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CENTERS FOR DISEASE CONTROL
NATIONAL INSTITUTE FOR OCCUPATIONAL
SAFETY AND HEALTH

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ADVISORY BOARD ON RADIATION AND
WORKER HEALTH

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SEC ISSUES WORK GROUP

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MONDAY
APRIL 7, 2014

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The Work Group convened via teleconference at 1:30 p.m., Eastern Daylight Time, James M. Melius, Chairman, presiding.

PRESENT:

JAMES M. MELIUS, Chairman
JOSIE BEACH, Member
MARK GRIFFON, Member
GENEVIEVE S. ROESSLER, Member
PAUL L. ZIEMER, Member

ALSO PRESENT:

TED KATZ, Designated Federal Official
BOB BARTON, SC&A
NANCY CHALMERS, ORAU Team
HARRY CHMELYNSKI, SC&A
JOE FITZGERALD, SC&A
JOHN HANSON, Office of Congressman John Shimkus
DeKEELY HARTSFIELD, HHS
TOM LaBONE, ORAU Team
JOYCE LIPSZTEIN, SC&A
ARJUN MAKHIJANI, SC&A
JOHN MAURO, SC&A
JAMES NETON, DCAS
DANIEL STANCESCU, DCAS
JOHN STIVER, SC&A
TIM TAULBEE, DCAS

T-A-B-L-E O-F C-O-N-T-E-N-T-S

P-R-O-C-E-E-D-I-N-G-S

(1:33 p.m.)

MR. KATZ: Welcome, everyone. This is the Advisory Board on Radiation and Worker Health SEC Issues Work Group. The meeting today has a couple of documents. And I need to apologize to members of the public on the line because those documents are not posted yet.

Both of them had issues with Privacy Act clearance and clearance for making them intelligible to people who can't see, which is called 508 clearance, and they're not posted yet. But we will get them posted just as soon as possible so that at least you can go back after this meeting and see what those documents include in detail.

And those you'll find on the NIOSH website, under the Board section of the NIOSH website for the OCAS program, the DCAS program, under today's meeting date.

So now to go on with roll call, I'm not going to do conflict of interest per se. But keep in mind, everyone that's Agency-related on this call, that there may be some discussion of Savannah River Site or Fernald and keep in mind whatever conflicts you might have with those two sites.

(Roll call.)

MR. KATZ: Okay, the agenda for this meeting is posted on the NIOSH website where I said. Just let me remind everyone before I turn it over to mute your phones unless you're speaking to the group. And if you don't have a mute button, press *6. That will mute your phone and then press *6 again to come off of the mute.

And, Jim, it's your meeting.

CHAIRMAN MELIUS: Okay. Thank you, Ted. And welcome, everybody. This meeting is sort of a follow up to our longer meeting from a month ago, a few months ago, I can't remember exactly when, where we had

started discussing coworker model issues and discussed a number of points.

And we've had some discussions both at the Board level and then we had a short Work Group call since this time. But we're really looking now at two of the things that we had requested at that meeting.

One was the NIOSH effort has been looking at what's -- I guess what we're referring to as a practically significant dose. I guess that's the PSD. And the other issue is the OPOS, or one person-one sample, or one person -- I forget, we had other terminology for it -- but which is a review of that. We asked for a more comprehensive review of that issue by SC&A.

So we're going to start looking at the practically significant dose issue. So I'll turn it over to Jim Neton.

DR. NETON: Okay. Thanks, Dr. Melius. I'm going to try to use Live

Meeting. Can everyone that's on Live Meeting see the cover page of the report that we put out on February 25th?

MEMBER BEACH: Yeah, I've got it, Jim. This is Josie.

DR. NETON: Okay, good.

MEMBER ROESSLER: I can see it. This is Gen.

DR. NETON: I didn't prepare slides for this. I thought I would just sort of skim through this report and hit the highlights and then we can discuss from there, because it's a fairly short report if you don't count the multiple pages of graphs that I=ve appended onto the end.

So this is a report of an evaluation of what we did call practically significant dose. We issued this report in February, end of February, after some analysis that we did. And as Dr. Melius pointed out, that was in direct response to a discussion we had at the Work Group

meeting on September 26th.

