
US ENVIRONMENTAL PROTECTION AGENCY

SCIENCE ADVISORY BOARD (SAB) STAFF OFFICE

CLEAN AIR SCIENTIFIC ADVISORY COMMITTEE

(CASAC)

# OXIDES OF NITROGEN PRIMARY NAAQS

# REVIEW PANEL PUBLIC MEETING

MARRIOTT AT RESEARCH TRIANGLE PARK

4700 Guardian Drive

Durham, North Carolina 27703

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8:36 A.M.

U.S. ENVIRONMENTAL PROTECTION AGENCY
CLEAN AIR SCIENTIFIC ADVISORY COMMITTEE
PUBLIC MEETING
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DR. HENDERSON: I want to thank everyone for being so timely in submitted your paragraphs to Angela, and I thank Angela for bringing it all together. Now that what's being distributed - -

SPEAKER: Hello?

DR. HENDERSON: Hello.

SPEAKER: Rogene, can you, you need to speak into the microphone.

DR. HENDERSON: Okay.

SPEAKER: Thank you.

DR. HENDERSON: What's being passed out is a compilation of what was submitted, and these are all, everything, it's truly a compilation, but I've read it through it, and I compared it with the list, this small list is, these are the points we listed yesterday afternoon that we thought should be included. So, you might, quickly, compare this list with what's in, what you'd submitted to see if we left anything out.

But the consideration that we're going to be making is, is this the substance, does this include



everything you want to say to the Administrator in our letter. And, it's not the exact words, because Angela and I will have to go through and make it sound like it was written by one person instead of a committee.

But, that is, it's not, it's going to be smoothed out, but does it contain the substance of what we want to say? Can we agree? Do you feel comfortable with what is written here as a compilation of everything that we want to say to the Administrator in terms of our peer review of the first draft of the ISA? And, while you're reading that, I think with, I'm going to, I have neglected to let Angela do a roll call of who's on the phone. So, I will turn it back to her while you're reading it.

DR. NUGENT: Thank you, Rogene. As we start this second day, and we complete the discussion of the ISA, and then move ahead to the discussion of the methods document, I wanted to welcome the people on the phone, and make sure everyone in the room knows who's on the phone, and then talk a little bit about the public comment period, here. So, may I ask, please, what CASAC panel members are on the phone today? Are the CASAC panel members on the phone right now?



DR. NUGENT: Good morning.

DR. LARSON: Tim Larson.

DR. NUGENT: Good morning.

DR. ULTMAN: Jim Ultman is.

DR. NUGENT: Jim?

DR. HENDERSON: Jim Ultman.

DR. NUGENT: Ultman. And, Lee Anne, are you on the phone? Okay, all right, and just a note about public comments. I'd mentioned yesterday that we were inviting public comments on yesterday's discussion relating to the ISA. No member of the public has asked me to speak this morning about the ISA. I'll ask one more time, because we want to be a little structured about how the discussion proceeds. Are there members of the public who'd like to present some comments?

MR. HICE: Angela?

DR. NUGENT: Yes?

MR. HICE: This is John Hice on the phone.

DR. NUGENT: Yes?

MR. HICE: I'd like to make a very, very short comment, if I could.

DR. NUGENT: Thank you, okay. I'll write that down, and we'll turn to you in a moment.

MR. HICE: Thank you.



DR. NUGENT: Let me also mention that we didn't explicitly list on the agenda public comments for the methods document. And, I would like to know whether, once we complete this ISA discussion, there are members of the public who'd like to present some brief comments on the methods document. Okay, hearing none, I think we should proceed. Rogene, John Hice has some remarks, and I propose that we take them now.

DR. HENDERSON: Now would be a great time.

DR. NUGENT: Thanks. I think your audio's working well for us here, so please, speak into your phone set, and we'd love, we'd like to hear your comments now, please.

MR. HICE: Thank you very much. I just wanted to reiterate that we'll be providing written comments for the record to EPA by that deadline, it was October 31st. And I'm sure several other groups will also. And I would just ask that the CASAC folks take a look through those comments, at their convenience, and add those thoughts to their own as they think about the review of the next draft. That's all.

DR. NUGENT: Thank you.

DR. HENDERSON: And I thank you, too. I, now, can people hear me if I hold the mike up like

this?
SPEAKER ON PHONE: It's fine, Rogene, for me.
DR. HENDERSON: Okay, that's good. This is probably easier than dragging that hand mike. Okay, have, Angela sent the list of substantive material that we want to have in the letter to the Administrator. Have people had a chance to look at it?
SPEAKER: Rogene, you talking about the short list or you talking about the big one?
SPEAKER: Big one.
DR. HENDERSON: I kind of meant the big one. This list, this small list, that doesn't have a time on it, is just the notes I jotted down when we were talking at the end of the day yesterday, when I said, you know, what are the substantive issues we want to convey to the Administrator. And these are simply my notes. We were in agreement yesterday that this list included everything we wanted to say.
Now, would, what I'm asking you, now, do you think these were captured in the more formal listing that Angela pulled together from the people who summarized each charge question? Well, that's a good idea. Though some of these overlap quite a bit. We have charge question one that, have you had a chance to



look at it? Would you like to have ten minutes just to look at this one, okay. Gary's nodding his head. Okay, let's, we will just, we're not breaking. We're just giving you time to read it, because this is important enough. I'd like for you to have had a chance to look at it carefully.
(WHEREUPON, the members read the document.)
DR. HENDERSON: I gather from the conversation that is starting that people are approaching the end of their reading. Are you about ready to move on? Okay, what I'd like to hear from you first is, is there anything left out of this that should be added?
SPEAKER: Are you asking just about question one, or about all of the questions?
SPEAKER: Let's go question by question.
DR. HENDERSON: You want to go question by question? Okay. We'll take charge question one. Is the response written her, does it include everything that you think should be included? Ron?
DR. WYZGA: One of the things that I think could be useful could be, if they could have more quantitative discussion about the rates of transformation of, I guess, emissions into different species of NOx and what are the influences on these



rates. I don't know if that information is available. It's not my area quantitatively, but I was looking for it, and I didn't see it in there.
DR. HENDERSON: Okay.
DR. CRAPO: Also, with respect to question one, I think that this is an appropriate place where we need to ask if there could be a better assessment of issues related to background, and peaks, and variations in exposure, more data about the variations in exposure across groups, so that we know what the, what percent of, or some idea about what fraction of the country are people, or indoors, or outdoors, is exceeding, or not exceeding the current standard, but substantially higher than the current annual average. So, that the, the focus on an average annual number makes it really hard for me to analyze what the exposures really are. So, I think we need more data on that side of the table.
DR. HENDERSON: Okay.
SPEAKER: Well, I think that actually falls directly under question two.
DR. CRAPO: Two, that be great.
SPEAKER: That's where ambient mon-, concentrations are. Some of it's there, but maybe just what more might need to be there.



DR. HENDERSON: Okay, we're looking at it again. We come to two, does anybody else have things on one, yes, Terry?
DR. GORDON: Just the general, when I read over this, I got the feeling that we were, I mean, it's, the ISA is supposed to help us assess things, and seems like some of the things asked to be added were just making it more criteria document like, just making it longer, and not, not helping us decide things.
DR. HENDERSON: Well, that's the strug- -
DR. GORDON: Just a caution.
DR. HENDERSON: That's the struggle that's going on, and some of this might go in the annex. I mean, but, we ask that it be condensed, and that the only policy relevant information given. And what you're saying is, now, we're asking to expand it in - -
DR. GORDON: In some areas.
DR. HENDERSON: In some areas. Mary?
DR. ROSS: Well, that was a point of clarification I was going to ask for in general. It says in the ISA's to include material. Maps, in particular, will make it longer. So, one of the questions is, can we balance between annexes and have, expand the ISA a little bit more, but add more of the

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annexes, too, and just a clarification if that's what CASAC means when they say in the ISA, or it really mean in the ISA.

DR. HENDERSON: Okay. That's a very good point, and if we say ISA, do we really mean the annex, so.

DR. WYZGA: And Mary, if these could be cross references to the annex, I think that would be helpful, too.

DR. HENDERSON: We'll go on to question two, because that is what James asked for, you think, is that included in this answer to question two?

DR. POSTLETHWAIT: Actually, as a present follow up to James' point, I'm wondering about this issue about getting a little better handle on, first of all, exposures. I don't know what data is available, but even if some relative analyses of speciation of NOx could be included, just to give us a feel. I mean if NO2 is 95 percent of it, then the rest of it's fairly trivial. If it's 25 percent of it, then, you know, there's certainly other issues to consider. And, I think those two things ought to be in the ISA, and not in the annex, so the reader has that, sort of that, visceral feel as he, as they continue on to the health effects portions, et cetera.

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DR. HENDERSON: Present those, the two points again, so I'll be sure and get them right.

DR. POSTLETHWAIT: Well, again, to speciate NOx, whatever's available, and then the issue of what we know about personal exposure, temporal paradigms.

DR. HENDERSON: Okay, some of that may not be available in any of the exploits, but we, and I agree with you, then, by healing what you want. Yes, Ted.

DR. RUSSELL: If I might, and this, also, is captured in response to question three. There's the discussion about the importance of the height of the monitors that shows up both in the last, sort of, section on the response here, as well as in, there's a fairly large bullet in the next one.

There's, currently, a pretty large section in the ISA on the impact of monitoring height, and I, actually, found that was much larger than it should be, and maybe even a red herring as such, in terms of how it might be addressed in the ISA. For one, there's a lot of information out there where you could compare the values between different height monitors, as opposed to just looking at one special study where they did it. Which, I think, would, gives you a biased

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view.

So, my recommendation would be much the opposite as, maybe, minimize this, say that monitoring height could be important, but if they're going to address it in the ISA, they should do it in a more conclusive fashion, and look at more monitors where this, where they could pick up this impact.

DR. HENDERSON: Okay, I know, Dale, you - -

DR. HATTIS: Yeah, I want to slightly disagree with the fact that that's over-emphasized. I think that's a critical component of the analysis that, if anything, should be extended to an analysis of, actually, what the biases are in, as-, you know, would be, in assuming that the distribution of levels of the existing monitoring sites are representative of outside outdoor levels, because it does mean that you can't really directly com-, without an analysis of that problem, you cannot directly compare the levels inferred from monitors with the, it helps you reconcile, to a degree that it's possible, the, any concentration response relationships you infer from it, the epidemiological data, with concentration in your response you infer from things like the Australian study and the indoor, other indoor studies, which are

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based on - -

DR. RUSSELL: But you now, tremendously larger impacts horizontally and spatially than vertically, so I think that that's being blown out of proportion, versus where you're placing a monitor close to a road, or you know, four or five hundred meters away from a road in a park, because that's where you're going to have the bigger differences.

DR. HATTIS: Well, I think that's, also, an important area, but this is a systematic error, you know, and the other may well be much more - -

DR. RUSSELL: No, it's, they're both systematic.

DR. HATTIS: The health studies are based upon aggregate exposure, agg-, exposures within big cities, okay. And those includes both stuff near roadways and not near roadways. So, essentially, that tends to be biased by the verticality, although, there are, in fact, some sub-populations within cities that are even more exposed, okay, because of their, you know, proximity to roads. So, I think that the influences are different, even though there may be a bigger overall number, ratio in the near roadway, far roadway. This other effect, really, is a substantial, why, I say, now, I don't think that it's overemphasized

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in the existing document. I would like to see a fuller analysis of both kinds of effects.

DR. HENDERSON: I want to be sure I understand what you're saying here. What is the difference, say, between, you know, vertically. Does Albuquerque have a different from San Diego, I mean, they, is that what you're talking about, I mean?

DR. HATTIS: No, no, no. This is a matter of the fact that, the monitors for all the cities are high.

DR. HENDERSON: Yeah, and people are breathing down low.

DR. HATTIS: And people are breathing down low, so that means that, systematically, the epi studies are based upon concentrations that are measured, that are underestimated.

DR. HENDERSON: And what is, what is the difference, the degree of difference, I mean, that you're taking?

DR. HATTIS: Well, I think that, that from the, you know, the brief discussion that I remember from the ISA, that that difference is two-, three-fold. But that's different heights of monitors. If you go down to the ground level, it looks like, you know, that could even be a larger factor. The fact

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that it's a systematic, you know, biases of several fold can have a big impact on what you might infer is a level that was, you know, protective of public health.

DR. LARSON: This is Tim Larson. I think the EPA monitors are sited, in most cases, in such a way that the inlet height biases are not capturing what you're thinking about, which is the vertical distribution in urban areas, primarily, in confined urban areas. And that, I agree, is a significant gradient that can be threefold. But, you're not going to see that at most NO2 monitoring sites, because their, the way their sited, they're, they tend to be in open areas. And the differences in heights of the inlets in those are-, in those open areas just don't capture the kinds of gradients of exposure that are important.

So, doing an analysis of all the inlet heights for all the NO2 monitors that EPA has isn't going to really capture that. And, unfortunately, there's just not a lot of data on the vertical distribution of the heights in the urban areas that are systematically done. We're doing a big study in New York City right now, trying to capture some of that, and there is some European data on this subject, but compared to the data that's measured at or near street

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level, it's fairly sparse.

DR. HATTIS: Well, whatever the best sources of information are to estimate the effect, you know, they need to be used. The fact of the matter is that, the existing epidemiological studies are based upon, what appear to be, biased measurements of the concentrations people actually receive. And, therefore, they are not directly comparable with the indoor measured concentrations that led to the observations in the Australian study and in the, well, Australian study. So, that's a big problem that needs to be addressed.

DR. LARSON: I'm unaware of any, or many NO2 EPA monitors that are actually sited on top of it, is that what we're talking about? I don't think that's true.

DR. GORDON: Well, it just seems that, from this discussion, I'm agreeing with Ted, now, 'cause I thought there was a big verticality problem. And if there is more data out there, this chapter doesn't get that across to me. It says there's a big vertical problem, but they might be variable by site, and that's not brought out. So, maybe Ted's right. It should be condensed but expanded in other areas. I mean they both should be discussed.

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DR. HENDERSON: Well, I hear-, what I hear people saying is that in urban areas, there may be a difference in, there may be a problem with the siting of the monitors, as far as the vertical differences in concentrations with NO2, but we don't have much information. I hear people saying, we don't need them, we don't know if that's true, so would you like, Dale, in the letter to say that this is a potential problem? That should be addressed.

DR. LARSON: There is some literature on this. I mean, if you could cite that, I, there, it's just not a lot of it.

DR. HATTIS: Well, whatever the literature is that's relevant to estimating the population exposures, that are true versus the population exposures that are estimated in the epidemiological studies, that's relevant to judging the levels at which you expect how many of X.

DR. HENDERSON: Sure.

DR. LARSON: But I think I'm on balance on Ted's, come down on, with Ted on this. I think relative, the NO2 EPA monitors in urban areas, the biggest gradients are horizontal. And they're not proximity to roadway per se. They're, actually, proximity to confined roadways, where you can get up

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factors of three to five times differences relative to the same traffic, of the same distance from a road in an unconfined location. So, you're not talking about twenty percent here. You're talking about three to five hundred percent differences. And similarly, factors two to three in the verticality at those confined locations with height of, those are big effects, none of which are being captured by any of this.

DR. HENDERSON: For any epi studies, there's always the problem of exposure. I mean, we're never happy with the exposure. Now, and, I think this is an example of some of the issues that come up. I think it should be mentioned in the letter. As I recall in reading through the document, it was discussed quite a bit, but - -

DR. LARSON: Well, the inlet height effect of the monitors is discussed, which I'm not sure is the important parameter.

DR. HENDERSON: I think in the letter, we do, we confirmed the fact that we are aware that the exposures, there's always a problem with measuring personal exposures in an epi study.

DR. HATTIS: Yeah, but this is not just the usual problem. This is not, the usual problem is a

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random error. And we know how to deal with that.

DR. HENDERSON: I understand. You're saying that this is - -

DR. HATTIS: This is a systematic error.

DR. HENDERSON: - - systematic because the, you think the inlets are consistently higher than the level of - -

DR. HATTIS: Look it, all I know is what I read in the ISA, and this seems to be, you know, what the ISA seems to say. And then I, sort of, believe that they will have located the monitors at elevated levels. You know, maybe, and if it's not true, then fine, you know, but.

DR. HENDERSON: Well, I, our charge is to advise them on how to improve the ISA, and are you saying you'd like the - -

DR. HATTIS: I'd like that, and I think that if it's, you know, if the analysis, if the statements in the ISA are correct, then, you know, maybe they need to be modified with, including the information from a larger literature base. But, you know, if they are, then it's worth an a-, worth some much more quantitative analysis, because it creates a serious difference between the types of measurements that are used as the basis of the epi studies, and the

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types of measurements that are used in some of the, you know, the better direct studies establishing the effects of the NO2.

DR. HENDERSON: To point out the uncertainties associated with the other, go ahead, George.

DR. THURSTON: Yeah, right, well, yeah, I agree with that last part that the problem is when you go to compare it to, like, indoor measurements and those measurements. But, it's not a problem with regard to interpreting and the epidemiology, I think we have to keep that clear, and applying it to for standard setting. Because, ultimately, you know, you're applying the standards at the central site monitors.

So, that's what you want to use in the epidemiology, and the fact that, let's say, those levels, let's say, they were fifty percent of what people were actually exposed to, it, then you would take all the numbers, double them, and then when you go to set the standards, divide them by two. I mean, it would be a waste of time.

So, I think that it's a fact, but it's not a problem that there are differences in the absolute levels between what's at the central site monitor, and

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what people experience on, at street level. But, only, the only place where I, you know, I think it is a problem that I can think of, you know, I agree.

When you go, if we're going to put some importance on these indoor studies, we ought to remember that those concentrations are not directly comparable to the central site concentrations. And that's, I think, the key that Dale brought out.

DR. WYZGA: And the clinical studies as well.

DR. THURSTON: Yeah, and the clinical studies as well, yeah, that's true. Because the actual concentrations associated with the NO2 exposures that we measure at the central site monitors are, actually, higher. And so, that might explain some of the differences that we see between the exposure studies, the indoor studies, and the ambient results. So, it, yeah, so that's going to have some importance later on in interpreting the results, so that is an important point to bring up in that respect.

DR. HENDERSON: Yeah, I can see that- -

DR. HATTIS: A condition of the central, there is always random error, addition, to effect, you know, and that's also a problem to be analyzed, but.

DR. HENDERSON: Well, okay, I see the

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point that, George, that, you know, you just made, and Dale, too, that there is, the, how something comparing the clinical and the indoor dose response first to what you may see in epidemiology. That can be, I think, clearly stated. Yes, George, do you have - -

DR. THURSTON: I just have one separate comment. I guess it, I'm not sure if it goes on two or three, but I think two, that I brought up something that I, in my quick review, I don't see reflected with, yesterday, which was that we need to, more clearly, delineate the difference between personal exposures to all NOx versus personal exposures to ambient NOx, and their respective relationships to outdoor central site monitors. I didn't see that written in here anywhere, and I did bring that up. And I hope that that's included.

DR. LARSON: Well, we had a bullet in section three on trying to look at the alpha, I guess I, the ratio of the outdoor to personal ambient.

DR. THURSTON: Is that what that bullet means?

DR. LARSON: Yeah, alpha.

DR. THURSTON: I didn't get it.

DR. LARSON: Okay, we'll fix it.

DR. CRAPO: Could I ask a question for

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clarification as I listened to the conversation. When we get an average annual level expressed for us, is that what, is that the average over the whole 24-hour day, then averaged annually. Or is that the high for the day averaged annually. Are we talking about - -

SPEAKER: Everything.

DR. CRAPO: - - everything averaged together, so when NO2's have the peaks during the traffic periods of the day, and it goes down very low at night, you're taking these high levels that occur during the day and averaging it out with twelve to twenty hours with, of low levels and getting a fairly low level out of it. That's, so, we need a lot more information about the peak, 'cause, probably, the average annual is about the last thing we want to look at to assess this st-, this substance.

DR. HENDERSON: You know, I think, that's what I have written down for your, what I wrote down for this. And we need to remember about the pattern.

DR. HATTIS: I've made a series of plots, actually, of the distributions of, for different average-, of NO2 levels for different averaging times from the existing data in one of the annex tables. And, so, we can talk about that later. Yeah, that's the, yeah, that's the graph, so, essentially, so if you

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want to talk about that in the context of the ISA, fine, or context of the other is fine, too.

DR. HENDERSON: Were you proposing that, well, this would be quite a few individual comments, but can you explain it to us what it's saying?

DR. HATTIS: Yeah. What this, I need to get it in front of me. What this is, is, essentially, plotting the, it is, basically, a lo-, what these are called is log normal probability plots. And, essentially, what's being plotted is the Z score, which is, essentially, the number of standard deviations that each value represents in the distribution.

So, that, for example, the first data point here is, generally, the first per-, is the one percentile level. The next is the, I think the five percentile level, et cetera.

But, plotted on a probability scale, so that, if, in fact, the date corresponded to a log normal distribution, which is the usual expectation, then the points would fall on the straight line. The regression equation in each case is an estimate of the, the intercept is the log of the geometr-, it's an estimate of the log of the geometric mean, and the slope is the, an estimate of the log of the geometric standard deviation, okay.

