these studies looked at in a timely manner, and if there is a need to have some relatively modest amount of support to make that happen, I would hope that the Agency could look at that issue.

In terms of a review process, I mean, HEI certainly is one option if HEI was willing to take that on. I would also say that maybe this committee or a subcommittee of this committee could serve as that peer review process with expanded outside experts that the Agency could bring to the table, if that is necessary.

But, I mean, I think there needs to be a centralized process, because otherwise, if you rely on people sending stuff back to journals, this process is going to go on far too long, and I think it's a disservice to this process and, frankly, to the public to do that.

**DR. HOPKE:** Jon?

**DR. SPEIZER:** There is an issue here with regards to what the process should be in terms of doing the fine. If we do this properly, we are talking 12 to 18 months

to do it right. I don't know that we have that much time in terms of delaying our process.

The other thing is if you try to give this to HEI, HEI's process does take into account the validation of the underlying data. Now, they can't do that for the studies that they have not been involved in unless they go through their process with it, and, certainly, to put that back on us as a committee to do is something that would be almost impossible.

**DR. SAMET:** A few comments just back to Fred. I mean, I think modeling has always been, if you will, an art form, but it has to draw on what you...on what one knows, and I don't think...I don't want to leave anywhere here with the ideal that modeling is simply a black art, as it is sometimes made out to be.

But I want to go back to the workshop point. I think one benefit of having a workshop would be, in fact, to identify the most key sensitivity analyses so that they would be run in a somewhat uniform way across the data sets, and I think what we heard yesterday points to some of the key issues around sensitivity controls for weather and other time variables that...where investigators do often make individual choices, sometimes arbitrary, where I think some of these standardization sensitivity analyses, I think, would be very informative and actually strengthen the whole Criteria Document and Les' ability to interpret.

So, I do want to speak in favor of holding a workshop. I think it is going to take a while for the

literature to short itself out. So, I think, for the Criteria Document, if these studies are to be considered, I think we need to have them, the key ones, looked at in a box.

And, Frank, that may mean, in fact, that investigators, as always, have to take account...have to stand up for the validity of their own data without an HEI or some other stamp of approval. That is their job.

**DR. HOPKE:** Let me take one quick sidestep here and ask Dan, since we are bandying about his good offices, would HEI, if we were to decide that was what we wanted to do, would HEI be in a position to help us out in that way?

**DR. GREENBAUM:** Dan Greenbaum, president of the Health Effects Institute. I appreciate both the suggestion and also the discussion you are having. This is a key issue of how to let the science process move in the way it would in a normal, self-correcting manner but also how to meet the needs of a risk evaluation and, ultimately, a regulatory decision process.

A few thoughts. First of all, certainly, we have already begun to mobilize to organize ourselves to deal with our own studies, let alone...beyond NMMAPS. That is not a large number of studies, but that was part of the idea. We knew we would have to do that. Of course, if you guys told us they weren't important, then we could put them off, off the shelf...or off the table.

So, to some extent, we already understand this to

be the process. Sverre referred to that.

Secondly, what is being posited here, I would tend to agree that there needs to be some systemization of this, not a lock step straightjacket for every investigator and let's do a, b, c, and d, but something to allow you, at the end of the day, to be able to compare the new results and understand why there may have been more of a change in one study than in another, because you would know the degrees of freedom that were used, you would know some of the other things that were used, and there would be a very well-done data base of those in one place, and that would be valuable.

I would say that that kind of review...and Frank raised this a little bit...is different from the sort of normal review that HEI does or studies it funds itself, and, obviously, we would need to think about what those distinctions are, but one could envision a certain protocol that was developed, maybe in a workshop, maybe not, of techniques that are to be expected in these things and some certification process that these are done and some mechanism for HEI to certify that that has been done and some reporting mechanism for HEI to summarize those.

This could not...I mean, I think it would be crazy for any organization to think about going back all the way to the original data for every one of the studies. I think you are not going to be able to do that. All you are going to be able to do is say well, if we use these different techniques, what happens in the analysis, and then others will be able to

interpret it.

So, I mean, I have a little bit of trepidation about this discussion, but, obviously, HEI is established to help in similar situations, so if there was a mechanism, then we would certainly...and if CASAC thought this would be a valuable thing, we would be interested in talking with EPA and figuring out if there was a way to do this.

We do have mechanisms in place that would allow, you know, sort of fairly rapid organization of this kind of thing, and we have done that before, and we can do that again so that there...One thing I would like to make clear. I would not think it was appropriately the HEI's role to be one who was deciding which of the studies are important or not. I want to make that really clear. Somebody alluded to that. That needs to be EPA with advice from you, and then, given that, then there is a process that could be set up.

**DR. HOPKE:** Joe?

**DR. MAUDERLY:** You know, we have as dilemma, but it is not a new dilemma. I mean, it is magnified under the current circumstances. I mean, science always moves continuously. That is not a new problem. There is always that next step that one would like to have before you make a decision.

You know, the dependence upon the epidemiology in setting this standard and the excitement that is being generated by some of the newer studies magnifies this problem, but it is not a new problem, and the role of the

committee is to advise the Agency on the state of the science, the interpretation of the science as it relates to air quality standards. It is really the role of the Agency to make a regulatory decision based on the state of information at any given time.

And, you know, the interest in or willingness of the Agency to delay recommending a decision, whether that be to change the standards or not...I mean, the law says that you are supposed to complete a review by a certain time. The law doesn't say you are supposed to change the standard by a certain time.

So, I think the discussions among the committee as to whether the wait is worth it becomes, you know, sort of fatuous. I mean, that is the Agency's decision as to whether the wait is worth it. Ultimately, the Agency is going to have to decide, presumably in the staff paper, what they think of current information is worth bringing forward and what they distill from that in terms of recommending a standard.

Now, this problem, although I think many of our understandings of it have been refined in the last 24 hours, has been known now for several weeks, and, presumably the Agency has been thinking a lot about this. It seems to me that, again, our role is to render opinion in terms of which of these bodies of information really needs revisiting and which it doesn't if it is going to be meaningful, but that is separate from the decision of the Agency as to whether they

think it is worth the wait in terms of meeting the legal requirement in the review.

I mean, it seems to me that we are sort of mixing two issues that are sort of separate issues. I would be interested in the views of the Agency at this point, which they must have views on that issue, that is, to what extent is reanalysis of the specific studies that exist now that we think have been affected by this problem is going to actually affect their vision for, you know, the indicator, the level, the averaging time, the statistical form of the standard. That is really the basis on which it is decided whether to move ahead at this point or not.

**DR. HOPKE:** Roger?

**DR. MCCLELLAN:** Well, I think Joe implied in a certain way you have said is a bit of emphasis on the time schedule, the legal element. I think there is another, much more critical element here, and that is that the genie is out of the bottle in terms of the science. The science, at this stage, is somewhat chaotic. We do not know where it is going, and the Agency, ultimately, has to make decisions, and we have to provide advice to allow the Agency to make decisions that are viewed as having been made in a reasonable fashion and avoiding a decision that is arbitrary and capricious.

I would submit that if we were to try to say get the damn genie back in the bottle, it didn't happen, go ahead and make a decision on a time schedule, that would be an

arbitrary and capricious decision. And I don't think the committee should be a part of that. I think we are a part of the process that says is the science sound so that the decision has the sound scientific underpinnings that would avoid its being overturned as being arbitrary and capricious.

**DR. HOPKE:** Joe and then Jane.

**DR. MAUDERLY:** Yeah, I really have to respond to that. I am sure that Roger doesn't think that I was suggesting that somehow we can stuff the genie back in the bottle, that this didn't happen, you know. I would hope that that was not his interpretation of what I said.

**DR. MCCLELLAN:** No, no.

**DR. MAUDERLY:** What I intended to say is I think that in this discussion, we shouldn't forget the fact that there are two issues at play. There is science, and there is policy driven by law and a policy process.

The science is most important, in my mind, because that should drive the policy, but I think it is the Agency's purview to decide whether or not they can move ahead at any given time on that legal schedule, based on the current state of the science. The current state of the science in this area is, as Roger says, very chaotic.

**DR. HOPKE:** Well, then, that puts them in a very precarious situation.

Jane?

**DR. KOENIG:** I guess I wanted to...I

think I have been hearing comments that we...I am beginning to get worried that we are letting this one major...you know, it is a major...I am not trying to diminish the problem with the statistics that have been discussed, but we have a very large compilation of information about the health effects of PM in Chapter 8, and, you know, David Bates has told us many years ago that the coherence of the data are very important where we need to look at acute studies, hospital admissions, pulmonary function, and all these various ways of looking at the health effects of PM, and the only one that is of real concern now are the mortality studies, the time-series mortality studies.

We did have presentations yesterday showing that when the reanalysis is done, it changes maybe the lag times, it maybe changes the relative risk a bit, but, basically, it doesn't change the conclusion. We have redone the analysis of the Phoenix mortality study, you know, we have done some continued analysis in Phoenix using GLM compared to GAM, and it doesn't change the relative risk. It certainly changes the T statistic a little bit.

So, I don't think that when these reanalyses are done that it is going to be a complete C change, that with one statistical method, you find an effect, and with another one, you don't. I really don't think it is going to be like that. And then, again, we have to remember we don't know that the analysis that we do in the next three or four or five months is going to be the ultimate one that is perfect

anyway.

So, I think we should try to take a little broader look at the health effects of PM and see what we conclude, what we know, and try to understand if a few of the mortality studies no longer can be depended upon, would that really change our opinion. How many people feel that they have changed their opinion about the health effects of PM because of this problem of GAM? I don't think I have changed my opinion.

**DR. HOPKE:** Yes, but the question is when this has to flow to the staff paper and to setting levels and forms of the standard, then these values matter.

Warren?

**DR. WHITE:** You could reformulate the question as do we have any reason, do we have any new evidence, to change the form of the existing standard. We all deliberated on this five or six years ago and came to a reasoned judgment at that time that we had, considering the body of evidence, as Jane says, which doesn't...I guess I am concerned to think that it turns on a hand...on a small number of black box studies. If that is really critical to the standard, then I think that is a pretty weak basis for it.

I think the standard rests on a whole understanding of physiology and morbidity and epidemiology.

If it is not a question of...if we are not really contemplating saying oops, we really goofed last go-around

and we want to get rid of the standard, then it seems to me that Joe's point about there being two different time scales at work here, one, the time scale at which science proceeds and, one, the requirement for a regular review of the scientific basis for the standard.

We can get a review of this...we can issue a...we can complete a review now and say there remain substantial uncertainties about many of the pieces that we have to support the standard, but our judgment is that, taken all together, the standard should stay as it is or there is no reason to change the standard at this point but that we need to continue review.

**DR. HOPKE:** George?

**DR. WOLFF:** Let me just remind us what this group decided last time, and I think we had pretty it much unanimous, almost unanimous, that there should be a PM 2.5 standard. Where the disagreement came in was the level. There was absolutely no agreement on the level, and there are many ways to look at it, but if you look at those tables that were generated afterwards, the consensus or the mean of the group for the level of the annual standard was well above the level it shows.

So, these discussions are very important from the perspective of the level.

The other thing I would like to point out is, I guess I took over this committee in 1993, and every review

that we have had since then has been a, quote, expedited review. We have never had the opportunity that we would have liked to look at the facts so that we could make a decision, and now, I have to agree with Roger that the science is a little chaotic right now. In fact, it's a train wreck, and we need to stop and let the facts fall out and not rush in.

I also look back and say if we had the results of NMMAPS that we have now and the analysis by Suresh that shows such little relative risk...and that was the first study...would we have gone down the road that we have gone down? We would have gone a different direction.

So, I think...and what I worry about is that I see the investigators that are redoing some of these analyses. They are not taking a step back. Instead, they are just redoing the calculations and stuffing the results into the paradigm that was established a number of years ago, and I really think that, at this point, we need to slow down and figure out what the most logical course is and follow that course.

**DR. HOPKE:** The question is, again, one of how slow. I mean, you know, this science could go on, you know, really trying to get at...we heard yesterday that Rick is planning another three years of study on the algorithms. I don't see that we can wait that kind of time frame for, you know, sorting the science out. I mean, the point is we had thought that these kinds of models were appropriate and, you know, they had been peer reviewed and accepted and published.

But now, we find that the numerics...this doesn't change the underlying models that were developed and used. It changes the numerical outcome because of certain problems with the computation.

So, you know, it seems to me that the logical step...endpoint for the current step...is to try and fix those numerics as quickly as we can, come to some reasonable...come to closure as to this is as good as it gets now, with the understanding that there still may be a whole lot of booby-traps out there in the mind field that we haven't yet stepped on, but that is going to be the task in the next five years, and, hopefully, many of those things will be resolved when we all come back again, that much grayer, in 2009.

**DR. WHITE:** But, Phil, I think it is understating the problem to say that it is just a matter of the numerics and not the models. You change the numerical outcomes and you will change the models that are preferred. I mean, using certain models, because they were the ones that gave the clearest and most interpretable results...

**DR. HOPKE:** No, but that tells you something. Okay? Now, if what we thought was a sensible and interpretable model becomes less significant, that is information.

**DR. WHITE:** The second point would be to...I think the question isn't just how much to slow down.

It could be restated as how to slow down. One way to slow...I am concerned, I think, as I understand George to be, I am concerned about trying to drive the science at the speed and in the direction needed by the regulatory decisions, and one way to slow the...as long as we have the scientific activity harnessed to the regulatory needs, that's a problem, I think.

I think, clearly, the scientific community doesn't need any further focus on what the important questions are right now. That's clear. So that just a decision by CASAC and EPA to say this is the best we can do right now, we have many uncertainties, and we are just going to acknowledge the uncertainties right now, and we'll have a better understanding in the next review five years down the road, that's not...that is one way of slowing the process down, slowing the pressure on the science down, allowing it to proceed at a rate that will take care of the business that needs to be thought about.

**DR. HOPKE:** But don't we want to at least give a little bit of time to solve the obvious problems so that at least the...we've got the current models fixed or, at least, the numerics to solve the current models to the point where we get the bottom line numbers in a reasonable way?

Roger?

**DR. MCCLELLAN:** Well, Warren's focus probably is heavily on this speed issue, because he just

bought a new car. I did ride in it. He drove it here to RTB, but I would just ask hm to back up and think about the decisions he made about the quality of the car he bought, and I think that is what we are probably talking about, the quality of the science here.

Clearly, we don't know where the road is going to take us, and we could spend the rest of the day debating a schedule filled with uncertainties. I think there are certain things that are pretty clear.

We have heard from one of the key investigators in the area the importance of a workshop for him and his colleagues to really try to understand where we are, where we go. We have heard from Les a proposition that he is prepared to give us a prioritization of the studies that need reanalysis, reevaluation, that we can take a look at. We can offer them feedback on that. We have had suggestions, I think very good ones, about the possible role of HEI in some kind of uniform review. We also recognize, I think, as Petros has suggested, that it is going to be important for each of the investigators to deal with a journal as they traditionally would.

So, it seems to me the path forward is there, and it is perhaps premature for us to think about what that schedule will be.

**DR. HOPKE:** Oh, absolutely.

**DR. MCCLELLAN:** So, I would just suggest that we maybe move on with the process, that we have an awful

lot of discussion about it. Keep in mind that another key element of this that is on hold relates to the underpinnings in terms of the risk analysis that is going to be conducted by the Agency as a prelude to their development of the staff position paper and where that will fit in.

**DR. HOPKE:** So, you know, let me suggest that we wrap up...I mean, I think we have got what I think may be a sensible way of proceeding, and that is, you know...did you want to...

**DR. GRANT:** Yeah, I think, having heard all the discussion, several things probably can be noted. First off, obviously, the Agency is not in a position to have this Criteria Document and the process just remain open indefinitely. We are going to have to take whatever actions within some fairly reasonable time here in the next number of months to wrap up whatever the next steps in revising the Criteria Document are and getting on with revising the staff paper and so on.

That means whatever else goes on beyond whatever steps we take concerning the options you have just described, for example, we can't wait a year and then catch up with whoever on whatever their time schedule is with the analyses, provides whatever submittals to journals or notes or whatever. So, that is one clear thing. It won't be an option for us to simply sit back and wait for all this to unfold to go ahead and complete whatever we have.

The second thing, it sounds to me, that, indeed, if

we are going to make the kind of progress that is going to be needed that, you know, it really is up to us, the Agency, taking responsibility to sort out some specific steps or whatever, for the process.

And this may mean, for example, a combination of some of the things you have just talked about. I think Jonathan examines reasons...the need for some sort of a workshop to pull together some of the investigators at least for, other than a tournament, these studies that you think would be very important to be able to take into account here in going the next step and wrapping up the document and feeding into a staff paper.

It may well be, and I think we probably have, the wherewithal to help pull together such a workshop with some of these investigators, bring together some who have already started the reanalyses. We would be able to get others already going to some extent on it, but, certainly, that workshop would help bring some commonality or whatever, approach or understanding, I think, would likely be a pretty worthwhile thing.

And then, afterwards, once you get these reanalyses done...and there has got to be some time as a target date for them, they have to be done quickly, the investigators willing to do it, and to the extent we have the appropriate funding or whatever to help facilitate it, then, afterwards, whatever peer review steps, again. That may well mean that if the Health Effects Institute is willing to take it on, perhaps we

are able to work it, you know, the way they are going to be looking at the other impacts.

**DR. HOPKE:** So, let's then, you know, we were talking before about, you know, you thought that within about two weeks, you would have your prioritized...you could prioritize the studies. So, you know, what I am suggesting is that, basically, in about two weeks or so, you send us a game plan...

**DR. GRANT:** Yeah.

**DR. HOPKE:** ...which would have the prioritized list of studies that we could comment on, some idea as to why those were chosen and, in general, why others might not have been, what you want to do about a workshop and when you would see the timing of it being and what it would do, and how we are going to handle the acceptability of any of the reanalyses, and then, where does that get us with regards to potentially revised documents and, you know, looking towards a meeting where we could review that and potentially close on the document.

Does that make sense to...

**DR. KOUTRAKIS:** I think it is important to ask the key players in this area, Francesca and Schwartz and Rick, if three months or six months or nine months is enough to solve this problem. I think we really have to have the opinion of the investigators what constitutes a reasonable time.

**DR. HOPKE:** Right, right, and that can be, you know, in the two weeks, you know, as Les puts his list together, he can be contacting the investigators to get feedback from them as to the feasibility and the time frame, and then we are going to be in a position to have information to make sensible decisions which I don' t think we are in a position to do now.

**DR. MILLER:** I just have one quick comment relative to the workshop. I think it would be a mistake to only include what you have identified as the three or four key groups. There are a lot of people that have done different studies, and that workshop ought to bring everybody together that is using GAMs and so forth, because they are going to go off on their own time schedule even if it is not then included as one, so you are going to want to have all of those relative groups involved in that session so they can benefit from...

**DR. GRANT:** I think, Fred, the essence of a workshop would be, obviously, if you are going to have, you know, certain of these studies reanalyzed and it goes beyond, you know, the groups we heard from today, there are additional effects. We need to have them in. I think we probably would need to have perhaps some additional experts beyond even those investigators be in as part of that whole discussion that would help inform a paper or whatever.

**DR. HOPKE:** Now, the other thing at this

point is that we had not, at this stage, gotten detailed comments to Les on Chapter 8 in most cases. I would suggest that now that you have got Les' list of those studies and what might or might not be, people can at least go back and look at Chapter 8, particularly the primary reviewers, primary and secondary reviewers, and start to get some comments together. Again, we don't want to leave major issues on the table that we haven't had a chance...you know, we are not going to have a chance to discuss in a lot of detail here, but let's get those comments into Les and his team so that those can be addressed in addition to any of these other problems.

Again, we want to be in a position next time where everybody can be satisfied that the document does, in fact, adequately reflect the science of the time, and we can move on.