We were hashing about ideas as to, you know, how we were comparing these different strata of coworker models and the idea came out, well, you know, how do we know if there's a practical difference? There are statistical tests that we can do, but let's talk about practical differences.

We hit upon this idea of practically significant dose. That is, if you change the dose to a case, how much dose do you have to add to really have a meaningful difference? And we hit on the idea of using the NOCTS data set that we have.

As you recall, we have over 40,000 cases in NOCTS. And we decided that if we looked at the cases that fell between 45 and 50 percent of the PoC, that would maybe give us an indication of -- and added in a little increment of dose to those cases, that would give us an indication of

how big an effect dose had on the PC calculations.

So we did that. We looked at the cases between 45 and 49.99 percent. And we identified, and this was surprising to me, there were only 175 cases that met this criterion out of 40,000 cases. That is, they were between 45 and 49.99 percent and had a single cancer. That's another key that we had to think about, only one cancer made up that PC value.

So we looked at these cases and the idea was to add 100 millirems to each of these cases to see what happened to the PC. I would point out that a fair number of the cancer models were represented in this analysis, although not all. I think I have, yeah, 25 of the 33 cancer models were represented out of the 175.

And about a third of the ones that we selected were represented by the lung cancer model, which is not surprising,

because I think my recollection is somewhere in the order 60 percent of lung cancer cases have PCs greater than 50 percent.

By the way, this report was distributed to the full Board some time ago, so you should all have a copy of it.

We looked a little bit at some of the demographics behind the cases. And on this page, Figure 1, shows what I think is a fairly interesting statistic. It's the distribution of ages at first exposure and the age at diagnosis.

And you can see from this that the age of first exposure, the median value is somewhere around 27 years of age, and the age of diagnosis is around 68. Well, that tells us, and this may be useful in our discussion later, that between those two there's about 40 years= worth of exposure that occurred that would need to be reconstructed, between the two median values, that is. And of course there's a

gradation between that.

So, nonetheless, many of the cases have very long exposure periods that need to be reconstructed. And if you recall, we decided, as an initial test, that we would add 100 millirem dose to each of these cases at the point in their exposure scenario that we felt would make the biggest difference in PC.

And that is, we would add the dose for solid cancers at the year of first employment, and for leukemias, I think we decided that if we added it five years before the diagnosis of leukemia that would be the most claimant-favorable, or give us the biggest change in outcome.

There were three scenarios evaluated. The first scenario was really just sort of an artifact of the situation where we changed IREP models. We are now running IREP Version 5.7. And not all cases had been run on 5.7. So we just went back

and re-ran, we made sure that all the 175 cases had their initial starting point as a Version 5.7. That's what we would call Scenario 1.

Scenario 2 is the situation where we added zero millirem as a constant to each of the cases at the point in their exposure that I just talked about, that is, at the beginning of employment for solid cancers, or five years prior to cancer diagnosis for leukemias.

You might wonder why we added zero dose. Well, it turns out when you add a line of input to IREP you change the sequencing of the random number seeds. So if we didn't have a zero dose addition and a concomitant 100 millirem dose comparison, we would not be comparing the differences in the pure excess relative risk, we would also be evaluating differences due to the uncertainty associated with the random number seed sampling. So that's why we had

to have a Scenario 2 which was a zero dose.

And then in Scenario 3 we added the 100 millirem to each of the cases. So in reality the real comparison that we need to focus on is the difference between Scenario 3, which is the addition of 100, compared to Scenario 2, which is the addition of zero.

Those two scenarios were run using the exact same random number sequences, so that when you have a difference it is in effect just due to the effect of the addition of the dose.

A couple of other things about the addition of the dose. We decided to make it an acute exposure to photons greater than 250 keV. And that just sort of simplified the analysis. Photons less than 250 have an uncertainty associated with them and we didn't want that to weigh into the analysis. So essentially it's truly a constant value that was added.

And, let's see, what was the other thing I was talking about? The 250 and, oh, the acute. Acute scenarios don't have any adjustments to them, whereas chronic might influence the outcome. So it was an acute exposure greater than 250 keV photons, 100 millirem.