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So, essentially, these, so these, if these log transformed values were normally distributed, they should fall more or less on the line, and they more or less do. They are not perfect log normal distributions. In fact, the actual data have, don't have as fat a, in the tails as they should for a perfect log normal. But, essentially, what this does is to show the change in the slope is, means, essentially, the longer averaging time or, you know, more tightly distributive than the shorter averaging time. So, the shorter the averaging time that you take, the data are further spread out, just because of regression of the mean effects. And this says how, how, what?

DR. HENDERSON: I mean that's what you need said, isn't it?

DR. HATTIS: Yes, and this, basically, quantifies how much less the dispersed the lo-, the yearly and three averages are relative to the one-hour averages.

DR. HENDERSON: And that's what James is saying, that they didn't give us much information, I mean, yes.

DR. CRAPO: So, let me just ask a real practical question from a real simple mind. How many,

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if I, and instead of doing the average annual and saying that was fifteen parts per billion, what would be, if I took the highest one hour from each day, would that be two hundred parts per billion?

DR. HATTIS: Those data are in the table, and I didn't plot them.

SPEAKER: Actually, they're in the ISA, too.

SPEAKER: They're in the hot spot.

DR. CRAPO: Right, so what's the answer?

SPEAKER: 201.

(WHEREUPON, there was a discussion off the record.)

DR. CRAPO: Did I guess, I guessed it right on the money?

SPEAKER: Yes.

DR. HENDERSON: You get a gold star this morning.

DR. CRAPO: And the excursion, the high end excursion is from that? Do we have a significant if the population is exposed 500 ppd?

SPEAKER: No, that was an excursion.

DR. CRAPO: That is an excursion, I was, that is the excursion, okay.

DR. HENDERSON: Well, okay, Ed, go ahead.

DR. POSTLETHWAIT: Well, if there are

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estimates made of personal exposures, won't that capture that issue, as opposed to, when we compare data back just to annual averages, which gets back to the central issue of how much stuff are people really inhaling, versus, you know, what's the average floating around.

DR. HATTIS: Not exactly, because it depends upon, on the averaging time for the personal exposures, where you also will have a similar - -

DR. POSTLETHWAIT: Well, that's where, that's where temporal plot, if it was possible, would be really useful, even from a qualitative standpoint.

DR. HATTIS: Yeah. But essentially, you'd have to have comparable, you know, different lengths of time averages to be able to compare. And I, offhand, I don't know whether the internal, the indoor exposures are more variable with time than the outdoor. So, you can have a different, you could have different comparability depending upon the, you know, how, what that looks like.

I mean, there's, also, a likely case that the indoor exposures will be correlated with differences in breathing rate. So, for example, it may well be that while I'm up and about, one of the things I'm doing is cooking on my gas stove, and exposing myself to

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proportionally more while I'm breathing more.

DR. CRAPO: Ted has just pointed to me that the 200 ppb that we were talking about is probably at fifteen feet up and not at ground level, so that the ground level might twice that level. What?

DR. LARSON: Ron, wait, no way, no way.

DR. RUSSELL: More likely at four meters, aren't more of your monitors at four meters than - -

(WHEREUPON, there was a discussion off the record.)

DR. LARSON: Those kinds of gradients don't exist.

SPEAKER: What?

DR. CRAPO: You say gradients of that nature don't exist?

DR. LARSON: Not that, I mean, not that strong a gradient over three meters.

DR. PINTO: Yeah, no, I think you're right, I mean. I think what I was trying to say was, no, this particular data point, okay, where it was a change in Lakewood, California, downtown Los Angeles, in other words, and is one of the roadside monitors, so you would expect it a, first of all to be very hot; b, you would also expect the inlet to be at, you know, the standard there, at the standard height, which of the order of three meters or so.

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DR. CRAPO: The reason I'm bringing this up is that I think those of us that are really focusing on the health effects are not even in our heads not even correlated to the right thing. And we're sitting here looking at the ambient levels and thinking 15 ppb average annual, and we're seeing health effects in asthmatics and people living near roadsides. When, in fact, the people near the roadsides are getting 200 ppb. And our correlation, all these correlation coefficients on the things that we're looking at are, at least, I'm not sure that because we've used a, such a bad metric to correlate what's going on, I don't think that we're thinking correctly on the health effects side.

DR. HENDERSON: I think one thing we can emphasize in our letter is the importance of the temporal and spatial variability in the NOx exposures, and how that will vary.

DR. CRAPO: Because this makes our biological plausibility, the discussion yesterday, change directions completely. It puts us, it, we were arguing that we weren't exposing enough to NO2 to get the level. If these things, if these exposure metrics change, then our whole argument yesterday, the biological plausibility is met, becomes much more

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likely.
DR. RUSSELL: No, maybe Jill wants to go into this further. I mean, again, the high monitor is Lakewood in downtown Los Angeles. It's a roadside monitor, so it's going to be high. You know, actually, some of these monitors are sitting really near freeways.
DR. CRAPO: Well, so am I.
DR. RUSSELL: Right, but what I'm saying is that, keep in mind, when you're talking about, these monitors, many of these monitors are capturing very much the highest levels that you're going to get, except in a very confined street canyon.
DR. CRAPO: Okay, and that's what I'm thinking, is that the high levels that are causing the disease that we're seeing, and we're not understanding who's got that high level, and where it is, and why. As well as, at least, the medical side of us are, because we're not dealing with the numbers in the form. So, I'm just wondering if the, if this is, a large part of our discussion yesterday wasn't confounded by some of us not quite understanding the exposure levels that our sub-populations were being exposed to. And, you know, the fact that your, having those, no NO2 all night long is irrelevant to the fact that you get up in

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the morning and get a big dose from 8:00 a.m. to 12:00 noon or whatever.
DR. BALMES: This is John Balmes. I have to, I need a clarification. I thought I heard Tim Larson say that most of the site, and I don't have any map in front of me here on the phone. I heard Tim Larson say that most of the regular monitoring sites are not, they're in open areas and are not necessarily near freeways. But I just heard that a lot of the monitors are by freeways. That makes a big difference to me.
DR. LARSON: Not a lot of them. Some of them are, but not a lot of them.
DR. BALMES: Right, I think that's important to know.
DR. LARSON: Most of them are not.
DR. BALMES: Yes. That was my understanding, too.
DR. RUSSELL: Yeah, so I misspoke when I said a lot, but you do have a representative population of ones that are near freeways.
DR. BALMES: Right.
DR. RUSSELL: And those are the ones, or very heavily traffic roads, and those are the ones that you do see on the one extreme of our population. If

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you were, had actually got, a see-, cumulative distribution function, that those are the ones you'd see at the upper tail. So, I think we are capturing those. And, actually, in response to your question about the biologic plausibility is, I think it goes both ways, is that in many cases, I think we might be looking at overestimates of what the potential exposure to NO2 is in a general population. Because a lot of people live out in the suburbs, and you know, again, I'm sort of parochial in knowing at Atlanta, is that, we've got more monitors near busy areas, than we do sort of in the general suburbs.
DR. HENDERSON: I, well, again, I think maybe we can cover this by a paragraph discussing the importance of the temporal and spatial variability of the pollutants and this is not special to NOx. It's always a problem, and that we, that this should be emphasized to discuss in the ISA. And it is true that we'll extend, but I don't hear anything that's, that couldn't be covered under the importance of temporal and spatial variability, and the, what we listed, as far as monitoring and determining exposures that we, we had discussed this yesterday afternoon, there's the, you know, you have the indoor outdoor exposures, the spatial and temporal variability, the siting of the

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monitors, all of that is something that we've already said is very important. So, I would like to just summarize that in a paragraph in the letter, and emphasize how the differences between the more precise measurement indoor in the clinical studies, and, as opposed to outdoor ambient studies.
Does that, would that co-, I mean, we've, you're absolutely ri-, and if you don't have the correct exposure, the response then is, it can't be related to the amount of, precisely towards lead and, but that stands, that's always a problem with epi studies. They don't have it for very long exposures.
DR. AVOL: Just one small point of information, I think what Joe meant was Lynwood, California not Lakewood. The Lynwood station is alongside the Long Beach Freeway, and gets several hundred thousand vehicles a day.
SPEAKER: Yeah, thanks, Ed.
DR. LARSON: Well, as my comments yesterday, and you know, at each of those, you know, two sites, there is a information in the database on distance from major roads. And you could compile that fairly easily, and probably, compare that with the population, U.S. population at large.
DR. HATTIS: I think that'd be a good

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thing to do to try to see what biases one should expect and what, you know, how do we characterize the variability and the likely exposures in relation to the variability that we see in the monitors.

DR. HENDERSON: Is that something, Mary, that could be done?

DR. ROSS: We can look into it.

DR. PINTO: I mean, perhaps, with help from the program offices, I mean, I tend to think that that sort of effort if, you know, if done well, I mean, could take a bit of time and maybe, even, longer. I'm thinking in terms of longer than the time scale for setting the next draft to come out. But we'd have to look into that, Rogene.

DR. HENDERSON: Okay, well, let's, I think we've had a good discussion of this issue, which is a, certainly, an important one. Can we look now beyond the first three charge questions to going to the health, unless there's anybody else has something else on the first three charge questions. The next four charge questions relate to the health effects. And, was there, were there things that were left out or that, yes, Ed.

DR. POSTLETHWAIT: As part of the charge four things, and this just may be simply an issue of

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verbiage. On that third line, where it says only the key studies that support an NAAQS should be included. I wasn't sure what that meant, in terms of, to support what we have now; to support a new one, I mean. And when you read that, it almost sounds like you, as we discussed yesterday, you could, inadvertently, introduce selection bias on what studies you were reporting, positive versus negative.

DR. HENDERSON: Well, this still is from the, has a little history behind it. And that's what I, how I interpret it. If you looked at the CD, it includes everything from, you know, a 500 ppm exposure of a toad frog to, you know, something at ambient levels. And you're right. How do you choose the key studies. But I think the meaning of this statement is that, that chapter three could be condensed to even more to make it less like a CD, and more, just includes studies that are relevant for setting a standard. I think that's the meaning of it, but you're bringing up a problem which we have discussed, CASAC has discussed,

and who chooses, you know. But we came down that it was more beneficial for us doing this review to have the Agency choose what they felt were the key relevant studies.

DR. BALMES: But that, this is John

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Balmes, again. I think the last sentence in the bullet here, is, contains key information about that the ISA would be improved if a plan or process for integration and study selection is clearly laid out. So, that it would be clear to some, to a reader, such as Ed, why studies were included.

DR. HENDERSON: That's a good point. Yeah. Are there other things?

DR. WYZGA: Rogene, I had a couple of things on five, but.

DR. HENDERSON: Okay, Ron, and then Joyce, go ahead.

DR. WYZGA: Okay. I guess, first of all, I'm flattered that my name is mentioned, but I would also mention that John, in number five, John Balmes mentioned some toxicological studies that weren't included. And I would change the wording to say that, instead of several of the latest NOx human field studies is, basically, several recent epidemiological studies that examine the association between health outcomes and NO2, were, either, not included nor studied correctly, and say, especially, in describing the impacts of other pollutants on the NO2 health associations.

DR. HENDERSON: Certainly, and nobody's

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saying it's going to be mentioned in here, I mean.

DR. WYZGA: Okay.

DR. HENDERSON: You know, I mean, as I said, I mean, this will not be covered - -

DR. WYZGA: But, I guess, part of it is, it's broader than simply the epidemiological is because there's some toxicological studies as well.

DR. HENDERSON: Okay, yeah, okay. And, is that ment-, it's a tox study, yeah, Balmes, oh, yeah. No, we, it's mentioned there. Sure, Ron, never in my wildest dreams would I mention names.

DR. COTE: This is an opportunity, though, for me to ask people if you, if there are specific papers that you're aware of that we don't have, please give us the references. Because, you know, we've done this careful lit search, for whatever reason those papers have not popped up. So, you know, if it's a flaw in the keywords or whatever, so please help us by giving us the specific references rather than.

DR. BALMES: So, I will include, this is John Balmes. I'll include the ones that I referred to yesterday in my written comments. But the nitrogen dioxide will get the one paper published in 2005. You don't have to get fancy with the keywords.

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DR. COTE: Thank you.
DR. HENDERSON: Okay, so, Ron and John will provide, you will provide those in your written individual comments. Then that, then in the letter, we can refer to it. We can, see individual comments of, with them, okay. Anything about question six that people have problems with or would like to add.
DR. THURSTON: Well, as to the question five.
DR. HENDERSON: You back to five, okay.
DR. THURSTON: Yeah, well, I mean, actually, the reason I put Ron's name in there was to, so that I knew he would respond to that and clarify that sentence with it. I figured that, otherwise, he might get ignored and he would make sure it was correct. So, we could just write members also pointed out, or something, instead of put, naming names here. The other thing is, in the iterations, I don't know, either I didn't have it in the beginning, or it got left out or something, but I would add at the, in the last sentence, just, well, I'm just going to get this, finally, examining the epidemiology results, and I would say, after results, add the words across outcomes as a function of. Because, the whole idea was to look, not just individually, but look across outcomes and

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look for coherence. That's it.
DR. HENDERSON: Okay, and I will remind you, as far as wordsmithing, when we finish here this morning, Angela and I will be drafting the actual letter, based on the substance of these comments. And you will be receiving it for concurrence and review. So, small wordsmithing, you can take care of at that point if you want. Can we go on to charge question six, then?
DR. WYZGA: One, on question five.
DR. HENDERSON: Five, I'm still on five.
DR. WYZGA: And, is Lianne on the phone?
DR. HENDERSON: Lianne wasn't coming on till when, 9:00. What's Angela's time.
DR. NUGENT: Rogene?
DR. HENDERSON: Yes.
DR. NUGENT: Is Lianne on the phone? She said she would be on the phone.
DR. SHEPPARD: Yeah, I'm here.
DR. WYZGA: Okay, Lianne, this is Ron Wyzga. You said something yesterday, number five, something about, and I wanted to see if I could capture it, about looking more systematically or in a better organized way at the, how one deals with co-pollutants and interpret studies using co-pollutants. Did I hear

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you say that yesterday?
DR. SHEPPARD: I don't think I was the one that brought that up.
DR. WYZGA: Okay.
DR. SHEPPARD: Probably is an important point.
DR. HENDERSON: Okay, are there more comments on the substance of answers to question five? Go on to six, then.
DR. AVOL: I have a question on six. This Ed Avol. My question is this. About seven lines in, there's a comment about sensitive populations. There's no comment about genetic susceptibility in that, and I just have a question for whoever wrote this, if that was a conscious exclusion because they don't believe it's sufficient - -
DR. CRAPO: It wasn't conscious. It was late at night in the middle of a bad Rockies game.
SPEAKER: That was a good game.
DR. CRAPO: So, let's add that, let's just add that.
DR. HENDERSON: So, what line, at what line, yeah, where is it, what line is it, that - -
DR. AVOL: It's about seven lines down, the last just in, I'm sorry, there's evidence of

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adverse health effects in sensitive populations such as.
DR. CRAPO: And how would you say that, though. The only ones that have really been studied are the ones that are mentioned here, really. I mean, genetic is a theoretic thing, but there's no hard study that says this is a gene that creates susceptibility to NO2.
DR. HENDERSON: You could add a sentence - -
DR. CRAPO: I mean, I believe it's true. I just don't think, I can't think of a study that would prove it.
DR. HENDERSON: You could add a sentence saying, genetic polymorphisms may also influence the response.
DR. AVOL: I mean, there is some published information from our lab and others on GST, and the sensitive to oxidative stress mechanistic pathways.
DR. HENDERSON: We can put into the, genetically perception.
DR. POSTLETHWAIT: Will that fall under, stuff under question seven. I mean, does, six and seven are, essentially, addressing the same chapter in

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the ISA. And there is this issue of defining susceptible populations.

DR. AVOL: Yeah, that's, I mean, I think that's fine. I'd be happy to put it into seven. I just pointed it out there, because it seemed like it was - -

DR. POSTLETHWAIT: Right, yeah, I mean, this becomes redundant, just like, you know, I said it's redundant.

DR. HENDERSON: Okay, I noted that that should be mentioned. Are there other things for six or seven?

DR. RUSSELL: Rogene, before going on, I'm actually curious. On the last sentence, that, I mean, to me that's a rather important sentence.

DR. HENDERSON: Which question are you - -

DR. RUSSELL: Oh, six. That we concur on the findings and, et cetera, directly result in adverse impacts. And this comes, you know, I was sitting here a little uncomfortably yesterday about the use of the word likely causal when we, they say the strongest new evidence comes from epidemiologic studies of ED visits and hospitalization. And I'm an air quality person, so I, the medical end is somewhat beyond me, but,

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recognizing that the epi studies that we've talked about the problems with the monitoring and the spatial variability. There are some that find associations. There's others that don't. And, it almost struck me that, I was sitting here going, the strongest new evidence, and you have some studies that go the other direction, and I recognize EPA was, sort of, sitting on the fence on this one, too. Directly result may just overstate how I think I feel on this. And I'm wondering how others feel, too.

DR. HENDERSON: I think that's a strong statement considering our discussion. I agree with you. I don't find, I think we're all trying to figure out is there something here or not, and - -

DR. SHEPPARD: Yeah, I agree as well. I think that's pretty strong.

DR. AVOL: I think, in fact, that yesterday in the discussion, John Samet challenged the consistent coherent issue.

DR. POSTLETHWAIT: James, yesterday, you and I were talking, and you came up with a really great multi-word descriptor, you know, that might soften this a bit. And I'm trying to remember what you said. It was something about, you know, NO2 appears to be a key player, I mean, you said it better than that. And

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whether, in verbiage that, while it may not be the chemical species NO2, per se, certainly, there's a linkage between NO2 in the air and all the other goodies and these adverse health outcomes.

DR. CRAPO: I don't remember exactly what I said. I can tell you that I, last night, I deliberately wrote this sentence very strong, 'cause I wanted to make us talk about it. I think we have to decide, I mean, this is, I think, the heart of the paper right here in that one sentence. It tell them whether we really agree or don't agree with the fundamental conclusion of the document. The, when I get, at the end of the day, I'm impressed that the, it's not, we have to cite the few studies that were negative; but in fact, this is a, it's a ten to one vote in favor of positive, but it's not an equal, half were positive and half were negative.

These are, the most of the studies that come out are showing strong effects. And I do think that it's likely the effects are tracking primarily the products of combustion, which the paragraph says. The, but the, but there are, overwhelmingly, strong data showing an association that we haven't really dealt with. And I'm concerned that the biggest problem is in our exposure metric. I think that our correlation

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needs with, needs to be with the highest one-hour average.

Not, like ozone was before it changed to an eight hour averaging time. And if we converted all of our data to one-hour averaging time, we might have a lot more confidence in this conclusion. But I don't, but I can't walk away from the strength of the data that's summarized in the ISA. It's a very strong document with studies from every dimension from every, from lots of different countries, consistently finding associations with products of combustion that metric was within all.

DR. BALMES: So, the, this is John Balmes. I agree with you, Jim, James, that the epidemiologic data taken as a whole from a stratospheric level are pretty impressive. My problem is that I don't think the coherence is, necessarily, there with the toxicologic data. We talked about that yesterday. And I don't, actually, personally, have a problem with the Agency moving ahead with a new standard if that's the ultimate outcome, based on epidemiologic data. I do epidemiology.

I appreciate its value. But I think it's, I don't think the toxicology is really there to support the epidemiologic findings. And it's often that

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toxicology is behind epi.
So, I think we should recognize that, I mean, if we have to say that. Because, otherwise, people will criticize the document for not, sort of, fairly representing the literature. And I think, with regard to respiratory infection risk, I think the toxicology is there.
But I don't think that we understand why NO2 causes, or is associated with a kind of lung function decrements that the children's health study found. I think that's a very important finding that should be very strongly emphasized in the document. But I don't, I, certainly, don't understand how that occurs.
DR. CRAPO: Would you say the toxicology does support it if we're speaking about 200 ppb instead of 15 ppb?
DR. BALMES: Uh - -
DR. CRAPO: 'Cause I've changed my mind on that one.
DR. BALMES: Well, I think that's a greyer area, but I'm not sure that 200 ppb, the toxicology supports 200 ppb.
DR. LARSON: James, Tim Larson, again. 15 ppb is your annual average. The 200 ppb is your one-hour max. So - -

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DR. CRAPO: Well, that's one-hour max in monitors on certain places. It's not the one-hour personal max.
DR. LARSON: Right, but what's the, what is the annual average at that monitor. I mean, that, in terms of, if there isn't, I mean, there's two things going on here. One of them is spatial, you know, proximity to roads, et cetera. The other one is the annual average versus the one-hour average. Both cause differences in these numbers. But, when you say 200 versus 15, one's a chronic exposure and one of them's acute exposure.
DR. CRAPO: Well, I know that, but the toxicology's almost all acute. And the peaks are acute. And I, see, yesterday, I was sitting here thinking about the 15 ppb and saying, I've got an order of magnitude or two orders of magnitude difference in my toxicology and my epidemiology. But, in fact, I don't. It's, they're coming together. The lowest threshold effects for NO are, you know, are in some, a few hundred ppb. We saw that yesterday, where they looked at the lower limits of toxicology having effects. And now, we've got peak levels at fifteen feet up in the atmosphere, in certain locations, pushing the same levels.