So, you know, those of you...you know, I didn't think it was very useful to look at this document in Chapter 8 without having a better feeling for the material that Les provided in his letter that gives you some idea as to which studies are in which category, but I think now, we can ask the people who were assigned to do Chapter 8 to please put their comments together and get them into Les in a reasonable time, you know, potentially, again, the next couple of weeks, so that he has got the big picture of what needs to happen in Chapter 8.

That way, he is going to be in a better position to develop his full plan and move ahead.

Ron?

**MR. WHITE:** Do you also want comments on Chapter 9 as well?

**DR. HOPKE:** Yeah, I think we need to start making sure that...you know, again, Chapter 9 should flow primarily from the summaries of the individual chapters. So, I think as we solve some of the summary problems in individual chapters, Chapter 9 may begin to come together. But it would be good...again, those of you who have done Chapter 9, you know, following our discussions today, everybody should have a better feeling for where we are, and, you know, I think at that point, comments on Chapter 9 would be quite appropriate.

Jon?

**DR. SAMET:** A comment, actually. I did already provide written comments on Chapter 8 which is why I can't stay awake anymore, and, you know, there is just a theme that needs to be picked up, and it comes from yesterday' s discussion as well. I just want to remind everybody of this.

All the discussion about, quote, confounding by other pollutants which pervades Chapter 8 and other aspects of the document is based on one formulation of how air pollution works and the idea that it is multiple...that pollutants somehow independently affect the health outcomes. We sort of pretend that game, in part, because we are writing a PM standard, so, therefore, other pollutants become

confounders.

Yesterday, we heard a lot about how we never control for confounders and don't consider them. This is all based on one model of how the world works that, I think, inevitably, can't be exactly correct. And I think throughout the document, and this starts right from the beginning of it, this issue has to be taken on head on, and this is not a matter of epidemiologic interpretation or anything else. This is where all the science has to come together.

I would just say that when I read Chapter 8, Chapter 5, and just sort of the beginning of the document, I really felt, you know, what you really have to do...it is almost a justification, a biological justification, of having a PM standard, in a way. I know the law says we have one, but we don't have to model data the way the law tells us to which is kind of what we are doing.

So, I would like to see some real thoughtful taking on of this issue, because all those who claim confounding, you can always claim confounding. That's silly, but it should be based in some real formulation of how, you know, nature works, and I just don't think that is in the document right now.

To me, that is the major deficiency of Chapter 8, Chapter 5, and, in part, the whole thing.

**DR. HOPKE:** Okay, Allen?

**DR. LEGGE:** I haven't said anything up to

this point, but I think, in response to the previous speaker, I should say you should read Chapter 4. Chapter 4 goes into the environmental aspects, and one of the key points that is made in Chapter 4 is that if you really want to look at how the environment is responding to stress, you have to look at the chemistry. The mass of the PM is irrelevant, and that comes across time after time after time in Chapter 4.

But I don't see that statement anywhere in the rest of the document. I mean, I think you should be questioning the use of PM mass as a surrogate to look at adverse health outcomes as perhaps the wrong way to do this. Maybe you should look at the chemistry. I think the chemistry is the key, and the reason you are finding such low associations is that you are looking at the wrong indicator.

So, I think there are some fundamental reevaluations, because what I think has happened is the modelers and the statisticians have highjacked the process, and the science gotten lost.

**DR. HOPKE:** Well, it is a question of functions.

**DR. LEGGE:** Right.

**DR. HOPKE:** To bring up one of Roger's...okay? We have only just started doing urban national composition measurements, and right now, there isn't the data base sufficient to let you do much. In another few years, there will be, and we can expect, and we certainly hope, that

there will be lots of good things coming out of that.

The other thing is that, certainly, the toxicologists have been challenging their animal models with a variety of things. There has been an effort to start understanding the differences in responses to different types of CAPs.

You know, it is not an easy problem, and getting a big enough base of data that we can start to look at other species as indicators is certainly something that all of us would really like to get at, but even with mass, we only have data every third day for 24-hour integrated measurements. You know, we have an appallingly weak data base, and, you know, and although we berate looking under the lamp post, it is the only game in town.

Jane, did you...

**DR. KOENIG:** Well, I was just going to say, you know, I think that that genie that you let out of the bottle just now...it hasn't been kept in the bottle, of course...is equally important to the uncertainty that we have on this document as the statistical models, and it just points out that we cannot...we are not going to reach a point where we are going to be able to make the kinds of decisions that we really wanted to make, because, as you say, we haven't...you know, we are beginning to...there are a few studies now and the data are available that we can start doing these compositional studies.

But it seems to me it would make almost as much

sense to wait until those come on as it would be to wait until we get a perfect statistical model, so...

**DR. HOPKE:** That is why we will be back in 2009, or, at least, somebody will be back.

**DR. WHITE:** It does seem inconsistent to say that...to hold this process hostage to clearing up the statistical problems but not to treat the lack of chemical resolution the same way. I am with Jane.

**DR. HOPKE:** Well, let me suggest that we need to move on to the individual chapters. We do not have as much time as we would normally spend on these chapters. On the other hand, these are, you know, the third go-around on them, although the first time was sort of...what I would like to urge everybody very much is to stick to the major scientific points. We all have lots of wordsmithing questions and issues, and minor, you know, questions of interpretation.

What we really want to try and focus on in the next, you know, period of time up through this afternoon is on the big ticket items. You know, are there significant misunderstandings, misrepresentations, misconceptions, other kinds of things which fundamentally need to be changed?

We can then, you know, provide the comments we have already and any additional comments we want to get in to Dr. Grant and his team, and we can then get finished up.

What I would like to do, I mean, looking at the

comments, I haven't seen in all of it, you know, any real show stoppers so far, but we haven't seen comments from everyone. So, what I would like to try and do is at least come to, you know, a tentative closure so that, you know, pending the fix-up, clean-up things that we all need to know, we all need to, you know, have suggestions on and which we will expect to have proffered, we are not going to revisit these chapters in depth again.

You know, Les has already indicated that they will revise the literature up through April 30th, 2002. You know, we'll be able to do some minor tweaking of these chapters again down the road, but, you know, what we would like to be able to do is basically finish up whatever we can. If there are still problems, we'll leave those chapters open, but let's finish up, to the extent we can, each of these chapters so that the effort can be refocused in other areas, both theirs and ours. Okay?

All right, so let's get one or two of these done, and then we can take a short break. So, let's start off with Chapter 2, and the primary reviewer there was Dr. Zielinska. Will you lead us off?

**DR. ZIELINSKA:** Okay. This was the second time I reviewed Chapter 2, and I think that the current version is a significant improvement over the present version, and in my opinion, it is a pretty good job in portraying the current state of the physical intensity of particulate matter, but it is pretty accurate.

Of course, I had several comments, several inaccuracies where there are several repetitions that could be avoided, so the chapter could be improved, but this is not really anything major, and I don't really think that it needs major reconstruction of the chapter.

So, pending all of the small things which could be improved in the chapter, I would...in my opinion, this chapter would be pretty close to being ready. There are several other people from the CASAC committee who reviewed the chapter, so I think it would be good to also listen to their comments as well.

Petros?

**DR. HOPKE:** Okay. Petros?

**DR. KOUTRAKIS:** I think I agree with Barbara. This is the third time we have seen this document, this chapter, and I think it is now ready to go. I agree with Barbara, again, that there are some few places where there is some repetition, and some areas are more developed than others, and it is not well balanced, but I think, overall, it is well done, and I have about five or six minor comments that I will provide with my written comments.

**DR. HOPKE:** Okay, great. Rich?

**MR. POIROT:** I agree. I thought it was well done, and all my comments are relatively minor.

One general area that I think could use just a little bit more careful attention is it is an awkward

organizational concept to try to talk about semi-volatile material and artifacts. Obviously, some discussion of artifactual sampling losses belongs under a heading of semi-volatile material, but there are also these various positive artifacts that aren't necessarily in any way related to the volatility. It is more a difference of physics versus chemistry, and a little more discussion of some of the positive artifacts might be helpful to avoid leaving the impression that all we are doing is losing stuff every time we try to sample.

**DR. HOPKE:** Okay, great. Warren?

**DR. WHITE:** I endorse Rich's point, and I felt that there was some sort of awkwardness involved, because there is this sort of split personality with regard to chemistry versus size differentiation as a principle for cutting the aerosol into pieces which returns us to this issue of the role of regulating gravimetric mass rather than chemical fractions.

The chapter starts off with the usual discussion of fine and coarse modes and trying very...going into quite a bit of discussion distinguishing the idea of mode from a cut, coarse mode from the...or the fine mode from the fine cut from the PM<sub>2.5</sub>, all different entities.

It is very difficult to do that discussion correctly and unambiguously without bringing in the different chemical composition of different particles. If you have a

particle between 1 and 2 microns, you can't really say whether that particle belongs to the fine mode or the coarse mode just from size distributions, but the particle itself isn't in the fine mode or coarse mode unless you bring in chemical information about the particle.

So, that is a conceptual problem, I think, that needs to be addressed, and I have comments on that.

I guess my other main comment would be that in terms of things that have been clarified in the last five years since the last Criteria Document, certainly, one of those has to be the distinction between...for carbon measurements between the two different basic approaches to measuring and analyzing carbon as exemplified by the two major EPA networks, national monitoring networks, that report particle carbon.

There is a discussion of the differences between TOR and TOT, but there is essentially no discussion of the difference in the way artifacts are handled. The sampling artifact, the positive, reactive filter artifact that Rich is talking about, there is no indication of the magnitude of that artifact which is very large and no indication that it is handled...that it is ignored in one network and adjusted for in the other network, and those are important facts for interpreting the carbon information, carbon concentrations, that are given elsewhere in the document and that were given in the last Criteria Document and cited here.

**DR. HOPKE:** Okay. All right, Mort?

**DR. LIPPMANN:** I thought it was a very good chapter overall. I did want to mention a few things.

There is a very highly detailed discussion to section 2.2.6 on inorganic elemental analysis and section 2.2.9 on continuous monitoring which I thought was far more than was warranted for this document at this time. My suggestion is that the main chapter text for these sections be greatly condensed and be supplemented by tables outlining the specific attributes of each method. If you want to retain the detailed text, it would be an appendix to the chapter.

And then, I'll refer to page 2-77 which has six text lines below and a diagrammatic representation of a dichotomous sampler. This is a big failing, I think, of this chapter to simply say a few descriptive words about this technique and to let it go at that.

There is a lot more that could and should be said here about the current state of the art of virtual impactors and their potential application for the measurement of thoracic coarse particles. That is an issue which has come up even in our discussions here, and there is no reason why the Criteria Document shouldn't provide a firmer scientific base for possible eventual use of that technique in the monitoring network which we haven't discussed, and that may be...it may or may not be...but it may be an approach that needs to be developed in more detail.

I will stop there. I have other comments in my

written.

**DR. HOPKE:** Paul?

**DR. LIOY:** I didn't have any comments on this chapter.

**DR. HOPKE:** Al?

**DR. LEGGE:** No.

**DR. HOPKE:** Gunter? Roger? Jane? No? George? Okay, good. Does anybody see a serious problem here that prevents us from, basically, saying we are done?

(No response.)

**DR. HOPKE:** Okay. So, I'll take that as, you know, we can fix this up and move on.

All right, let me suggest that we take ourselves a 10-minute break. I think it is a good time, and then we'll move on to Chapter 3.

(**WHEREUPON**, a brief recess was taken.)

**DR. HOPKE:** Reassemble, please. Let's keep things moving.

Okay, let's move on, then, to Chapter 3, and our primary reviewer here was Mr. Poirot.

**MR. POIROT:** I thought, starting out with Chapter 3, that it was especially critical to remind ourselves this was a supplemental CD, and I think that is fairly evident in the CD in Chapter 3 that reflects back...well, it's Chapters 5 and 6, I think, in the last round

of reviews which, in some ways, were a lot more, intentionally more comprehensive, more broad based, and this was very focused on filling in some of the holes. That, in and of itself, makes it possibly appear to be somewhat less than it is in the sense that it is tightly focused in a few areas and then includes a lot of reference back to the original CD which, I think, is very appropriate.

That being said, I thought, however, that there were some areas here where we are kind of painting in broad brush strokes the general spatial, compositional, east versus west, primary versus secondary, the general information that I think we put...you know, we are all familiar with but maybe a little bit too carelessly, a little too casually, a little too fast in some of that summarized general information that is actually presented, I think, fairly coherently in the previous CD. And I think it is just a question of being a little more careful with a few of the things, and most of those, I think, would fall under the category, I think, of minor comments that could easily be fixed just with one more look through.

I did...and then, in contrast to these broad brush strokes, then there is a lot of detail provided in a couple of areas, and one, I thought, that was worth singling out was the spatial variance information that is largely based on Joe Pinto's excellent paper that looks at that question, specifically within different urban areas around the country, and I kind of thought...well, and then we have all kinds of

detail and maybe too much detail than we need, and there was a comment that I wrote here that I noticed myself making in other parts of the CD, in this chapter and elsewhere. It is kind of this general thing of too much information, not enough knowledge.

After I realized I was doing this time and time again, I finally recognized where these things were coming up. They were coming up every time we got to the frontier of what we really understood, and then, the job kind of became one of simply describing the conflicting information or the detail of the information that kind of define the frontier.

After reflecting on it a little bit, I thought well, that is actually a fairly appropriate way to handle that sort of information. This is stuff that was called for, it was demanded by the previous reviews, and presenting the information regardless of whether a consensus and even summary was possible from it, I thought, was probably a good way to handle it.

I did feel, however, that with this focused effort on the spatial variance within urban areas, I heard at least three commenters yesterday in the private session in the afternoon reflect back and quote from this section talking about oh, my God, spatial variance of PM is just huge, we don't know anything, and I think that is a bit of a misinterpretation of the intent of the studies, certainly.

So, I think maybe that it would be helpful to consider other ways of interpreting that information and in

presenting it. I think it is as much a comment on the nature of what we are doing for monitoring programs and how we site our monitors as it is a real commentary on the actual aspects of spatial variation of the data.

You know, with experience as a State guy who has to site monitors, it is a really hard job, and it is getting harder, especially when you say I am from the State, I am here to help you, can we put a monitor, you know, next to your school, and you get all this politics involved, and you get some Congressional districts that demand to be protected with a monitor and others that don't want, you know.

So, actually, I think, you know, having seen some of the...well, some of the Harvard sites and other of the research monitoring sites, in many cases, actually supported some of this information. They do a better job, often, in siting representative population-based monitoring sites than we are able to do in the States.

That, in general, I think, was the one thing I thought I would mention there. So, I didn't feel like the chapter was far from completion at all, especially when taken in combination with the more broad-based information presented better, in some cases, in the '96 CD.

I did think that some of the language, the summary careless language, could be just cleaned up and that that would be fairly easy. It is almost like it is stale. We have rewritten the same story so many times that it is hard to write it again, but one more try to just clean that up a

little bit. Again, a little bit maybe of qualifiers on this spatial variance. Those are things, I think, that probably should be done.

Les also mentioned the possibility of including some of the newer data, and this is another difficult situation. I picked on it for including only the one paper, but the data haven't been out there and available for very long, and yet, they are huge.

So, it is nobody's fault, but I think the ability to have, if we could, one more year...and I don't even know if 2001 is yet available...but presenting that data is not the kind of thing, to me, that needs an extensive peer review process. If you are just presenting summary data, it is your data. It is our data. Just present it. I don't think, necessarily, that needs any kind of extensive peer review, and I think it would be real helpful, because a lot of these patterns really start to clear up after you get just a little bit more data, and we are almost there. So, I think that process will be helpful, and I think that will also feed back in to being able to do these broad-based summary statements a little more clearly.

That is about all.

**DR. HOPKE:** Okay. Dr. Legge?

**DR. LEGGE:** I won't go through any of the detailed comments, because they are...the specific comments, because I think they are straightforward and self-explanatory

in the written submission.

I think the one thing that becomes clear is that if you want to look at coarse, don't use the difference method. It is quite clear that measurements are required, so I would support what was said earlier with respect to...this was in the previous chapter related to the dichots, because I think this ties in very nicely, because, in later work and discussion, you are talking about negative values which, you know, are somewhat problematic, to say the least.

The only point that I would like to bring up is related to the reference to Kaleel and Rasmussen's paper on page 3-68. I would recommend, and I said this in my specific comments, look at the paper by Garin, et al from 2001 with respect to isoprene emission capacity, because the way in which the paragraph is interpreted based upon Kaleel and Rasmussen, it really is an emissions inventory issue, and the way in which Kaleel and Rasmussen had done their work with respect to actually taking the measurements, they had some problems with temperature control and what not, so I thought the interpretation needed to be changed in the light of Garin's paper.

The one point that I would like to make with respect to this chapter and all the other chapters...and I am sure my colleagues around the table will agree with this...please identify your research needs for the future on a list as you are reworking these and put that list someplace so that when you put together your research plan for the next

cycle, you have got that list. This is just to help you.

**DR. GRANT:** Yeah, that is a helpful suggestion.

**DR. LEGGE:** And that is it.

**DR. HOPKE:** Okay. Dr. Zielinska?

**DR. ZIELINSKA:** Yeah, I think it is a pretty good chapter here. I just have a few specific comments.

One is connected with the discussion of the background PM<sub>2.5</sub> in section 3.2. It is quite a brief section, at least, some definition of background, but there is really no clear recommendation from the document which definition should be used for the background and what values should be used, and this seems to be an important problem in the view of the risk assessment and the document which was done before for PM risk assessment. So, I think it should be a little bit more elaborated on the background issue.

The other problem which I think is maybe not so important, but I think it should be clarified a little, the section says in a few places that secondary fine particles are basically dominating the mass, and this is maybe true for nitrates and sulfates, but it is not necessarily true for organic carbon.

It is actually not obvious yet from the scientific evidence that secondary organic carbon is really so important. It could be, but, at the same time, it might not

be, especially in urban areas. There is a lot of work done in environmental chambers which shows that secondary organic compounds form, but there were only a few of these compounds which were really identified in the atmosphere.

So, it could be that this is a very important problem, but it might, at the same time, be, like some people think, that the primary organic is still very important emission, so I think it should be a little bit more careful here in these statements.

The other thing is also that this is the chapter which really has the most information about the chemistry of chemical composition of the PM and everything is in appendices. I think this is a pretty good job, but maybe it would be good in the summary section to say a little that it really would be in the future studies very important, really, to get some more information about the chemistry of the PM.

**DR. HOPKE:** With regard to the background, the last go-around, we had considerable discussion with regards to what we would define as the background. So, it may be useful to just pull that definition from the '96 CD and stick it in there for clarification.

Let's see...

**MR. PINTO:** The definition was pulled right out of there.

**DR. HOPKE:** Oh, is it there? Okay. I'll

have to go back and check.

Paul?

**DR. LIOY:** I have got simple comments. They may not be simple to answer, but they are simple comments.

I think that the issue of coarse fraction really needs to be put more in a statement of research needs and development of data bases based upon the development of new samplers. I do not think that PM<sub>10-2.5</sub> is adequate at all.

In fact, in the conclusion section, I would basically drop that whole paragraph talking about coarse, because I don't think it adequately describes the problem, because I don't think we have adequately addressed the problem. I think it is a whole area of research in PM that we have to consider and consider thoroughly for the future.

So, therefore, a lot more research needs, I think, should be coupled between Chapters 2 and 3 about this very important issue of coarse particles.

I do believe that we should try to put in as much new data in on PM<sub>2.5</sub> as possible, and I'll leave it to your discretion as to where the cutoff date is. There is an issue of quality assurance of that data, so, therefore, it would have to be only the data that is quality assured up to a certain point that I think we should be including, and that, to me, would be adequate peer review.

In the summary and conclusions sections, you spend

some time talking about annual averages and the range of annual averages, but there is no discussion about the peaks for 24 hours. Since we have a standard that has two components, an annual standard and 24-hour standard, I think it would be appropriate to add a paragraph or two on that issue to explain what peaks have been seen and whether there have been any violations of the 24-hour standard and where they were, and I think that would be a reasonable addition to the conclusions.