So we ran all three of these, we ran these scenarios over all 175 cases, doing what we normally would do for cases that fell between 45 and 50. That is, we would run the IREP analysis with 10,000 iterations each 30 separate times and take the mean of those runs.

That's standard practice for any case in our program that falls under those parameters. So we did that. And we ended up with the statistics that we can see summarized here in Table 1, that the maximum value under each of the scenarios, and particularly I would call your attention to Scenario 2 and 3, none of the maximum values

exceeded the 50 percent PC.

That is, out of the 175 we ran, all either had zero change or increased slightly, but did not result in a change in compensability decisions.

If you look at Table 5 on the following page where it's highlighted in yellow, if you look at the solid cancer and CLL line, Scenario 3 compared to Scenario 2, there were a 170 solid cancers. The minimum difference was zero. The median difference was .02. The mean was .06. And the maximum change was .34. There were only five leukemia cancers included in this analysis. And you see on the last line of Table 5 the statistics associated with that.

And there were some differences. The minimum change was .08. The median was .3. The mean was .28. And this is percent. And the maximum change is .34 percent. There was slightly more increase in the PC values in leukemia cases, which we might

have expected because leukemia in itself tends to be compensated at a much lower dose. So a 100 millirem change to a lower dose would more than likely have a larger effect, at least that's my interpretation of that.

So if you get to the bottom line, this is a change, this slide here, Figure 5, shows the distribution, the changes in PCs between Scenario 3 and 2 for all cancers.

And you can see here that the median change, the dashed line, is .02. The mean change is .06. And the maximum change is .34, as we said before. So it's log-normally distributed. It's very heavily weighted towards a very small change. There are some larger changes out there, not very large.

So that's what we ended up with. So it's a pretty simple message here that, you know, the addition of 100 millirems in

these cases didn't do a lot, didn't change anything, although, you know, I'm not saying it's -- it may be fortuitous that none changed because we were on the borderline for a couple that could have just as likely gone over.

But nonetheless, they didn't change much at the maximum point where they would make an effect. So the next step beyond this is -- I'm not quite sure. I thought it would be obvious when we ran this. But now I'm very interested in hearing some feedback from the Working Group as to where we go with this.

Clearly, you know, if you had ten years of exposure the change in PC wouldn't be .06 times 10. It's not a linear function. And in fact when you get closer to the cancer diagnosis, the exposure has less and less an effect.

As you get within ten years of the cancer diagnosis there's sort of this

asymptotic, or S-Shaped function that kicks in where you get virtually no credit for the cancer being caused by a radiation within the last two or three years of exposure prior to diagnosis.

So, anyway, that's it in a nutshell. I'd be happy to answer any questions that people might have.

CHAIRMAN MELIUS: Okay. Thanks, Jim. Board Members first, do you have any questions?

MEMBER ZIEMER: No questions here, this is Ziemer.

CHAIRMAN MELIUS: SC&A, do you have any questions?

MR. STIVER: This is Stiver. I don't have any questions on this particular aspect of it, no. I don't know if Arjun might want to say something.

CHAIRMAN MELIUS: Arjun or anybody?

DR. MAKHIJANI: Sorry, I was on

mute. I didn't realize. I forgot.

This came up in the last conference call. I think they are more or less similar findings that were presented last time, maybe more complete now.

But my comment was that, you know, a lot of what we deal with in SEC type of situations is uncertainties in relation to internal dose. External dose is generally reasonably well-known, and I think apart from the neutron case in Rocky Flats, I don't know that any SEC is being granted. I might be wrong.

So I don't know what significance this particular analysis has, you know, that you check for adding 100 millirem to the external dose. I think trying to identify the uncertainties in internal dose, which can be quite big -- say, the difference between an 84 percentile and a 95 percentile dose in various situations can be quite big.

And applying that and going by

radionuclide, because it's a radionuclide-dependent problem and on organ-dependent problem, certain analysis becomes more complicated, but also it's more relevant. I don't know that this external dose analysis is very relevant to SEC investigations. I mean, it's theoretically interesting.

CHAIRMAN MELIUS: Are you suggesting a specifically different analysis?

DR. MAKHIJANI: Yes, yes. I'm suggesting that an analysis that adds a fixed external dose to see if people are put over the top of 50 percent of the Probability of Causation criterion is, to my memory, not very relevant to SEC cases.