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DR. LARSON: I'm not disagreeing with your general conclusion, but I'm just saying, to be more precise, those epidemiology studies are probably looking at 24 hour time series. And those 24 hour averages are certainly at a max greater than 15 ppb.
DR. CRAPO: Yeah, and I'm, but I'm also saying that is a, I think that NO is not driven, NO's health effects are not driven by the daily average. That's probably driven by the peak, and - -
DR. LARSON: Right, but - -
DR. CRAPO: - - and the, and we never looked at the peak in terms of comparison of.
DR. LARSON: Right, because a relevant comparison would be the 24 hour versus daily max hourly average. Because the type, and the epi are based, primarily, I believe, on the 24 hour, but I'm just saying, those are the two numbers to compare.
DR. CRAPO: Well, it is except that we're looking at fairly profound health effects, and, I mean, in many of these studies, and - -
DR. LARSON: Well, and I'm agreeing with you. I'm just saying that the change from one day to the next is greater that 15 ppb. And, you know, in some cases, the one-hour max could be several hundred, and the change from one hour to the next could be

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fairly large, too. So, I mean, the 15 ppb, it seems like, is, it's not even in the range of what we're talking about. I mean, that's an annual average, and it just gets washed out, as you say, by all the seasonally flow seasons and all the midnights and everything else, so.
DR. AVOL: This is Ed Avol. Not to go back to discussion of the health effects, but since the lung function changes in the children health study we brought up, let me just point out one perspective. And that is that in, of course, in looking at lung function growths or decrements in lung function growth among children, we're looking at long-term changes of children that are moving around their communities, and we're looking at those annual averages from those central site monitors in those areas. And so, while it may be true that close to roadways or at traffic peaks, there are several hundred parts per billion concentrations, in fact, our relationships with those changes in lung function are with the annual average.
DR. CRAPO: Well, I understand that factor. I'm just hypothesizing, I mean, I'm saying that the health effects appear to be real. And I, biologically, couldn't explain them with the annual average, but then it occurs to me that what's likely

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happening, maybe I only need to hit my kid with 200 ppb once a week in order to cause adverse changes in his growth of his lung. And I take him on my freeway for three or four hours a week while I'm driving various places. So, it could be that that's the problem, and we have-, but my point is, we haven't even analyzed it that way.

DR. LARSON: Right.

DR. HENDERSON: Well, there is no - -

DR. CRAPO: But the health effects are real. That's what this sentence says. The health effects are real. I don't know why yet, but I, there, and it might not, and it might be a surrogate, but they're, but they are so uniform across so many studies, that we have to take them serious.

DR. HENDERSON: Now, as far as - -

DR. BALMES: This is John Balmes. I agree with that. It's, but I, so the, the coherence in the epi, I have, I'm comfortable with. It's, if people are assuming from that statement that we mean coherence with the toxicology, I don't think we're really there yet. That's all I'm trying to say.

DR. THURSTON: Could I say?

DR. HENDERSON: George?

DR. THURSTON: Yeah, I don't really think

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we're at with, we may end up where this last sentence is, but I don't think we're there yet, in my opinion. So, I mean, I would just say, concur that the epidemiologic findings, you know, indicate, let me see. I had it written down here, too. Yeah, concurs that the epidemiologic findings indicate that current ambient NO2 exposures are associated with adverse effects on the public health. But the document needs to better document, or better, you know, lay out the plausibility, a consistency in coherence. I think that work, that needs to tightened up, and that's where we ought to be focusing this next iteration. I don't think we're done yet, and this gives the impression we're done.

DR. HENDERSON: That we're done. No, I would agree with that, and I'll let Mary talk on it. Would you write down your modified sentence so that.

DR. ROSS: While you're on that subject, I just want to draw your attention to a sentence a few sentences earlier. CASAC recognizes that the primary associations are between products of combustion and adverse health effects. That's also a strong conclusion that will have policy implications. And just wanted to make sure if that's something you agreed with. It's helpful if you provide why, you know, what

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supports that, too.

DR. CRAPO: Well, I'll say it, 'cause, actually, I wrote it with, we said it several times yesterday, but when, every time you do the study, you find that there's an adverse health effect, which you can link it, like, to the roadway, or to the children's study with an open fuel on their furnace in the home, the powerful correlations that go with this, the fact the primary source of NOx is combustion. So, it seemed like an obvious to me.

DR. RUSSELL: Yeah, that one I have no problems with.

DR. HENDERSON: I have no problems with that, either. I think that's a solid statement, but George, would you repeat your modification of the last - -

DR. THURSTON: Yes, I may have it here. CASAC concurs that the epidemiologic findings indicate, we'll see, that current ambient, is directly, no, are associated with. That's what epidemiology tells us, associations. Are associated with adverse impacts on the public health, comma, but that the document needs to better - -

SPEAKER: Articulate?

DR. THURSTON: Well, you could say the

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ISA needs to, yeah, the ISA needs to better document that these findings are plausible, consistent and coherent with, now do we want to say with toxicology or something with other evidence?

DR. CRAPO: Well, to me, I would say, in looking at lots of different medical kinds of issues, I see more consistency of this data than anything, virtually, anything that I make medical decisions on. A lot of consistency across broad settings, where the issue has been plausibility or coherence with the toxicology. And that was a dose issue. It was not, there's plenty of toxicology at high dose. There's no question about if you're talking about 10 ppb, I mean, 10 ppm, there's no question it correlates. So, the whole issue is, to me, the only issue is dose.

SPEAKER: Well, yeah, I mean, that is a big - -

DR. THURSTON: Well, I just think it needs to be better. I think you're probably right. There is, having read it, you know, there is a lot of that evidence, but it hasn't been laid out in a way that makes it obvious that where the coherencies are.

DR. BALMES: Well, one thing that might be useful is to look at the relationship between these one-hour peak exposures and the annual averages.

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DR. HENDERSON: I thought that was done in there, but I - -
DR. HATTIS: We do have direct evidence in a table in the ISA on that point, that essentially, the 99th percentile of the one-hour maximum is like 72 ppb. It's not the highest is like 200, but that's the highest of 288,000 measurements. So, I mean, you're a little bit far out on the scale there with the 200. But, certainly, the 99th percentile is about, is 72 parts per billion whereas the 99th percentile, the one hour of the yearly averages is 33 parts per billion. So, you have a couple fold there, which gets a little closer to the toxicology, but.
DR. HENDERSON: Mary?
DR. ROSS: You know, when we talk about - -
DR. HATTIS: But that's again, for the monitors that, some of them, which may be close to roadways, but they're still a little high up, so it may, may still be some additional distortions.
DR. HENDERSON: Mary?
DR. ROSS: We tried to evaluate the short-term exposure studies that looked at different indices, and there's a small discussion on page 5-5 of 24 hour studies versus one-hour max studies. And they

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don't find, there's not a lot of difference in the epidemiologic. Now, that is one-hour max on a given day, but, you know, we did try to evaluate that, and we'll look at if there are any further studies.
DR. HENDERSON: Okay, Ron?
DR. WYZGA: Rogene, I would say, I guess in the spirit of what we said, if you look at the previous sentence, we, basically, say NOx is a significant factor, and I wonder, given what we said later, if we could change the is to can be.
DR. HENDERSON: Yeah, I know, I see (WHEREUPON, Dr. Henderson reviewed the document.)
DR. ROSS: And can I ask one more, I'm sorry to keep bothering you but, when you say NOx, do you mean NO2 or NOx, and it's one of the things we battle with all the time is selecting the term.
DR. CRAPO: I use them interchangeably, because we did it yesterday. I don't think we know, exactly, what the species is, but NO2 seems to be a good surrogate for it, so you could use NO2, but, in fact, you're measuring the, you're measuring the, well, you're using it as a surrogate for NOx, so probably, I think NOx is your better term, because you don't really know it's NO2, do you?
DR. WYZGA: Except the studies have

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tended to look at NO2.
DR. CRAPO: Yeah, so I mean, you could say it either way, but since they interconvert, you're a little bit wondering what it really is you're. I mean, is the NO2 a surrogate for NO-, for all the other species. And so that's why I use them interchangeably, without being very discretionary. I knew, I need, you should use the same term.
DR. HENDERSON: So, you're saying, I mean, what you're suggesting, Ron, is that NOx can be a significant factor?
DR. WYZGA: Yes.
DR. HENDERSON: Does anybody have an objection, I mean, can we agree on can be?
DR. CRAWFORD-BROWN: Now, is that can be in the sentence of can be under some circumstances?
DR. WYZGA: Well, we've avoided making definitive conclusion in the last sentence, and we're saying, you know, we're waiting for the document to, basically, organize and, you know, give us a redraft. And it seems to me to make that conclusion that it is, it can be, and I think that's one of the things we're waiting on, you know, the next round, to see whether or not the document supports, you know, it is a significant factor.

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DR. HENDERSON: Yes, that's the sense that I understood. Okay, did we, for the NOx issue, we decided to keep the same term. What did you decide on the - -
DR. CRAPO: I like NOx better, because it - -
DR. KENSKI: I actually would prefer NO2 in the, you know, all of the epi stuff is based on NO2 measurements, and the tox stuff is NO2 measurements, and you know, yes, they are, they do interconvert, but you know, the peak, peak, I mean, you know, what we measure as NOx is, what we measure as NO2 is, you know, the difference between NOx and NO-, so I, I don't know. I just think it's better to be consistent and keep that, you know, link with NO2.
DR. HENDERSON: The toxicity data is based on NO2, I mean.
DR. KENSKI: Right.
DR. HENDERSON: Yeah, I mean, the clinical and the - -
DR. KENSKI: And what's repor-, and what's reported, granted, it's not, you know, absolutely pure, you know, true NO2, but it's as close to it - -
DR. CRAPO: Well, I wouldn't be, I'd be

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happy to accept either one, as long as that, someplace in it, you defined that three was interconversion and that NO2 is as, is a critical species in the sequence. So, you just make, as long as you define what you're using, that's fine to use the other term, as far as I'm concerned.

DR. KENSKI: It just might be good to add a sentence, you know, up front saying that, you know, we acknowledge that, you know, the NO2 that we measure is not, you know, true a hundred percent - -

DR. WYZGA: But I think the other thing is that, that we use NO2 with the relationship between NO2 and the other components of NOx may change temporally and spatially, and we don't really have enough evidence to say that it's consistent. And if that relationship were consistent, then, I think, we could jump to NOx, but it's not consistent.

DR. KENSKI: Right, and we're asking for a better, you know, definition of some of those.

DR. HENDERSON: Can we go on to seven and eight. I put in on seven about the genetics. I thought, I don't know who wrote eight, but I thought that was well written. It was very clearly written. Somebody wrote that. It's Doug. Oh, we, we'll get a my kudos to Doug. I thought that was well written.

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The, we've talked about the multi-pollutant aspects, and I'm, hope-, I think Ellis, probably, you contributed that. And, that will be, can be worked into the letter as a major point that, you know, after all our discussions, we still have this problem of the multi-pollutant aspects for, when we try to assess the risk of air pollutants, particularly the different oxidant pollutants. But, let's see if there's any big changes in seven and eight that we want to make. Particularly, anything we want to add.

DR. BALMES: I thought I heard yesterday that some people were uncomfortable with the idea of defining a susceptible group relative based on their where they live. That's the first bullet in, uh - -

DR. HENDERSON: Page seven.

DR. AVOL: I think Tim's right. There was some discussion about moving the issues of high exposure locations and near roadway into exposure.

DR. POSTLETHWAIT: Yes, and when I put this together during the Rockies game - -

DR. CRAWFORD-BROWN: I don't think the Rockies actually had a game.

DR. POSTLETHWAIT: That's what I was thinking. Yeah, I mean, that's, it can go wherever. The question is is whether it does, does increased,

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inherently increased exposure represent susceptibility.

DR. HENDERSON: Oh, okay, or whether it goes in the exposure.

DR. COTE: Just as a point of clarification on that. We tend to talk about susceptible and vulnerable populations, and susceptible is a more innate quality. And vulnerable being people at increased risk, or individuals at increased risk for some not intrinsic attribute. So, exposure would be increased vulnerability.

DR. POSTLETHWAIT: Then the first bullet needs to be changed to incorporate, not only defining susceptible, but defining vulnerable. And then, depend upon what the panel feels, you can leave the high exposure in there, or not.

DR. HENDERSON: Okay, I see, you, there is the, the people near the roadway are vulnerable because of the high exposure. That makes sense. I, and that's what the question asks, susceptible or vulnerable.

DR. ROSS: And to expand on that, the vulnerable population includes the two sub-categories, other than the biological, the socio-economic and the geographic were, generally, extrinsically sensitive. So, we could split that vulnerability up into two

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components, and that would address, I think, Dr. Avol's questions.

DR. AVOL: Yeah, but I think there is a interaction here in the sense that vulnerable populations, those are the high exposure alongside roadways, are likely, are disproportionately likely to be lower SES and get into issues of environmental justice. And then, they may have biological in that sense, be the former susceptible. They may also fall into the susceptible population as well. So, they get, sort of, a double whammy. But I think that it is true that there are susceptible and vulnerable sub-categories here.

DR. HENDERSON: Okay. Any more for charge question seven?

DR. COTE: If you have time, I had a quick question. The two on this, on the page five, the partial bullet at the top, the last sentence, the chapter did not address biologic plausibility with regard to specific populations, thus it's difficult to attribute health outcomes to direct causal. I think we're all in agreement when you have biologic plausibility, you're much better off. Or is this intended to mean, though, if you don't have mechanism of action information, then you can't say there's a

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causal outcome?
DR. POSTLETHWAIT: Well, my intent was to, sort of, throw that open for discussion that, would it make the document more robust to have, why would an asthmatic be more susceptible to NO2 than a normal. For example, what is it about the biology of NO2 that induces susceptibility in a specific subset of the population. Yes?
DR. COTE: Yeah, I think we can make that stronger. I'm not sure we can actually, and in each case, can be successful, do we not.
DR. CRAPO: The asthmatic has a more responsive airway, and greater responsive inflammation, and the NO2 is an irritant, so it could easily be an oxidant. So, it could easily be - -
DR. POSTLETHWAIT: That one's easy. Some of the others may not be so easy. And we can't - -
DR. LARSON: Are we doing, dealing with a likely causal, and that term. I mean - -
DR. POSTLETHWAIT: Yeah - -
DR. LARSON: - - causal is a diff-, is a higher standard than likely causal. My understanding was, you don't need the biological plaus-, I mean, you don't need the detailed mechanism to go to likely causal.

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DR. POSTLETHWAIT: Well, in a perfect world, the detailed mechanisms would be wonderful, but I'm not sure we're there yet, or even close.
DR. HENDERSON: And regulations have to be decided on, you know, even in the absence of mechanisms for sure.
DR. COTE: The second question I had is in the next bullet, the word unique. I wasn't and sure what was intended. So, it says a unique and probably susceptible - -
DR. POSTLETHWAIT: Hey, Jim Ultman, you're up.
DR. HENDERSON: Jim, are you there. You were there. Not answering.
DR. POSTLETHWAIT: He sent me this. I cut and pasted it in, so it's his fault.
DR. HENDERSON: Oh, okay.
DR. COTE: That's o-, it's not, it's not a deal breaker either way, so that's okay.
DR. HENDERSON: Well, I - -
DR. COTE: Thank you anyway.
DR. HENDERSON: Okay. We can find out.
DR. POSTLETHWAIT: I mean, there is some uniqueness in children because of the superimposition of exposure on top of growth and development. So,

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you've got injury, repair, growth, and development.
DR. COTE: Okay.
DR. POSTLETHWAIT: And, which is not, two of those factors are, don't occur in the adult.
DR. HATTIS: Yeah, if you want to back off from unique, you might say distinctive.
DR. POSTLETHWAIT: Sure.
DR. COTE: Thank you.
DR. HENDERSON: Okay. Did you get that, Angela, distinctive. Let's look at charge question eight and, uh - -
DR. AVOL: Could we just go back.
DR. HENDERSON: Oh, sure.
DR. AVOL: I'm actually, I mean, I think that Ed is right. It is unique because of the growth aspect. The tissues are in the period of growth and are more sensitive. And I think that is a unique attribute. But it's not a unique population, anything in the population that makes them unique, susceptibles population.
DR. HENDERSON: I think we can work that in. Let's see.
DR. LARSON: The first part of the sentence refers to the children's health, California health studies. The second part refers to children in

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general.
DR. HENDERSON: Yes.
DR. COTE: I thought the concept of the injury, repair, growth, development was what was useful for me.
DR. HENDERSON: Yes, I, and, maybe, we can put that in, that children, I don't know, are unique in that, you know, injury, growth and repair.
DR. POSTLETHWAIT: Actually, you could throw in a fifth variable, which would be dose, 'cause their running around breathing harder, we hope.
DR. HENDERSON: Okay, now can we go on to eight, and I, Doug wrote this. It just seemed like it was very clear and captures many of the concerns that the committee had. The, a multi-pollutant aspect, I think, it will be something we'll bring up at the end of the letter as a, you know, general concern we have for all airborne pollutants, and maybe we'll suggest the need for, in the future, striving to address, you know, multi-pollutants, rather than one pollutant at a time, a one atmosphere approach, which the Agency is trying to take anyway.
DR. LARSON: But, I also thought, based on the discussions yesterday, that there was a general scientific consensus that nitric oxide was not a

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confounder either in the palliative, its palliative effects, or its, you know, irritant effects. There was no, really no information at these concentrations. I guess, we don't really have the EPA summary of all the nitric oxide concentrations, but it just seemed like we had, sort of, generally, concluded that if, in fact, it is a mixture, it's, it doesn't seem to be the nitric oxide that's doing much of anything. And then, when you, when you, if you eliminate that, you're, sort of, the next most abundant thing is NO2, and then you start going way down in abundant for these other species that we don't know much about in terms - -

DR. HENDERSON: I agree, or what I was thinking of multi-pollutant was ultra fines and ozone and - -

DR. LARSON: I agree with that, but I'm just saying that, even though we can't, necessarily, say much about that, I think we can say something about the biological plausibility or the lack of it for nitric oxide. Because that seemed to be a point of confusion early on in yesterday's discussion.

DR. HENDERSON: Okay, I think it's pretty clear in the document. That's where I read it, so in - -

DR. LARSON: Yeah, I mean, we're just

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re-, I mean, I was just reading it. It seems, it still seemed to be a point of confusion.

DR. HENDERSON: Okay, I got it. We're coming to the end here, and as again, this is the first time we've tried this sort of process. And I need to know if everyone on the phone and sitting around the table is co-, if we modify as we have discussed here this morning extensively, if we modify the content of these points, are you comfortable with these, this being the substance of the letter that we send to the Administrator. Now, I'm not talking about wordsmithing, et cetera. Because, what will happen is that this draft letter will go to all of you, so if, you know, if you have wordsmithing problems, don't worry about it. It's the substance of what's in the letter that I want to know if you're comfortable with. And Mary, why are you raising - -

DR. ROSS: May I ask one final, about question number eight.

DR. HENDERSON: Okay.

DR. ROSS: We had actually intended that the entire ISA be the document that serves as support for risk and exposure assessment. If it is intended that only the conclusions chapter be the resource for risk and exposure assessment, what that's going to lead

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to is a major reorganization of the document to move a lot of information from the earlier parts into chapter five. That's not what we intended, though.

DR. CRAWFORD-BROWN: I need to answer that, though. I mean, I certainly would agree that the entire document is the resource to which people need to turn, but I just don't know what findings and conclusions mean if it isn't a summary of the most important and relevant points from the previous chapters. I, you know, I would think that there will be people who are going to say, look, I don't have time to read your whole document.

Tell me what I really need to know as a policy maker, as somebody who's going to try to do a risk assessment, and so forth. Tell me what I really need to know in order to be able to make those determinations. You're the scientist. I'm not the scientist. So, I just, you know, that chapter needs to be a chapter that does summarize everything from the past as far as relevant conclusions are.

DR. COTE: You know, I was going to, I meant to ask this yesterday, if there were specific examples where there were more important conclusions in the body than in the chapter five. If somebody could note those, just when you see them. Things were

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actually were written by the same people, and I think chapter five reflected, as we were working, perhaps, more refinement of thinking, and so, it's a little disturbing if it was better the first, rather than the second round of thinking, so if you ju- -

DR. CRAWFORD-BROWN: If we combine a list of the things that are back in the earlier chapters that - -

DR. COTE: That should be - -

DR. CRAWFORD-BROWN: But I think the main issue had to do, also, with the fact that the writing of chapter five does need to be the bridge to the user of this document, and what that user needs, as important information, for the kinds of decisions he or she is going to make. And that's where I didn't, you know, I, personally, I know Ellis felt the same, didn't feel that that connection was quite there, where somebody at chapter five began to ask, what are people actually going to use this for in the end. And that's why I raise this issue of integrated. I don't think there's such a thing as integrated outside of the context of the question that somebody is trying to address.