I think that also provides a path forward for the risk assessment sections of Chapter 9, and I think that would be very helpful.

The final point is I think one of the things about source apportionment that has given trouble to all of us who have done source apportionment at any one time or another is the fact that the automobile tracer is really nonexistent except in very isolated circumstances where you have been able to collect molecular markers of organics.

I think that statement needs...I think something needs to be stated about that somewhere in this document, because we could be either overestimating or underestimating the contributions from automobiles and also from trucks, and I think it would be useful to let people know there is a large uncertainty in that number.

And that when we start trying to do epidemiologic regressions associated with source apportionment for automobiles, we have to be very cautious, because exposure

data, especially, is not there in terms of what the composition is, and only in limited studies, mostly Glenn Cass' study, God rest his soul, did I really feel confident in some of the numbers on the source apportionment for the automobiles or the truck traffic.

Those are my major comments. Otherwise, it is an amazing summary of all the information that is out there.

**DR. WHITE:** I just have one question. Appendix B which gives the aerosol composition data from the speciation network describes the carbonaceous species as having been determined by thermal optical reflective switches, the BRI/Improved method. Is that correct? This is the data from the feasibility or the intercomparison. Joe is nodding his head. Okay, thank you.

So, it was done by a different carbon method than is used in the speciation and trends network?

**MR. PINTO:** That I am not entirely clear about, Warren. We can check into that.

**DR. WHITE:** Okay. Given the differences in the methods that are discussed, that is an important point.

**DR. HOPKE:** George?

**DR. WOLFF:** I just want to bring up two points at this time. The first one goes back to the background.

I guess I am happy with the definitions, because

they came after a long discussion, but I am not happy...I am uncomfortable with the levels, and I want to see a range, and I think EPA is working on that, but I would also like to point out that I was impressed with the methodology that Alan Lefohn presented yesterday as a way to estimate the background, and I think some consideration should be given to that as a better way to estimate the background than the way that we have.

And the other thing that I just want to mention, the initial figures in the chapter...there are maps showing the concentrations of the various measures across the country...I think they would be much more useful if the cut points on those maps corresponded to the standards so that you could look at it and not only see what the concentrations are but see which areas are in attainment and nonattainment.

**DR. HOPKE:** Let me toss in a little more with regard to the background. One of the things that discussed and agreed upon with regard to the risk assessment is that they would look at a distribution. So, clearly, we need that distribution in the Criteria Document. So, you know, somehow, we need to get a distribution of backgrounds that then can get passed on to the risk assessment team as the basis for their...so, we need to look and somehow come up with a sensible way of providing, rather than even a range of backgrounds, a distribution which is what we had discussed needing as a part of the risk assessment.

Okay, let's run down. Petros?

**DR. KOUTRAKIS:** I only have a few comments. I think this chapter has been substantially improved since the last time. The last time, very little was there, and I think the authors went out and really took everything that was available themselves and tried to summarize them, and I think they did a good job.

Still, of course, we really don't have solid data on emission rates, but that is reality.

I think, now, the chapter is too long, and if they could find some ways to make it a little more concise, I think that would really help.

Also, there is somewhat of a lag between this chapter and Chapter 2, especially, for instance, particle formation process. Both chapters talk about that.

Otherwise, I have some very minor suggestions which I have provided in my written comments.

**DR. HOPKE:** Ron, comments? Jon, comments? Sverre? Fred? Jon? Jane? Warren? Allan, you have something else?

**DR. LEGGE:** I just have additional question. On some of these speciation tables, could somebody explain to me how the minimum measured value is smaller than the minimum detection limit?

**MR. PINTO:** That is a good question, Allan.

**DR. LEGGE:** Yeah, yeah, there should be

some indication, then, in the text if that is the reason.

**DR. GRANT:** Yeah, a clarification for that.

**DR. LEGGE:** Right.

**DR. GRANT:** Let me just note on the new data to be added in, we do think we will have enough quality assured data all the way through the year 2001 to add in. That is what we are hopeful for and have pretty good reason to think we can.

**DR. SPEIZER:** Can I just comment on that?

**DR. HOPKE:** Yes, Frank?

**DR. SPEIZER:** I was going to raise before you said that a generic issue, and that is that I am concerned that...I don't know what the right number is, \$500 million being spent on speciation activities, and they are basically occurring during the period where they missed out on the '96, and they are going to be missed out on this one, and then they are going to be forgotten for the next.

So, unless we can figure out a way to update, as Les just suggested, through 2001, maybe even further than that, I am not sure, because I think you can get data now through March of 2002...

**DR. HOPKE:** Not that has been fully QA'd.

**DR. SPEIZER:** Yeah, maybe it hasn't. I am not sure, but I think, certainly, updating that data is going to be very important to have somewhere in this document,

because, otherwise, we just spend an awful lot of government money, and it is going to get lost.

**DR. HOPKE:** Jon?

**MR. BACHMANN:** We are about to put a summary of 2001 speciation data...I'm sorry.

**DR. GRANT:** Jon, the microphone is over on this table here.

**MR. BACHMANN:** Jon Bachmann, Office of Air Quality Standards. We have prepared a summary of sort of the first full year of speciation sites for over 40 sites. We are going to put it in the current trends brochure which is due out very soon which means we have gone through some QA process and we have a way to report the information. We want to report some of the details that you are concerned about as well, but if that is something you want, we can obviously provide it to you.

**DR. HOPKE:** That, I think, would be very useful.

Dr. Lippman?

**DR. LIPPMANN:** No.

**DR. HOPKE:** Okay. Let me just throw out another development that is going on. I met with Linda Sheldon this week. Those of you on the monitoring subcommittee saw my email to her in which I suggested that because we were going to have some delays in completing the CD that this gave us an opportunity to look at alternative

coarse monitoring opportunities.

So, they have agreed that they will be moving ahead with some testing of sequential dichots and continuous coarse monitors as well as the current side-by-side, so we should have, potentially, more choices down the road to look at when they are starting to prepare the FRM decisions.

So, I think we are moving ahead with, potentially, some better measurement technology in terms of getting coarse monitoring.

**MR. POIROT:** Phil, can I come back to the one...this background point that is, obviously, very important? I just wanted to put in a little bit of a qualifier. It is a very interesting and engaging topic for discussion. Lots of people have lots of ideas about how it should be done better, but, really, you have almost got to go back to John Fragonas' guess for the APOP SOSTs, and even there, we had to hire our best gambler, our best guesser, and the actual process of really trying to improve upon that intelligently is not easy.

I just wanted to put that qualifier in. Let's recognize it. I think it is something that a lot of people are working toward. I would almost relegate it into that category of something that is going to come, but it is not going to come fast. So, maybe, as I say, what we are looking for here is just an improvement by degree so that we can talk about a range without really demanding that we actually somehow codify this natural background.

**DR. HOPKE:** Well, I mean, I think, at this point, we need to just ask them to look and see and do the best they can. I mean, we would like to try and get a distribution. I mean, that was one of the things we talked about extensively in the February 27th phone call. So, to the extent that it is possible to do, you know, we would like to see it, and, obviously, the place for it to be is in the Criteria Document.

So, then, again, the question is, are any of these things sufficient that people are going to want to review this document, this chapter, again in detail? Does anybody...would anybody see a need for a thorough re-review of this chapter?

**DR. WHITE:** When we provisionally sign off on these chapters, are we keeping open the possibility of revisiting the summaries for the chapters? For example, we are talking about putting in the speciation and trends summaries in this...

**DR. HOPKE:** I mean, again, we are not closing them off entirely, but the point is that we are saying, you know, let's get in the literature up through April 30th, as Dr. Grant has suggested would be done, let's fix these things that we have said, and next go-around, we are not going to spend a lot of time in the meeting going over individual chapters. We will ask for whether there is anything that is a serious problem, particularly if all we

have to do is fix summaries to make the final approval, then that is a pretty easy task.

In other words, I want them to know, basically, what the final rules of the game are to get this done where we will be in a position to say it is over.

Fred?

**DR. MILLER:** I would like to just follow up, though, on what Warren has brought up, because I think that the integrated synthesis chapter really should rely on those summary sections. So, I wouldn't like to wait. I would like the next time to see it...and it is a general comment for, particularly, 6 and 7, that there is more emphasis on the summary, that it is the kind of material that you are going to want to move forward to synthesize.

**DR. HOPKE:** Right, exactly.

**DR. MILLER:** And yet, we will still have one more shot at it, that don't just leave it, because I can guarantee it is going to be kicked back on a lot of them.

**DR. HOPKE:** Yeah. Okay, so, we are done with Chapter 3. Chapter 4, Dr. Taylor?

**DR. TAYLOR:** This is going to be an easy effort. My comments really fall into three categories, and the first is really an overarching issue that continues to permeate the CD, and then the other issues are the ones you have in written form from me, and I think you can handle those pretty expeditiously.

Now, on this overarching issue, my personal assessment of PM effect in the environment places a very low risk on the environment, and the processes and pathways by which I arrived at that decision are certainly not documentable, certainly not to me, certainly, in any quantifiable manner. And I get the same sense from Chapter 4 that the Agency has made the same conclusion that there is a minimal risk.

However, I can't follow the pathway and the process by which the Agency worked to that degree of closure, and I think it is important, unfortunately not at this point, but certainly for future CDs, I simply think we are at the stage now, after three decades or more, that we lay out the assumptions, we lay out the process by which you develop the way the Agency goes about the risk.

I think it is fortunate, at this point, that PM probably is a minor issue with respect to the environment, but there are likely to be issues down the road in which the environment will play a larger role, and without having some developed approach for how we bring that to the table, fold it into an integrated summary, is going to leave me and maybe other colleagues with the same dilemma. So, we are fortunate in where we are right now.

In light of the above and assuming what PM issues those of us will make comments on that are major or minor, I conclude that the chapter, at this stage, can come to closure.

I did exhort the Agency just to recognize that this development of a coordinated and integrated framework for addressing the risk in the environment, we have been way too long in doing that. I think we come into a chapter in which we have disparate pieces pulled together. When you get to the end, there is no way of taking that information in a cohesive manner that gives us the ability to recognize what the risk is. I don't feel comfortable with that. I don't think you are in a very good position to defend it when it gets to an issue that is really important.

So, I would exhort the Agency to sit down now while you have a breather on the environment, develop some sort of general model by which you are going to walk through that effort, so that we have that in place, that there is some agreement. The worst case would be where if we come to an issue that truly is a risk issue that needs to be addressed, I don't think we are in a position to address that.

Then, there are other issues that I have. I think you have that in writing. All of those can be handled in probably less than a week's time, at most. My colleagues may have some others, but I think we can easily bring this to closure.

**DR. HOPKE:** In terms of the framework, have you looked at the EPEC framework?

**DR. TAYLOR:** Yes, I think the EPEC framework has some components to it that could easily be

adopted by the Agency in how we pull together these issues. There probably need to be modifications, because that was done for a specific purpose.

**DR. HOPKE:** Right, but that might be...again, in looking ahead to the ozone document where one expects the ecological effects to be much more important, that might give you a unifying framework in which to look at the risk, the ecological risks, in a sensible way that we really can evaluate them appropriately.

**DR. TAYLOR:** Right, I agree with that, and I, you know, I think, as you look through the document, when you go to the integrated summary which I was asked to comment on which was really easy for me, because in the integrated summary, there is no mention at all on the environment. And I understand that you rested on the NRC report, given the focus of this, but at the same time, if you don't have a game plan for bringing that to the fore, there is going to be a point in time in the future that we will be at loggerheads over how to deal with the issue of risk to the environment.

**DR. GRANT:** I think the point is well taken for, especially for, the ozone document that we are in the process of bringing along and have the committee, you know, review the plan for the document sometime this fall. So, yeah, certainly, George, we will take a look and see the extent to which we can sort out something of the sort that

you are recommending.

**DR. HOPKE:** Dr. Legge?

**DR. LEGGE:** Well, this is going to be very interesting, because I totally disagree with my colleague, but I guess that is why we are here.

I thought this chapter was a substantial improvement over the previous one, and in contrast to Dr. Taylor, I found that, in fact, this chapter shows really quite clearly that there is a signature of response of PM deposition in the environment.

The problem, I think, goes to the whole way in which standards are being formulated and set. In this particular case, it is made abundantly clear in this chapter that PM is a mixture. It is very difficult to isolate which is the role of PM in isolation from the other gaseous pollutants as well as...criteria pollutants as well as organics.

Further, the averaging times that are being considered are 24 hours and annual. Well, ecosystems just simply don't work that way. You are dealing with a cumulative response, and, basically, what you are seeing in some of the measurements that are being made in both terrestrial and aquatic systems is you are seeing a signature of a response of these ecosystems to long-term cumulative stress.

So, what this is suggesting is that we need to look at ecosystems in a different way with different averaging times, in a more comprehensive way, because the ecosystem is

telling us that things are happening. We just have to be smart enough to figure out how these things are happening and how we can stop...decrease the rate.

So, I think PM is an issue, but I think we have to look at it in a different way, in a different form. So, I think, in this case when you are talking about primary standards and secondary standards, it is going to require some imagination with respect to ecosystems, and I make the suggestion that perhaps some modification of the critical load approach that the Europeans have taken might be the way in which to do this.

I am sure Jon is just going oh, no.

**MR. BACHMANN:** I love it, but it is not allowed under the Clean Air Act.

**DR. LEGGE:** I understand that. I understand that, but I don't see any other way to deal with it, because it is a cumulative issue.

**DR. HOPKE:** Are you suggesting something different in terms of how the document, this current document, should be framed?

**DR. LEGGE:** I am suggesting that in the summary that it be recognized that there needs to be a paradigm shift away from simply dealing with pollutants in isolation, and they are going to have to be dealt with from an environmental perspective collectively. We have to go there eventually.

I mean, we have been really successful in decreasing exposure of receptors to acute concentrations, and that has been great, but the catch is the receptors don't die any longer. The receptors just simply get sick, and it is difficult for us to determine what part of the milieu that the receptors are being exposed to are the responsible agents. In fact, in the case of the ecosystem, I think it is very straightforward exposure, and it is cumulative over time.

So, I think we need, as we go into chronic, long-term exposures, we need to change the way we are looking at cleaning up the atmospheric environment and its potential impacts on the terrestrial and aquatic systems.

I have specific comments, but I won't...they are not crucial.

**DR. HOPKE:** Okay. We have written comments from Dr. Rowe. We have specific comments from Dr. Rowe. Again, most of these are...you know, there are no real show stoppers here. A number of specific comments in terms of improvement of the presentation, but I didn't see any here that I saw that represented really significant problems.

The one thing that he comments on is the section on economics where he comments: With one unfortunate exception, economics has been deleted from Chapter 4 and the entire CD. There are few new relevant welfare effects studies since the last CD, e.g., damages of air pollution on cultural materials, reanalysis of prior visibility studies, and limited other work.

If these other past economic studies can be used in subsequent standard setting steps without reference in the CD, omission of economics or human perceptions and values in general is okay. However, without this literature, there is little in Chapter 4 to indicate the welfare significance to humans of the actual or potential visibility materials in ecosystem impacts identified.

So, that may be something that is worth looking at again.

Warren?

**DR. WHITE:** Well, I hesitate to get into the game between George and Allan here, but there was something I didn't under...maybe I don't understand. Much of the discussion in the ecosystem section, it is not clear to me that it is about particles specifically. For example, there is reference to a major concern is nitrogen saturation, the resultant deposition by large amounts of particulate nitrates, and that is indicated that that is happening throughout the East.

I am surprised that there is enough...people don't see very much of particulate nitrate in the air in the East. I am surprised that the amount of particulate nitrate in the air would be sufficient to be a problem in the ecosystem.

**DR. HOPKE:** 3 to 5 mics per cubic meter in the wintertime.

**DR. WHITE:** And is that enough to...

**DR. HOPKE:** I don't know, but, I mean, there is...in the wintertime, there is a reasonable fraction of that fine particle mass that is nitrate, and given the effectiveness of snow as a scavenger.

**DR. WHITE:** I would submit that that is fine nitrate, largely fine, and I am still surprised that that would be a problem in terms of deposition, but perhaps the point is that...is to echo Allan's concern that we are in an inappropriate straightjacket in being forced to look at things by specific criteria category so that this is, in some sense, for the ecosystem, for vegetation, it is not important whether this stuff is in particle or gas form.

Also in the ecosystem section, the turbidity discussion, I think, would benefit from a review by EPA's own visibility people. It is a bit outdated, and I have comments, specific comments, on that.

On visibility, the visibility section is much improved from the previous version. My major concern, my major remaining concern, is that it still doesn't really address the connection between visibility and fine particle mass which is the primary standard that we are using for PM. It talks about visibility in terms of chemical constituents and makes a sliding reference to a noisy relationship between visibility and PM<sub>2.5</sub>. That relationship isn't all that noisy, a.

It would be easy to put examples in from our

existing improved monitoring data, and that would be a powerful support for connecting real-time exposure to fine particle mass to communicating, in real time, people' exposure levels. Visibility is easily monitored in the continuous real-time manner, and also, the connection between PM<sub>2.5</sub> and visibility which, again, is easily monitored continuously, that addresses Phil's observation earlier today of the sparsity of data available for epidemiological analysis on PM<sub>2.5</sub>.

We have real-time continuous indicator of PM<sub>2.5</sub> in the form of methylometer and transmissometer and ASOS visibility monitors that are available hourly every day, and it is just a real...I think it is a hole in the document to neglect the existence of this very real connection.

**DR. HOPKE:** Rich?

**MR. POIROT:** I agree with everything Warren just said about visibility specifically, including I thought the summary information was very good, the appropriate references, the other more detailed information were very good. A lot of the illustrations presented in this chapter are taken from the improved network data and so forth.

One thing that I think is missing is really I am not seeing this actually opening the door clearly to the possibility of a secondary standard for the purposes of protecting visibility in non-Class 1 areas, the rest of the

98 percent of the country. I really think that aspect of things could be emphasized a little bit more strongly.

And, as Warren says, the fine mass visibility relationship wobbles, but it is not all that wobbly, and it is actually very sound. Actually, I could...I don't have it with me. I could show you a diagram out of the 1969 EPA Criteria Document for sulfur oxides that, if you put it in the right units, it is  $3 \text{ m}^2/\text{gram}$ . We have known this for a long time, and every PM review, we always consider the possibility of a secondary fine particle standard. Generally, we find a way to reject it, better ways, oh, my God, we can't do the same thing east and west.

Well, I don't know. If you look at some of the peak 24-hour concentration east and west, it is not so different. You could actually do something, if you had to, that would do quite a bit of good east and west and everywhere. So, I would like to emphasize that particularly.

The second general comment I have on the chapter relates back to our controversy between our ecologists as well, and I noted that, in some cases, the chapter seemed to be having a hard time deciding whether do we need to actually stick the particles. There is a lot of really good information on particle deposition per se in isolation, and it is partly a question but partly a comment.

Can we only hound it if it is deposited as a particle and then as a fine particle or as a coarse particle, or what about a particle that gets a little humidity and

swells up, and then we count it as deposition of a coarse particle, and then a little more humidity, and all of a sudden, it is in a cloud droplet, and it gets deposited. A little more, and it rains.

So, we are having a hard time deciding can we only count the particles. The ecosystem doesn't know this, you know, and there is other stuff going on that is complicated, and there is that need.

One way to think about this, deciding what can we count and what don't we count and which constrains CD review or not, is that at some point, were EPA to consider a secondary standard for ecological purposes for fine particles, were they to go that route, they would then need this criteria information to make a justification of why the standard is set at this level and what the benefits of setting it at this level would be.

You could argue the same information equally belongs in the SO<sub>2</sub> criteria document. It has got to be somewhere, though. It has got to be somewhere, and it could as well be included here. So, that is the other.