What is generally relevant to SEC cases is whether we have the data on how accurate the coworker models might be. So in relation to the latter question, accuracy of coworker models and what we know and what we don't know, if we try to gauge the

uncertainties in regard to, say, thorium dose in a particular situation and examine that for its effect on Probability of Causation, that might yield a more interesting result in terms of practical applicability to SEC sufficient accuracy questions.

DR. NETON: Arjun, this is Jim. I don't disagree with you but I think until this analysis, prior to this analysis, we had no idea how much a dose would change a case, especially looking at the population that we have in-house. So, I mean, I think it's very informative to know that 100 millirems is sort of on the cusp of making changes.

I mean, I wouldn't know if it would have been 5 millirem, 10 millirem, 100 millirem. So we at least know that now. I mean, and the nice thing about external is you get rid of the baggage of these other uncertainties so at least you're sort of

able to focus in on a quantitative change based on constants.

Now, I agree, then the next step is more than likely to fold in the uncertainties maybe. I don't know. It's hard to say, because, as I said, internal dose tends to be delivered over time, as you know. Doses that are delivered within ten years of exposure have less and less influence on the outcome. It's hard to predict.

DR. MAKHIJANI: Yes, well, I actually agree with you that, you know, so I'm not saying the effort that you've made, obviously it's a useful effort because we know something quite important today that we didn't know then. So I didn't want to imply that it was a wasted effort, because it's not. I agree with you.

So the question is, you know, what's the comment and what the next step and where should we go? And my comment was

simply directed at the idea that the sufficient accuracy question generally comes up, as you know, in relation to internal exposure.

And if that's the issue to resolve, then, you know, maybe in the same way that you've done external exposures there could be a single sort of incident-related exposure at the start of employment, you know, in the way that you've done the sort of Savannah River, you know, what was it, high-five model, a similar approach to, you know, applying a dose corresponding to the uncertainty at the start of an employment, or an intake at the start of an employment and letting the doses and Probabilities of Causation unfold from that might tell us something about how accurate we need to be.

I mean, if it's even a very large dose doesn't change the outcome, then, you know, you're in pretty good shape. But, you

know, if a few nanocuries can make a significant difference, you know, then there will be pretty big issues.

DR. NETON: And maybe the situation would be to look at the subset of these 175, because we're looking at cases between 45 and 50 that had internal exposures that contributed to the PC. My gut feeling is that many of them did because that's when you get the biggest doses.

It's pretty hard to get a PC that's in the 45 percent range based on external exposure, has been my experience, except maybe for those people that worked in the very early years, like at Mallinckrodt or something. For solid cancer you need tens of rem exposure to get into that range, if not higher. And that's only usually doable with internal exposures to what I would consider as target organs or metabolic organs.

DR. MAURO: Jim, this is John. I

have a question along these lines, because Arjun has a great question. If we were to assume -- this is a thought problem. Now, you delivered 100 millirem to organ of concern. Take the time period prior to diagnosis that you felt, this is a judgment call, would sort of maximize the latency consideration.

Now, if that dose, that 100 millirem were delivered by, let's say, tritium to the organ or delivered by an internal photon emitter or beta emitter as an internal dose in that year, would anything change?

DR. NETON: Yeah, I mean -- well, I'm not sure about tritium. But I know for all internal doses the minimum uncertainty is a GSD of three on the internal dose estimates.

DR. MAURO: So you would deliver it that year, but instead of it being a fixed value it would be 100 millirems

delivered to that organ. But it would have a distribution on it which could give you an end tail that could change the picture.

DR. NETON: Yes.

DR. MAURO: Okay.

DR. NETON: But you've got to be careful. That's a GSD, that's a log-normal distribution, then I'm not sure what you're comparing it to. See, now you're talking theoretical. You would add -- I don't know what you would add even.

DR. MAURO: Thanks. No, no, I didn't realize that -- if you did it as an internal as opposed to a fixed, deterministic number of 100 millirem, you would be forced into a situation where you would have to factor in this --

DR. NETON: 95th percentile values for internal are put in as constants.