DR. COTE: Was it that there weren't

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of information were missing, or both?
DR. CRAWFORD-BROWN: I, but I mean, my personal opinion is that what happens with chapter five is that, it is, what often happens with concluding chapters in theses, for example, where it's just a compilation of things from the earlier chapters. Here's a thing from chapter one, and here's a thing from chapter two. Rather than somebody, systematically, sorting through and saying, what do we think we really learned from the earlier chapters that are relevant to the kinds of applications that we thought we were directing this report towards.
DR. CRAPO: I think a good example is the issue I was talking about a lot this morning about the dose metrics being annual average, and not telling you what the people, the populations were exposed to, actually, in terms of the more toxic elements of the high level exposures. And then, a discussion of that, so that the person who tries to interpret the health effects data, in relationship to the possible exposures, both for what they know and don't know, is not there in chapter five. A person that would read that and just think you had, it would just jump right from the exposure data, think it had totally supported all the findings. And so, I think, that disconnect

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that we struggled with for two days here needs to be obvious in chapter five.
DR. HENDERSON: And I lay a few, John Samet had quite a bit to say about chapter five in his comments. And he had the, since so many people had the same conclusion that it was really just a listing of the, what, of items from the previous chapters, excluding some, because several people said that, and not an integration of, you know, all five. So, I think that it really does need attention.
DR. COTE: Clearly.
DR. HENDERSON: You don't have that many people giving almost the same comments without there being something that - -
DR. COTE: No, no, I wasn't disagreeing. I was just trying to get more - -
DR. HENDERSON: Just get more examples and - -
DR. COTE: Yeah.
DR. HENDERSON: Yes, Ellis.
DR. COWLING: I would offer two comments. One is George's suggestion yesterday that, and it's relevant to what Doug was just saying about, what is relevant to the decisions that were made next. And it seems to me that he was suggesting that a scan be made

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of these 47 statements, or however many it becomes, and that those that are directly relevant to the issue of making a judgment about the standard be highlighted or marked in some way, and that the, so that's the first point. And the second point, in chapter two, you were asking for examples of then something that was mentioned in chapter two, but didn't show up in the summary that was in chapter five. And all of the nine statements in chapter five are relevant to the issue of monitoring alone.
DR. COTE: Right, I heard that, yes.
DR. COWLING: So, I was just thinking to mention those examples.
DR. COTE: Thank you, and what you provided on criteria for judgment, I thought was very good, too.
DR. CRAPO: I'd like to add one more thing. I think the biggest thing that might come out of this review of NO cycle is a recommendation that we go to a one-hour daily average instead of an annual average. And, no matter what the level is set at, it would totally change our science. But, we ought to set, I think that's what's needed more than anything else, because I think that we're measuring the wrong thing. And, I would argue that our document ought to

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set the, ought to, appropriately, set the background for that type of a recommendation, 'cause that's where I think we're headed. And it's not in there now.
DR. HENDERSON: Has the shorter averaging time been considered in the, by the Agency, because in our discussion, I had the same thought, James, and I thought, well, gee, maybe we're looking at the wrong averaging time.
DR. CRAPO: Well, both daily and, sure, I mean, one-hour and dailies is, those are two changes to it.
DR. HENDERSON: I'm just curious if the Agency has, that's ever come up.
DR. ROSS: Well, I mean, you can look in the history of the rule making, and in 1993, actually, you'd have to ask Karen Martin the specific history, but we made an effort to try to breakdown into short-term and long-term exposure discussions. And within a short term, there are a range of different levels. Many of the epi studies use 24 hour, but we did try to discuss the evidence at, related to averaging time. Tox studies use a whole variety of different exposures. And then, we try to make that available, to the extent we can say something about peak exposures, we will. There aren't many epi studies that look at peak

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exposures. I'm not even sure there are many tox studies, but we'll try to bring that up as much as we can. I mean, we're taking that ho-, as a comment that we need to address.

DR. CRAPO: Remember if the ozone field goes that direction, for shorter averaging times and it's, because it's been there for decades, it has really influenced the thinking of the evolution in that field. This data would suggest that NO2 has a toxic profile similar to ozone. In fact, it interacts with ozone to make it this toxic product. So, there's no rationale for having a different, an annual averaging time for NO2, and a short averaging time for ozone. I would just argue that you can use the science of the ozone science to justify a lot more evaluation of why NO2 ought to have the same type of short-term evaluation on it. And part of our problem is we set it up wrong thirty years ago, and we've got a bad collection of data to compare everything to.

DR. BALMES: I guess the other point that we should emphasize, this is John Balmes, is that if asthma exacerbation is one of the major endpoints that we feel the epidemiology supports, and I certainly think it does, then it makes no, you know, an annual average does not protect asthmatics from exacerbation.

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DR. HENDERSON: Okay, thank you. I was thinking of the ozone and, you know, the eight hour standard make sense because it's much higher during the daylight hours.

DR. CRAPO: And so NO2 is the same- -

DR. HENDERSON: Is, is NO2 in the same - -

(WHEREUPON, there was a discussion off the record.)

DR. CRAPO: NO's shorter than the ozone peak, isn't it?

DR. RUSSELL: It's actually a very different shape.

DR. HENDERSON: Yeah, I think we'd have to be a little careful, but you know, I - -

(WHEREUPON, there was a discussion off the record.)

DR. HENDERSON: Terry, Terry has his hand up, or you want to go to Dale?

DR. GORDON: I had a feeling that this conversation was going to go this way, and I was wondering if it did, we went to shorter term. Are we going to lose something. It sounds like people are leaning toward a short term, not a long term, and how would that effect the true long-term studies, such as the children's lung growth studies, which might be more correlated epi wise with annual averages. I mean, to

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me, the epi drives it. We'd, logically, might think, oh, it's a short term for that day that really drives it, but we have to come up with a value, and if all the epi is driven by lo-, the annual averages, we got a tough task.

DR. HENDERSON: That's a good point.

DR. CRAPO: For particulates, we have two, so we could keep both, then. We could put a short-term and a long-term standard in. Well, we couldn't, but the Administrator could.

DR. COTE: And if you were, if you're thinking about two different kind of health effects, like lung growth and asthma, there's no reason to think it would be the same. It might be, but I'm not sure, I don't know.

DR. BALMES: And, there's also no reason to have the same type of siting criteria for your monitors if you're going to go to a short-term standard. Because, I can walk down a street canyon for an hour and get a completely different exposure than I will at a EPA monitoring site for an hour.

DR. ROSS: Just to remind people, we're a little ahead of the process here, talking about the standards already and the sited criteria.

DR. HENDERSON: No, we tend to jump over

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to the endpoints, so let's, but, I really would like to draw this together so that we complete our peer review of the ISA document, and Ellis, would, I'll give you the last call before I ask.

DR. COWLING: Well, I would just like to support what Jim Crapo has suggested here, with the additional suggestion, and this is where they did do what Karen Martin told us yesterday. What was in the mind of the Administrator, and what are the policy implications of having an annual standard, and what are the policy implications of having a daily standard, or any other standard. And it seems to me that we ought to know what was the rationale in 1971, when an annual standard was selected. And now, and then, we have the other iterations in '93 and so on, what was in the mind of those who made the decisions at that time. And I think if that is clarified, it would provide a more rational basis for a decision about what is the proper averaging time.

DR. BALMES: Ellis, I can tell you one thing. I was, way back in my youth, I was in the public health service at EPA. And the very first criteria document, as you know, were very thin, and committees were about five or six people, and the process took a day, so.

DR. HENDERSON: Oh, you're making us all jealous. Anyway, I do want, we are skipping way ahead. We're going to the next step. And we, before we go there, we need to complete our review of the ISA, which is looking at the science. So, I want to know if everyone in the room and on the phone is comfortable with the substance of what we're going to put in the letter. And you will see this, the draft come-, the letter come out, and you will get to, we will seek concurrences.

We always do, so, is there anyone who is not comfortable with it? John Samet, are you on the phone? Oh, he's coming this afternoon, okay. Well, we have a quorum of the chartered members of CASAC here who are all comfortable with this, so I consider that the charter members have approved this, the substance of this letter that's going to go out.

What comes out next is going to be the draft letter, and with Angela's able help, I hope we can get it out fairly soon. And then, you must look at it very carefully, and we will seek concurrence before it actually goes in. And any questions about that process? Well, I thank everybody for cooperating so well with this new way of doing things. We'll see if it works out. I don't know if it, it hasn't quite



reached it conclusion, but all of you, by participating so readily, I think have helped it, and we may continue to do this.

The next thing on our agenda was to move on to the next document. I think maybe it's time for a break, and we'll take a fifteen minute break, then we'll come back and we'll hear from the Air office. And they are going to move us in the direction we keep trying to go.

(WHEREUPON, a break was taken.)

DR. HENDERSON: If everybody could take their seats. Thank you, Doug. Okay. We're going to be moving on, here comes Ron, if others could take their seats. We're going to be moving on to a consultation now for our next document, which is the exposure risk assessment methods document. And, as we've been saying, we keep jumping in this direction from going from the science assessment to wanting to participate in this part of the process. And this is our opportunity. As a consultation, this is where we can, early on in the development of this process, provide advice to the Agency on the methods for exposure and risk assessment. So, we had quite a bit of discussion on exposure assessment this morning. It is, we're going to hear first, then, from the Agency,



and I would ask, the first speaker is going to be Lydia?

MS. WEGMAN: Yeah.

DR. HENDERSON: Okay, and Lydia, maybe, you know, as you go through, you can introduce the others from the Air office who are going to be participating. So, it's a real privilege to have Lydia with us. She always clarifies things.

MS. WEGMAN: Well, I don't know about that, Rogene, but thank you very much. My name's Lydia Wegman, and I am the Director of the Health and Environmental Impacts Division in the Office of Air Quality Planning and Standards. And we are the folks who will be working on the exposure and risk assessment, and ultimately, the advanced notice of proposed rule making and the proposed rule and final rule. And I do want to introduce the folks who are with me, or the ones who have done the real work on the scope and methods plan for the exposure and risk assessment. And Dr. Karen Martin, who will speak in a moment after I'm done, Dr. Scott Jenkins, Dr. Stephen Graham, and Dr. Harvey Richmond.

MR. RICHMOND: I'm no doctor.

MS. WEGMAN: Oh, no doctor, you should be a doctor, though. You do the work of a doctor. So,



this is our team on the exposure and risk planning for the NOx review, the primary NOx review, and we'll be coming to talk with some of you next week about our NOx and SOx secondary review.

I first want to say thank you all for taking the time to review the work we've done, and to spend the couple of days you're spending here in RTP, either in person or by phone, to offer us your comments. Your comments are invaluable to us, and without the work of CASAC, we would not be able to perform our work. And I just want to say how very important your work is to us, to the Agency as a whole, and to public health. And thank you very much for all the work that you do.

I, also, just want to make one point, as you offer us comments on the scope and methods plan. As you have seen, and I know several of you have commented on, we've got a tiered assessment, both for the exposure and risk assessments. And, one of the reasons we have the tiering is that, we don't know whether we'll have the scientific evidence to go through all tiers of these assessments, and we are very much looking to you for advice on how to prioritize these assessments, and what we do need to do, based on what

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are the resource constraints that we face in our office. We have constraints, not only in terms of people and money, which are constraints that we always face, and it does seem that we face them more every year with declining budgets. But, we also have a time constraint in this case. As you know, we have a court order. It's currently under review by the public, but we very much anticipate having a final court order that gives us firm dates by which we do have to complete the proposed and final rules, as well as the ISA. And, that does limit what we can do. And I want to alert you to that, because I know that there is a desire on all of our parts to do the maximum amount of assessment that we possibly can do with the science that we have. But we will, in fact, be facing some constraints, and I want to seek your help in knowing what is the most important thing to do within the time and resource constraints we have. So, as you think about these issues and give us your advice today, I'd appreciate it if you kept that in mind.

And now, I'm going to turn it over to Karen, who is going to offer a few thoughts on multi-pollutant assessments.

DR. MARTIN: Just, while this is, you all have been talking some about the issue of multi-

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pollutant approaches, and multi-pollutant standards, and multi-pollutant interpretations of scientific evidence, and the question is, the tangentially related to the subject we're here to talk about, our plan for doing exposure and risk assessment, but it's, obviously, more broadly related to our ultimate review of these primary and of two standards, and our review of standards in general. And I just wanted to take a moment and make a few observations about the discussion, and sort of, our view of it.

In the context of science assessment documents, it's clearly extremely important that those assessment documents do everything they can to tease out, what do we know about any individual pollutants effects, and what do we know about the interactions of that pollutant with other pollutants, and to what extent can we define specific effects related individual pollutants versus to what extent does the evidence limit us to only making more general observations about associations of air pollution more broadly.

All those issues are extremely important, and your discussions are helping, I think, to sharpen the science assessment document in that regard. It becomes important for us, of course, at least as an initial

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step, in deciding how to approach our exposure and risk assessments; what is it we're assessing the risk of. We can, obviously, make some up-front assumptions, and my comments yesterday were intended to help get your, at least, preliminary thinking to help us do that. But our assumptions can, then, be further refined, as we go through the process of doing a first phase and a second phase of a risk assessment, so that, in the end, we can, are in the best position to characterize what, in fact, we think our quantitative assessments reflect the risk of, in this case, only SO2, SO2 in combination with other pollutants, SO2 as a surrogate for other pollutants. All those things are things we are, in the end, going to have to speak very clearly to. So the more you help us, at this early stage in the game, with some of your thinking at this stage, and recognizing we can further refine that as we go about characterizing, in the end, the results that we do produce.

Beyond that, the issue of multi-pollutant standards and multi-pollutant strategies, obviously, has much broader implications for all of our NAAQS reviews, and for what the Office does in implementing programs to address the NAAQS. And I would just make the observation that, some of the comments I heard, I, perhaps, unintentionally, have the, sort of sounded

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like, there is an inherent mismatch between setting standards for individual pollutants, and crafting control strategies that most efficiently and effectively get at the mix of pollutants that are, in fact, of concern.

And I would offer the observation that I don't, really, perceive that to be a mismatch. It's clearly a distinction, but one can, clearly, have standards for individual pollutants in conjunction with air quality management programs that are very multi-pollutant oriented, and seek to find the most efficient strategies for addressing all the pollutants for which we have standards. And, you all, I mean, different people have different views on that, but I just wanted to make the observation that there isn't, necessarily, an inherent mismatch, or contradiction in doing those things.

The one pollutant that we truly have a multi-pollutant standard for is, of course, particulate matter, which is a collection of thousands of pollutants. And if you think about it, we have established that as a multi-pollutant standard under the guise of PM mass, and a great deal of the research right now is focused on trying to tease out what are the differing relative toxicities of the individual

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components within that mix. So, when we do find ourselves faced with what truly is a multiple pollutant standard, what we set about to do is trying to figure out how to separate it out. And I think that's sort of informative as to what utility there might be in trying to aggregate all the other pollutants into one standard, with interaction terms, wouldn't our next step, logically, be trying to sort out the relative toxicity.

So, I just wanted to offer those observations, in terms of, the issue is really an important one, but perhaps, it's not as much of a mismatch or contradiction as one might originally think.

Those were the points, observation points I wanted to offer before we get into it, so if there's nothing else we need to deal with, why don't we just jump in to the overview presentation we wanted to make.

DR. HENDERSON: I think that's, that would be good. Donna has a question.

DR. KENSKI: Well, just a response, I guess, to the idea that single pollutant standards don't, necessarily, preclude multi-pollutant controls. Well, I, you know, it's clear that, you know, a control on one pollutant will almost always, you know, have an

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effect on other pollutants, it still, you know, the burden on the states to comply with the single pollutant standard requires that they produce a, you know, state implementation plan. And in that plan, they have to provide for how they're going to control that single pollutant, not multi-pollutants. So, I think the, you know, it would, while we get these, sort of, indirect, you know, controls on other pollutants, it would be more straightforward, I think, to, you know, have a multi-pollutant approach that really, you know, dictated this, you know, need to control all pollutants, not just single pollutants. So, while, you know, while, yes, we do get controls, still the burden on states is to demonstrate their control of a single pollutant for a single standard.

MS. WEGMAN: Yeah, and I'll just respond briefly. We are very mindful of the air quality manager port that the NRC issued, and we did, there is, in fact, a subcommittee of the Clean Air Act Advisory Committee that has looked at all the recommendations coming out of the air quality management report, including the one to develop multi-pollutant plans, and we, in fact, have a project going on in our office to pilot multi-pollutant planning with three states, North Carolina, New York, and Illinois, Missouri, four

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states, it's the Saint Louis area. And so, we, in fact, are very mindful of that issue. As far as the planning goes, I think Karen is addressing, you know, the way in which we set standards right now, which does not, in fact, preclude multi-pollutant planning. And we can set-, you know, at this point, we do need to look at the pollutants individually, but that doesn't prevent us from moving forward to multi-pollutant planning. And that's, definitely, what we are trying to do.

DR. HENDERSON: Thank you. And so, Karen, are you going to, who is our first speaker for the - -

DR. MARTIN: Scott's going to take the lead in covering the opening, and Stephen and Harvey will round out the opening presentation.

DR. HENDERSON: Okay.

DR. JENKINS: Okay, thanks. My name is Scott Jenkins, and I'm the health lead for the NO2 review and OAQPS. And I'm going to be talking through, probably, three or four slides on giving a little bit of background on the current approach that we have proposed in the scope and methods plan. And then, Stephen is going to talk through the exposure part of it, and Harvey is going to talk through the risk part

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of it.

Okay, so we're all aware, by now, that our purpose here to solicit feedback on our proposed approach to assessing risks and exposures. I just went through this, so I'm going to talk through, a little ahead on the schedule a little bit, talk about the previous review, and give a little bit of what, I hope, is historical perspective. And then, talk about the scope of the plan.

Okay, first schedule, and Mary presented the same slide yesterday, so I'm not going to go through anything in detail, other than to point out that the next time we will be soliciting, or will be meeting with CASAC will be Spring of '08, where we'll be asking for feedback on the second draft of the ISA, and the first draft of the risk and exposure assessment, and then, again, September of '08, for the second draft of the risk and exposure assessment. And then, the final date here, this is our, the date that we anticipate will become our court ordered date. This is about five months earlier, just to point out, five months earlier than the dates we had originally proposed.

Okay, so a little bit of background, and this, and I'm going to expand on this side a little bit, just based on the conversation that we just had

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prior to the break, and that is, providing a little bit of historical perspective for how the original standard was set.

So, the original standard was based on epidemiology studies that were conducted in Chattanooga, Tennessee, basically, where the long-term annual average levels of NO2 were correlated with health effects. The issue that arose later with those studies was that the issue of confounding with other pollutants, an issue of the measurement approach to, for, from measuring NO2 in the studies.

So, what happened was that, the original standard was set based on those long-term epi studies. And then, every review since then has focused, essentially, on the short-term issues. And the crux of the decisions that the Administrator has made are how well does that existing long-term annual standard protect against short peak exposures.

So, I think that'll become clear when I go through the slide a little bit, but that just gives you a little bit of a historical context.

So, and their talk-, specifically, about the last review of the NO2 NAAQS, and the Administrator had a, made a couple of conclusions regarding the sufficiency and the necessity of the existing annual

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standard. The first conclusion was that the existing annual standard will maintain annual NO2 concentrations well below levels, long-term levels that are of potential concern. And those long-term levels of potential concern were derived from the animal tox literature. And this is, basically, a fi-, based on findings that if you expose animals for relatively long periods of time to relatively high levels of NO2, you get emphysema-like lesions in the lung. And then, we're talking about, at least months of exposure to, say, at least 5 ppm NO2 here.

So, it's pretty much, it's pretty easy to see that, yes, the existing annual standard of .053 ppm will protect against those sorts of long-term effects.

The other conclusion, and this is, really, more of the focus of the last review, the other conclusion was that the existing annual standard will provide protection against the short-term peak NO2 levels that are of concern. And those short-term levels of concern were derived from the human clinical literature. This came from a set of studies showing that, in asthmatics, if you expose asthmatics to levels as low as, say, .2 to .3 ppm NO2, you can get increased airway response in this.

So, the way that the second conclusion was

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arrived at was that we conduct-, we and OAQPS conducted an air quality assessment, essentially, evaluating the relationship between the annual average NO2 levels and short-term one-hour average NO2 levels. And, as part of that evaluation, we looked at the number of exceedance as a very short-term benchmark values, with the assumption that were just meeting the current standard.

So, those benchmark values were derived, again, from these clinical studies that I just mentioned, and, basically, the result was that, if you assume that the existing annual standard is being attained, the short-term levels of NO2 of potential concern would be very unlikely in most parts of the country. I think Los Angeles had a few exceedances at the .2 ppm level, but that was the only spot where those exceedances were found.

So, that was, this was the structure of the la-, the con-, of the decision framework for the last review. And now, I'm going to move to the current review, and talk just for just a minute about the scope of the planned risk and exposure assessment, and then I'm going to turn it over to Stephen.

We hit on this a little bit yesterday, this, using NO2 versus other oxides of nitrogen. Obviously,

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NO2 is but one of the oxides of nitrogen that include both gaseous and particulate species.