**DR. HOPKE:** Dr. Lippmann? Dr. Vedal?  
Dr. Wolff?

**DR. WOLFF:** Yeah, I have some comments. In fact, I have some comments I am very concerned about that pertain to the climate section, the effects of climate.

This section can be divided into two parts, a

general part where we talk about the general aspects of climate change, and then a second section that focuses on the effects of particles. I am going to talk about these two sections separately.

The first one is when they talk about the general global climate science, and they touch on a very...on a number of controversial issues here on which there is no scientific consensus. There are two ways in which they can approach this. One is to rewrite it in a completely objective way, or, an easier way is to skip it, because it is not necessary for the discussion on particles, and that is what I recommend they do, is to skip this discussion.

Then, turning to the section on the effects of particles on climate, this is a very disjointed discussion that doesn't flow in a logical way, and I suggest that they do it in a logical way by following the following framework which would be, first, to discuss the role of scattering particles; second, to discuss the role of absorbing particles; and then, third, to discuss the role of cloud enhancement due to particles.

Now, they rely heavily on the IPCC Third Assessment Review, and I think that is probably okay for the discussion of the role of scattering particles.

There have been a number of new papers that have come out since the IPCC report on clouds that needs to be incorporated, and, unfortunately, most of what we know on the issue of black carbon which is the primary absorber has been

discovered within the last two years, and none of those references are covered in this section. So, they are going to need to get hold of the latest literature on the effects of black carbon in climate.

**DR. HOPKE:** Can you provide those references?

**DR. WOLFF:** I can. I didn't do it. I didn't spend the time to do that.

**DR. HOPKE:** Okay. Dr. Speizer?

**DR. SPEIZER:** I want to pick up on Warren's comment. Do we have enough...are there data out there that would allow us to use the co-location using methylometer data or visibility data against particle data to come up with some kind of correlation?

**DR. WHITE:** There are many sites in the improved network that have methylometer data co-located with the aerosol data. Those are remote sites.

There is also the ASOS system operated by the Weather Service which is more or less co-located with some monitors in which Rudy Husa is looking at, on behalf of EPA, and, in fact, there is a mention in this draft that they expect that ASOS PM comparison to be included in the next iteration, and I have seen Rudy's work, and that also supports the...my claim that there is a good correlation between methylometer and PM<sub>2.5</sub>.

**DR. SPEIZER:** I think it would be useful

to have that, if we could. I think, in fact, when it comes to that paper, you are going to want to use best available levels, and that might help inform it.

**MR. POIROT:** Can I only add one point to that, that this ASOS data is available, so called, but it is available and an unfortunate decision was made in the archival storage processing of this data. It is still quite useful under very polluted conditions, but the data have been truncated and so forth, and maybe this isn't the place for it, but I was kind of thinking it might be nice to have a little bit of an editorial reference to that in this document using the term unfortunately. Unfortunately, these data are not available.

Because there is interest within NOAA actually in making the data available, but they don't have the budget support to do it. It would be extremely valuable, the fit between that data and some of the continuous fine particle data. When it is accessible in its raw form with appropriate adjustment for humidity, it is possible.

Really, it is unfortunate. It might be worth slipping that term in.

**DR. HOPKE:** Yes?

**MR. GARNER:** Dick Garner with EPA. EPA has been for five years developing an ecological risk paradigm, and, currently, NCEA-Cincinnati is awarding contracts for the study of deposition on wetlands and what it

might do to affect aquatic areas. The authors of this chapter in this document looked at that paradigm, and they agreed with the general group of ecological...terrestrial ecologists, I should say, who have looked at it also and felt that it did not fit for terrestrial areas, and that is one reason why it was not used in this document.

Thank you.

**DR. HOPKE:** Petros, did you have any? Fred, do you have any comments?

**DR. MILLER:** No.

**DR. HOPKE:** So, is there any, again, do we need to look at this again?

**DR. WHITE:** Returning to Rich' s point about the importance of laying a foundation for any secondary standard, as it now stands, this draft does not permit consideration of a secondary standard, because it does not make any connection between visibility and fine particles as measured by the FRM.

**DR. HOPKE:** Okay.

**DR. WOLFF:** And I would like to see the climate section.

**DR. HOPKE:** So, it sounds like this one may need to have a little more looking at the next go-around. Is that a fair statement? Okay, there are some things here that probably need a little more attention, then.

**DR. GRANT:** Yeah, I think the things just

mentioned under visibility, we are going to have to, obviously, take a pretty good look at that.

**DR. HOPKE:** All right. Let's move on, then, to Chapter 5. Paul?

**DR. LIOY:** Sure. Chapter 5 has been improved quite a bit since the last version. I do have three main points that, I think, still have to be considered by the authors, and then, also, within that, there may be a need to determine where dose fits between Chapters 5 and 6, because I haven't seen a dose calculation yet, which I think we do need something, and I have a couple of ways out of that, but let's go through my three main points.

One is that I think one of the things that troubles me is that there is a continuing lack of coherent discussion about how these exposures related to any biological effects, whether it is derived from epidemiology or whether it is derived from toxicology. There needs to be some discussion, not on page 80 through 97 but on page 1, in this chapter that starts out saying we are worried about exposure, because there is a potential for biological effects.

We know, at this present time, that we have a standard for 24-hour average and a standard that is associated with an annual average, but there could possibly be other considerations, maybe even 8-hour or whatever, especially with peak concentrations. We don't know at this point in time what the toxicology and maybe the epi will tell

us at some time in the future, but I think you need a plausibility argument of why we are worrying about this in terms of population and the general environment.

So, I think a real serious one-page discussion is necessary explaining this in the context of exposure and linking it to what one be thinking about in Chapter 8 when you start talking about epidemiology and in Chapter 9 when you are starting to talk about issues of risk assessment. That wouldn't be on page 1, but I think that kind of issue needs to become part of the argument within Chapter 5, and I don't see it.

The second thing is that when you look at that and try to look for an argument as to what are the important features of Chapter 5, I am left at the end with a laundry list, and I don't think that that is appropriate when you start looking at a risk paradigm. I think what you really have to do is decide what are the most important features of this chapter that relate to why we have to consider exposure to ambient aerosol as part of the risk paradigm and as the data or, at least, the summary information necessary to use it in Chapter 9.

We have figure 9.1, and I have a general comment that every chapter should start thinking about their summary in terms of how you take the essence of each chapter and driving it into one of those boxes for use in the risk assessment in Chapter 9. I mean, I don't see the summary...I think some summaries are better than others. In one section,

there is no summary, and that is Chapter 3. I just see a little bit of information here or there.

But I think that that will help Chapter 5 a lot, you know, prioritize what the major points are. I think that you have a good starting point, and either William, you wrote it, or Les, you wrote it, or both of you wrote it, because the initial letter to us this past weekend has a good starting point for four bullets in Chapter 5 that have some value for moving this forward from Chapter 5 to Chapter 8 and to Chapter 9.

We just don't have that at this point in time. I think it is very important, because it is an important chapter. It starts beginning to bring in health effects and how we translate from ambient pollution to exposures and dose relationships.

That brings me to the topic of dose. I think that...well, when I read the dosimetry chapter, and I read the exposure chapter, I said, where is the calculation of dose? We really do need some.

I mean, we have to say well, when is the dose too long that we are receiving of these aerosol particles? There is nothing in this document relating to that, and I think that is a critical path that has to be walked, and a critical analysis has to be done.

You are fortunate in one regard, that there has been just finished, but I don't think it is published yet by my group, but it is finished, an analysis of the first

population-based exposure-dose model has been done for Philadelphia data, and it actually does come up with doses to the general population that can be derived from the ambient pollution in Philadelphia for 1999. It might be worthwhile to work with Dr. George Opolos of my group to get that report or Dr. Ostinet from EPA, because they worked on it together.

And that would be a very good way to start, because the calculations have been finished. They use a good...they use the lung deposition model that has actually been cited in the dosimetry chapter, and it will help out in terms of coming up with what the doses of fine particles are to a relatively large robust population, Philadelphia, Pennsylvania.

So, I would recommend working with that data base, since it has already been done, and I will encourage Dr. George Opolos to get the peer review publication out, but I think the data alone would be very valuable for EPA to work with to come up with a dosimetric calculation, because I think that that is the important linkage between Chapters 5 and 6 and 7 that is just not there.

I think there is another...the other final concern I have...and this could probably be handled in a paragraph somewhere in the beginning...we talk about distribution functions for various activity patterns and inhalation rates and all this other stuff which affects human individualized exposure or subpopulation exposure. However, none of the equations of a distribution function in it. They all are

based upon single people. I gave a couple of references to find a couple of equations that will help.

But I think, more importantly, is that you need a section that really clearly defines, in the beginning, one paragraph that says when you are dealing with personal exposure, you are dealing with a lot of variability among individuals and that when we are dealing with ambient air pollution, we have to recognize that although there may be a very...you know, we are being driven by the outdoor air pollution problem, and that is the way the standard is being designed, but one has to consider the variability of any indoor contribution if you are trying to assess the differential between personal and ambient exposure.

That is not to discount the ambient exposure and, in fact, to actually indicate that some of the ambient exposure that occurs indoors from aerosol penetrating outdoors will be dependent upon where you sit on the frequency distribution for either infiltration, age of the house, you know, level of activity you have in the home.

So, there, I think, it is important to recognize that it is not just in terms of decrease of the outdoor air. It is actually coming up with a better profile for the total ambient exposure which you have nicely laid out in the equations that Williams described in the chapter.

And I think that is it. I do have one concern that needs to be revisited when this chapter is revised, and that is the dose. I would really like to review it and make sure

that it is done properly and comes up to a standard where we can start looking at how it links to other chapters. Also, I would like to be able to review how the summary reflects how it is linking to the risk assessment in Chapter 9.

So, those are my concerns. Most of the rest of the chapter, I think, has been a vast improvement.

**DR. WILSON:** Paul, if we were to put the dose calculation in Chapter 9, since we will have the exposure and we will have the dosimetry, then we could use that as part of the integration to integrate exposure and dosimetry and have a section in Chapter 9 on calculation of dose.

**DR. LIOY:** As long as you link...as long as the basic work with the PM shed model that was used by Ostinek and George Opolos and any other data that you might find are found at the end of Chapter 5...all right...which would be fine, or at the end of Chapter 6 or some combination of the two, because I am not sure how...

**DR. HOPKE:** Just make sure it links back properly.

**DR. LIOY:** You have to link to each other in some way, shape, or form, but I think you can work it out. I think fine, leaving it in 9 as the data, but I think you have to have a basis for that, and that would be in Chapters 5 and 6, and I think you have some good data to work with right now, and I think you should utilize that, and it will

help facilitate the process.

**DR. HOPKE:** Petros?

**DR. KOUTRAKIS:** Well, this is the third time...

**DR. HOPKE:** In the mike.

**DR. KOUTRAKIS:** Yeah, I said that this is the third time I reviewed this chapter, and I must say that it has come a long ways, and I think it is pretty much done right now. I think the strong points of this chapter is that...the strong point is that it really provides a very comprehensive review of the recent studies. They have used many tables to tabulate information.

I think, finally, provides a balanced view. It originally started where only outdoor pollution is bad and don't worry about anything else, and I think many authors participated and now really present many studies rather than just selecting some studies here and there.

I think where the chapter fails and, to a greater extent, the executive summary fails, is to really articulate the findings of the recent studies. Although it presents all studies, very inclusive, I think it really fails to highlight what we have learned, you know, over the last several years.

And I am just going to say, to my opinion, what we learned and how this is different from what the thesis of the chapter is. I think we learned that personal exposures correlate to other concentrations, but there is a tremendous

intra and interpersonal variability, and that variability depends on many factors, such as indoor sources and the variability of the penetration of outdoor pollution to indoors.

And from the initial studies like the team studies and Harvard Six-Cities study, we always assume that it is the indoor pollution, you know, that really weakens the correlation between personal exposure and percent concentrations. However, these recent studies really suggest that it is the home characteristics also can introduce some variability, because the impact of outdoor sources can vary, and depending upon the penetration efficiency of particles and depending upon the air exchange or use of air conditioning. And all these factors might be different by season and geography.

Now, in the chapter, especially in the executive summary, there is again back to this simplistic approach that says well, if we were able to measure all the people outdoors and take the mean, that will correlate. It might be intuitive, and I am not saying that I don't believe that, but I think there is no data and there is no logic path to substantiate that statement.

The other thing which really bothers me a lot is this, I think it is, Wayne Ott's approach which was adopted by the chapter and the executive summary especially where they took personal approaches in three different cities, I think one in Canada and two in the United States, and they

regressed them on the outdoor concentrations, and they came up with the correlation was very scattered at the intercept, and they said well, the slope is the penetration of particles wherever you go in the United States or in Canada, and you can even use that in Australia, and here is the entire science, and the intercept is what comes from indoors.

That is a very simplistic approach, and I don't have the time to go through it, but this is the main thesis of, you know, the exposure in the Criteria Document, and I think, really, it is quite sad after, you know, 20 years of exposure assessment studies to have that kind of simplistic approach.

Then, the Criteria Document for the risk itself, on the one hand, everything is the same and we use a slope, and then, they go and they prepare the Janson paper where she went and she took the heterogeneity among cities, and she was able to explain some of that variability on air conditioning use which says that there is variability of outdoor impacts and indoor concentrations. So, that, again, is quite troublesome.

There is a great deal of references to the Espoli study in the chapter, and I personally think that the way that the Espoli study was designed is not appropriate to address the very specific issue of personal correlation versus outdoor concentration. If you remember, the Espoli study had two samplers that one was turned on when people were outside, and one was turned off when the people were inside, and also, it has a limited number of measurements per

individual.

Now, I know we all get too excited about NRC 1 and NRC 2...I am talking about the research priorities...and about the validity of the epidemiological studies, and we really have forgotten about chronic exposures and exposure assessment, and I think probably it is too late now, but maybe in the next Criteria Document, I think we should really start thinking about these issues and not just focus on the, you know, the correlation of personal exposures to outdoor concentrations.

Also, I would have liked to see a little bit of the implications of exposure assessments in the particle health effects arena. I think we have been concentrating on the epidemiology, and we have got a little bit sidetracked, but we really have to bring exposure assessment and have epidemiologists to provide a better interpretation for their results and also the toxicologists, and I think, you know, the Criteria Document, in the toxicology and epidemiology sections, they talk about these issues, but I would like to see them as well in the exposure assessment side.

Otherwise, I think the chapter is very comprehensive, and in spite of my, you know, few comments, I think, really, it is well done, and it is almost set to go.

**DR. HOPKE:** Okay. Jon?

**DR. SAMET:** I actually think Paul and Petros have made my main point already which is the lack of linkage between Chapters 5 and 8 and probably on into 9. It

just stands by itself, and I think it could do a better job of cross linking to Chapter 8.

In fact, Chapter 8, as it stands right now, includes a lot of the same material as in Chapter 5, but it is not as well done. So, in fact, what really should be done is a better linkage from Chapter 5 to Chapter 8, and we could probably remove a lot of the exposure-related stuff in Chapter 8.

I have a few other minor points. There seems to be a premise that it is, actually, lung dose that is of interest, but I think there should be a reminder that it is, in fact, dose to the whole airway that is of interest in the document. That is stated firmly up front, and that actually needs to be sort of restated and fixed.

Otherwise, I thought it was improved. Of course, there have been a lot of new exposure studies since the last Criteria Document, so there is a lot of new information to bring forward into the chapter.

**DR. HOPKE:** Okay. Frank?

**DR. SPEIZER:** I don't have much to add. I had a lot of written comments that are sort of relatively minor.

I was concerned about the way the chapter started, that it was defining exposure too narrowly in the sense that it was sort of taking a reading on exposure which really was more in the province of Chapter 6, in some sense, that this was solely environmental exposure, and much of the

measurement is being made in the environment, so I think we need to be clear about that.

The other is sort of a relatively minor issue, but I think it is probably something that ought to be looked at. In a number of the tables, there is not a consistency in what is reported in the various columns of the tables. For example, in table 5, in some places, the summary...some of the...you have got measurements that are sort of listed as either in the chronic section or as actual values and listing values where there are blanks in places that could have had some of those values. I think just more consistency could be generated in that.

I don't have any more to say than that.

**DR. HOPKE:** Okay, thank you. Dr. Zielinska?

**DR. ZIELINSKA:** I agree with Petros and with Dr. Samet that there are some problems with this section, especially in different places, specifically, some of the summary especially. It is kind of contradicting whatever is in the discussion in the chapter.

It is just like you are saying in the chapter that it is so important that the personal exposure is very complex, it is indoor/outdoor, and then, in the summary, it says but still, because indoor is independent of outdoor, we can go ahead and just do outdoor and forget about the other part which doesn't really seem to be very logical. Nature

just doesn't work this way. It is everything is kind of important.

So, about the PM spatial variability, it says in the chapter that there is some variability which is important, but in the summary, it says well, basically, it is uniform. So, it is kind of contra...it is not very consistent. There are a lot of problems with this.

I am also not totally convinced that sulfate couldn't be used as a surrogate for outdoor PM concentration, especially the difference in distribution in the fine and things like that, and I am not so sure that there are no really indoor sources of sulfates like, for example, some humidifier with water which could be actually introducing some sulfate in the indoor.

So, I do have some type of problems, but other than that, I think it is a very good review of the existing literature, and it is probably very close to being done.

**DR. HOPKE:** Okay, thank you. Mort?

**DR. LIPPMANN:** Some of what I wanted to say has been said. It is a thorough review, it is pretty competent, and doesn't need a lot, but the introduction is really the pits. It just doesn't do justice to the chapter, and it doesn't make the bridges that need to be made to the other chapters and the epi and the dosimetry, as Paul has mentioned.

It seems to me that one of the easier ways to get

it in the right framework, as a start, is to take page 2 from paragraph lines 3 to 11 and move that up front. The words are there, just in the wrong place. And then start to build a bridge to the epidemiology and the reliance, of necessity, on the ambient monitors as a surrogate for exposure and how that ties together with that and the interpretation one can give to the epidemiology.

The first paragraph, as it exists, just, you know, it doesn't add up. Lines 13 to 15 are very poorly written, human exposure data and models provide the link between monitoring data and atmospheric models and lung deposition models. In what way? How? It doesn't recognize that we have estimates based on models; we don't have reliable values based on models. Models serve a purpose, but this sort of implies that models can do a lot more than they are capable of doing.

So, I put that in my written comments, and I suggest that that, together with the tighter ties to what this really means in terms of delivered dose and to the interpretation of outdoor monitoring data in relation to epidemiology is the really critical failing, but that should be relatively easy to fix, and I don't know that we need to hold up the chapter from its completion.

**DR. HOPKE:** Warren?

**DR. WHITE:** No.

**DR. HOPKE:** Allan? Jane?

**DR. KOENIG:** Les, could you just remind

me again, what was the date cutoff for this chapter or do we...

**DR. WILSON:** I didn't quite hear you.

**DR. KOENIG:** The cutoff.

**DR. HOPKE:** At what date did you stop including literature into this chapter?

**DR. WILSON:** The contractor that did the literature review, when we wrote his contract, we were more hopeful than we should have been, and it was cut off, I think, in October. So, we have added a few things in later, but we do need to add a few more important papers since then.

**DR. KOENIG:** Well, I guess I would say I know there are a couple papers that have been published in the Seattle panel, say, and I think it would be good to...

**DR. HOPKE:** Could you speak closer to the microphone?

**DR. KOENIG:** It would be good to get the Seattle panel data in if it fits within your framework.

**DR. HOPKE:** Joe?

**DR. MAUDERLY:** I have a difficulty with something here that, since no one else has mentioned it, this may be a singular deficiency in my understanding, and maybe my colleagues can resolve this for me over lunch.