DR. MAURO: Okay. So then would it be correct to say, if we defined this as an internal scenario that we actually did,

that was actually done, but you said that, no, we're going to assume it's an internal scenario where we have a fixed constant 100 millirem at the 95th percentile, which was 100 millirem.

DR. NETON: Right.

DR. MAURO: Would you have the same result?

DR. NETON: Wait a minute. Say that again.

DR. MAURO: In other words, I'm trying to find a way to see if there is any parity between what you did and how it might have relevance to internal exposure.

DR. NETON: Right.

DR. MAURO: And the way I'm thinking about is you explained that internal does make things more complex because when you assign that internal dose to an organ, in a given year, you would assign a distribution. You would have a distribution around that 100 millirem.

But if we were to define that 100 millirem, no, no, that wasn't the median of the distribution. It was, the 100 millirem is your 95th percentile deterministic internal dose.

Does that question make sense? In other words, define the internal dose in terms of the bounding dose, and saying if it were 100 millirem for the bounding without any uncertainty, but it was delivered internally on that year to that organ, would the results come out the same?

DR. NETON: I'm still not following you.

DR. MAURO: Is the question coherent? I'm not sure if I'm even posing a question that -- it seems -- I'm just thinking about -- see, depositing energy in tissue and in organs, in my mind, does it really matter if it's depositing that energy in that year by an internal emitter or by an external source? And so I'm just thinking,

in the simplest way, well, why should that make a difference?

DR. NETON: Well, you know, it also just came to mind that you also have the radiation effectiveness factors folded in there, too.

DR. MAURO: Yes.

DR. NETON: So those make a difference.

DR. MAURO: Right, both beta and alpha have that factor.

DR. NETON: Part of this is leading me to think that there's so much variability in the internal that it may have to have a big change in order to see a difference, because, you know, you're adding a slight -- you know, we're talking about a ten percent change.

You know, I think in September we were talking about coworker models that maybe had a ten percent change in value. Okay, let's say the value, the dose value

changed by ten percent. Well, you know, you've got to raise the effectiveness factor uncertainty, you've got all these other uncertainties in there that -- although, you know, if you do change, as we well know, if you change the central estimate you're going to change the PC by a proportionate amount because, you know, it's not changing -- changing the distribution is a different beast then just changing the central estimate. I don't know.

CHAIRMAN MELIUS: So, this is Jim Melius. Is there an example we could develop that we could try to illustrate that? I mean, is there a scenario that you could -- what's the next step that would be useful? Do we want to try look at that in some sort of example?

DR. NETON: I think it could be. At the top of my head, I can't think this through right now. But it's possible that we could come up with some other test.

CHAIRMAN MELIUS: I know they want to try to do it sort of comprehensively because there's lots and lots of --

DR. NETON: I would like to explore the idea that I sort of broached last time, though. Maybe it's embedded in this analysis. I don't know.

But, you know, we were discussing the fact that, you know, we have a coworker model that, in my opinion, is -- well, I'll call it a general exposure model. And that general exposure model admittedly includes a series of potential strata, because it's one size fits all.

We've acknowledged that. And so there may be embedded in that model different strata that have different distributions, agreed. But what we've done is we've developed sort of an approach where we have sort of a two cell exposure matrix now where we said if we believe that the exposure to that unmonitored worker, you

know, you have a monitored worker exposure coworker.

But now you're going to apply that, a monitored exposure distribution of workers, you're going to apply that to the unmonitored worker. If that worker does not appear to have been involved in heavy activity and intermittent exposure, that sort of thing, we'll use the 50th percentile with the full distribution, because clearly his exposure would not have been high end.

But then we've got the other approach where we say, well, this person looks like he could have been exposed because he was working in radiological areas and doing something that could have generated airborne materials. By default, then, and this would apply to all construction and trades workers, we will assign the 95th percentile of the distribution, recognizing that we know that there's a number of other strata buried in

there.

But we're saying we're willing to accept the fact that there's at most a five percent chance that his exposure was higher than that. Now, if we go and pull out the strata for these construction workers, now we have a better representation of the potential exposure of that group, I would suggest that we wouldn't give the 95th percentile anymore.