There are really two issues, I think, embedded in this. And that is, first, that is using NO2 as a surrogate for the gaseous nitrogen oxide, and the other issue is using, is focusing this review on the gaseous nitrogen oxide.

So, regarding the first, the first statement, you know, and I think this was borne out yesterday, we're thinking-, we're planning to use NO2 as a surrogate for the gaseous species, basically, because the lack, relative lack of health effects data, and actually, it came out yesterday, also, the relative lack of monitoring data for gaseous species other than NO2.

In the case of the particulate, the second point that I made, the particulate nitrogen oxide, and we made this point in our integrated review plan, and we, this point, also, came up at our last consultation with you last spring, that the particulate species are addressed by the current NAAQS, and the rationale provided right here, basically, the last review for the, of the PM standard concluded that size fractionated particle mass, rather than chemical composition was the most appropriate way to address

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ambient PM.
This conclusion, obviously, is going to be reassessed in the next review, or I should say, the current review, since it's already kicked off. We had the opening workshop. But at present, it would be redundant to, also, use the NO2 NAAQS to protect against the health effects of particulate nitrogen oxide.
Other than that, I just want to point out that the assessment is going to evaluate, this will be a recurring theme throughout Stephen and Harvey's part of the talk, that the current assessment, we're planning to assess both recent ambient levels of NO2, ambient levels that are associated with just meeting the current standard, and ambient levels that are associated with just meeting the potential alternative standards, which will be identified as we move forward. And the assessment's going to focus on both short- and long-term exposures.
So, that's all that I had to say in the way of background and introduction. I'm going to turn it over now to Stephen, who is going to talk us through the proposal, proposed plan for the exposure assessment.
DR. GRAHAM: Thank you, Scott. Could you

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work the clicker? Sometimes I have a habit of talking with my hands. Okay, all right, thank you. So, of course, the general, broad goals of this exposure assessment are to estimate both short-term and long-term exposures, short-term being hourly, and that is associated with these current levels of ambient NO2, and assuming alternative levels of NO2.
Also, to develop these quantitative relationships, based on the form of the current standard, which is long-term, annual average and the relationship between that average and the short-term peak concentrations, which was done in the prior review as well. But in addition, I want to, also, consider local source influences, which we saw was important in the review of the ISA, and the impact on the exposure estimates.
As far as the approach, it's already been mentioned that we have three tiers. The tier one is air quality characterization. And I'll go through each of these in greater detail, I guess, or of course, it's been in greater detail in the scope of methods document. Populations considered include the general population, as well as the individuals identified as susceptible or vulnerable. And the assessment of uncertainty is also going to be approached in a tiered

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fashion, that is going from, in a sense, a qualitative evaluation and progressing to a quantitative evaluation if, of course, data exists to support that type of an evaluation.
So, the tier one, as I mentioned, is a air quality characterization, and the purpose there is to estimate the potential exposures, using the current, as well as historical air quality data that we have available to us, and use that as a surrogate for exposure. In addition, we are proposing to take a glance at some of these near roadway exposures, using the ambient data, using enhancement factors. And then, of course, any available concentration data and emissions data that may be available to look at the influence from sources, particular sources that may be outdoors or indoors.
The locations that we considered are outlined, based on the, those criteria that is, air quality trans data availability, you know, number of monitors, whether the data are quality assured and comprehensive, and in addition, to some other criteria. And we've selected Los Angeles, Houston, Atlanta, Philadelphia, and Chicago, and possibly, aggregation, based on some of the analyses that are going to be performed here.

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The expected output is, of course, descriptive statistics for NO2 in some of these selected locations; relationships between the short-term peak levels and the long-term average levels; and, of course, identification of additional areas to be modeled in the tier two and tier three, dependent on the analysis outcome.
Uncertainty will, primarily, be qualitative at this stage, and of course, these tier one exposure assessment, the outcome is going to be used for comparison with some of the health benchmarks, once they are identified.
So, in tier two, we've got, the purpose is to improve that relationship. So, now, we're trying to link the actual concentrations, themselves, to persons, to humans. And we are going to, of course, consider both the on roadway and, as well as, near roadway, using dispersion modeling and or enhancement factors as well.
The model concentrations for other outdoor sources, if there are any identified, as well as the indoor sources, if they are identified as being important in influencing these exposure estimates or, shall I say, the relationship between, I'm sorry, the contribution, the relative contribution between the

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two, that will be done as well. And, of course, consider influential factors, that is, time that people do spend in particular microenvironments, as well as the limited decay of NO2 indoors, and populations residing near roadways.

The locations, of course, are going to be, it's going to be a more focused analysis, and it's going to be focused on the locations that have been identified in the tier one analysis.

And the output is going to be broken up into two different exposure metrics. We've got short-term exposure outcome, where we have, in addition to the temporal and spatially resolved ambient air quality concentration fields, that account for local sources, like emissions from roadways and other sources that are identified as important. We've got estimates of the number of individuals who may experience exposures of concern. Not to suggest that it's an individual analysis. It's more of a cohort-based analysis.

And then, of course, long-term exposure estimates will include annual average exposure levels within a given census tract, and could be considered at a more finer resolution, say a block group or block. And it's not just the annual, but also, I believe, we'll be able to estimate the daily average.

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And, in addition, we've got the ratios of exposure to ambient, which could be useful for extrapolating to other areas that we had not modeled. And uncertainty would be addressed, of course, through various sensitivity analyses, limited sensitivity analyses, based on input distributions and other model inputs, as well as measured comparisons, if there are data that exist for particular microenvironments. That would be compared to model estimates.

In tier three, of course, it's a more refined approach, and here we are focusing on addressing more particulars about human physiology, including time, well, that's not physiology, but time, location, activity patterns, and their physiology. Using the air concentration fields developed from a tier-two approach, that is where we have the on and near roadway concentrations, and using the EPA's APEX model for estimating exposures.

Locations, of course, are built upon what had been identified in the tier one and used in the tier two analysis. And, oh, I forgot to mention, of course, the APEX model is capable of estimating individual exposure estimates. It's a time series exposure model. And we also have capabilities to estimate indoor sources using that model.

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So, as I said, the locations are the same as those identified previously. The expected output is going to be the counts of people exposed one or more times to several NO2 levels, based on, of course, health information obtained from the ISA, and because APEX is a time series model, and the averaging time, that is of interest, can be taken out of the, or shall I say developed as an exposure metric. And we also have counts of personal occurrences of a particular exposure.

And the uncertainty can be a little bit more quantitative in a sense. We can look at, again, model inputs, where data exists for describing both a variability and the uncertainty in them, and of course, model formulation. If we have estimates of personal exposure that are available to compare that, as well as microenvironmental concentrations. That's it. Thank you.

MR. RICHMOND: Thank you, Stephen. I'm going to walk you through a few slides on the risk assessment. First of all, overview goals of the risk assessment are to estimate the number of occurrences of short-term air quality events and number of people exposed at, or above, various potential health effect benchmarks associated with alternative NO2 scenarios.

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If a tier two assessment is conducted, we'd also provide health risk estimates for NO2 health endpoints associated with alternative scenarios. And for any tier, we'll, of course, identify and characterize key assumptions and the variability and uncertainty associated with the assessments.

As Scott and Stephen have said, the scenarios evaluated are for both recent air quality, simulating the current standard, which is a difficult challenge, given the levels are much lower than the current standard; and air quality levels just meeting potential alternative standards, which could be short- or long-term standards.

There's a two tiered approach here. Proposed one is the, in tier one, potential health effect benchmark levels, which will be based on a review of the revised ISA, would be compared to, first, air quality and then, exposure estimates generated by the tiers that Stephen's gone through.

Tier two, if it's judged feasible, and they're, and of sufficient utility for decision making, we involve combining concentration response, if it's based on epi; or exposure response based on controlled human exposure data, with exposure estimates to generate population risk estimates. It's what we'd

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like to have, ideally. We may or may not be able to get there.

And next slide, okay. The tier one, as I've said, the air quality levels from a tier one exposure assessment, or estimated exposure levels from tier two or three, would be compared to potential health effect benchmark levels for several example urban areas. Those would be the same areas that Stephen's talked for the air quality and exposure tiers.

We have identified, very tentatively, in a benchmark of, in the .2 to .3 ppm one-hour averaging time range, based on the controlled human exposure studies, of effects that have been observed in asthmatic, both children and adult asthmatic. There's uncertainty about those health effect benchmarks that we see, we'd be using alternative benchmark levels to illustrate the impact of alternative choices about the lowest exposure levels of concern.

In terms of variability, we address that by doing the analysis in different geographic areas. Population variability in response but it would have to be addressed qualitatively. We don't have, I think, data to distinguish that very well. And the projected outcomes would be the number of occurrences of air quality levels at or above several benchmarks, or

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number of times in a given year that a population or individual experiences various exposure levels of concern.

To our next slide. And a tier two, if conducted, would estimate the number of individuals in selected populations for several example urban areas expected to experience specified health effects more similar to the ozone and PM risk assessments that we've completed in the last couple of years.

We judged that it would be more likely that would be based on the epidemiological literature. Preliminary judgment is that controlled human exposure studies don't provide enough information to identify credible exposure response relationships. There's enough information to judge benchmarks for the health endpoints, but it's difficult to see how to get exposure response relationships across the range of interest.

We're still evaluating. We're, obviously, listened carefully to what you've said over the last day and a half. And look forward to seeing how the revised ISA responds to those, in terms of whether there's sufficient epidemiological evidence adequate to conduct a credible quantitative risk assessment.

The criteria listed here for determining if a

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tier two assessment would be conducted, including the outcome and insights gained from the tier one assessments, both with the exposure and risk assessment, and availability of information and data required to conduct a tier two assessment on the adequacy of concentration response functions, baseline, and getting baseline incidents data for things like hospital admissions and emergency department visits for the example urban areas.

Then, the utility or value added to the decision process beyond the insights provided by a tier one assessment, and the feasibility of conducting the assessment within the time constraints that we have.

Next slide. Based on our preliminary analysis of the first draft ISA, the most likely candidate endpoints are listed here. I think that was, generally, in agreement with what I heard yesterday in the discussion on ISA. But the strongest evidence from the epi would be for respiratory related morbidity endpoints, including hospital admissions, especially for asthmatics; respiratory related emergency department visits; and respiratory symptoms, such as cough and wheeze, particular in children and asthmatics.

Risk estimates, if we do proceed to this

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stage, we would propose to conduct both sing-, use both single and multi-pollutant models. And uncertainty would be addressed similar to how we've handled in PM, the statistical or sample size uncertainty, that we would provide confidence intervals around point estimates of risk, and representing a range of results, based on different epidemiological studies.

Expected outputs are listed here, in terms of we would look at estimated incidents that can express the results in a number of different ways. Incidents per hundred thousand and or percent of incidents. And this would address hypothetical change in incidents associated with moving from just meeting the current standard to just meeting potential alternative standard.

The final part of the risk characterization is several things that we've tried to either put the more limited example, like, you know, urban areas analysis, is one to summarize U.S. air quality information, and discuss the various health effects that we were not able to quantify from the ISA. So, that would certainly be part of the exposure risk report to provide context for those things that we do deal with quantitatively, and would include those air quality statistics for all air as the U.S. based on the

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NO2 monitoring data. And that we'd also provide information, national scale information on the size of potentially susceptible or vulnerable populations as part of that.

DR. JENKINS: Okay and this slide just has the charge questions to CASAC. This is actually a condensed version of those charge questions, because we actually had too many to fit on a single slide, but I think this captures them.

DR. HENDERSON: Thank you. Karen, do you have more to present?

DR. MARTIN: I don't believe so, unless there are some specific questions.

DR. HENDERSON: Okay, now, Lianne, you're on the phone?

DR. SHEPPARD: I am.

DR. HENDERSON: When are you leaving? I'm just trying to - -

DR. SHEPPARD: I have two more hours.

DR. HENDERSON: Oh, okay. I was going-, that's good, Lianne. I just wanted to allow you to ask questions if you were leaving.

DR. BALMES: Rogene?

DR. HENDERSON: Yes.

DR. BALMES: This is John Balmes. I'm

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going to have to leave to teach in a few minutes, and I will be returning in time for the health effects discussion, which is currently scheduled for, what is it, 2:15 your time?

DR. HENDERSON: We may be getting to that a little earlier, because I plan to have a working lunch.

DR. BALMES: Well, I just, I have to teach, so I won't be able to join the call till a little bit after 2:00 your time.

DR. HENDERSON: Okay.

DR. BALMES: Just so you know.

DR. HENDERSON: Okay.

DR. BALMES: I don't have a specific question right now, though, just letting you know.

DR. HENDERSON: Okay, and if you, let us know when you join in. Okay, I found it fascinating our discussion just before we started this about, you know, the annual average standard and how that relates to peak exposures. And this group has, obviously, addressed that, and I, in a statement, if the existing annual standard is obtained, short-term NO2 levels of potential concern would be unlikely in most parts of the country.

That, would, addresses some things we had a

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lot of concern about this morning. But let's start in on the discussion of the air quality section, which is very brief in this report, and has lots of discussants. So, we may have more discussion and, than there is text, here.

SPEAKER: Than material.

DR. HENDERSON: But, what I'd like to do is run through, you know, there's three, the air quality section, the exposure section, and the risk assessment section. We're going to have, open the discussion up to anyone who has any questions. We tried to group people as to their interest, rightly or wrongly, so let's start out with, on the air quality, Ellis, did you have some comments you wanted to make, or you know.

DR. COWLING: I must say that the general impression I have is that the approach is being, that is being proposed is reasonable, and that I have confidence that it will be pursued within the limits of time available that were mentioned. The five months shorter time frame, I'm sure has caused some anxiety within the staff about how to get all the things done that they had hoped that they can accomplish. But, I'm satisfied that the approach being proposed is reasonable.

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DR. HENDERSON: Thank you, Ellis. Donna, do you have any comments on this, the proposed methods for air quality evaluation?

DR. KENSKI: Well, I guess I have a question.

DR. HENDERSON: You need to get close to your mike.

DR. KENSKI: Okay, sorry. In answer to the, I guess, the charge question about whether it was appropriate to use historic data, I thought that was the logical approach. I, the question I had was in the, how you're modeling expected exceedances, and it gives an exponential model here, and I just wondered if there were any discussion about that choice of model, and whether you considered other models.

DR. GRAHAM: That's a good question, thank you. We've got, that, actually, had been used in the previous review. So, as I was looking to, I guess, duplicate that effort, but in addition to that, we are also going to look at an alternative model that looks at, like a logistic regression, so it'd be more probability based.

DR. KENSKI: Okay, yeah, I think that's appropriate.

DR. GRAHAM: Thanks.

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DR. HENDERSON: Is that all, though, or did you - -
DR. KENSKI: Oh, well, another question about your choice of, and I'm not sure if this really fits in, maybe it does. Your choice of cities, New York wasn't on this list, and that seemed odd to me that, 'cause it was one of the higher, definitely one of the higher concentration cities. So, if you're looking for peak exposures, it seems like you'd choose those urban locations, and it has lots of monitors.
DR. GRAHAM: Right, I think Philadelphia was selected over New York, per se, because of, it was representative of a northeastern region, but the key feature there was the availability of additional data, including very refined roadway counts, and other data that had been developed previously through other research. So, I thought it would be a slam dunk, per se.
DR. KENSKI: Okay.
DR. HENDERSON: Is that all? Tim Larson, are you on the phone?
DR. LARSON: Yes, I am.
DR. HENDERSON: Okay, did you have comments on the methods for the air quality section?
DR. LARSON: Yes, a couple. It wasn't, I

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guess, I have to calibrate my thinking here. The short-term standard, the health effects for that are based on the analysis of existing monitoring sites for short-term NO2 levels, I assume.
Is that the, I mean, is, it seems to me that the relationship between the short-term values and the long-term values, and how you do that, depends on what sort of the health basis you're deriving, using to derive that short-term value. If it's the epi, then that's one thing, and then, would you just, sort of, use the statistics from existing sites.
If it's independent toxicology clinical human exposures, et cetera, then it seems like, potentially, there are different relationships between the long-term and short-term values for parts of urban areas that may be more relevant than ones at the monitoring sites. So, I'm not clear, it's not clear to me which is the basis for your health risk assessments.
To the extent that it's the epi, then I suspect that the existing monitoring statistics are relevant. To the extent it's other, then I would suggest that the relationship, I mean, in the extreme case, for instance, the one-hour peak exposure is while you're commuting, which has nothing to do with any of the statistics or distributions at the monitoring. So,

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I guess, the question is, how do you see that going down?
MR. RICHMOND: Okay, this Harvey Richmond. Let me try to address that. In, if we can, the risk assessment has said, at first one tier, there's, if we're looking at results of either the air quality in tier one or exposure, either from a tier two or tier three, either APEX or otherwise exposure estimates, we're comparing, we're using all of the air quality information.
We're using the monitoring, but also, enhancing that with additional information to try to estimate, either, a surrogate for exposure or getting the distribution of exposures. That's then going to be compared with a health benchmark levels that are based on the controlled human exposure studies.
So, we're trying to match exposure with an exposure response or an exposure, you know, an effect observed in a clinical setting. That's one use of it. And separately, if the epidemiology is deemed that it's sufficiently one that is likely causal, or you know, whatever we decide to go down on that continuum of causality, that we're going to quantify, if we quantify an effect from the epidemiological literature, those studies, I agree with you, are based on the ambient

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monitoring fixed site monitors, usually the average across several monitors.
And if we were to do a risk assessment, based on epi, it would not be based on the exposure analysis. It would be based on the ambient fixed site monitors. I hope that clarifies it.
DR. LARSON: Yeah, that helps, thank you. Well, at least to the extent that it's based on the human clinical studies, I would suggest caution here using your near roadway or traffic related impact as models, because I think you get very different relationships spatially and temporally in a flat road, than you would in a built up urban area. So, I mean, the residential areas of Philadelphia or parts of Chicago or Houston maybe that's, your approach is fine.
But we're doing studies in Chicago, and I know for a fact that, is part of our cohort lives in downtown Chicago, and we can't and don't have any success using those kinds of approaches in that area. So, if there was some way to qualitatively screen those parts of the urban areas that are subject, is more complicated confinement effects, so that you would limit your exposure assessment in some way, based on that.
I would think that's more defensible. You

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get a qualitatively different in a distribution and it's not only, then becomes determined by the geometry of your urban area, but also you end up with this question about the vertical distributions within those confined areas.

And then it, then you really up, you really, you know, it's an open question as to where the, whether you've got buildings with open windows, or whether you've got inlets of a building in a residential apartment on the roof or on the ground or whatever, and it gets real complicated in a hurry. And the, I guess, the basic point is that a simple, sort of, Gaussian dispersion model do not have much skill in those parts of the urban area.

So, I mean, maybe it's a qualitative way to assess, you know, there are methods for doing that. You know, you can look at building footprints, and overlay building heights. We've done that in New York, and we're doing it in Chicago. And you can, sort of, identify the areas that are, you can just look at Google, actually, and probably do the same thing, but more quantitatively, you could do it that way. But I would say your proposed approach air mod, et cetera, is fine as long as it's, sort of, single family residential, but otherwise, it's questionable.

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DR. HENDERSON: Do you have a response to that, I mean, to that, Harvey?

MR. RICHMOND: One thing is I'll note historically, it's one of the reasons why there hasn't been an NO2 exposure analysis in the reviews that I was involved in '85 and '93, is doing this is much more challenging than doing an ozone exposure assessment. And we acknowledge that.

I think we're, you know, we're saying, we're trying to push the envelope as far as we can, and we're still in the learning phases as to how far that is, and we'd certainly be interested in the kind of information that, Tim, that you've cited that, you know, if we, for some of the example cities, if you have relevant information, or ideas on how best to do it, or if we, simply, you think if the advice of this committee is we, simply, aren't able to credibly do certain parts of the analysis.

Obviously, from a public health standpoint, you'd be interested in those levels in those places where you're saying it's most difficult to conduct the assessment.

So, that's the challenge we face, and this is a general road map. We'll see as we get into it, but we look to the advice of this committee and experts in

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the exposure field as to what they think about that.

DR. HENDERSON: And that brings me to a point that I had meant to bring up earlier. For all of you who have not yet submitted your individual comments on this methods document, that's just essential in this case, because the letter will not, it will be more pro forma when it's not going to list the consensus. So, the advice that you want to give to the Agency in this consultation will come in the form of your individual written comments, so that increases their importance. Tim, is that, are you, have you completed your comments on the air quality section?

DR. LARSON: Well, I, yeah, I think that's, wait a minute. It certainly, EPA, I think, is sponsoring some of the work I mentioned, so, you know, we certainly can do our best to work with the, provide whatever information we have. We have quite a bit of, Lianne is involved with this, too. We have quite a bit of NO2 passive monitoring data, saturation data in several cities that we're talking about.

DR. HENDERSON: I'm sure they'd appreciate having all the information you can give them. Ted, would you - -

MR. RICHMOND: Can I just ask one clarifying question?

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DR. HENDERSON: Sure.