We also sit in on discussions about engine emissions and other kinds of source emissions. Now, in those discussions and those documents, some of them long-awaited,

you know, much is made of near source exposures. For instance, if we want to talk about health risk, why, we invoke people standing near a bus stop in New York or some other place. If we want to invoke, and especially in the current atmosphere, particle effects from vehicles which this document claims is also important, we talk about gradients of effect from roadways, school children having all kinds of problems, which I don't argue with.

But here, we have a statement on page 5-107, again, one of the main conclusions from this chapter is that the available data indicate that PM mass concentrations, especially fine PM, are uniform and that if you have a few monitors in town, you can correctly estimate people's exposure and, if we get this whipped into shape, dose.

Now, maybe I am missing something here, but I have a hard time reconciling those two concepts.

**DR. LIOY:** Can I...I think that is part of the issue where the averaging time and the biologically relevant exposures come in. I mean, they are basing it on the 24- hour average and the annual average. There could be peak exposures that are gradients that are associated with other, you know, local, near-source issues that have been ignored, I think, in the way they have established the exposure paradigm for this chapter, and I think you are doing a disservice to the science by not including information like that.

**DR. MAUDERLY:** But if we think we have

evidence, I mean, to support this, again, if we think we have evidence that proximity to a roadway or, presumably, any other source of potentially hazardous materials is related in a significant way to health outcomes, then, you know, I think we are denying something here. You can't have it both ways. There are issues here, and they are not addressed.

**DR. MILLER:** I have a comment, but were you going to enter into this discussion?

**DR. KOUTRAKIS:** No, no, I just wanted to tell Joe that we are doing a study in St. Louis where we put people on the bus, and we go from busy and not busy roads and try to understand, you know, the variability of exposures and that kind of thing. I don't know if that is sufficient for you, but...

**DR. MAUDERLY:** Well, there is plenty of literature, you know, that exists that gets quoted in other venues. My point is if there is a disconnect between those points that are made strongly and the point that seems to be made strongly here, that we don't need to be concerned about that.

**DR. SPEIZER:** I would have to agree with Joe. That statement, the more that I look at it, is actually wrong.

**DR. HOPKE:** Okay. Fred?

**DR. MILLER:** I wanted to ask Dr. Lioy if the Philadelphia study that you were referring to, the model

that is used in that, has that been published?

**DR. LIOY:** The model itself?

**DR. MILLER:** Yes.

**DR. HOPKE:** The dosimetry model, you mean?

**DR. LIOY:** The dosimetry model has, yes.

**DR. MILLER:** Well, but the incorporation and putting it into...

**DR. LIOY:** It is in the PM sheds framework.

**DR. MILLER:** What I am getting at is as long as the components of what was done in Philadelphia are represented in the Criteria Document, OAQPS can use that kind of an approach in looking at other areas in that, and it wouldn't rely on having, quote, that Philadelphia study published, and I just wanted to clarify whether or not the components that were put together for that have each been published, because if...they need to appear in this document somewhere.

And my reason for bringing this up is that I don't know if you did cohorts through time and space and demographic patterns that would, to me, represent the kind of thing that was needed. So, that is one kind of dose right there, and we get into a different thing for extrapolation purposes in Chapter 6, but I was just wanting to understand, because it would be very important that the components are, in fact, cited.

**DR. LIOY:** Right. The CHAD data base that was used...CHAD data base was quoted in the Criteria Document as the data base for population activity, near source, far source. I believe the PM sheds was quoted in the Criteria Document. If not, I'll have to check, and I know the dosimetry was, and, also, the atmospheric model has been used. That is the EPA Models 3 that has been used throughout various Criteria Documents, especially ozone.

So, the components, the modeling components, have been vetted. It is just that the analysis which has been done has not been published yet, but the data is available.

**DR. HOPKE:** Other comments, Fred?

**DR. MILLER:** No.

**DR. HOPKE:** Sverre?

**DR. VEDAL:** Yeah, I have just one point that I want to discuss, and it relates to one of the concluding bullets in the chapter which haven' t been brought up yet which is that multi-pollutant...personal exposure studies have suggested that ambient concentrations of gaseous pollutants serve as surrogates of personal exposures to particles rather than as confounders, and that is dropped, and there is discussion of why that statement is made, but this is a big, big deal, to my mind.

This chapter is not the place to do justice to that, and it doesn' t. It rears its head in a much, much bigger way in Chapter 8, and I think that is probably

appropriate.

You know, as a cynic, one might say, you know, there's been this historical move with respect to how to view confounders, gaseous pollutants as confounders. Initially, it is an issue that well, yeah, they are there as potential confounders, but they don't do anything with respect to the PM effect.

That is variably true and not true, depending on studies. Since, I think, to some extent, that has not been an entirely tenable position, now, one next step is to discredit them as confounders by viewing them as surrogates.

And in some ways, the gases can be viewed as surrogates. I don't think that is a silly position at all. Where the difficulty comes in is that now, the next step, assuming that there is some primacy of PM here...and that is not an entirely silly position, either. The PM is different qualitatively. It is not a gas. Perhaps the exposure information suggests that there is some primacy to PM, that there is a much, much better linkage between either personal exposures to PM and the ambient measurements as opposed to the gases, and there is an argument there.

But now, raising the issue is that gases are not confounders in this chapter is a big bomb to drop here, and the issue is huge, and it wasn't resolved well in Chapter 8, and it certainly isn't resolved in this chapter.

I don't know what to do with it here. It is an issue that deserves a lot of discussion. It isn't going to

die in the way it was treated in Chapter 8.

I don't have any suggestions as to how to deal with that here, but it is left quite loose, and it is not just a throw-away line. It is a huge issue.

**DR. WILSON:** Would it be satisfactory just to have a note that this will be discussed in more detail in Chapters 8 and Chapters 9?

**DR. VEDAL:** Yeah, I think rather than just leaving it hanging like that, that might work.

**DR. WILSON:** It seems that it needed to be raised in Chapter 5, because it is an exposure...

**DR. VEDAL:** Yeah, I was torn as to whether it was an appropriate place to raise it, but I think it is an appropriate place, you know, to raise it.

**DR. HOPKE:** So...

**DR. KOUTRAKIS:** Did you want to see more results or just...

**DR. VEDAL:** No, the results are there. They are presented there, the basic data on which the contention is based are presented there.

**DR. HOPKE:** So, a pointer to what it means in Chapter 8 would do the job?

**DR. VEDAL:** Yeah, I think so.

**DR. HOPKE:** Okay. George? Ron?

**MR. WHITE:** I was actually going to raise

the same issue, but I think Joe was making the point about the issue of shorter-term averaging times and a little bit more discussion of that in this chapter and then maybe some linkage as to what the...to Chapter 8 and 9 and what the potential health significance of those shorter averaging time information might be.

**DR. HOPKE:** Sure. Well, and, particularly, as it looks like we are moving to potentially more continuous monitors in the monitoring network where it would give us more access to data on short-time exposures to a much larger fraction of the population. So, a heads up to that evolution might be useful, too.

**MR. WHITE:** Certainly, you know, people are contending that the PM increments are so small that it is not biologically or otherwise, you know, possible to see health effects. Certainly, one avenue to explore is whether or not in children from averaging times we are seeing much larger increases that may be more biologically feasible in terms of having a health effect.

**DR. HOPKE:** Yeah. Okay, can we...

**DR. LIPPMANN:** Phil, can I say one more thing?

**DR. HOPKE:** Sure.

**DR. LIPPMANN:** Picking up on what Ron and Paul had said, perhaps we shouldn't...should have remarked on this earlier, but taken as a given that the short-term PM

standard should be 24 hours is probably a mistake. At least, we should begin to address that as an issue. What does the science tell us about the adequacy of the 24- hour averaging time as the right averaging time for PM, acute PM, health effects?

So, in revising Chapter 5, I think the concept should at least be raised as an issue. We could say traditionally, you know, we have used 24 hours for practical reasons as the appropriate averaging time, but it is not necessarily locked...you know, cut in stone that it has to be so, and what are the implications of considering other averaging times.

**DR. HOPKE:** Yes, Fred?

**DR. MILLER:** I want to go back to the statement about the gases and surrogates. I didn't pick that up, but I, clearly, would not agree even as surrogates if you are talking about coarse mode particles, so I don't know the context in which it was brought.

**DR. WILSON:** We weren't.

**DR. MILLER:** Okay, but even with...I wouldn't even agree with fine unless you made it less than 1 in terms of the aerosol science and the distribution of the data I have seen. So, I think you really need to clarify that and present a more solid argument if you are going to go forward with that.

**DR. KOUTRAKIS:** Or even ultrafine.

**DR. MILLER:** Yeah.

**SPEAKER:** Ultrafine is a whole different issue.

**DR. HOPKE:** All right. Other issues with regard to Chapter 5? It seems to me there are still enough open things that we probably better take another look at this. We are very close. I mean, I think we are in good shape for finishing it up, but I think there are some things here where people would feel more comfortable seeing that linkage from 5 to 8, from 5 to 9, and 5 to 6 that...

I want to take a slight detour here, because Dr. Speizer will only be on the phone until the end of this morning's session, and since he is commenting on Chapter 7...and I am stalling here to give him a chance to find his notes...I would like to pick up his comments now, and we' l l come back to Chapter 7 later, but I don' t want to miss the opportunity to discuss anything that Frank has to say about Chapter 7.

So, Frank, could you pro...

**DR. SPEIZER:** I am still looking.

**DR. HOPKE:** Okay. I am sorry. I should have stalled a little more. Then, what I thought we would do at that point is let' s break for lunch, and then we' ll come back fresh and hit the last two chapters.

**DR. WHITE:** In the meantime, you could ask Petros to tell you some about Robin Williams' routine last

night on...

**DR. HOPKE:** Oh, I watched it. He was on HBO last night. Some of it was amusing.

**DR. MAUDERLY:** Most of us were studying the Criteria Document.

**DR. HOPKE:** So, Frank?

**DR. SPEIZER:** Yes, I have got my comments. I guess my general comment was that...and it is more of an observation than a complaint...is that a lot of the stuff that you have used on the respiratory side is appropriate, but it really isn't new. A lot of it has been seen in the previous CD, and there is really a relatively limited amount of work that is really new.

In contrast, cardiovascular work is new, and it seems to be where the major work is being done. This may be appropriate. That is where I actually think it was directed toward in the sense that that is the mechanism for stuff that we observe that needs to be worked on.

I think the important point that comes through, maybe not as strongly as it could, but it does come through, is that the cardiovascular effects that are being recorded by inhalation groups are occurring or seem to be occurring, maybe not totally but, certainly, in large part, without perceived pulmonary effects, when those are being measured simultaneously, which, I think, is an important point toward the mechanistic issue. It needs to be sort of...perhaps

could be stressed a little more in Chapter 9, and it might be already. I am not sure.

I had a number of minor comments that relate to, really, throughout the text and throughout all the chapters, relate to the use of abbreviations that are not defined very well and not in the general list of abbreviations that are provided.

**DR. HOPKE:** Okay?

**DR. SPEIZER:** Well, the one other issue had to do with metals. There was a discussion of metals. I am concerned that there is a sort of hint or a suggestion that there are experiments that have been done with metals at these concentrations that are, quote, too high, and the results are generally being interpreted as negative and, therefore, maybe not all that important.

On the other hand, it seems to me that the concern would be perhaps at lower levels, you might see effects. And I am sort of harking back to some of the work of Mauderly, not necessarily with metals but with diesel, that suggests that you could overwhelm the systems with high enough levels.

So, I think that there has to be some discussion about the potential for taking this into account in greater detail.

But, in general, I thought the chapter was pretty well written, and I actually thought that it was, you know, they had done a good job.

**DR. HOPKE:** Okay, thanks, Frank.

So, what we would like to do...I might as well bring this up now before people start to bail...is that let's ask people who want to revise their comments, add additional comments, to please do so by a week from Monday. That would be the 29th. And get them to Bob and me. That way, we can wrap up this and get the guys going with all of their comments.

So, that gives you two weekends to reflect, and although many of us will be busy reading PM committee documents this weekend in preparation for another fun-filled set of meetings next week...

**DR. MILLER:** Frank, could you clarify...

**DR. SPEIZER:** What?

**DR. MILLER:** Could I ask you, Frank, to clarify? You said that you didn't think that there were many new citations since the last time. Were you referring to the '96 or since the second draft, because just the last page and a half...

**DR. SPEIZER:** Sorry. I meant...what I thought was...I mean, there are many new citations, but it isn't a lot of new information on the respiratory side that we didn't already know.

**DR. MILLER:** Okay, I see, because the last page and a half of citations are all new studies. That is why I was just wondering.

**DR. SPEIZER:** Yeah. No, I was speaking...

**DR. MILLER:** Okay, but no new established effects.

**DR. SPEIZER:** It strikes me as more of just repeats of what was known before.

**DR. HOPKE:** Okay.

**DR. SPEIZER:** Can I ask that the committee, Bob, could send me the additional materials that were distributed?

**DR. HOPKE:** Absolutely.

**MR. FLAAK:** Absolutely, Frank.

**DR. SPEIZER:** Yeah, okay. All right. Well, enjoy the rest of your afternoon.

**DR. HOPKE:** Thanks very much, and congratulations to your parents.

**DR. SPEIZER:** Thank you.

**DR. HOPKE:** That is a great achievement.

**DR. SPEIZER:** Right.

**DR. HOPKE:** So, let's come back at...let's still make it 1:00 o'clock. We are doing so well, we will foolishly give an extra ten minutes.

(WHEREUPON, a luncheon recess was taken.)

**DR. HOPKE:** Okay, let's reassemble here. Okay, it's time for us to move on to dosimetry and toxicology,

so we want to move into Chapter 6, and our...hold on. Bob would like to go over travel arrangements so we can get cabs organized.

**MR. FLAAK:** I wanted to wait until everybody had arrived, but I see everyone has walked into the room.

**DR. HOPKE:** Except George.

**MR. FLAAK:** Yeah, George has an early flight. Most of the folks are leaving on flights that are around the 5:00 or 6:00 o'clock time frame. How many of you need a ride to the airport at about 3:00?

(Show of hands.)

**MR. FLAAK:** Okay. How many earlier? Nobody earlier than that? Oh, you are earlier than...are you going to go with George? He is on the same flight schedule you are on. 4:15? I wouldn't push it too much. It is going to be busy at the airport with the shutdown at Midway and its being a Friday. All right, we'll find something a little earlier. The rest of you are after that time frame? How many need rides to the airport after that time?

(Show of hands.)

**MR. FLAAK:** Okay, good. That should do it.

**DR. HOPKE:** Okay. Jeff, you are Chapter 6 and lead discussant is Fred.

**DR. MILLER:** I found the chapter much

improved. I have got specific technical comments, but I have five points that I want to bring up that, I guess, I would call in the more major category, not necessarily flaws but simply things that I think need to be included.

The first one has to do with age. The data in the chapter talks about for modeling where there is an increase prediction of deposition in the head with age, but the actual experimental data that are available from Beckrum show...I am sorry, they show an increase with age, and the mathematical models that are stated in the chapter show a decrease, but Beckrum's experimental data shows a clear increase with age, and he looked at children 5 to 11, 12 to 15, and adults.

So, there is, to me, a disconnect between the mathematical models that are cited there and the only real experimental data in that area, and that needs to be looked at, and I have provided the reference there.

In addition, in the age section, there is a lot of information, and I want to commend the authors for adding the numbers of figures. It is certainly much easier to follow a lot of the information.

But relative to age, there is enough information from scattered studies that are presented that I think it would benefit from including a graph, trying to make a composite of the different experimental data that is there. That would help to see if you can actually establish some trends that do relate to age. So, that is one barrier.

The second comment I want to provide is that in the

discussion on overload, information is given relative to Morrow and the volume hypothesis, but clearly evolved has been work by Driscoll and Gunter and others on surface area as a factor, and, actually, surface area relating to carcinogenicity of the PSPs much more so than volumetric. So, there is an uneven and inaccurate discussion of that material in that section.

The third major point was that I have to strongly disagree with the section where it talks about that there is inadequate data to model the retention of particles. The ICRP and the NCRP models are cited in here, and they handle both deposition and clearance, and I would think that the other reviewers would agree with me that that is just not a justifiable statement, that there is no ability at the current time to model the retention of particles.

The fourth area that I wanted to comment on has to do with dosimetry calculations or, I should say, the lack thereof, and to me, this is one that is an example of how it is collective wisdom that evolves. I just want to relate that the committee originally requested that calculations be made and added to the chapter. They still are not. That has come up here.

I got the feeling with our conference call with OAQPS on the risk part that this really wouldn't factor in in the way they were going to be going about it, so I have to admit that my own personal review of this while I was on vacation, I forgot to bring up again that the dosimetry

calculations were missing, but then I said well, why should we include them if they are not going to really use them.

But, interestingly, over dinner last night, my colleagues clearly pointed out the value, in particular, of putting into perspective some of the animal work and tying it to the human epidemiology, because just as a couple of brief examples, if you have a 1 micron particle, I can defend that a 500 Fg/m<sup>3</sup> exposure in animals is equivalent to about 50 in human, because there is a deposition and a clearance factor that ends up being about 10. The same way if it is 3, it goes up to a 20- fold factor.

There is nothing in the chapter that provides this kind of calculation and to put these things into perspective. So, I have to back off and say I was remiss in my draft comments that I did not include this. Clearly, that is why I cited as an example of collectively, when we end up getting together and discussing, usually, you end up with a much better result than what any one individual would do.

My last major comment has to do with the summary section, and here, I feel that the summary sections of these chapters that the major points that you want to take forward should jump out at you, and they do not in Chapter 6 at the current time.

In my comments, I just listed that these almost even ought to be bulletized. There are a number...and you can create a list of how many things you want, but just quickly, I was able to write down that there is a

statistically significant gender difference for coarse mode particles. That is something that should be brought forward.

There is nothing in here in the summary about exercise and how it increases respiratory dose. There is nothing in the summary about the fact that the deposition patterns are similar in animals and humans, but the absolute fractions are quite different.

So, you can go down and look at the number of different points, and I actually feel that you could create that list, and they ought to really be brought forward in the summary to actually explicitly state what the conclusions of the chapter are that you want to take forward for the synthesis chapter. To me, that is currently missing, and it needs an overhaul.

I have got a number of technical comments that, you know, they will be able to be self-explanatory in the written comments, but those were the major things that I had to comment. Again, though, I do believe it is much further along and it has had significant progress.

**DR. HOPKE:** Joe?

**DR. MAUDERLY:** Well, like Fred, I note that there are recommendations that were made last time and, I thought, made pretty clearly, that were not adopted in the revision. So, I think it is worth stepping back for a moment, and if it is not understood why they are important, to lay that groundwork.

I mean, we have to ask ourselves, why is there a

Chapter 6 and 7 here anyway? I mean, as Fred points out, the way the standard has been rationalized to date and may well be again this time is not based on dose. That is, it is not a dose-based standard; it is an exposure-based standard, a presumed exposure, modeled exposure, and that relationship to population health effects.

Now, that is not necessarily what would drive a standard, but in this case, it has been and it is likely to be. So, you could say well, the toxicology and the dose really isn't very important, and we don't need to include it, but, in fact, the toxicology chapter is invoked as supporting biological plausibility. That seems to be its main function, since it is certainly not used in any way to explore dose-response relationships, not as well as it could be.

So, let's just take biological plausibility, and I would propose that there are two arms of biological plausibility. There is the fact that something can cause an effect which is important and which is portrayed in Chapter 7, but there is also the dose at which that effect occurs, and I would propose that the dose issue is just as important a part of biological plausibility as a mechanism for seeing, you know, some potential hazard.

Now, if that is true, then we need a lot better support for understanding the value of...and I am not petitioning one way or the other...but for understanding the value of the toxicology information and how that relates to human exposure and human doses and human health outcomes.