We would assign the geometric mean and the full distribution to that population because it's a better known, better characterized population. So then the trick is, what is the practical significant difference? How high does the mean of that strata have to be to exceed the 95th percentile? The mean and the distribution applied to that worker, how much higher does that have to be to exceed the 95th percentile of what I'll call the general exposure model?

And I think that, to me, is a relevant test. I don't know any other way to put it. But it just seems that's the way one should approach this. I've thought about this a ton in the last week. And that's what I've come down to, at least in my mind, as an appropriate comparison.

DR. MAKHIJANI: This is Arjun. I think that sounds like a good idea. I mean, I haven't thought about it as much, hearing it for the first time. But it sounds like a pretty good idea to me.

But if we're going to apply some numbers, I would like to see some test where we try to gauge -- I guess this is one way of gauging the uncertainties, but we will be back, if we are to pull out the distribution for that stratum that you're going to compare it to where you're going to take a median or the full distribution and compare it in the 95th percentile of the general distribution, then you're going to run into

this problem of how you extract the stratum and how you develop a distribution.

And I think, you know, that's been a pretty big hurdle. I think, in principle, the kind of test that you're talking about would appear to be I think a good starting point.

DR. NETON: Well, I think all of the other caveats apply in that you have to demonstrate that the strata that you pulled out is that, you know, the workers were monitored, they were being represented as the highest exposed or represented the workers, you know, all the sort of things that apply to coworker models.

But then when you do that comparison, I think it might be doable with the approach that we were just talking about, because if you can add -- it's not intuitively obvious how the Probability of Causation -- what the difference of the Probability of Causation is if you compare

the full distribution versus the 95th percentile.

We have done this in the past. Dave Allen and I talked about this earlier in the week, or I guess earlier last week, that it seems to us that assigning a full distribution is very akin to assigning an 87th percentile as a constant. I can't prove that right now.

But I think that's kind of -- it's going to be variable depending on cancer levels. But that's probably a fairly good number. So then how much higher does that distribution have to be for that 87th percentile to exceed the 95th percentile of the general model?

And I think we can test that. I think that's a testable -- it's sort of similar to what we just did, testable over claims to come up with some ranges. And it's never going to be the same for everybody.

But I think we can show -- in general, I think what you'll find out is that it's going to take quite a bit of difference in -- the stratified model would have to have a pretty much higher geometric mean to overcome claimant-favorability of assigning the 95th percentile of the general model.

I'm almost certain that's true. But we have to test that.

MEMBER ZIEMER: Dr. Melius?

DR. NETON: Hello?

MEMBER ZIEMER: This is Ziemer. Yeah, I think what Jim is suggesting makes sense. But, you know, we're going to have to try that. We're sort of in the same boat as we were when we talked about the external adding 100 millirem and seeing what the results were. It seems to make sense conceptually, but I would certainly like to see what it looks like with some actual values.

DR. NETON: I agree, Dr. Ziemer. I really can't even begin to articulate how this would happen, but I think it is doable. We would have to look at the data that we have.

MEMBER ZIEMER: Right, right.

DR. NETON: And run through some general scenarios. And as we did before, I could actually, you know, put a straw man out for everyone to look at and make sure that we're on the right path and then move forward once I get, not agreement, but general, you know, feedback from the group.

MEMBER ZIEMER: And I think we'd get a better feel for some of Arjun's concerns, because those certainly make sense as well. And maybe this will give us some insight as to what direction to go at that point.

DR. NETON: Yeah, and we've kind of got the pieces of this for Savannah River, I think, in place to some degree. I

mean, we've got stratified.

See, the other situation is it's not possible to stratify everywhere. You can only stratify where you have, you know, the data, like we have in Savannah River. It's bothered me that we're saying, well, we're going to stratify. If you decide to stratify and you can't stratify another site, what does that mean?

I think this gives you sort of a semi-quantitative way of looking at data saying, you know, yeah, but look at how much is going to have to change in order for that to overcome the 95th percentile. So it may inform us at other sites as well. I don't know.

DR. MAURO: Jim, this is John. I want to understand this a little better. We could use the example of comparing the totality of the data against, let's say, the construction worker.