MR. RICHMOND: Tim, that saturation data, is it for short-term averaging?

DR. LARSON: It's, no, it's two-week average - -

MR. RICHMOND: Two-week average.

DR. LARSON: Yeah, so that's a problem, but, yeah, it's a problem. But it - -

MR. RICHMOND: Okay, I just wanted to clarify it.

DR. LARSON: It can identi-, I mean, we've done models, though. We, in New York, specifically, we've done, we've implemented the OSPM model for New York City, which is kind of an interesting exercise. And, to do that, you have to do, or you have to have information on building footprints. It's a massive undertaking, but so, we have, we have hourly predictions compared to our measurements. And they compare pretty well.

I mean, it is reasonably, if you expect to model that. So, they do have skill, and they, and we do have predictions on an hourly basis, both as an urban background model, and superimposed on that is a, is an OSPM model, and using Mobile Six and the traffic - - model for New York City.

DR. HENDERSON: Okay, let's move on to Ted.

DR. RUSSELL: Okay, very much like the prior individuals, I was, generally, pleased with the scope document. One of the things, I think, that comes out of just recognizing that you're going to be doing a number of these, if you look at it more than one a year, to get it down to a well-oiled, sort of, approach, is one of my first recommendations.

And I realize you all are, may not have tons of resources or whatever, but just something that could be done such that these things become very automatic. You know, I look at where we've come in other areas of the modeling world, and I think that this could be done when you're looking at exposure and risk analysis as well, just to make it so it's not as, such a huge effort every time.

A few things, one of them was, in regards to what you, when you were presenting this morning, you said something about locations considered, and you have the five cities, and then, an aggregation of others. And then you said, possibly, or maybe you said possibly before you said that. And I, it brings back what we discussed in the lead panel was that, we're, I think, as a whole, more interested in the U.S. than in



individual cities.

I'm just wondering how you can, how you would plan not to do an aggregation of others, because I think that would be somewhat more instructive to us, to show us, on a national basis, the exposures of concern. So, do you want to respond to that, how you're going to make that decision not to do an aggregation of others, or?

DR. GRAHAM: Delete possible.

DR. RUSSELL: Okay.

DR. GRAHAM: No, the intent was, in the original analysis, they had done Los Angeles as a separate area, and everything else was just lumped together. And here I was proposing, okay, we can do multiple locations, and if it's of value, we can look at these other locations as well. And the criteria, in a sense, for selecting the individual areas is based on the fact that, we do have some information on the fact that there are more peak occurrences.

In these other locations, there may not be. So, in a sense, the model for predicting peak exposures over a particular level, it just may fall apart, because there are no peak exposures. So, that's why I say possible.

DR. RUSSELL: Okay, though, the way I



read this, it wasn't just peak exposures. It was all exposures. So, I'm just hoping that you're looking at doing the exposure analysis at a national level, not just for five cities, both peak as well as long term.

DR. GRAHAM: The air quality data is going to be evaluated nationally. When we look at the focused exposure analyses, that's going to be on individual cities that had been identified.

DR. RUSSELL: I think we would have some interest in, maybe I'm not, maybe I'm singular here, of really the interest at a national level somehow extrapolating or doing something to get, to give us an idea of what's happening nationally, not just at those cities. Because it came up in the lead. It came up in the ozone, as well, that that would be some important information.

And, let's see, one, just a minor comment, in your model, in terms of how to go away from roads use--

DR. MARTIN: Just, if I may?

DR. RUSSELL: Yes.

DR. MARTIN: Just to come back to the point you just made. I can't not make the observation that, as we move to exposure modeling, what we and you both are looking for is to develop enhancements to



those models to be, to address the location-specific issues that are so central to understanding exposures to NO2.

Once you zoom out and now say, oh, let's do that on a national scale, you lose all your local specificity, which is why we would approach a national look on the basis of air quality, recognizing it's a pretty gross approximation, and looking on the local level, to try to tease out the nuances of exposures around roadways and building canyons and those sorts of things that we couldn't possibly do on a national scale.

So, I mean, we're not trying to be resistant to say, yes, it would be nice to know exposures on a national scale, but I think the best we can reasonably do is to do the more generalized air quality, look on the national scale and to tease out the details locally.

DR. RUSSELL: Dale has a comment, I think, in response.

DR. HATTIS: Yeah, but, yes, essentially, you've got three legs of a parallelogram approach here, at least, in your plan. You've got the local assessment of air quality. You've got the local assessment of exposure. You've got the national

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assessment of air quality.
I think it's not too much to hope that you apply the lessons from the comparison of the local assessment of air quality and the local assessment of exposure to make, at least, a preliminary national projection of the exposures, if the regularities you've observed in your fully analyzed cases apply to some portion of the national air quality data.
I mean, you, probably, wouldn't apply the Philadelphia comparison directly to South Dakota, but you, probably, want to apply it to some portion of South Dakota, maybe, in a fraction of Fargo or whatever, and, to some extent, get.
But anyway, that's the basic idea, is that it's, it might not be a tremendous expense and of effort to do that distributional projection for an appropriate fraction of the country, or the country as a whole, you know, even though you don't want to do, in detail, the country as a whole. You can get an approximation from that, from the comparison.
DR. MARTIN: And then, of course, you're left with making the judgment, does the approximation so assume away all the details that are important that you're left with, clearly we could create numbers, but would they be meaningful. And if they're not going to

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be meaningful, then we would argue, they're not worth creating in the first place.
So, that's what we have to deal with, and we can clearly look at it, but that's always the tension, as you point to with lead as well. And, I didn't want to just slip by this and so.
DR. CRAPO: I wanted amplify what you're saying, and maybe, even take it further the other direction, which is that, your data on local data is really still coming from your primary monitoring stations, I assume. That's correct? I mean, your, like your, near roadway monitoring stations, and things like that, gives you local data that you'll use for looking at some of the variation at the more local level.
But, in fact, what we're learning, as we, or the mornings is, or what we're learning is that there, the local level has even tremendous variability within that. There's each gra-, I mean, gradients across the roadway are falling away as a, you know, being 10 feet versus 100 feet versus 1,000 feet for roadway has a huge impact on the levels. And even being in a car dramatically changes the level.
I was told during the break that the school buses are 4.6 times higher than ambient inside the bus,

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as opposed to standing by the roadside. So, I guess that I'm thinking that a lot of your, most of your key data that's going to explain health effects are going to come from understanding local variability.
And I, and it's where I'm going with this is, is the, you need to associate locally, but you'd probably have to have wide, a careful thought and discussion about the variances even locally, 'cause you're only very, barely touching that, that part of the parameter.
Sounds to me like the, if you're doing a near roadway, for example, comparison, you might have various people that are experiencing that for which, that have levels that are many, many times others that are in the same environment because of the way they, the way they were exposed to it. And so, I'm curious how you'd handle that variability as you let that average out.
And that's just, actually, taking exactly your comment and taking it the other direction, even more extreme at the local level that we, actually, need to understand the health effects.
DR. GRAHAM: Well, that is part of the plan.
DR. CRAPO: Yeah, I like that part, that

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you had one-hour average, I just really compliment you on the fact that your, you did have the one-hour averaging goals in there.
DR. GRAHAM: Well, and to take into account, specifically, roadway, on roadway and within, given buffer distances of the roadway.
DR. CRAPO: And what about inside cars?
DR. GRAHAM: Sure, on road equals in vehicle.
DR. CRAPO: 'Cause that could've, that could, actually, do you have, are you going to have personal monitoring measurements to give you that data?
DR. GRAHAM: No, based on modeling.
DR. CRAPO: You're just going to model it, okay. That would be key to this whole thing.
DR. HENDERSON: Okay, Ted, did you have more to - -
DR. RUSSELL: I think that was, primarily, it, and I'm not sure where we ended up on it.
DR. HENDERSON: Well, I heard that we need the local data to be able to relate it to health effects. I mean, that's, to me, that's, but - -
DR. RUSSELL: Right, I think we want the local data, and, just, when we sit here and talk about

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things later, I think we're going to want to know what are the national implications. And maybe I'm one of those who says, if you give me an approximate number and say it's really approximate, that's a fine thing. You know, I don't, that doesn't bother me, because I know what I'm basing my discussions on.

That is, it's a number and there's significant uncertainty, but it, at least, it's something that gives me an idea of what's happening nationally. So that was the, that's my major concern there. And, let's see. Also, one of the other issues that I, or thoughts I had on this was, how do you plan to provide ambient versus total exposure risks, total exposures and related risks in your assessment, 'cause I think having that comparison would be insightful.

MR. RICHMOND: Well, in the past, and we've addressed this in the CO exposure model, where we included passive smoking in gas stoves, we're able to, since it's driven by a model, the exposure part, at that tier of the assessment, to both report total, as well as, just with the ambient.

In other words, basically, turn the indoor sources off in the model, and how much is the ambient, both including ambient outdoors and the ambient that penetrated indoors, but in the absence of those indoor

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sources. So, we do try to provide that perspective of how much is due to the ambient problem, as opposed to indoor concentrations as well.

DR. RUSSELL: And that will be included in this?

MR. RICHMOND: Yes.

DR. HENDERSON: Okay, Christian, do you have?

DR. SEIGNEUR: Yes, I only have one point I want to address. It's, when it does a tier two exposure assessment and the use of the model used to calculate the air quality concentrations, in your document, you mentioned you plan to use AERMOD. You, also, mentioned the model CALINE4.

My understanding is that AERMOD was the route for stacks, dispersion of protons from stacks. CALINE4 is most specific to roadways. So, could you clarify why you're planning to use AERMOD other than CALINE4?

DR. GRAHAM: Absolutely. While it had been recommended to me that I use CALINE for, I'm sorry, AERMOD for few reasons, CALINE, from what I understand is, the developer of that model had recently retired, and Air B has no initiative to continue on developing that model. So, we can consider that an

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DR. GRAHAM: In a sense, it's no longer supported, so it may have been used traditionally, and it may look like a reasonable approach now. I guess, I'm trying to think of the future. And AERMOD is actually a little bit more advanced. It's based on boundary layer theory versus stability classes, and has additional capabilities addressing turbulence and meandering.

And, I know that the AERMOD doesn't have a line source option right now, but it is something that is being considered in the near future, not in time for this particular review, but it will have that capability. Right now, what we are proposing is to do link-based emissions, so, and I think it is being applied right now in New Haven, Connecticut, and there has been a paper published recently using CALPUFF, which is a similar type of dispersion model, to do this near roadway estimation.

So, it's, I think, not an unreasonable approach, and there will be, I guess, portions of it that, of CALINE that may be investigated. I think you had also mentioned in your comments earlier about the conversion from NOx to, or shall I say NO to NO2. So, that may be an important feature there.

But, again, it was to look for, look towards

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the future, and, in addition, the fact that we are, also, going to look at additional sources, some of which are stationary type sources. So, why not use one model to head all the emission sources.

DR. SEIGNEUR: Okay, yeah, that will be fine. My recommendations, though, would be that if you're going to use AERMOD for roadways, that it would be evaluated prior to, with data graded near roadways prior to its application. 'Cause EPA, typically, requires people to evaluate the models before they are applied. So, in this case, since AERMOD has not been formerly evaluated for roadway application, that, you know, EPA would do that.

DR. GRAHAM: Right, yeah, and I did forget to mention that, that AERMOD is the recommended model, at least for dispersion.

DR. HENDERSON: Now, does anyone else have something they want to comment on the air quality section, 'cause after this, we'll move on to the exposure. Yeah, Ron.

DR. WYZGA: I have some questions. Let me say that, I'm very impressed by the approach, and, I think, a really good understanding of the exposures here, and I think you're, really, getting it.

I think you, it's going to be a challenging

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job, but my question was, when you talk about just meeting the current standard scenario, I just want to see if I understand it.

The current standard is 0.053 ppm, and let's say, that you come up with a health benchmark, a new one, of .05. And that, if, let's say, one of your cities, your concentration is .04. Does this mean that, in your risk assessment, you're going to assume that the people are exposed to .053, as opposed to .04?

DR. GRAHAM: That's a tough one.

MR. RICHMOND: Our dilemma is, for our purpose, not an impact assessment. We're looking at, in the country, we have levels, typically, down at .03 and below. So, we're well below the current standard, annual averages for the current standard.

How do we assess what the risk is for meeting the current standard. It's not the risk from recent air quality, which is lower. Is there a scenario, you know, that we look at as a hypothetical scenario, that matches exactly the current standard at the monitoring network, in the design monitor just meets the 53, you know, ppb.

There are two, you know, sort of, basic choices, and I'd be interested in comments from the committee. The one we put forward but were, like to

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hear views on, is to use recent, meaning recent the last time places did not attain or were just in attainment of standard. In L.A., it wasn't that long ago, had levels that were approximately the current standard.

That's one approach to use historical air quality in the '90's, generally, when some of these locations were just meeting the current standard. The other choice is to use some kind of roll up approach. And then, the question is, do you do it proportionately and roll all the monitors up from current levels to just meeting standard. And, I believe, UARG had some comments about that very issue, so I'd encourage you to look at that.

They were actually arguing not to use the historical approach, but that it would be better rolling up the monitors that were nearest the road, and then, rolling up the other monitors not as much based on relationships between near roadway monitors and the other monitors. So, that's an alternative approach. And I don't think we're fixed, yet, on exactly which approach, but we put forward as, to get reaction, at least. You know, how else are you going to do it. Otherwise, we don't have any results for risk or exposure or air quality that approximate the current

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standard.

DR. WYZGA: My only concern is that, I think, the risk estimate that you come up with is going to be misread as to, this is the current risk, and - -

MR. RICHMOND: Right, and it's not, and I appreciate that.

DR. WYZGA: - - and I think that's something that, really, if it's done this way, you need a very strong statement telling people what it is not.

MR. RICHMOND: Right, and we agree. It's a very hypothetical, and I agree, sort of, with your comments that if we go down this path, whichever way we do to simulate the current standard, we need to make it clear how unlikely that is, given current NOx stationary controls, given NOx vehicle controls, you know, that's a very unlikely scenario. But, that is, sort of, the baseline if you're looking at, what are the risks that would be, if you were just meeting the current standard.

DR. HENDERSON: Important point. Yes, Kent.

DR. PINKERTON: Although this may be somewhat of a trivial question, I noticed in figure two, when it shows the NOx emissions that, where they're coming from, and I understand that the focus

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has been, primarily, on urban areas and near roadways, but I noticed that close to 20 percent of NOx emissions come from off highways. And so, I'm just curious if rural areas or areas of high agricultural activity, do they contribute to NOx emissions, and are we missing something by only focusing on urban areas or near highways?

MR. RICHMOND: I don't know if we're prepared to say much. The one thing I will note, I think we were going to look at an air quality tier one, was major power plants sometimes are sited. I know in, I think it was Charlotte Mecklenburg, I know the case where it was sited, just outside the ozone non-attainment area, coal-fired power plant. And we have the ability of modeling to see what kind of NOx levels, NO2 levels would we expect around some of those point sources.

They may or may not be peaks of concern. Maybe they're still, with controls that we have on, don't reach those levels. I don't know if on, have any information on that, but that's the kind of thing we will look at in the screen analysis, do we have any potential problems outside due to some of these may be that we know which sources from the emission inventory are major contributors to that.

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DR. KENSKI: Kent, maybe I could clarify a little bit. That off-highway category includes sources like construction equipment and marine, you know, boats, lawnmowers, all those things. And so, you could make the assumption that they, generally, follow, sort of, a population distribution. I mean, the distribution of emissions in that category would be highly correlated with population. So, to that extent, you could assume that it was more urban and less rural. Although, certainly, you know, farm equipment is a part of that category.

DR. PINKERTON: Okay, thanks.

DR. HENDERSON: Okay, I think we've, actually, already moved into the second section, the, our exposure section, and - -

DR. SHEPPARD: Rogene, before we continue, I wanted to comment a little bit more on the air quality modeling.

DR. HENDERSON: Go right ahead.

DR. SHEPPARD: You know, well, before I start, if everybody who's on the phone could mute their line. That would be really helpful. You can press star six if you don't have a mute button. So, the complexity of the modeling, I think, is ex-, of the air quality model is extremely challenging. And Tim

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touched on that a bit with the street canyon issue. And there's so many assumptions that are in here. And it, it's, also, I was, it really hit home, the comment about the resource limitations. And this is a, potentially, a huge effort to get it right.

I think simplifications are possible, depending on the purpose of the analysis, and I'm, it strikes me as this air quality modeling is being done for many different purposes, which means that simplifications, if you had only one purpose, may not be as easy.

You know, if you just want exceedances, you might be able to simplify in different ways, than if you wanted predictions. Because you're going to be using the predictions, for instance, in the APEX model. If you're focusing just on long-term exposure, there are simplifications; but if you want the short-term, one-hour, that means a lot more complex model.

It's not so clear that temporal and spatial variation in NOx are separable in the sense that, when you're really near roads, the temporal patterns are, probably, really different than locations far away from roads.

So, thinking about which monitors are representative for the analysis becomes really

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important again, depending upon the purpose of what, what the analysis is trying to do.

The other comment I have, beyond that, is, if it could simplify the work, or at least make it clearer to those of us who are reviewing it, how much each tier is completely conditional on the previous tier, and to, perhaps, take out anything that's overlapping. For instance, between tier one and two, that looks like there's some different overlapping efforts that are going to be done, and can those, can some of that be removed and done in only one tier.

DR. HENDERSON: Do you have a response, anybody want to respond to a question about the overlapping of the tiers. Again, we've gotten into the exposure area, but that's fine. That's where we're supposed to go. No comments.

DR. GRAHAM: We'll take a look at that.

DR. HENDERSON: You'll take a look at, okay. That's all we need. Thank you, Lianne. Did you have more to, comments to make?

DR. SHEPPARD: I do, but maybe I'll wait until other people talk about exposure, and then chime in later.

DR. HENDERSON: Okay, well, I know you still have, you'll still be there another hour or so?

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DR. SHEPPARD: Yeah, right.

DR. HENDERSON: Doug, you have comments on the exposure method, the tiered approach, et cetera.

DR. CRAWFORD-BROWN: There's no lunch first, then?

DR. HENDERSON: No.

DR. CRAWFORD-BROWN: Just wanted to know where we stood with lunch, that's all.

DR. HENDERSON: Oh, well, lunch is coming in thirty minutes. Oh, lunch is ready. I suggest we have a working lunch. I thought, maybe, according to our schedule, we would go to, we would have lunch at 12:30, that we might make a little more progress, but if hunger pangs are striking, I don't mind.

DR. CRAWFORD-BROWN: I'm not taking the rap for this here. I just wanted - -

DR. GORDON: Let me take the rap.

DR. HENDERSON: When you said to know, it's good to know what the plan is. Let's work a little longer, I feel like.

DR. CRAWFORD-BROWN: Okay, I don't care.

DR. HENDERSON: I'm not hungry yet.

DR. CRAWFORD-BROWN: Is this on? Is this one on? I'm not, is there a reason you're holding the?

DR. HENDERSON: It's just because I can't

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reach and yeah, it's on.
DR. CRAWFORD-BROWN: Okay, well, first, I like the exposure section, as I mentioned in my comments. It, really, is very much in the line of a wide range of other kinds of assessments that the EPA has done over the years. And it, really, is, I would say, you know, partially in answer to Ted's issue, the exposure and the risk side is starting to get pretty automated these days.
The models are not quite plug and chug, because situations change quite dramatically. I was very comforted when you said that you would use the epidemiological results with air quality information and the clinical studies for the, I hope I'm getting this right, for the actual inter-subject variability kinds of calculation, 'cause I always worry about using the epidemiological results to get your slope factor, or whatever, and then, also, doing inter-subject variability.
Because the epi results, in fact, already have that convolved inside of it. And so, I hope I'm understanding that correctly.
MR. RICHMOND: That is correct. And if you'll look at the ozone staff paper, and risk assessment, you'll see that's exactly what we say - -

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DR. CRAWFORD-BROWN: Yeah, exactly the same thing, yeah.
MR. RICHMOND: - - where we had clinical data and epi data. We made that point.
DR. CRAWFORD-BROWN: Yeah, good, okay. I wasn't quite clear on one thing, which has to do with, as you move from tier to tier, are you moving from tier to tier because of things that you see in the previous tiers assessment, like a screening method, for example, that say, oh, if I look at the upper 95 percentile, boy, that's really large.
So, I, that risk is large, so I better do a more detailed one. Or I look at it and it's very small, so I don't need to do the more detailed one. Or are you moving from tier to tier based on whether the data are available to move to the next tier. I'm assuming, maybe, a little bit of a combination of those.
DR. GRAHAM: Right, I'd say both. And the hope would be that the prior tier is, in a sense, more conservative or, well, I don't want to say, hopefully, it's more uncertain, but we want to reduce the uncertainty in progression from going from, say, a tier one to a tier two or tier three.
DR. CRAWFORD-BROWN: Okay, 'cause is

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you could do is, you could imagine that the different tiers are different levels of uncertainty, or you can imagine that the different tiers address different kinds of questions of one, the lower tiers having to do with questions about the upper percentiles of exposure. And the other ones covering the whole exposure realm. And then, the only other comment I would make now, the rest are all in my written comments, is, I do think on the uncertainty side, you've got a significant amount of work to do there.
You always will have that. You've got this challenge of combining the, what are going to be necessarily qualitative aspects of uncertainty with more quantitative aspects of uncertainty, aspects of uncertainty that have to do with scenario specification, and so forth, and other aspects having to do with uncertainty in parameter values.
And I'll be interested to see how you fold those things together into some, sort of, overall judgment of uncertainty here. I agree with the direction you were, sort of, heading, which is to make it, you know, to leave this sort of expert judgment as, and sort of semi-quantitative uncertainty bounds in the assessment.
I think that will be important, rather than

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thinking that everything can be reduced entirely to the kind of more quantitative probability density functions on uncertainty. But, in the end, you'll just have to figure out how you're going to present that as a story, the overall uncertainty. But I thought the methodologies were quite good. That's all.
DR. HENDERSON: Thank you. Terry Gordon, do you have some assessment, or advice to give on the exposure section?
DR. GORDON: Well, I'd say quantitative risk assessment is a weak point of mine, so I don't have really much to say, except exposure.
DR. HENDERSON: Well, this is exposure, yes.
DR. GORDON: Well, see my confusion of the terms shows - -
DR. HENDERSON: Well, we're talking about the exposure section, not the risk assessment. I mean, the tiered exposure approach.
DR. GORDON: So, not the-, we're on the health effects or not?
DR. HENDERSON: No.
DR. GORDON: Oh, no.
DR. HENDERSON: So, are you still, are you just still, okay, that's fine.