So, we heard in Chapter 5 that there needs to be some consideration of dose, and part of that was not whether or not it should be there but the fact that it is missing from the document altogether and it shouldn't be. Now, it was proposed well, maybe we can fix that by tossing into Chapter 9. Well, then we don't need Chapter 6 or maybe 7 or maybe 5. That is not the way to fix it. The way to fix it is to deal with it when it is being explored.

Now, you know, having vented that, then let's look at the chapter. I don't think the chapter yet really lays out an adequate foundation for understanding chapter 7 or the relevance of the animal information to human health effects. It presents a lot of information about dosimetry, and most of that information is correct, and it is well done.

But one example is that if you look at the different figures that have these segments of regional dose for different species or different conditions and all the spots and the error bars, you have to know a lot about dosimetry to distill from that an overall picture of the relationship between deposited dose or fractional deposition in different regions of the respiratory tract and particle size.

Now, there are figures, you know, ICRP and NCRP that Fred invoked. There are figures that explain, very simply, this relationship in a reasonable way...this is a relatively mature science...in a reasonable way across the full spectrum of particle sizes, and it has been my

experience that when you show one of those to people that don't know much about dosimetry, they have this aha, now I understand. I mean, this can be simply portrayed, and just adding one of those figures, as was pled for last time, to the chapter is worth about half a dozen of the others.

Then, we need tables. We need some actual numbers to make sense of this. Now, Fred just gave us a quote here on a relative dose. That is extremely important. Most of the doses that are used to generate the effects that are discussed in Chapter 7 are very high doses compared to environmental, some of them ridiculously high compared to environmental, but are they irrelevant?

Well, to decide whether or not they are irrelevant, you need to understand the things that Fred just talked about, and the fact that we have made advances in our ability to model comparative doses between species is mentioned in the chapter, and it is cited, and it is done well, but no examples are given, no tables are given, and I think at least limited examples that let you put these things in context then will prepare the reader for what needs to be done in Chapter 7. And we'll talk more about dose in that chapter, but this is where that needs to be done, not in Chapter 9. It needs to be done here.

Beyond that, there are some minor comments that I will send in and some revised comments, but one thing that I think is missing in the summary...again, the summary, you have heard from all of us that that is very important...if

you would put me on the spot and ask me what are the most important advances in particle dosimetry in the last five years, I would point to two.

One is an improved ability to understand interspecies differences, and that is very important, and it should be made clear.

The second is the striking difference we have in deposited dose...in some cases, we only know total deposited dose, not regional dose...of particles between individuals. I mean, the fact that two people can be sitting in the same room or standing on the same street corner and because one of them has certain characteristics or lung abnormalities, they will receive twice the deposited dose as the person next to them, that is important, and it is very important for understanding the epi effects as well, and we know that to be true. In fact, the Agency itself has produced a lot of those data.

Now, those studies are mentioned in the body of the document, but that point is not even brought forward in the summary as a key point, and to me, that is probably the most key point to what the Agency will want to do with the epi data.

So, I think there are some overarching issues with the chapter. I think they are very easily fixed. I mean, you know, one person could spend a day doing this, and it would be a nearly perfect chapter. So, this isn't rocket science; it just needs to be done, just like we said last

time.

**DR. HOPKE:** Roger?

**DR. MCCLELLAN:** I'll start out on the one hand and then on the other. On the one hand, this chapter is a scholarly review of the subject. By and large, all the relevant literature has been considered.

Unfortunately, the chapter has some major weaknesses. It is excessively long and turgid with details. As an aside, the authors could reduce the length by at least a page by giving just a single referral to the 1996 CD in the first paragraph. There is hardly a page that there isn't a reference back to it. I will just make that point once.

Second, the chapter would be substantially improved and shortened if more emphasis were given to synthesis of the information and presentation of basic concepts, and we have heard some of those elaborated.

The chapter is poorly linked to the rest of the CD. In part, this may be the case, because very little of the information in dosimetry, in some people's view, has any bearing on the establishment of the national PM. If the authors disagree with that assertion, then I challenge them to highlight in the chapter the specific information that impacts on the setting of the NAAQS for PM and the interpretation of toxicological and epidemiological data. This exercise will aid the authors in identifying the contents of a substantially shorter, revised chapter.

A key component of the revised chapter should be a

brief discussion, perhaps including a summary table or tables, on the special aspects of dosimetry and key components of PM. This would include consideration of not only particle size and mass but also the specific chemical components, such as the carbonaceous fraction, sulfates, nitrates, trace metals that have received consideration as putative toxic agents that may have a special role in the toxicity of PM.

A table or tables might be created showing, for a typical subject, the estimated amounts of each PM constituent deposited per day for one or more typical aerosols. The tables would compliment similar tables in other chapters, especially the toxicology chapter both for animal studies and controlled human exposure studies and the epidemiology chapter. This set of tables would be useful in developing a more informative integrative summary chapter.

And I have some additional detailed comments, but, by and large, I would concur with the points that have been made by both Fred and Joe.

**DR. HOPKE:** Gunter?

**DR. OBERDORSTER:** I also agree with the points that have been made before, so I don't have to repeat them also at length, and I have some detailed comments listed here which I certainly will not go through.

Some general ones would be, along with what Paul said before, Paul Liroy for the Chapter 5, I think it would be good to start here with the exposure dose-response paradigm

to have the lead in it and then go full into the dose issue which is done here in the introduction to this chapter very nicely.

I also endorse fully about what Phil was saying about the figures. Certainly, it is nice to have one figure here showing the old deposition data which was developed showing individual variability of the data but then go on and have one more figure in here. As an example, I put here down the ICRP model.

**SPEAKER:** That's it. Yeah, there it is.

**SPEAKER:** That is exactly right.

**DR. OBERDORSTER:** But I was thinking of the MPPDEP model, because that model gives us a nice way to compare rats and humans side by side, the same simple way it is done here. It gives you right away an overview of what is going on where you have that figure here with hamsters, dogs, and mice and rats shown all together rather than pointing all over the place and you don't know anything about it. So, this is one general comment here about the figures.

Also, there are several instances where the document certainly should be much more critical in terms of evaluating the information that is given, specifically...we'll come back to that maybe later...with respect to translocation studies of ultrafine particles which are wrongly interpreted, in my view at least.

And I wasn't sure from the beginning what is the

differences in the terms clearance and translocation. In my view, it is pretty much the same. Is there any...it is not the same?

**DR. MCCLELLAN:** Clearance means you get rid of it. Translocation means you...

**DR. OBERDORSTER:** Well, by the way it is used here, it is interchangeable, and...okay, so that needs to be cleared up here, because that is what I interpreted, too, that one should be the further translocate and the other get rid of it, but that is not the way it is used in the document.

Another...yeah, I was coming to the gender differences in deposition. I wasn't really quite sure if what is stated here in the document is correct when it says that females have a higher deposition than males, given that most of the studies that are listed here with done with an academic breathing, men and women breath the same volume, same minutes inhalation, and, by necessity, you would expect women to deposit more, then, and there is one study by Frampton where they didn't do that, and there was no difference.

So, I am not sure if there is really that gender difference between...in deposition. Maybe you should critically look at those studies and point out the possibility that it might have been influenced by the academic breathing in those studies.

Also, in the figures that are given here and that I

didn't understand in the legend, it talks about the individual points as being MMADs. If that is the case, it depends very much on what the standard deviation is for a particular point, so I think that is what is meant here.

One thing is, also, there is some misconception here. It is incorrect here when the statement is made ultrafine particles, in general, have a very high deposition efficiency in the nose. It states that the nose is a very efficient filter for all ultrafine particle sizes which is not correct, and if you look at the ICRP model or the MPPDEP model, the nose becomes very efficient for particles below 5 nm, but above that, the alveolar region is the highest or even the tracheobronchial region on a surface area basis. So, I think that needs to be corrected here.

And these are some individual comments I have here which you will see.

Then, yeah, one thing I think that is quite important, it talks about here about so-called hot spots of deposition and somewhere else, and what I would like to see, if it is possible, to see how many false increases are there over the average, because this information is used to justify high in vitro doses or intratracheal installation doses, and as far as I can see, the whole increase is maybe a factor of 5, at the most.

I don't know, Fred, what your take on this is, but I think it would be good to have something said there, because you have that issue of dosing in vitro studies and later in

the toxicology chapter, and that should be made clear, that although we have these hot spots, it is not that they are an order or two orders of magnitude differences between the individual sites which I don't think is the case.

**DR. MILLER:** I would like to comment on that. I mean, I think the authors need to go to the manuscript by Zhang and Asgharian, and they did look at the hot spot aspect in the coronal ridge in bifurcation. I think it is more on the order of a factor of, at most, 10.

**DR. OBERDORSTER:** At most.

**DR. MILLER:** At most, but it is certainly not several orders of magnitude.

**DR. OBERDORSTER:** Right, right.

**DR. MILLER:** It is more than a two-fold, but it is somewhere in the ball park of a ten-fold. I think there is also Emory...there are a couple of manuscripts that have looked at in using CFD and, you know, and hot spots.

**DR. OBERDORSTER:** Well, with respect...

**DR. LIPPMANN:** It depends on particle size, too.

**DR. MILLER:** Yes.

**DR. OBERDORSTER:** Oh, yeah, sure, it depends on particle size as well.

With respect to...you mentioned CFD, Fred. I thought maybe this chapter was a bit too long in the CFD section of this chapter. I think it would be useful to have

some general introduction what is it good for. For example, the issue of hot spots might be easy to view the results with CFD computations than without. I don't know, though.

On the other hand, there is also some statements are made here that we need more models, that is, better models, and I don't know in what sense that is. Given the large individual variation, I think the present models are quite good, given that we have to expect there is a large completely round...round of data that have been predicted by those models.

So, again, I think the CFD is fairly extensive and maybe a bit too much in there, and it would be good to point out what it might give us in terms of improvements.

Let's see. Yeah, one problem I had was several places also stated that the minimum of deposition is between 0.1 and 1 Fm, and that is way too much, and I think I would narrow it down to minimum deposition is around 0.3 to 0.6 F m of diffusional and sedimentational deposition mechanism are minimal. There are several places that occurs, as you will see from my individual comments.

And here, coming back to, I think, what Joe, both, and Fred said was giving some examples about deposition. I think it might be also good to have just a simple table in there giving...comparing rats and humans in terms of their surface areas and sizes of the respiratory tract or specific areas in the respiratory tract and then give an example for a

few particle sizes, how much would be deposited there under normal breathing conditions, and give also normal ventilation rates for rats and for humans and just to get that comparison out so that people can understand what the differences might be, what they might have to expect.

Then, coming to the issue of what I mentioned before, the translocation of so-called ultrafine particles, there are three studies listed here. One is led by the Belgian group, the Nemerans group...actually, two of them...using macro-agitated albumin, and this macro-agitated albumin technician labeled has been used for quite some time in nuclear medicine, and it is well known that 10 percent of that is just normal albumin, not agitated. So, there is certainly some concern in that particular study as to whether it really shows, when they measure the label in the blood, that this is the macro-agitated albumin or just the albumin itself or even the label if that has come off.

The same applies to technician labeled carbon particles, the so-called technigasma, and there, too, there is no way...and I have talked about that with Woerk and Kreining and others who are expert in that field, because they have done it themselves...there is no way to make sure that what is measured in the blood is really representative of these inhaled technigasmas with the fine particles. It could just be the label has come off and then maybe has attached again to some other protein. So, you have to be a bit careful how to interpret those studies.

And another study that is cited here led by Takenaka, et al where they use ultrafine silver particles, and in the document it states here over and over again that these particles were found in the liver, were found in the spleen and the kidney and everywhere, but it is certainly the particles what was found, it is just the silver.

And it is well known, again, also from the BSF studies, that silver is soluble to a degree, specifically, if you are dealing with ultrafine particles. And I think Joe had done some study, reported those as ultrafine silver, and we have done some things with ultrafine, and we were also concerned about the solubility issue.

So, we cannot use these studies to say that this confirms that ultrafine particles have translocated to the blood.

I think I leave it here. Just one final comment. It was mentioned before it would be nice maybe to put down some short section at the end, future research needs, and that could include, then, maybe specifically some bigger list than what I just mentioned, the mechanisms or specific clearance pathways for ultrafines and also for other particles or solutes on particles.

That is it.

**DR. HOPKE:** Okay, thanks. Warren?

**DR. WHITE:** I agree that the chapter is significantly improved. One comment I had in terms of tightening this, it refers to the same paper over and over

again in five different sections and introduces the basic elements of that over and over again. There is really no need to do that. It should be tightened up.

And I have a number of small comments. And one comment that isn't in my pre-meeting writeup is stimulated by some of the things we heard yesterday in the public comments, and some people went to elaborate extent to calculate particles per unit surface. That is really nonsense in the context in which it was presented.

When you inhale particles, it is well discussed in terms of variations within the conductive airways, but there is nothing in here...and the key references are missing...about the non-uniformity of inhaled particles depositing in the pulmonary region.

There should be references to the work of Brody and colleagues and Warheit on measurements of deposition in the proximal airways. In broad terms, beyond the tracheobronchial region, there is deposition in the first branching of the respiratory airways which is about twice as great as the second branching level which is about twice as great as the third branching level.

And inhaled fine particles do not...nowhere nearly...deposit uniformly in the gas exchange region. There is certainly concentration toward the mouth of the region in the first branching airways.

Now, is that important? It may be. It should be at least mentioned in the non-uniformity of deposition

aspects, and then it should be cited in the section 6.5 on the comparison of deposition and clearance patterns of particles administered by inhalation into tracheal respiration.

By inhalation, you get this very non-uniform deposition, and installation gives you another kind of non-uniform deposition, but in the dependent regions where the liquid goes, it does go all the way to the peripheral sacs which it doesn't by inhalation. So, that is another reason why installation is really to be used only for certain limited purposes.

I apologize for not calling your attention to that in earlier drafts, but it was stimulated by thinking about what some of the public comments were. Certainly, if you want to assume that particles inhaled are uniformly deposited across the football field represented by the ventilated surface, you come up with very low densities, but it doesn't happen in the real world.

**DR. HOPKE:** You will put those in your revised comments?

**DR. WHITE:** I think they are taking notes.

**DR. HOPKE:** Okay. Gunter?

**DR. OBERDORSTER:** I think we have also to be a bit careful, though, with the taking the Warheit and Brody paper and extend it to all particle sizes. They have

used carbon iron particles, and I think the size was about...I have forgotten...maybe 1 F m or so, and they have done it with fibers, and they have found these coronal depositions, but that doesn't mean that this is so for all particle sizes, and it could be very different for, for example, ultrafine particles.

**DR. LIPPMANN:** It could be, but I doubt it.

**DR. OBERDORSTER:** Well...

**DR. LIPPMANN:** On aerodynamic grounds, but let's not go into that.

**DR. HOPKE:** Okay. Paul?

**DR. LIOY:** I have nothing further to add to the excellent comments of Fred, Joe, and Gunter, so I think you have to take them to heart and make this chapter very, very focused on getting a good understanding of deposition and how they related to both toxicological, epi, and risk assessment issues.

**DR. HOPKE:** Allan? Okay.

**DR. MAUDERLY:** Could I say one more?

**DR. HOPKE:** Sure, Joe.

**DR. MAUDERLY:** I just would like to follow up now. Professor Oberdorster needs no apologist, and I agree with everything he said, but I am concerned that some may misinterpret the aim of what he was saying.

Those of us working in the field are convinced, in fact, most of us feel that we know absolutely, that some ultrafine particles do translocate to other organs and from the blood, and, in fact, this has been known for many, many years, some of it going back to the radiation work.

So, the point is not that this doesn't happen. The point is that the citations that were given to support that fact do not support that fact well.

**DR. HOPKE:** Thanks, Joe. Fred?

**DR. MILLER:** I have...go ahead, Roger.

**DR. MCCLELLAN:** I agree with that. What is missing in some of that is quantitation. I mean, the emphasis is on the phenomenon occurring absent quantitative consideration.

**DR. MAUDERLY:** Oh, I agree completely. What we do not have are good quantitative data. In fact, Gunter is probably closer than anyone in the world to producing that now with some of his techniques.

**DR. HOPKE:** Fred?

**DR. MILLER:** I just wanted to clarify on the kinds of tables that Joe and Roger were referring to being added. As part of that, I was kind of prompted by his last comment there, and that has to do that in those tables, different dosimetrics should be presented for the animal versus the human, and that puts into perspective some of the different kinds of endpoints and how it may be mass or it may

be particle number or it may be mass per unit area, and the models can generate these information, and it really does end up being a function of particle size and getting dramatically different comparisons depending upon what size.

So, I think those are the kinds of tables they were referring to, but I want to make it clear that it is more than just mass that I would hope that we would see and, definitely, added tables. You did get the word. Right?

**DR. HOPKE:** Sverre? Ron?

**MR. WHITE:** I don't have a comment on the chapter, but I do have a comment on a recommendation that I thought I heard, and I may have been mistaken, which is that there ought to be the addition of some research needs added to the end of this chapter. Did I understand that correctly?

**DR. OBERDORSTER:** Yes.

**MR. WHITE:** I guess I would respectfully disagree. I really question whether this is the document to include research needs. I did find it in Chapter 8 as well which I did review. I didn't review Chapter 6. And I guess my view is that that is not the purpose of the document, to identify future research needs, and if it is, then it needs to be very explicitly done throughout the entire document, and it needs to be pulled together as a separate section. If it is not, then it ought to be taken out of the document and not added.

**DR. HOPKE:** I don't think we should be

putting research needs in here. I think we should be summarizing very well what we know and what we don't know so that from this could easily be derived a research needs document.

**MR. WHITE:** That's different from what I thought I heard.

**DR. HOPKE:** And that, I think, is where we want to go with this document, that it should be the state of the science, and if there are deficiencies in the current state of the science, those should be pointed out, but, then, let the next document translate those broader missing pieces of the science into more specified research needs.

**MR. WHITE:** I mean, as we all know very well, there is a whole other group that is looking at the whole issue of PM research and needs and so on.

**DR. HOPKE:** And that is Monday's meeting, yes.

**MR. WHITE:** That is Monday's meeting.

**DR. HOPKE:** George? Petros? Okay, do you have questions?

**DR. GRANT:** I think I understand pretty clearly what has been suggested or recommended and pretty much can take on doing them. Indeed, we will take note of the research needs as we go along for putting in the research needs document, but we will not be adding those into here, as appropriate to what you just said.

**DR. HOPKE:** Okay. You know, this one has still got some major holes in it. We need to hold off and see later on whether we get some of the things we have asked for before.

Okay, Chapter 7. Fred?

**DR. MILLER:** I have provided a number of detailed comments, and there are just a few areas that I want to highlight, because I am sure that some of the other reviewers will pick up different things.

One of the major things that I felt was missing was a more adequate treatment of the cardiovascular area, and I noticed that there were only two publications that were passed the previous document in that particular section, and I thought that that...I was particularly interested in the comments from one of the external public comments that talked about some of the cardiovascular effects not only in the animal but in the human. That particular area, I think, is going to gain more attention, and to me, it is not sufficiently treated at the current time.

I also felt that the organization of the summary section, right now, it goes through pretty much by particle type, and that may be appropriate, but I would like to see, similar to what I recommended for Chapter 6, that the points that you are really relying on taking forward actually are more explicitly wrapped up in a final section of that summary.

For example, the study by EPA where the

intratracheal installation of ROFA caused effects, and then the inhalation exposures at  $15 \text{ mg/m}^3$ , and they were seeing no effects puts a lot of that into perspective and ought to be a particular point that goes forward to the summary in terms of the relationship between intratracheal and inhalation.

So, there are just a number of places throughout the chapter where particularly important observations are made, and, yet, they don't appear in the summary section, and I could go through and list them, but I think, when you read it, you see. I mean, the Utah Valley study, for example, where the parts about copper are brought out and the absence and the washing off. There are a number of other studies that kind of give you insight into what might be potential actors or actresses, and that is just not really carried forward in the summary.