Let's say you had the data set,

you have a distribution which has, on the full data set, which has a 95th percentile value. Now let's say you were in a fortunate position where you have a subset of it, which we'll call construction workers.

And then you have sufficient data to build a distribution. Now, what would be the outcome that would be revealing? That is, if you found out that the 50th percentile of the substrata was below the 95th percentile, or would you be looking to see if the 84th percentile of the substrata was below the 95th percentile for the full distribution? What would be --

DR. NETON: In effect, that's sort of right. I mean, but you'd have to do some IREP runs and see how they came out. You would take the full distribution and use it. And you would take the 95th percentile and run it. And whichever one came out more claimant- favorable is the way you would go.

DR. MAURO: Now, if you found that the outcome of the full distribution for the substrata had a -- and I'm not saying the 95th percentile, I understand the points you're making. But let's say it turns out you decided that certainly if the mean came in below the 95th percentile for the full set, if the mean of the substrata came in below the 95th percentile of the full set, that would be informative.

If the 84th percentile of the substrata came in below the 95th percentile, that would also be informative and encouraging. But if the 84th percentile of the substrata came in above the 95th percentile of the subset, what would that mean to you?

DR. NETON: To me, that would mean you need to stratify because you're not -- you know, you have just demonstrated that the less than five percent probability of a person exceeding the 95th percentile occurs

in that strata.

DR. MAURO: So that's the thought process. So really the test that you're running is if you find that out that, that the 84th percentile of your substrata is less than the 95th percentile of the full, you have basically convinced yourself, and perhaps everyone else, that there's no reason to stratify.

DR. NETON: That's correct.

DR. MAURO: Good. That's very interesting.

DR. NETON: And that really, to me, is the nut of it all. Is the 95th percentile disenfranchising anyone because, you know, their data are all in this upper tail? And all I'm saying is, well, let's test that. Let's get the strata and test and see if the upper tail is not sufficiently, the 95th percentile is not sufficiently claimant- favorable. And if it's not then, by goodness, yes, sure, we'll

go and stratify and use that data set because that's been demonstrated.

DR. MAURO: I think you have just proposed a strategy for dealing with stratification that has an end point that's a manageable problem.

DR. NETON: I think so.

DR. MAURO: And I certainly, if everyone feels that way, that is, in effect, you're saying in dealing with any site where you have thousands of workers or hundreds of workers and you have reason to believe that there are substrata in there that may be different than the overall group, have their own distribution, and if you are in a fortunate enough position to -- now here's where the big problem is going to be.

We have enough data from the substrata. Propose the question you just raised. You could do that first and decide whether or not you need a substrata coworker model, or you could just use the entirety of

the data.

Do you think it's reasonable that we would be able to go through such a process? That is, are the data such that when a question is raised, like the subcontractor question, quite frankly, were we in the position to do that? I guess there are some sites where the subcontractor data were there. Is it possible to make this test that you just described?

DR. NETON: Not always. But I think, where it is, it needs to be done. And I think what's also going to be informative is, you know, what magnitude of difference does there need to be in order to say, yes, 95th percentile is not claimant-favorable anymore?

And I think we might be surprised at how high that is. I mean, because you have GSDs of three, which is the minimum GSD that we assign to any dose distribution, because that's the -- three is applied by

default if it's less than three because of the biological variability of the sampling, you know, the metabolic models and such.

That's a pretty large GSD. At the 95th percentile, the GSD -- I mean, the 95th percentile value is six times higher than the geometric mean. You take 3 to the 1.645. So the geometric mean would have to increase quite a bit in order to be higher than the 95th percentile with the distribution.

I don't know. Until we test it I'm not sure. But the answer is, where we can we would do that. Where we can't, I'm not sure what we do at this point. But we have that same issue whether we do this or not.

It's just a way of at least being able to test where we have the data, and then maybe we can say, well, you know, similar sites with similar -- I don't know.

DR. MAURO: You don't want to put

yourself in a position where if you do have a site, if you have lots of data, you have a sense that are some substrata down there, maybe a job category or something, the kind of work that people did, pipefitters and things, where you don't have data but you suspect that maybe there's a problem, of course, you know, you wouldn't be able to test it if you didn't have the data.