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DR. GORDON: Well, I was going to read Ellis' comment.
DR. GORDON: I have no experience in which to basically form judgment.
DR. CRAWFORD-BROWN: That didn't stop me from talking.
DR. GORDON: Well.
DR. HENDERSON: I got the message. Okay, Jim Ultman, are you on the phone? Have to wait for people to un-mute. Lianne, you said you wanted to save your comments. Do you have any further comments, and then I'll open it up to the whole group.
DR. SHEPPARD: Well, you know, I'm looking over what I wrote. And I prepared an extensive set of comments, but a lot of them are fairly detailed, and probably aren't worth discussing now. But the, my comment about the purpose of the tiers, and I also, it resonated with me, the previous comment about, exactly, what is the goal of each tier, and are they representing different kinds of questions, or are they, really, just progressions of better information. Because, in the exposure tier, it states pretty clearly that they'll be using interpolated hourly NO2 concentrations.
It says measurements, but presumably,

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there'll also be predictions, because they'll be over space as well. And, you know, that is just a, I mean, we're, as Tim alluded to, we're struggling with that here in the project we're doing.
That's a huge, huge undertaking to do that well. So, there has to be a number of simplifying assumptions to even do it at all. And, of course, you know, then you start to question how good it is. And, again, it depends on the purpose. I guess the only other comment, with respect to the exposure modeling is, it seems to me that the, well, when it moves to the level of the Monte Carlo simulation with the APEX model, that could be expanded to incorporate some key assumptions.
So, not just doing sensitivity analyses, looking at one or two different assumptions; but incorporating explicit structure for what those different assumptions or models could be. And, then, getting a more explicit estimate of the uncertainty that has to do with more than just the distribution, or just the underlying assumptions, but also variability in what those assumptions are.
DR. HENDERSON: Thank you, Lianne. Now, do others, as I say, these names listed here are just, trying to divide up according to interest. Obviously,

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I missed it on Terry, but anyone should have, should feel free to comment on the approach they're using for exposure assessment, particularly the tiered approach. Do we have any more comments?
DR. HATTIS: Yeah, I just want to just reinforce that, you know, I do think that if you stop at the some of the lower tiers, you'll probably not produce the kind of information that will later be needed in, at least, impact assessments, if not the primary decisions.
DR. HENDERSON: Good, and I believe Frank Speizer had a similar comment that he would be disappointed if you stopped at tier one.
DR. GORDON: Rogene, I - -
DR. HENDERSON: Okay, Terry.
DR. GORDON: I might be making myself more confused, but on page 22, it has a long-term exposure approach, as if it's going to be using annual averages. And then, when I get to page 31, I was going to talk about some, one health comment. It says they're not going to use that in the health risk assessment. So, if that's true, why are you going to do this work? I don't agree with not doing it, actually.
DR. GRAHAM: It was probably found, I

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don't want to say probably. It was founded in the current form of the standard. That is, it's a annual average.
DR. HENDERSON: Is that the answer you're, I mean, does that answer your question?
DR. GORDON: Tradition, yeah.
DR. HENDERSON: Yeah, okay.
MR. RICHMOND: Well, one of the, I mean, this is sort of the linkage to get back and forth between the exposure and risk. One could envision doing a long-term, addressing long-term air quality in the tier one, or long-term exposure, doesn't mean that quantitatively that we have enough information to address, or we don't, you know, depending on both causality and the level of information on concentration response relationships from the epidemiology, do we have enough to make a credible quantitative risk assessment, not qualitative con-, you know, concerns about the health endpoints that may be shown, but enough to, basically, move to that next step quantitatively. And, so I mean, there could be very much a distinction between whether we do long-term air quality or exposure, as opposed to a tier two, quantitative, long-term risk assessment.
The question on benchmark is it's difficult,

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given the issue that Doug and others have brought up, the epi studies long-term don't tell you, like the clinical studies, what's a benchmark exposure level. You don't know what the exposure was. You know what the ambient monitors were. That's all.

DR. HATTIS: Well, because you don't, they don't directly tell you about it, they certainly give you a clue, from which you can reason, given your other information about what they're likely to have been.

MR. RICHMOND: It, again, depends, there's all sorts of questions about is it really the cumulative long-term average, or is it, as Dr. Crapo mentioned earlier, is it that someone sees a peak so many times per week. There's all sorts of possibilities, from a health standpoint, in terms of what the real, underlying cause of those long-term effects are.

DR. HATTIS: Yeah, and I think you need to fairly characterize those uncertainties by doing it a couple of different ways, and say, okay, what are the differences in expectations that we get from these different possible states of the world.

DR. HENDERSON: Thank you, Ed?

DR. AVOL: I submitted some written

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comments. I won't go through all those, but one area I did want to ask about was the issue of the Tiger mapping, in terms of the road designations, and in terms of modeling and assessing the portion of population that may be within or near roadways.

There are ways, I point out one way that we, sort of, found out there was a problem and what we did about it, but there are other ways to do it. But I just wanted to get some confirmation that, in fact, you're either going to ground troop it or do some sensitivity analysis or something, or move to something other than that.

DR. GRAHAM: I'm sorry, I was looking at my notes. Yeah, we are aware of that data as well. And, it's not to say that we were just going to look at the one data source that I mentioned, but the Tiger road, it wouldn't be exclusive. But the Tele Atlas would be used.

DR. HENDERSON: Are there any other comments or questions people have about the exposure assessment section?

DR. SHEPPARD: Yeah, this is Lianne Sheppard. I have another question, and what does it mean to look at exposure for just meeting current standard, when so many of the measurements are below

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the current standard?

DR. HENDERSON: Yeah, go ahead, Harvey. We talked about that earlier.

MR. RICHMOND: Yeah, I thought we had discussed that about twenty minutes ago, but - -

DR. HENDERSON: Yeah.

DR. SHEPPARD: Yeah. Well, maybe, okay, maybe I just missed it.

MR. RICHMOND: Oh, okay, but, well, what I laid out is, it is a problematic challenge to, you know, to deal with how do you assess the exposures or risk just meeting the current standard. There are different approaches. One is to use historical air quality when the levels were just meeting the current standard back typically in the 90's for some of these example urban areas.

The other approach would be to rec-, you know, do some statistical adjustment just like we've done in ozone and PM, where it's been to ra-, you know, adjust things, air quality adjustment procedures to adjust the distributions downward to meet a standard, but effectively, rolling up distributions to just meet the standard. And there are different ways you could do that, as to whether it's proportionately all the monitors, or whether we make distinctions between the

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near roadway and non-near roadway monitors.

So, we were looking for feedback from the, particularly, the air quality experts on this committee.

DR. SHEPPARD: So, I guess, my question, then, is, should we even do that, since the mo-, since the current data are below the standard.

MR. RICHMOND: Right, the other alternative is, then, we, otherwise, have no exposure or risk associated with the current standard. It would really be the recent air quality and what standard that would be associated. So, if a place that only maximum has .03 today annual average, that they were, basically, looking at standards at that level and below. That's the choices we face, and you know.

DR. CRAWFORD-BROWN: Rogene, may I, several points have touched on that.

DR. HENDERSON: Yes, go ahead, Doug.

DR. CRAWFORD-BROWN: This worries me just a little bit, because the question comes up as to what do you mean by meeting the standards. If what you mean by meeting the standards is that everybody goes to 0.053, then that's one thing.

But my argument is going to be, that when people meet the standards, kind of like in water, it's

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the same issue, they put in place mitigation strategies that do drop significant areas well below the regulatory limit, and that is part and parcel with meeting the standard.

So, I don't think that a scenario in which everybody has gone up to .053 is, in fact, a scenario that is meeting the standard in the way that meeting the standard actually plays itself out.

MR. RICHMOND: Yeah, let me clarify that. When we say meeting the standard, standards, typically, have been implemented by, for example, large regional areas. The CMSA basis, it's not just L.A. County, but it's the L.A. at CMSA is, typically, a definition for a non-attainment area. When we say adjusting the air quality, we mean at the highest monitor in that area. We're not talking about using or adjusting air quality so that every single monitor in an area is just at the current standard. It is the design monitor within that urban area. So, it's like, for the whole New York area, if we did New York, or Philadelphia.

DR. CRAWFORD-BROWN: Okay, so in your - -

MR. RICHMOND: So that, so none of it, nowhere have we ever adjusted air quality in any of our analyses in the past so that all monitors with an area, when we do just meeting standard scenarios, it means

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only at the design monitor, and what are the relationships at the other monitors as they flow up and down.

DR. CRAWFORD-BROWN: Oh, okay, okay. Okay, there's something you said earlier that made me think it was different from that. Thank you.

MR. RICHMOND: All right, okay.

DR. HENDERSON: Well, and, I think Ron brought up the important point. You wouldn't want to say that the risk associated with meeting the current standard, or the current risk when it's, actually, lower. So, I, that's, you could misinterpret that. Dale, did you have something?

DR. HATTIS: Yeah, I think the concern is to have a realistic scenario. And in the, the realistic scenario that could get you to back up to the roll up, type methodology that you want to think about, is imagine a future of possible growth in traffic or other things that you could reasonably imagine, where you could be deteriorating the air quality enough to get you to near the, near compliance with the current thing. So, I think it may well be that your roll up scenarios are the easiest thing to do along those lines.

MR. RICHMOND: Right, and in that vein,

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one of the things, having looked at your comments, we may want to, at least, take maybe the worst case situation, maybe it's Los Angeles, and look, you know, look at the mobile models. What if we were to double vehicle things, would we still have a problem?

We still might not come up to that level given control technologies and given stationary technologies, that was the industry argument, that even given what's in place and can't be rolled back, that you can't envision the scenario that gets there, but that's something we could look through modeling in a more limited number of areas.

DR. HATTIS: Yeah, and I think that's a reasonable alternative, to say, okay, what is the worst possible deterioration that we can reasonably imagine under the current scenario. I mean, that can include, you know, non-attainment of ideal compliance with everything, but.

DR. LARSON: Harvey, this is Tim again. When your scenario of just meeting the standard is going to based on the actual location of the, the worst, the highest EPA monitor in that area?

I mean, what if you did your modeling exercise and found that there were a whole bunch of places that currently don't meet that standard within

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the urban area.

MR. RICHMOND: Well, what you, are you talking about the exposure modeling, air qu-, I'm a little lost as to which point - -

DR. LARSON: Yeah, I mean, your, yeah. I mean, is it based on the current, the - -

MR. RICHMOND: Whether you meet the standard, by definition, is at the monitors. It, you know, the mo-, we're supposed to be, have taken that into account.

We realize in setting the CO standard and the ozone standard that, no, the highest level may not, you know, depending on the pollutant, may not be at the monitor, but designing scenarios for alternative standards is based on the monitoring network, not, we'll then look at the implications through exposure analysis in modeling to see what's the distribution of exposures in the population, no matter where they are, but it is based on simulating standards that are met at the monitoring network and by definition of the standard at the design monitor.

DR. LARSON: Okay.

DR. HENDERSON: Okay, does anyone who is on the phone have any comments? I don't want to ignore you. I've already heard from Lianne and Tim. Okay, I

suggest that there seems to be a strong move towards lunch. We have lunch next door. I would like for us to use this as sort of a working lunch. Maybe be prepared to start our discussions again at 1:00 in here. You can bring your lunch in here and eat, or you can eat there, or do whatever you want to do. But I'd like to start the discussions at 1:00 and Vanessa has something.

DR. VU: Since we are short of time, I'd also like to invite OAR representatives to join, grab a lunch here so you can quickly go back here.

DR. CRAWFORD-BROWN: With us?

DR. VU: No, no, I mean, get the lunch and come back here at 1:00, since it's a, you know, sandwich buffet, whatever.

DR. CRAWFORD-BROWN: They get in line first, then.

DR. HENDERSON: Well, I think that's great, so we will begin our discussions here at 1:00, and you can use your time now to eat in there or eat in, to bring it in here, whatever you want.

(WHEREUPON, the morning session was concluded.)

DR. HENDERSON: We want to, very good. Doug is my bell ringer. We want to get started discussing this last section of the methods document.



That is the one on the health risk assessment. And I think there'll be a lot of comments on that. A lot of people interested in it. John Samet is calling in a 1:45, so we'll have his comments later.

But, we have all of our Air Office crew here. Well, that was a great lunch, and I thank Vanessa and, who has already left for arranging it for us. That was a nice way of handling things.

So, now, we're going to open our discussion on the health risk assessment approach, and what, and offer it, our advice to the Agency as to whether we think they're using the right approach, or if it could be improved. And Ed, you are one of the first discussants.

DR. AVOL: Okay, thank you. I have, I guess, two comments. One has to do with the risk assessment scope overview itself. The, what's laid out on page 31 talks about how the draft ISA leads to a suggestion that the strongest health findings are for one-hour and twenty-four-hour averaging times, so there's not going to be any risk assessment for longer term exposures. And that's disquieting, I guess.

The current standard is an annual, long-term standard. The document says, or this document says, we're only going to look at short-term exposure. There



is data from several studies looking at children's lung function, for example, which is a long-term, sort of, exposure. And so, it seems like there needs to be some reconciliation.

Yesterday, we had some discussion about, well, perhaps maybe there is a need for a short-term NO2 standard. But, so, I just want to offer that up as a comment for discussion, or at least for consideration. In any case, here, it just, sort of, says, well, so, we're just not going to do it. But I think it needs to be, at the very least, it needs to be, sort of, just supported or substantiated or something.

The other comment, which is a small comment. I, also, have some small written comments. But, there's a, in section 4.3, there's a discussion about health responses. And again, it, sort of, focuses more on short-term effects. And, sort of, disregards long-term losses in lung function. And yet, based on what we talked about yesterday and today, one of the conclusions in the ISA is going to be that long-term lung function is an important issue. So, it seems like the two documents are not going to be quite consistent.

MR. RICHMOND: In response, we said preliminary, based on what we saw in the first draft



ISA, which we're waiting, and we said we will make the assessments based on the second draft ISA that will be coming out before the risk assessment. So, we will look at and work closely with and see it to see how those issues are addressed in the second draft ISA.

DR. HENDERSON: Okay, now, is, John Balmes, are you on the phone?

DR. SHEPPARD: Rogene, I think he said he was coming back at 2:15.

DR. HENDERSON: Oh, that's right. I knew that. I'm sorry.

DR. SHEPPARD: Can I take his place? I'm leaving kind of earl-, soon.

DR. HENDERSON: So, would you like to make your comments now?

DR. SHEPPARD: Yeah, and I'd like to follow up on Ed's comment, because one of my main concerns was for each of the tiers of the risk assessment is that, I think we need to have very clearly stated criteria for what particular outcomes and populations and so on will be used. And those should be specified in advance. And presumably, they will come from the results of the ISA, as has been stated. But, the criteria for choosing them, for instance, would it be only the out-, the outcomes that

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are measure-, assessed as likely causal, as an example. Those, then, get brought forwarded to the risk assessment.

My other, fairly major comment, with respect to the risk assessment is, I think it needs to be expanded to have three tiers. And the first tier should be the qualitative risk assessment. And, so, that it doesn't, it becomes as important as the other tiers, and it also becomes the foundation for the quantitative risk assessment.

So, all the different outcomes are reviewed, but some of them, presumably, can't be easily quantified in a quantitative risk assessment, but they're still important, and they get discussed in the, in what I would suggest would be the first tier, which is the qualitative assessment. And then, some of them meet the criteria for being brought forward for quantitative assessment, and they, therefore, go up to the next levels. So, I think that's a fairly major change in the organization that I recommend.

I think the criteria for even discussing the quantitative or even conducting the quantitative risk assessment need to be specified in advance as well in this document. And I, actually, recommend that all tiers of all, both the exposure and the risk

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assessment, be discussed, even if the discussion is that these are the reasons why we can't do this, if that is the ultimate decision.

From what I've seen, I think that all tiers should be done, at least so far, but that remains to be seen.

And then my last, fairly major comment is the quantitative risk assessment needs to, also, incorporate some integrated uncertainty assessment that goes beyond the sensitivity analysis.

DR. HENDERSON: Okay.

MR. RICHMOND: Just on the last point, this is Harvey Richmond. Could you clarify what approaches, either in written comments or today, when you use the word integrated uncertainty assessments, what you would envision that, what approaches being used to carry out such integrated assessments?

DR. SHEPPARD: Yeah, and the devil of those, that kind of thing is in the details, of course. I'm sure that's why you asked the question. And I guess, the idea here is that the, and I'll try to expand a little bit more than I have already. The idea is that the, we go beyond sensitivity where we assume a different set of fixed assumptions to allowing for multiple different assumptions.

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I guess, looking back at the ozone criteria document, when we had a fair amount of discussion about the linear versus logistic function, you ended up using, doing a new analysis, which had different weights for the linear and the logistic function.

That is an example of moving in that direction. It was presented more as a sensitivity analysis, but the, you know, that's the, that's what I'm thinking, that a lot of, a number of different assumptions and uncertainties of those would be incorporated into the estimates that are produced.

MR. RICHMOND: But again, that was a sensitivity analysis. There wasn't an assignment of how much weight to put on the different choices. We put forth a base case assumption, and we looked at the impact of alternative assumptions. I'm hearing you say that you want us to do more than that. I'm still left puzzled as to what you would be recommending us to do differently.

DR. SHEPPARD: Okay, I'll try to articulate that more clearly in writing.

DR. HENDERSON: Okay, is that all you had to say right now, Lianne?

DR. SHEPPARD: Yes.

DR. HENDERSON: Okay, thank you. And

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then, James Crapo, do you have something?

DR. CRAPO: Yeah, I think I've made most of the points, so to make the, I like the risk assessment model and the health endpoints. I thought you were choosing the appropriate ones, and I like, particularly, that you were, included a focus on short-term exposures and short averaging times.

And, I assume, if I read it correctly, you're going to continue that as you do the tier two epidemiology. You're also going to look at the possibility of using correlations with something other than the national average, annual average, but rather the short-term exposure peaks, which I'd really encourage that.

Because I think that one of the most important outcomes that can come out of this analysis to help us develop data that would convince us it's important to change the form of the standard or not. Because I think that, I think form of the standard is, probably, one of the more important questions to address at this point in time. And I'd like to see the risk assessment provide us better information to make an informed decision on that. But I think that's already part of your goal as I read it, so I'm very pleased with what I see.

DR. HENDERSON: Thank you, James. Is Steve Kleeberger still here? I don't see him. He's not, he wasn't going to be on the phone, was he?

DR. NUGENT: That's correct, and he did send an email this morning saying he may be unlikely to be here.

DR. HENDERSON: Oh, okay. Then we'll go on to Kent Pinkerton.

DR. PINKERTON: Okay, again, I think this is a really well-executed document. I think the concern that I have is one that was also expressed by Frank Speizer. And that's just the concern that with the tiered approach, that one may be tempted to stop at tier one and not go beyond. And I think that becomes problematic, because there's such rare occurrences of excursions of above the set standard, that one could argue, well, there is no need to go to tier two and look at these potential health effects.

But since we see so many instances of significant health effects associated with ambient concentrations of NO2 that are well below the established standard, that I think it's just important that that be really emphasized, that many of these studies really need to go beyond just tier one and go on to tier two and, occasionally, to tier three.



But, again, I think the way it is written, the health endpoints seem to be very appropriate. Again, keep in mind, as you look at susceptible populations, again, to keep in mind children, those who have asthmatic conditions. Also, I don't know if we've really reached a point at this point in time, but are there potential differences based on gender, with regard to the health effects associated with nitrogen oxide exposures.

Again, I think, some of my questions about why only cities and not areas that are not city or population based are not being included, but I think, Donna, you helped me understand that a little bit better. So, and I think those are, pretty much, the extent of my comments.