I think that there is more balance in the current version, but there is still a need to tighten up the interpretation of some of the studies, because there aren't technical details presented for some of them that would maybe put a contrasting, and then I would go back to the aspect of the dose part whereby there are a number of studies that could actually be grouped together, because they form a continuum of the different exposure levels. If we then had the information from Chapter 6, the reader would be able to see that that...how they fit together.

So, those are my major comments. It is a very difficult subject to try to bring together, and, personally,

I am even more in a quandary, given yesterday's results and seeing, in terms of toxicology as opposed to being supplying the biological plausibility, and I am seeing the epidemiology with some of the issues emerging and saying now we are down to an even finer level of effect that we are detecting in some of these, they are still significant and so on, but how can you expect some of the toxicology studies to show and to demonstrate.

So, part of that becomes an aspect of plausibility, but it also becomes an aspect of dose that I think is needed as a translation from Chapter 6.

I will just leave it at that, but I will also say publicly I didn't mean to beat you with you did hear about putting the tables in, Les. That wasn't called for.

**DR. HOPKE:** Okay. Joe?

**DR. MAUDERLY:** Well, let me pick up again with the idea...and Fred has expressed it, but I really do think it bears being understood well, and that is that a key part of the utility of Chapter 7 is being able to put these various effects in a context and understanding to what extent we can use them to explain or undergird some of the epidemiological effects. In that sense, dose is important.

Now, assuming that we have laid the groundwork in Chapter 6, there are still some exposures that are quoted in Chapter 7 for which the exposure level or dose is not given, and those have to be oversights, because many of them have

been corrected, but there are still some holes there, and in one case, I know they are listed but incorrect.

But I think, in my view, one of the key deficiencies...and, again, I think it is easily remedied...is when we are talking...I don't care whether we are talking about the general category of cardiac effects or inflammatory effects or whatever the effects might be...I think it would be very useful to point out in the chapter in that section what the lowest dose or exposure that has revealed an effect to date is.

My preference would be to go ahead and do some translation in terms of human doses, but that may be a stretch, but if that is well done in Chapter 6, at least the reader can do that.

Now, this is not because, as was suggested yesterday, that we need NOELs and LOELs, because the standard isn't likely, although that would be an interesting thing to have, the standard isn't likely to be based on that. It is not important for that reason, but it is important, again, to understand the extent to which we think the laboratory findings at this point are or are not, you know, convincingly supportive of the epidemiology findings. So, that is why it is important.

Now, another point, a second point, is that, as has been mentioned before, I think the chapter and the effort suffers by the intentional avoidance of studies on source emissions such as engine emissions and done so on the basis of well, that is covered in some other document.

Well, that is not the point. The point isn't whether it is in a file somewhere. The point is, what is its relevance to the issue at hand? In fact, that is where most of our information on copollutants lies at this particular point. It is even stated in the document that we really have little information on mixtures except for some acid sulfates, and that is, you know, that is a curious avoidance of the fact that we have lots of information on mixtures.

Now, the extent to which it informs what we are seeing from epidemiology is a second point, but, in fact, we have a lot of information, but it has been avoided except in certain cases where it suits the authors' purpose like in the case of the ajuement effect to invoke diesel particles. Well, if it is important there, it may be important in other areas, too, and, in fact, that is an area where there is a paper published in the last year which showed, in an inhalation model, that over 80 percent of the effect of the whole emission was conferred by the non-particle fractions.

Now, that is not confirmatory as to whether or not particles are causal, but it is a very important piece of information.

A third point has to do with bioaerosols, and this is another one that is a repeat point, and if there are rationales for why these decisions have been made, it would be interesting to hear them. Bioaerosols is covered in this chapter by talking about endotoxin as if that is the only bioaerosol there is, but if you read this chapter, that is

the only one that is mentioned.

In fact, recently, I attended an indoor air conference, and those people talk a lot about bioaerosols, and I never heard endotoxin mentioned. Now, the fact is they have some different things to work with in indoor air, but the fact also is that there are a lot of biological materials associated with particles in the outdoor air, and to write a chapter and only mention endotoxin, I think, is doing a disservice.

The point is made in the summary part on bioaerosols, they are sort of dismissed based on the ' 9 document which stated that bioaerosols, quote, would not account for the reported health effects. Well, the point is not whether they would account for the health effects; the point is do they contribute to them.

A lot has been made of metals in the document, and a lot of room is given in this chapter to metals in the document, and I think that is appropriate, but in the summary here, it says it cannot be assumed that metals are the primary toxic component. Well, if that is our rationale, then we shouldn't be wasting time talking about metals.

The important thing is not is there a magic bullet; the important thing is what components of PM could be contributing to observed effects. And I would propose that there is a large and growing part of the population with asthma and respiratory allergies that would be shocked to learn that bioaerosols, inhaled bioaerosols, have no

importance to health effects.

**DR. HOPKE:** All right. Dr. Lippmann?

**DR. LIPPMANN:** I would like to get to the points not mentioned and perhaps to acknowledge that there were major reductions in this chapter that we called for, myself included, and that related to all that stuff on the mutagenesis and carcinogenesis, and the rationale was we have no evidence that ambient particulate matter is associated with excess cancer.

Well, it has changed since then. Hope, et al, 2002, provide evidence...some may want to not...but peer reviewed evidence that lung cancer is found in excess in proportion to ambient fine particles.

So, I think you have to come back and put something in there. In my view, this need not and should not mean the restitution of most of the discussion on mutagenesis and high- dose cancer exposure studies from the second draft which I am sure you have and could reinsert...I am not recommending that...but, rather, a selective discussion of mechanisms of, for example, mitogenesis or just the stimulation of cell growth which can be a secondary cause for the expression of cancer, and particles may play a role in it, and thinking along those lines in the literature could be discussed.

But there should be something now, especially if you are going to make anything out of excess lung cancer being a consequence of ambient particle exposure. There

needs to be something in this chapter that at least addresses what we know about the toxicology that might account for it if it can.

So, all my other written comments are pretty much editorial. It certainly is improved over the previous draft.

**DR. HOPKE:** Dr. McClellan?

**DR. MCCLELLAN:** This is a voluminous compilation of research findings of the health effects of PM in observational studies of human subjects and laboratory animals exposed to PM under controlled exposure conditions. Generally, the concentrations of PM are substantially greater than found in the ambient air in the U.S.

Although the introductory paragraph introducing the concept of various research approaches targeted to test hypotheses, the concept of hypothesis testing is really lost, virtually lost, in the rest of the chapter.

It is curious that, at the end of the one introductory paragraph, the chapter authors noted it, the chapter, may fail to adequately convey the extensive and intricate linkages among the cardiac, pulmonary, and nervous systems, all of which may be involved individually and in concert to represent the effects of exposure to PM.

It sort of says how it is going to fail, and I would have to say, unfortunately, they met what they said, they failed to do it.

I urge that the chapter be revised, and I think it could be shortened by just tightening things up and organized

in a manner that more clearly links the chapter to other chapters in the CD and, ultimately, the establishment of the NAAQS for PM. It would be useful for the chapter, after a brief introductory paragraph, to include three brief sections that link to the rest of the CD.

The first of these sections might relate what is typically found in PM and, thus, forms the basis for the hypotheses as to how PM may produce health effects. This should include consideration of all of the major constituents such as carbonaceous material, sulfate, nitrates, and trace metals, and a linkage back to the dosimetry chapter.

The second potential section would briefly relate the health effects found to be statistically associated with increased PM as a basis for testing hypotheses related to how PM might produce these effects.

And a third section really relates to the approaches available for testing hypotheses, i.e., controlled human exposure, laboratory animal studies, and in vitro approaches. For each approach, the strengths and weaknesses really need to be related.

The chapter, that last section, needs to really describe the very substantial challenge faced by the experimentalist trying to obtain data on hypotheses that must be linked, ultimately, to statistical associations between increased levels of PM and increased rates of adverse outcomes characterized on the order of 1 percent or less for increase in effect per  $10 \text{ F g/m}^3$  in studying populations that

are measured in hundreds of thousands of people or millions of people over periods of years.

The rest of the chapter needs to be more clearly organized around those PM constituents of concern, the types of adverse outcomes, and the approaches used, the human studies, laboratory animal studies, in vitro. Whatever the organization of the matrix of information, it should remain clear in terms of these three different kinds of approaches or orientations, if you will.

I have vacillated on the following point, but I think it is an important one, and that is some inclusion that there is a serious deficiency in the present Chapter 7 in the inadequate coverage of chronic exposure studies previously conducted in laboratory animals with particulate matter.

I suggest that the authors include a brief section that...much of it built around, perhaps, one or more summary tables that reviews existing knowledge from chronic inhalation studies conducted in laboratory animals. One group of studies are the multiple exposure level studies conducted with vehicle exhaust like the diesel exhaust that Joe has referred to. Some of those studies, especially those conducted by the Lovelace organization, evaluated a broad range of responses from biochemical indicators to life span of populations.

In addition, there are a small group of chronic inhalation studies conducted by the National Toxicology Program. Although much of the focus was on cancer as an

endpoint, they do provide relevant information with regard to other endpoints and, in all cases, involve multiple exposure concentration, something that is missing from many of the studies that are cited in the chapter today.

A few of those...a few other studies may be identified by considering data bases such as those of NIOSH, ACGIH, and HESDR. Now, it is recognized that these studies that I have noted above generally involve pure compounds and, thus, do not exactly mimic typical ambient PM, but they were selected for study, because they generally were viewed as being of concern from a toxicological standpoint.

In addition, the studies typically started, which is a potential criticism, with young, healthy animals and followed them for, generally, two years or, in a few cases, even longer. Obviously, near the end of life, that is no longer a young animal. They were, in fact, chronic exposures of aged individuals.

A review of this substantial data base and placed in perspective via the vehicle of the dosimetry chapter, I think, does provide us some valuable insights in terms of exposure, time, and health outcome responses and what one sees in terms of ambient PM in human populations.

Finally, the chapter requires a revised summary inclusion section that more clearly links it to the rest of the CD and, especially, the epidemiology chapter, the dosimetry chapter, and the integrated synthesis. This might be achieved by reference to several tables that summarize the

evidence as related to the points I raised above, that is, constituents of PM, adverse outcomes, and the experimental systems used.

The total chapter, especially the summary and conclusions, need, I think, to reflect a more neutral tone in describing evidence for PM and its specific constituents at ambient concentrations and, that is, the extrapolation of the findings at these higher levels to ambient concentrations that have been observed to have associated statistical increases in terms of adverse health effects. Again, I think we can do that by linking the kinds of tables that were called for in terms of dosimetry chapter into this chapter and then on to the integrative summary.

**DR. HOPKE:** Okay. Gunter?

**DR. OBERDORSTER:** Could I make a comment first, or question, Roger? When you are referring to the animal studies...and there are numerous of those, long-term inhalation studies, chronic inhalation studies, and there are also carbon monoxide studies, diesel studies, carbon black studies, nickel studies, and cadmium and so on, I mean, their purpose, as you said, were to look at the endpoint cancer, mainly, so they focused solely on the respiratory tract. Is it really...and the doses, of course, the concentrations were rather high, the lowest going down, I think, in Joe's studies to 700 Fg/m<sup>3</sup> and others 1 mg/m<sup>3</sup>. 350? Okay.

But can we really use those for the purpose of this

document, environmental ambient particles? And we are looking at more sophisticated endpoints, including cardiovascular system.

**DR. MCCLELLAN:** Well, I think the answer, obviously, as I referred to in my comments, is yes. I think it is very informative that you can expose laboratory animals to 350 F g/m<sup>3</sup> 35 hours a week for up to 30 months and a substantial population and not see significant adverse health outcomes.

In some of those studies, there was detailed pathology done. There were detailed biochemical studies. I think what is remarkable is the findings in those.

They were exposure-response studies. There were studies above those at 3500 F g/m<sup>3</sup> and at 7000. Again, the fact that animals could be exposed at those levels and there was no detectable shortening of life span in the highest exposure level animals, I think, provides, again, a perspective.

I think, when I reread the chapter and found that, you know, we...it's like that is another world and we shouldn't consider it here, to me, is a serious shortcoming, and I think those studies with both vehicle emissions and studies with other materials provide us some very helpful insights in terms of the total picture of what is our understanding of the biology and pathobiology of inhaled particulate material.

**DR. MILLER:** Before you go, Gunter,

though, I just would point out, too, though, that there are studies conducted by EPA of a chronic nature with ammonium sulfate and ammonium bisulfate, and you saw in the sclera cells in the deep part of the conducting airways a structural remodeling. That was 500 Fg which, as I said, translated to a 50 Fg/m<sup>3</sup> exposure in humans.

So, there are also other studies that don't involve carcinogenesis that would add to the data base that Roger is talking about.

**DR. MCCLELLAN:** Right, and it is not only positive. I mean, I think we have to be even handed in laying evidence on the table of both positive, quote, findings and negative findings. We do have, I think, one...I believe the Heider, et al study is briefly mentioned in here, but it is, you know, mg/m<sup>3</sup>.

**DR. MILLER:** Right.

**DR. MCCLELLAN:** But those studies give us some insights that, I think, are absent today. It is like they put their blinders on in terms of what they wanted to review.

**DR. OBERDORSTER:** No, I mean, I have nothing against citing those studies. The only question is how detailed do you want to review those.

**DR. MCCLELLAN:** Well, again, I think you can do some of it in a summary fashion. You may refer to

details in terms of use of appendix tables, but these are very important body of information, as they say, of the biology and pathobiology of particles.

I would be happy to, you know, discuss further on it. I just...

**DR. OBERDORSTER:** I mean, much of it has already been said, so just a few comments here.

Again, of course, the issue of high doses which has very nicely been addressed in the chapter here, at least as far as the studies concerned were described, but then, when it comes to the section of potential mechanisms, it seems to have been completely forgotten.

The mechanisms are pointed out here based on these high-dose studies as if that would be happening under environmental conditions as well. So, I think a bit more critical writing in the mechanisms, potential mechanisms, section would be very useful here to really put some caveats down here that this is a mechanism that has been observed at these high doses, and it may or may not be true for the low doses as well.

And at the beginning on page 3, line 20, it stated that high doses using animal inhalation and installation studies are necessary and without really saying why they would be necessary. The question, of course, is are they really meaningful.

And one problem is that, most often, healthy animals are used, and the epidemiological events have been

found in compromised humans. That, of course, poses a difficulty in selecting or deciding or validating animal models, because all what we are doing here is creating acute animal model, whereas the human condition is a chronic one.

That makes it very, very difficult, and maybe these difficulties could be pointed out here when discussing this issue in that context.

In some of the tables, table 7-2, for example, that deals with inhalation and installation studies...by the way, I would suggest to divide those, make a separate table for inhalation and a separate one for installation studies.

And then, the particle sizes given under installation studies as well as on the inhalation studies, at least in many cases, and the installation particle size is also given as MMAD, which I don't know what it means, probably the particles when they were collected from the air when they stayed on the filter, that was their size then, but when they were instilled, they may be completely different.

On table 7-4, I have a bit of a problem here. For most of the studies here, again, I would not think of them as being ambient surrogate particles as is said in the title of that table. The first study is an overload study which was at very high concentration, and the next three studies are actually all petrol studies which I also would not think as surrogates for ambient particles, so I would not list those here.

Just a comment also on animal model or animal

models in general. The mono-protaline model is being described here, at least, not described, but the results are listed here, and I think it might be good to also have a critical, brief description of that model in here.

This, again, is a very highly acute, induced model, and I am not sure, although it causes pulmonary hypertension, is it really relevant for the human situation. So, I think a sentence or two about the validity for the human situation would be helpful here.

The in vitro studies, in general, I think it should also be pointed out when these studies were done that the doses used here are really very high compared to what really you would expect the cells to see after an inhalation study. Also, in particular, table 7-10 that deals with in vitro studies, there is a column of exposure techniques that are listed throughout in vitro studies.

That could be taken out, and it would be much more useful to have a column in here what the dose per  $10^6$  cells, for example, is. That would give you much more information and compare the studies among each other.

I think these are...I have many more individual points here that you will get when you get my written comments.

**DR. HOPKE:** Okay, thank you. Okay, Petros?

**DR. KOUTRAKIS:** Well, I think the chapter

really does not highlight the major achievement since '96 which I think is very important. It really goes through many studies, and there is not the big link and the big picture, and I think, to my opinion, somebody should really communicate, you know, what has been achieved since '96 was that people can produce responses with lower doses. We don't have to blast the animals now. We are able to use lower doses to have a response.

There is better animals models based on the epidemiological studies. They started from the bronchitis, and now they go to MI and, maybe in the future, diabetics. So, there is a consistency between the epidemiological and the toxicological studies.

Also, there are more sophisticated biological response methods. The way they measure now ECGC is better than before, but now, you can do systemic measurements, chemical measurements of systemic response.

So, I think a lot of things have happened since the last review, and I don't think that somebody gets that picture by reading this.

Also, there is no link between the different outcomes and what they mean, if they mean something. In the Center's report, for those who have read it, there is a kind of an effort to link and trying to see if there is any relationship between different outcomes and give you the big picture, especially for people like me who are not toxicologists. That is lacking from the chapter, and I think

it is important.

Also, I think the most important studies were lost in the shuffle. I think a lot of ROFA studies where there are many other studies which might not be relevant, and, really, the most important studies, where the chronic studies or the concentrator studies or some other human exposure studies really were a small part of the big picture, and I think that was not a good idea.

Although the chapter has sections for different types of particles, there is not a synthesis or a contrast of the different methods, you know, concentrators versus source emissions, source/biological versus different types. Rather, it just goes and says well, this method can do this, and this method can do that, and there is not a critical synthesis.

I also found the organization very convoluted. I am sure there is a better way to present the material. The way it was presented, you had to read the same studies about five times. You know, you had the studies when you did different animal models, and you had the same studies when you talk about source types, the same studies when you talk about source apportionment and chemical characterization, and, really, you went on and on which I thought was kind of not very clear.

So, I don't know if it is too late, but think about, you know, how to organize the chapter so it is easier to present information.

I think, overall, we might not know the exact

mechanisms, we might not know the exact particles that cause these effects, but definitely, I think, although we have a limited number of studies, we get some responses, I think, and those data support the epidemiology.

And I think we are now to the point that epidemiology might reach its limits, and we might not like it, and I think it is the toxicology working together with epidemiology which might tackle some of the issues like confounding, et cetera, and source types.

Again, this chapter does not really make the links with epidemiology and exposure. It does not really give some interpretation of the epidemiological studies. There were some epi studies there, but I don't think there was so much.

So, that is all I have to say.

**DR. HOPKE:** George? Ron? Jon?

**DR. SAMET:** After hearing so much about the black art of epidemiology, I am pleased to hear that there is uncertainty in toxicology as well.

**DR. HOPKE:** Sverre?

**DR. VEDAL:** Yeah, just on a discordant note, I found an aspect of the summary section actually quite refreshing which is I think it was appropriately qualified in terms of the conclusions. I think they did address the limitations that are present in the studies. I really like that aspect of the summary.

Having said that, the summary could be helped, I

think, by one main thing. It is my opinion that, at this stage, for better or for worse in toxicology, the primary purpose is biological plausibility. People can argue with that, but that is all right. Secondary purposes are dose-response and mechanisms, but the primary purpose is biological plausibility. I don't think you have to apologize for that.

Having said that, the summary gets bogged down in the organization of having to go down the list of particle types and loses that primary purpose. You need to cut bait on the issue as to whether you think biological plausibility has been enhanced by the recent toxicologic findings. I think they have, and you can make a case for that, but I think you should state it, and that is one way of providing a linkage to the subsequent epi findings.

**DR. MILLER:** I personally don't think that the chapter needs to be reorganized. I think if some of the things that were brought up here relative to the synthesis and the linkaging, with the exception of adding some aspects on the chronic, that it might suffice for what Petros is bringing up by actually referring less to describing the studies when you have already introduced them once.