DR. HENDERSON: Thank you, Kent. Dale Hattis observed that I'm not too sharp here this morning. I skipped him. That was not intentional, Dale. So, we'll hear from Dale right now.

DR. HATTIS: That's all right. Anyway, I want to second the thing that some of the, many of the comments that, in fact, Kent Pinkerton has just made. But just to say, a little more strongly. I'm going to be really disappointed if you stop at tier one. Of course, avoiding disappointing me is not a huge



national priority - -

DR. HATTIS: - - but I do think that getting an idea of the quantitative significance of the health effects that you think are likely is important from a national priority setting standpoint. You know, one, of course, your main job is to inform on decisions about the revision of the criteria, this particular criteria standard.

But, also, it seems to me, that you are also feeding into a national discussion about how we should devote our resources to changing the mix of air pollutants that we are exposed to, and, as well as other problems. And so, trying to be as thorough as you can about allowing people to project national impacts is an important function, okay.

Because this isn't going to stop at the, with your meeting of the deadlines that you have in front of you. And, you know, people are going to continue to try to understand how, you know, how they should be devoting resources to this problem. Because of that, in part, I think you ought to really, seriously, consider stretching a bit to include the kind of effects that are based upon the chronic observations, particularly the children's lung function growth.

Let me say that that's important because it



sets, if, in fact, it's true that the NOx or NO2 changes that, that sets the baseline for lung function over a lifetime, which deteriorates, which grows through childhood and early adulthood, and then starts to deteriorate over time until you get to less and less function as you get to our age. And so, that's, and that is, in fact, directly related to mortality as well.

So, that has, sort of, long term implications for lifetime function and survival that might not be apparent from just saying, okay, well, we're going to lose X percent of FEV1 for kids who have more than they need to begin with, you know.

So, I think that's, so I think that's a reason to take that possibility seriously, and to, it's worth a little bit of a stretch, if you have to admit that you have three or four or even tenfold uncertainty in that, well, okay, it might still be important.

DR. HENDERSON: Thank you, Dale. I'm going to ask Ronald Wyzga to make his comments, and then we'll open it up, and everybody can make comments.

DR. WYZGA: Thank you. I think the plan as written is a very good plan. I think it's very thorough, very thoughtful. I think the difficulties are going to be in the implementation. It's a

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formidable task. You have a tremendous challenge, and I think that to come up with something that's going to be, with your resources available and with the data available, is going to be, accepted by a wide community is going to be a challenge.

But, I applaud the approach you've taken. I think, when I think, you know, particularly, tier three, and you look at the current epidemiology studies, they tend to look, they tend to use linear models, which suggest that there's no threshold. And, that's one area, what worries me particularly, where you're looking at the just meeting current standard, in the sense that if an area is still well below any standard or proposed standard, because you're using a linear model, you're going to overestimate the risks for that area.

And I really worry that that could be misinterpreted, and I urge you to, sort of, think about both how you present that, and is there some way to get around that problem. I don't have an obvious solution to it. I think you've done some thinking about it, but I urge you to think further about it, and to the extent that you can't resolve it, it's going to be very important how you present the results so that they don't mislead the public. But, otherwise, thank you, I

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think you've done a great job.

DR. HENDERSON: Are there other people who want to make comments on the health effects. Doug, I think does.

DR. CRAWFORD-BROWN: Just one small one, and it's more of a medit issue. As we've been having this discussion about the epidemiological studies, and the contribution of NOx and ozone and PM and so forth, this, probably, is a time for you to start thinking about looking at, what I would sort of call, the mass balance of the various risk studies that you're doing to see if they add up to something more than the total decrement that's seen in the epidemiological studies. I just wonder, if you add it up, what you calculate for NOx, and what you calculate for ozone, and what you calculate for PM.

They're all based on, sort of, the same kind of epidemiological results from which, we hope, we're tearing apart the various relevant contributions, but I just don't know. I don't know. If you added them up, would this be something like TRIM, for example, where TRIM had problems with more stuff coming out of a compartment than ever went into the compartment, you know. It's sort of a mass balance, kind of, thing there, that I thought I would find interesting at some

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point in time.

DR. HENDERSON: I think that's the problem of double counting, are we double counting. I mean, how many deaths, how many times can a man die. I mean, I'm just joking, of course, but what I mean is - -

DR. HENDERSON: - - is there any double counting. I think that's a logical question.

MR. RICHMOND: No, Rogene, no, we didn't, really, indicate mor-, we didn't include mortality in that preliminary list. It's morbidity endpoints, and the hospital admission studies, that have NO2 may, or may not, be some of the same studies that pointed to ozone or PM where they were using - -

DR. CRAWFORD-BROWN: Yeah, I don't know. I just get a sense that I keep seeing the same kinds of studies appear in documents, and, you know.

DR. HENDERSON: Yeah, you're right, it's the morbidity we're concerned about, but, okay. Is there anybody on the phone who wants to make a comment and has not? We are - -

DR. POSTLETHWAIT: I think Ted wants to comment.

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quick. We've got all the time in the world.

DR. RUSSELL: No, I prefer making it quick. Just, carrying on something from what James said is that, if we're going to be looking at a, possibly, a new standard, when you look at your table two, or any of the other analyses, just keep in mind that, maybe look at various alternative standards and forms of standards for our assessment.

DR. HENDERSON: Yes, I think that would be very good for the analysis to see. Well, it's been a very productive day and a half. I'm, I really want to thank everybody for working so hard, and for staying, most of you staying to the end of the meeting. And, I hate that we're going to miss John Samet, apparently, but he has written, has he sent in his comments, his written comments?

DR. NUGENT: I don't think we have comments on the methods document, but his assistant said he'd be on the line at 1:45. This was scheduled for 2:15 on the agenda.

DR. HENDERSON: Oh, I know, I know the problem, but I'm just sitting here. I don't think people want to sit fifteen minutes to wait, I mean.

DR. HATTIS: He can sign on and say his piece and that's fine, but we won't hear it.

DR. HENDERSON: But you all will be a the airport.
DR. CRAWFORD-BROWN: I think it's $14.38 we'll earn during that time, so keep at it.
DR. HENDERSON: Okay, well, it, I do value John and, the two Johns comments, but I think that they have, since we're not trying to reach a consensus, I mean, we're trying to get all of everybody's comments, that we can just get their written comments, which is what is needed. And again, if you haven't turned in your written comments, well, be sure you do that. Ed is wanting to say something.
DR. AVOL: Yeah, I would just ask that if the Agency staff have any questions, based on what they've heard, that they would like to get clarification on.
MR. RICHMOND: I have one.
DR. HENDERSON: Okay.
MR. RICHMOND: We put forth, I know it's preliminary for putting aside the long-term children's health study, but for short-term, from the clinical, we identified a preliminary range of .2 to .3. Are we in the right ballpark, or do the people who are familiar with the clinical evidence think it's something other than that range for one hour, based on the controlled



studies that we have, based on the evaluation in the ISA.
DR. CRAPO: I have a question, what do you mean by .2 or .3. Are you looking for, are you going to model the - -
MR. RICHMOND: A level of concern, if you're going to compare either air quality or exposures. We did this in ozone, as you remember.
DR. CRAPO: Right.
MR. RICHMOND: But we had .06, .07, .08, so we don't have to settle on a single level, but is that lev-, a range at which we, at least, are interpreting our evaluations, because - -
DR. CRAPO: All right, well, let me be sure I unders- -
MR. RICHMOND: - - I think that that's where the clinical studies start to, kind of, you know, the lowest level at which effects in asthmatics are being observed.
DR. CRAPO: I like this, except I'm not sure how you're going to model it. Because, in fact, we don't have any documented exposures at that level from the air monitoring stations. You have to extrapolate into cars and buses and - -
MR. RICHMOND: Well, that's what



we're - -
DR. CRAPO: - - and homes and things like that. So, you're going to extrapolate that that might be there and use that. I like that idea.
MR. RICHMOND: But I'm saying, on the health side, are we in the right range - -
DR. CRAPO: On the health side, but the, so you're going to, actually, look to see if there's health effects, and you're going to model with that, perhaps, might be that will be - -
MR. RICHMOND: Well, we're going to see if there are exposures of, what we call, our term is exposures of concern, which doesn't mean that everyone who sees that exposure will, necessarily, be affected, and we've explained - -
DR. CRAPO: I know, and I understand that. But this going to be all extrapolation data, based on modeling from - -
MR. RICHMOND: Model data that's a combination of both ambient and modeled inputs through the exposure model.
DR. CRAPO: I think that's a very good idea. I'd love to see the data, 'cause it addresses exactly what I've been talking about.
DR. HENDERSON: And I think he was,



Harvey was probably asking Ed clinically that was what you would consider appropriate levels. Haven't you done studies with children?
DR. AVOL: Not children in chambers at .2 or .3, no. I mean, the work we did in chambers was a higher, was with adults. So, I don't know that it's, I can directly relate to this.
MR. RICHMOND: You talking about, there were a number, there's a table summarizing a number of asthmatic studies that go down as low as .2.
DR. AVOL: And so, I mean, in that sense, again, as James said, I mean, I think, what you lay out is fine. My, not withstanding my previous comment about long-term studies, long-term is more - -
DR. HATTIS: Let me make a somewhat modest further comment on that, and that is that, you should, when you measure a statistically significant decrement at lung function, or a change in the responsiveness, you're talking about, not necessarily, a uniform response or a uniform susceptibility within that group that's measured.
And we have prior information about how variable people are in their susceptibility in a large number of other context. We have a database of that that's on our website.

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But, anyhow, so, in pharmacodynamic variability, in that kind of local responsiveness, happens to be, tend to be more variable than lots of other stuff, basically, of the order of geometric standard deviation of three or a bit more for that kind of variability, if I remember correctly.

But, you know, so, you can, in fact, by imposing a, kind of a log-probit function, with that amount of spread, you can make a, just as you can make distributional characterizations of the exposures, you can make distributional characterizations of the likely variability in susceptibility, and get something more that may, in fact, you know, say, you know, for your first percentile population, you might have sensitivity that's outside of the range that you've measured for the average concentration that's capable of changing this group, right.

And so, any how, so, it is possible to do a slightly more involved analysis that, maybe, take you half hour rather than fifteen minutes, that you might do for the una, with single variable analysis.

You also asked the question about how do we do an integrated, you know, characterization of uncertainty. And there's a, this is, perhaps, a longer answer, but basically, you characterize the

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uncertainties in the exposure, and it's faster to say that than to do it, and the uncertainties in the susceptibility and concentration response slopes and other things of that sort, and you, basically, convo-, you know, basically, convolute those two with a Monte Carlo simulation.

But you do have to, you know, sometimes these are better done than other times, and it is a matter of an evolving art as to how to choose the distributions that you use to characterize each of the uncertainties.

MR. RICHMOND: And in this area, it is not straightforward. The clinical data, even when I'm suggesting .2 to .3, some asthmatic studies, controlled studies, have found effects. Some have them have been repeated, and haven't found the same level under the same kind of conditions. So, this is no easy matter to assign probability or simply pick distributions out.

DR. HATTIS: Right, and so, you might want to, you know, do some combined analysis that says, well, there's some chance that the population distribution of susceptibilities is in this range, and some with this kind of mean in standard deviation, and some chance that it's in some other range that would be compatible with the observation that, you know, was not found in a particular population. So, anyhow, so,

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there are ways of dealing with this, although, they do require a bit of creativity and maybe creativity is a bad word.

MR. RICHMOND: A lot of creativity on work.

DR. HATTIS: Yeah, you know, but, nevertheless, you know, it's possible. And I think it's possible without inordinate resources. I mean, I think of the, you know, the poor guy who's over in the other part of ORD dealing with trichloroethylene and he's having to deal with Markov chain Monte Carlo simulations of to do uncertainties and variability for trichloroethylene and project from animal data to people. And, you know, and he's large-, mostly one guy, you know. So, lots of people have, you know, resource constraints, but you know, it's a hard problem to do quantitative assessments. But it can, you know, it's not impossible.

DR. HENDERSON: Thank you, Dale. You almost took up the fifteen minutes, but not quite.

DR. HATTIS: I'm sorry.

DR. HENDERSON: No, it's okay.

Yeah, I can just change it. Kent, go ahead.

DR. PINKERTON: This is a, just a question about, under the risk assessment overview, you

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had mentioned there that the EPA would not develop risk estimates for NO2 related effects associated with long-term NO2 exposures. And, I think you stated that you wouldn't do that, based on the fact that the findings are inconclusive, or at best, suggestive. And I'm just wondering, does that mean that you think that in doing short-term exposure assessments, you might be able to address issues that may have, with regard to NO2 exposures, that may have long-term effects?

MR. RICHMOND: No, I don't think that's what we're saying. One, as Lianne mentioned, there, we have applied in the past and was envisioning here, it's, selecting which health endpoint is first looking at causality, and in the past, we have and proposed here to do things that were likely causal, not to quantitate risk, or develop risk, quantitative risk estimates for things that were only suggestive or limited whatever final terms the ISA ends up.

So, we are, that is, part of the screening criteria in terms of determining how far we go, and then, looking at what kind of information we have as well, in terms of even once you get past. There were endpoints for ozone like inflammation, which were clearly likely causal, or causal.

But we didn't have sufficient information to

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generate, we felt, a credible exposure response relationship, and we still considered that in the review, that endpoint, in the discussion and evaluation, but we didn't do a quantitative, let's produce how many people have different degrees of inflammation.

So, just because we don't quantitate something in terms of producing some number of people have this many health effects, doesn't mean we're ignoring the other health endpoints.

DR. HENDERSON: I have a question that has occurred to me as I sit here. I seem to remember that some of the toxicology studies suggested development of a tolerance to NO2, am I right, does that happen, or am I getting it confused with ozone or - -

MR. RICHMOND: I'll defer to Ed.

DR. HENDERSON: Are there development, are there animal tox studies showing development of tolerance?

DR. PINKERTON: I think there are, yes. Oftentimes, NO2, as people are likely to be aware, behaves in a similar manner to ozone. It's just that you have to have much higher concentrations to get the equivalent response. But I do believe that there is a

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tolerance that is developed with persistent exposure to NO2.

DR. HENDERSON: And that's very hard to take into account at setting any standard, I'm sure, but. Well, okay, I think we, now. I will do as Ed did earlier. Anything, any advice or that you were expecting to get that you haven't gotten and would like for us to comment while you have this great group of investigators here?

DR. GRAHAM: After your other comment, I did have a question specifics about, we had selected, I think, five locations, and I briefly said there were criteria in their selection. And, I think it was Ed had commented, why not Phoenix and Denver, and I was just wondering, why those might want to be included?

DR. AVOL: I picked those two in looking at previous annual standards in violations of the standards, and just thinking about distribution and representation of the national picture that Phoenix and Denver offered other sorts of geography and exposure issues than just the urbanized cities like New York and Philadelphia, sort of thing.

DR. HENDERSON: Any more advice for the Agency. We will be seeing this again, of course, but the consultation comes first, and then there's the

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first draft of the actual document and the second draft. So, we should be seeing this document two more times, and - -

MR. RICHMOND: Just to clarify, no, you won't be seeing this document. You'll be seeing a draft exposure risk assessment report.

DR. HENDERSON: Oh, okay.

MR. RICHMOND: I mean, there's a huge difference. This was the road map, this plan. We don't, we plan to take into account your comments and the comments of the public in figuring out what we ultimately do. But the revised methods and what we actually do will be in, along with the results, in the first draft risk assessment, that's targeted for March.

DR. HENDERSON: Your report. Okay, that's good, and I'm glad you - -

MR. RICHMOND: I just want to make sure they do, and on the scheduling and we don't, under the new process, we don't produce a final of this plan.

DR. HENDERSON: Oh, no.

MR. RICHMOND: The plan is a living - -

DR. HENDERSON: No, no, no, no. I'm just, but this is leading to a document that will be reviewed two more times.

MR. RICHMOND: Right.

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DR. HENDERSON: But thank you for correcting. This has gotten so complicated with the new process, but it's good to be precise, so I'm glad you corrected that. And, perhaps, we can - -

DR. MARTIN: If I might, perhaps, it might be worth saying, just a little bit of clarification about what you can expect to see in the first draft - -

DR. HENDERSON: Good.

DR. MARTIN: - - of the risk assessment report versus what you can expect to see in the second draft of the risk assessment report. And I'll just layout an initial major distinction, and you folks can add to it as you will. We talked about estimating exposures and risks associated with various alternative standards.

And first of all, looking at just air quality, current levels of air quality, and then, just attaining the current standard. Those are the scenarios that we anticipate putting into the first draft of the risk report, and that you will be seeing those results and estimates associated with those two scenarios in the Spring, at the same time you see the second draft integrated science assessment.

Subsequent to that, in the second draft, we

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would then, at that point, decide what alternative standards we would then, additionally, do exposure and risk estimates for. Because at that point, we would have the benefit of the second draft science assessment, and the benefit of your review of that document, to help inform an appropriate range of alternative standards that would reasonably be applied to finish out the exposure and risk assessment.

So, those results you'll see in the second draft assessment.

DR. HENDERSON: Okay, that's helpful.

DR. MARTIN: And I wanted to make that point, because in the past, when we've come out with the first draft assessment, what everyone's looking for is, what is the risk associated with the range of alternative standards, and that, that's what we'll do in the second draft.

DR. HENDERSON: Second draft, in the first draft, you'll have the risks associated with the current exposures and the, if you reach the higher levels of the - -

DR. MARTIN: And it relates to the comment I made yesterday. We really don't want to get ahead of ourselves. We don't want to start projecting to what alternative standards may be appropriate to

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consider until we've had the benefit of your review of the second draft of the science assessment, where the inferences and conclusions are more sharply defined.

DR. HENDERSON: Good advice, Karen.

DR. MARTIN: Did you offer anything.

SPEAKER: No, that's okay, well stated.

DR. HENDERSON: Good.

SPEAKER: Rogene, somebody may have just - -

DR. HENDERSON: That's what I thought. Is there someone that had come on the phone?

DR. BALMES: ;Yeah, this is John, hi.

DR. HENDERSON: Oh, you have no idea how happy we are to hear from you, John.

DR. BALMES: Yeah, no, I just listened.

DR. HENDERSON: Okay, well, we would like your comments on the risk assessment part of this methods document. And, I'll tell you that the response before you has been generally positive. You probably didn't get to hear all that, but - -

DR. BALMES: No, I, you know, I'll tell you, Rogene. I don't, I didn't provide written comments on it at this point. I didn't have, I guess, very much to say, because, in a sense, it was such a general template that I didn't see too much to say

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until I guess receive sort of the next step. So, as a starting point, I think it was fine. And then, I think we'll have to see what comes.

DR. HENDERSON: Okay, John. Yeah, and we've had a very good clarification of what the next steps will be. Did you get to hear that?

DR. BALMES: Yeah, I did hear that. I heard that, yeah.

DR. HENDERSON: Okay, so that was very informative. And, okay, John. Well, we hope you didn't rush over to, we were just waiting for you to, in order to adjourn, to tell you the truth.

DR. BALMES: Oh, okay, well, then. I'm sorry to hold anybody up from adjourning.

DR. HENDERSON: Well, we've had interesting discussions. Really, this last discussion was most helpful, and we wouldn't have had it if we hadn't have been kind of waiting for you.

DR. BALMES: Oh, okay, okay.

DR. HENDERSON: So you contributed.

DR. BALMES: I'll be in person next time.

DR. HENDERSON: Okay. Thanks a lot, John, for calling in.

DR. BALMES: Okay, bye.

DR. HENDERSON: Okay, I think we are

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finished in our, it is the job of our DFO to adjourn us.

DR. NUGENT: Well, thank you all for being here, and then the next steps will be for me to send around a draft of the document we spoke about this morning, and send a draft of the minutes around for your comments. And I guess, even before I do that, I'll be contacting you about scheduling the May meeting to get your availability, so, I look forward to seeing you again and thank you. Meeting's adjourned.

(WHEREUPON, the PUBLIC MEETING was adjourned at 1:45 p.m.)

CAPTION

The foregoing matter was taken on the date, and at the time and place set out on the Title page hereof.

It was requested that the matter be taken by the reporter and that the same be reduced to typewritten form.

Further, as relates to depositions, it was agreed by and between counsel and the parties that the reading and signing of the transcript, be and the same is hereby waived.



CERTIFICATE OF REPORTER

COMMONWEALTH OF VIRGINIA

AT LARGE:

I do hereby certify that the witness in the foregoing transcript was taken on the date, and at the time and place set out on the Title page hereof by me after first being duly sworn to testify the truth, the whole truth, and nothing but the truth; and that the said matter was recorded stenographically and mechanically by me and then reduced to typewritten form under my direction, and constitutes a true record of the transcript as taken, all to the best of my skill and ability.

I further certify that the inspection, reading and signing of said deposition were waived by counsel for the respective parties and by the witness.

I certify that I am not a relative or employee of either counsel, and that I am in no way interested financially, directly or indirectly, in this action.

MARK REIF, COURT REPORTER / NOTARY

SUBMITTED ON OCTOBER 25, 2007

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