But I think the thing that is really missing is the ability to get the summary of it in perspective. So, I guess, I, for one...and maybe I am too close to it...don't feel that you need to scrap it and go to a totally different organization.

On the other hand, the three paragraphs are kind of twisted that Roger brought, putting it into perspective of the risk assessment and the methods and so forth. That would be good introductory material to kind of put the thing in perspective.

So, I think some balance or mixture of all the comments you have received from us is something you can sort out and maybe come back with. I actually wouldn't endorse scrapping it all and starting from ground zero.

**DR. HOPKE:** Rich? Jane? Allan? Warren?  
All right, well, this has been, again...do you have questions?

**DR. GRANT:** No, not questions. I would just note one thing. Going back to examining different individual components or whatever and having, you know, information on them, of course, that was part of a tack we took back in the '96 document at the start and had quite a lengthy...once you go down that track, you can end up with quite a lengthy additional amount of material that you end up putting in. Ultimately, at the advice...the committee took it out of the '96 document, this treatment, you know, of different metals and so forth.

So, you know, we are going to take a look at what has been suggested here and see what might be done. I suspect, to the extent to which we are putting in some things along that line, that, you know, it may well be that

substantial amounts go in appendices and then key points are brought out, you know, into the chapter, but the committee has to understand and recognize now that this may result in a significant lengthening of that chapter, you know, if we go down that track to do much of, you know, a component-by-component...

**DR. HOPKE:** I think the key is to be looking at, you know, what have we learned over the last five or six years in terms of mechanism and mode of action and where the action is and are some of those single component studies, then, relevant to our understanding of what is going on, and to the extent they are, they help build the bridge.

**DR. GRANT:** Yeah, we'll have a look at it and, you know, make efforts in that direction. Again, I' 1 1 repeat, the committee just has to realize what that may mean in terms of length and the amount of material that gets added in and, yeah, we'll have to figure out how to put it.

**DR. HOPKE:** All right. Joe?

**DR. MAUDERLY:** With respect to, you know, the amount of material and what has to be done, I just want to endorse the concept that Fred advanced. This is a better chapter than it was last time. It is not a really bad chapter.

There are some things that need to be done, and they are important things, but I don' t see that as either terribly difficult or requiring a great deal of extra length,

but then, I am an eternal optimist. That is what keeps me coming to these meetings.

**DR. HOPKE:** So, you are signing up for 2009?

Okay, well, thanks very much. I think this has been a very productive session. You know, I think we have, as I say, we have looked at where we are going to go at this state. Let me try and recapitulate where I think we are, and then you can tell me what really is happening.

I mean, again, the question is what to do with Chapter 9. I mean, part of the problem with Chapter 9 is that, you know, as we have all talked about, there isn't an adequate flowing from the summaries at the ends of each chapter to build to Chapter 9. In fact, in the case of one chapter, there is no flow from the chapter into Chapter 9.

So, you know, I think that, again, it is useful to provide your comments, but it seems like we still have a lot of work to do on Chapter 9, because the individual chapter summaries are still in need of significant work in virtually all of the chapters. So, you know, one of the key components of getting this together is going to be getting concordance between those chapter summaries and the flow in Chapter 9.

Now, you know, Chapter 9 has...you know, and I think, again, providing our comments, individual comments, to it, but the tone of Chapter 9 really is a little hard to judge where it is until we see, I think, a little bit more as to what shakes out with Chapter 8.

So, I am not sure that it is tremendously valuable for us to spend a lot of time working on that. You know, I think if we come back...you know, at this point, we have, basically, 4, 5, 6, and 7 for which there is still some modest amount of work. 2 and 3 need so work, so that I think, you know, we still are going to be able to bank out those chapters pretty quick.

That will give us a good chunk of time next time to work on 8 at the point where we are going to have to take what we have in terms of our understanding of the epi and fold that into 9, and that also gives, then, Les and his team a chance to rework the summaries and try and build some of that concordance which, I think, is one of the things that we will all go around the table and say is needed.

So, you know, I think that...sure.

**DR. MILLER:** I don't disagree at all with what you are saying, but I was wondering if the committee could...is in agreement to say the structure of what is there is what we would expect to see as opposed to if we got it and say oh, no, we think it should be organized differently. I am not saying the content, but, you know, is that something that we could do that would help ensure that while the subsections, you know, and the material going in it, that do we have a basic agreement that what they have laid out here structurally is the way we would like to see integrative synthesis?

**DR. HOPKE:** Warren?

**DR. WHITE:** Is the absence of Chapter 4 in the Chapter 9 intentional?

**DR. GRANT:** I sort of hit a point where, in trying to draw together under some very short time frames...I will just note we lost about four months of work on this document to the World Trade Center events, and that is partly consequences as far as myself and other staff members helping to work together with other colleagues from EPA on it, also some of our consultants, like from NYU and so forth, getting drawn in, so that there was a lot of time that, you know, quite unexpectedly but, obviously, had to be taken out and devoted to that, dealing with the World Trade Center thing.

And then, coming back and starting to get some input that we didn't have for a number of months, in trying to move this along, we were really sort of running out of time, in a sense, to go ahead and try to bring this on out. We hit a point where the basic structure, if you follow, you know, the NRC framework and the set of questions or those types of questions which was aimed more at the health side, you know, and I think George Taylor, you know, appropriately noted, in a sense, that that was the main thrust.

So, we sort of hit a point. Very difficult to see how quickly you are able to draw in and bring into play some of the things from Chapter 4 into 9 in that structure. I think there are some things that in the discussion even here probably are going to help us to some extent. Some of the

points that Allan Legge made earlier on the chronic impact, for example, on biological systems, the ecosystem side of things, certain analogies, perhaps, to be taken into account.

That is not to say at all that there are not also differences, but we believe, indeed, acute exposure effects on the human health side are extremely important here, but, in addition, there are some analogies.

So, there may be ways that we can bring in some of the stuff from...indeed, from Chapter 4 into Chapter 9 as far as an overall, you know, integrative synthesis. We will have to be thinking through and be creative, perhaps, about just exactly how one approaches to fit in the overall flow that we now propose to set up, and that is sort of in line of the question and so forth or addressing issues of the type laid out in topics 1 through 10, for example, coming from the NRC report. You know, we can see what we can do.

**DR. WHITE:** The NRC report is clearly focused on health.

**DR. GRANT:** Yes.

**DR. HOPKE:** Well, are there...yeah, Petros?

**DR. KOUTRAKIS:** I have a question in here. Somebody else might help me. Is the integrative...is the synthesis a catalog of headlines or highlights of the review, or is it something that has to be concise and really address specific questions across disciplines? Because the

way I saw it, it was just a catalog, but I am not sure what is the definition of synthesis for a Criteria Document.

**DR. HOPKE:** Well, I mean, that is why there is a problem with the current summary chapters...chapter summaries. The current chapter summaries are recapitulations. They are not syntheses of what we know and what we don't know.

I mean, the idea of having this document is, ultimately, to have a clear description of the science as it currently is, including what we know and what we don't understand, and if we work a little less at recapitulation and a little more at really review and real synthesis in those chapter summaries, then we can move to a synthesis chapter which really gives us a better feeling of where we are, you know, what are the relationships between sources, ambient concentrations, exposure in the ecosystems and people, effects on both of those systems as informed by dosimetry toxicology and informed by exposure and epidemiology.

Now, you have got a, you know, still following along with the basic risk paradigm, you have got a flow where you come away with, you know, a set of bottom lines that, I think, provides much more use to the reader in terms of what we know about the science of airborne particulate matter and its adverse ecological and health effects.

**DR. KOUTRAKIS:** In that case, I agree with you that that should be, but I am not sure if the

existing document really provides that.

**DR. HOPKE:** I don't think it does.

**DR. KOUTRAKIS:** Okay.

**DR. HOPKE:** But that, you know, I think we can, by providing these kinds of comments today and more detailed written comments, we can help to focus them in those kinds of directions, but I think the key starting point is those chapter summaries, because, you know, if we can start to move so that those chapter summaries are much more informative than they currently are, then I think we have made a big step forward in making it much easier to put together the summary chapter.

Mort?

**DR. LIPPMANN:** It is impossible to scan this at this point and talk about what is not there, but, clearly, there is a lack of explicit address for two mixing issues. One is the coarse particles. EPA has to address it, because it has to consider whether it should establish a coarse particle standard. It can't use  $PM_{10}$  anymore in a standard, and, admittedly, there is far too little information to come to some really firm judgments.

But I think, as you rewrite Chapter 9, if nothing else, at each point, you say we know very little, we wish we knew more, but this is the state of knowledge so that the people writing the staff paper can deal with that issue, having your authoritative statement of what we know and what

we don't.

Likewise, we know much less about the relevant dosimetry toxicology and other aspects and exposure related to the annual mortality and its consequences for the annual standard. So, in writing Chapter 9, again, I urge you to summarize and synthesize what we do know, and there is considerably more than about coarse particles, and coarse particles do not seem to be associated with mortality either in the annual or the time-series, but to at least explicitly address the issue of setting the annual standard based on fine particle effects on mortality and anything else it is affecting.

So, you have got this richness of information that we traditionally looked at, but there also needs to be a specific recognition of the paucity of information on some key issues that OAQPS will have to face.

**DR. HOPKE:** Ron?

**MR. WHITE:** Well, I think Chapter 9 right now, in terms of the structure, they took the advice of the committee and formatted it according to the risk paradigm from the NRC report. I still think it is...and maybe this is what you were saying about the summaries from the chapters, but it is essentially, in a lot of cases, just reiterating what is in some of the earlier chapters. It really doesn't pull it together, I think, the way we are expecting it to and, I suspect, maybe the Agency would like to do, given more time to work on it.

I think it would be, I think, helpful for all of us to offer some suggestions on how they can do that, and whether that means posing some additional questions that they ought to be responding to beyond just the specific risk assessment paradigm questions that are in the NRC report or giving them some other way of pulling these things together, I think this just doesn't do it.

I mean, this just really is getting the same tables and studies, and it is not what I think we need. In fact, it is probably a lot longer than it needs to be in terms of trying to pull together an integrative synthesis of the information that is in this extremely long document, and I think a lot of folks around this table are concerned about the length of this document and how much is in it and why does it have to be this long.

Well, you know, it may need to be as long as it is for a lot of reasons in terms of making sure you have all the science in there and covering your bases on that, but, certainly, this chapter ought to be, you know, where you are really pulling everything together in a very concise way, addressing the key questions, and not feeling like you have to recapitulate all that information.

**DR. HOPKE:** Absolutely. I wholeheartedly agree. So, I think the key is for those who have suggestions to, again, get them together with your individual chapter assignments, and let's get these all to Bob and me by July 29th. I know that is a tight deadline, but we really want to

keep this process moving.

Now, at the same time, over the next two weeks, Les and his crew will be looking hard at trying to prioritize the studies, get us together a game plan of what his top picks are in terms of the studies they would like to see reanalyzed and included, get some idea from those investigators, to the extent possible, for reanalysis of the key studies, what they are going to do in terms of having a workshop and when that would be, what their suggestions are with regards to a uniform review process by which we could judge the reanalyzed studies, and get that to us, as I say, in about two weeks.

What we will do, then, is distribute it and ask you to start sending your comments in as soon as you get that so that they can start to see what we think about those ideas. What we will try and do, then, is to plan a teleconference for the last week of August, because we have to have a 30-day magic Federal Register notice in order to have a teleconference, and, since in the third week of August, I am going to be in Christ Church, New Zealand, it doesn't work until we get to the fourth week.

**SPEAKER:** That's your problem.

**DR. HOPKE:** Yeah, that's my problem. Okay, anyway, that way, you know, we can look...you know, we will have been feeding back our ideas to Les from the time we get them. We can come together as a group, develop a consensus. If there are some manipulations of things, we can suggest those, try and work together to come up with a final

game plan.

I would, at the same time, hope that I would have the summary of this meeting together, roughly, a week after the 29th, somewhere around the 5th or 6th of August, which we would circulate to you for your comments and which we could potentially approve at that same teleconference.

**DR. LIPPMANN:** Question. Should we be sending our further comments to Bob Flaak or to Les Grant or to both?

**DR. HOPKE:** To Bob.

**MR. FLAAK:** Forward them to me with a copy to Phil, and I will forward them to Les. That way, they are a part of the record.

**DR. LIPPMANN:** That is what I thought. I think Phil might have unintendedly said that Les should get our comments.

**DR. HOPKE:** Only on the plan. In other words, what we would like to do is to start some informal feedback to Les after the game plan comes out.

Yeah?

**DR. GRANT:** I think what Mort means is your comments on these chapters, Mort, into Bob, and in the meantime, we will also be sending out our thinking about prioritization of the studies and the approach for a workshop or whatever to begin...you know, send out by email or whatever to begin getting some ideas back, feedback, and then

the conference call that Phil mentioned.

**DR. HOPKE:** And, hopefully, by then, we will have some approximate time lines. Obviously, Bob and Zisa will be getting in touch with you with regards to your availability later in the year, because we will, obviously, need to have a meeting somewhere, and my guess would be that problem January is where we would be looking at as a likely date, but, you know, until we see a little bit more the lay of the land, it is not quite clear how we, you know, can be making final judgments.

But I think we come away with two chapters essentially finished. We have got four chapters that are in pretty good shape that need, you know, some fix-up, clean-up stuff and we would like to see again but we are not going to take enormous amounts of time to go through, and then we can put our full attention onto 8 and 9 and executive summary and pull this together in the next meeting.

Now, also in the fall, we will have the outline of where we are going to go with developing the ozone Criteria Document, so, some of you will...you know, the CASAC members for sure and, potentially, some of the other people will potentially wind up on the ozone panel, because you are multi-talented. So, we will have, again, a teleconference somewhere down the line to go over that and start looking at the time lines for pulling that together.

At this point, let's ask Karen if she can give us, then, some idea as to where we are going with risk assessment

staff papers and the other side of the process.

**MR. FLAAK:** Karen, please identify yourself for the record.

**MS. MARTIN:** Karen Martin of OAQPS.

**DR. HOPKE:** Okay, a little closer.

**MS. MARTIN:** Is that better?

**DR. HOPKE:** Yes.

**MS. MARTIN:** I can give you a very short update on where we are, and I doubt that anything I will say will be a surprise to you. In the very near term, we will work with Les on the game plan to try to bring as much focus on priorities most directly relevant to the review of the standard, as you all discussed earlier.

We are continuing to work on air quality analyses to try to bring air quality information as up to date as appropriate and working in conjunction with Joe Pinto and others in regard to that.

We are continuing to work on the risk assessment that we have discussed with you all on the methodology for the assessment. Clearly, we are not going to get ahead of the Criteria Document. We are not going to get ahead of dealing with outstanding issues on epi studies to actually move forward to do the quantitative aspects of the risk assessment, but we did have consultations with you with regard to methodology with regard not only to the aspects of the assessment that deal with fine particles but also

broadening that to looking at coarse particles or PM<sub>10</sub>, as we discussed with you earlier, and we will continue to incorporate that input into the methodology, but, as I said, we are not going to get out ahead in doing quantitative assessments until we are more comfortable with where we stand with regard to what epidemiology results we really want to use to feed the quantitative assessment.

Neither are we going to go beyond where we can in terms of other aspects of the staff paper until we can appropriately link that to revisions yet to be made in the Criteria Document.

So, I have no schedule to offer. Our schedule will follow the development of the game plan and schedule related to the Criteria Document.

**DR. HOPKE:** Might I suggest that, you know, one of the things that probably could be useful is when the dust has started to settle a bit more on the questions of these epi studies and you feel, you know...because, normally, you have started on the risk assessment before the CD is closed. It might be useful to again think about a teleconference to just, you know, again, talk about...see where we are in terms of the reanalysis and what these studies are and, again, just review what studies are going to be used and how they are going to be used and how, you know, you got to the point where these are the sensible things to put into the risk assessment.

**MS. MARTIN:** I would agree that would be a reasonable forum, following along the teleconference we had earlier this year to address some of those issues.

**DR. LIPPMANN:** I can certainly understand the reluctance and, in fact, the necessity of waiting for the resolution of the time-series data before doing any risk analysis, but I thought I...at least, the message I got from this meeting was that there was no call for or need to wait on the annual mortality risk assessment, because we have not asked for any changes in the treatment of that in the Criteria Document.

That, clearly, is one of the major components you have to deal with in terms of your risk assessment. Are you waiting to start that also?

**MS. MARTIN:** No, we are not waiting to start that. That is one aspect of the assessment, and that work, the methodology for that, had been well along on that with regard to the fine particles. So, that is...that is a reasonably straightforward piece to continue to carry out, but it is just one piece of the broader assessment.

**DR. LIPPMANN:** But since it is such a major piece affecting the annual standard which, we all know, is really the controlling standard in most parts of the country, I would think that when this committee meets again, you could brief the committee on how that aspect of the risk assessment is coming along.

**MS. MARTIN:** We will see where we are on that in relation to the timing of the upcoming meetings.

**DR. HOPKE:** Roger?

**DR. MCCLELLAN:** Somewhere along as this moves along, I personally think it would be very useful if you and your staff were to lay out for us, absent the quantitative information at hand, whether, in essence, the decision structure that you propose to use in the staff paper addressing, basically, how you use that information to arrive at your decisions, in a broader sense, how low is low enough, and I think if we probably were to poll people around the table, certainly as I have talked with them individually, some individuals feel it is very clear how you arrived at decisions in terms of the previous staff paper in terms of your ranges and then how you moved from those ranges to actual specific numerical values you selected. Other individuals say that was kind of a black box mysterious process to them.

But I think we are now in a position where it is going to be very important to lay that out, that rationale of the decision structure, and it seems to me that perhaps you could expose the committee to those, your thoughts on that, in advance of actually having analyses in hand. In fact, the discussion might even be better, might be richer, if you will, without having it contaminated, if you will, by specific number setting in front of us. That is my personal

view.

**MS. MARTIN:** To add to what you are saying, we certainly made every effort to spell out in the last staff paper and in the rationale for setting the standards to try to be as clear as possible about exactly what the thinking was that fed into it. There was certainly no desire to present a black box, and we did make every effort to be very clear.

I would just reflect for a moment on the purpose of the staff paper, and the staff paper is not a decision document. It doesn't lay out the reasoning for the final standard. What its purpose is is to lay out a range of alternatives reflecting the science as we understand it as well as the range of differing views about how one should interpret that science in the context of setting standards. And that range of alternatives and what different alternatives imply in terms of how they interpret and weigh differently the elements of the science that comes to us, that is the purpose of a staff paper.

So, the staff paper, I cannot articulate a decision framework in the context of the staff paper, because the staff paper isn't the place where we really reach a decision about the standard.

**DR. MCCLELLAN:** No, no, what you have just explained to me as the purpose does have a decision structure around it. It stops short of what your final decision is, clearly.

You know, I would also...let me just go on and say I think last time, the CASAC was remiss in not exercising its option to actually comment on the proposed standard. I would hope, this time around, that CASAC would afford itself that opportunity.

I think perhaps the use of the word decision analysis structure is what is putting you off, I sense, but ultimately, I think that it is going to be increasingly important to be able to...for people to clearly see how one arrives at the standard and start getting the committee familiar with that, including an aspect that rarely gets any real discussion in terms of the group, and that is the statistical form of the standard.

So, I think there is some work you could do in terms of educating CASAC on that that is going to make it easier for the CASAC panel to come to closure on the staff position paper and will have put them in a better position to review that next piece of the puzzle.

Just a comment for your consideration.

**DR. HOPKE:** Basically, it may be good, in sort of a short document, to lay out how you map the science that is in the CD onto the policy questions that need to be answered and how you then start to pull those things together to come up with alternatives and, you know, potential ranges of standards, et cetera. In other words, a bit more of how the rationale and the process works in terms of seeing how you move from a to b to c.