So it doesn't really solve the problem. But I guess it would only give you some -- when you do have the data you could start to build a sense of whether or not this 95th percentile is fairly robust and will deal with most substrata.

DR. NETON: Exactly. I mean, I think until we get through a few different tests maybe that will be informative. I think what it's going to show is that ten percent differences aren't sufficiently large to move things over.

And by and large, that's kind of

what we've been seeing. You know, there are some exceptions. But I think it would give us something to hang our hat on to say, you know, is the 95th percentile really as claimant-favorable as we felt it is?

Because that's honestly the reason -- I got to thinking about this. That's why we picked the 95th percentile in the first place, because we don't know where that person falls on the curve. So we said, well, let's go way at the high end and there's a five percent chance at most that his value exceeded that. So, anyway.

CHAIRMAN MELIUS: This is Jim Melius. I'm just sort of keeping in mind we're just trying to get at the issue of sufficient accuracy not the issue of claimant-friendliness.

DR. NETON: I agree.

CHAIRMAN MELIUS: And so, depending on how the data sets are made up and, you know, for the sample size and so

forth --

DR. NETON: That is true.

CHAIRMAN MELIUS: -- yeah, this could lead us astray also. I like the idea of doing it. I just think we need to sort of keep in mind it's not just proving claimant-friendliness that we're trying to get at, though it certainly, you know --

DR. NETON: Well, it's a part of it. But I do agree with you, Dr. Melius, that, for example, if you have a similar geometric mean but you end up with a GSD on the stratified model of 9, then you end up in the situation where, you know, the upper bound is some huge number that may or may not even be a plausible value. You're right.

CHAIRMAN MELIUS: The other thing that concerns me is, and it actually comes up a lot when we talk about OPOS, is that a lot of times our issue is dealing with -- these are not perfect, you know, random

samples. And we often don't have complete information on how, you know, the monitoring was done.

And it certainly often appears to be done differently between production and subcontractor workers and even among groups of subcontractor workers. And so I think that we have to keep in mind is how do we deal with those sort of issues? Which I think comes down often to sort of a judgment on how these monitoring programs were done and are they really that different and so forth, and we'll probably talk a little bit about that with the OPOS review next.

But that's all been as important a question as sort of, you know, how much of a difference is there? So it gets you, before you're trying to -- you know, what sort of statistical assumptions are we violating and how important are they in the kinds of comparisons that we're proposing to do?

DR. NETON: Yeah, I one hundred percent agree with you. I mean, can you really stratify in the first place? Well, first of all is the coworker valid, the general model valid?

CHAIRMAN MELIUS: And then my final point would be that the other sort of practical issue that comes up in this is do we even have enough information to be able to, you know, really identify people within stratas? And often it's complicated because people may have moved from one strata to another as their job changed and so forth. And that complicates it also.

But I think that's stuff we can talk about. I just think we should be careful to keep those sort of practical issues in mind as to when these kinds of testing and conclusions are appropriate.

And I have a feeling we'll spend more time wrestling with the practical evaluation of the monitoring programs and

the strata than we necessarily will with the statistical comparisons, if we can get there.

DR. NETON: I agree.

DR. MAKHIJANI: I agree with you, Dr. Melius.

CHAIRMAN MELIUS: Other comments from Board Members or SC&A?

MEMBER ROESSLER: This is Gen. Yes, I have a comment. Beginning with Neton's response after Arjun brought up the concerns about the internal dose, he said a lot of things that really, to me, were very convincing.

And then as everyone else is talking, including John Mauro, they're all convincing. But to me, this is pretty complicated stuff. I don't deal with these kind of statistics every day.

So I think as Jim goes through this process, if we decide he should, I would like to see him write down what the

hypothesis is and then put some words with it so we understand what all this generation of numbers means and what the application would be, if there is one.

CHAIRMAN MELIUS: One point, Jim sort of talked about the process we did for sort of developing the current report, and he sort of laid out the methodology and we commented on that. And I think that sort of laid out just what you asked for, Gen. So I think he's proposing to do that again this time.

MEMBER ROESSLER: Yeah, because like John Mauro said, he wants to understand it better and certainly I need to understand it better.

CHAIRMAN MELIUS: Yeah, you're not alone.

MEMBER ROESSLER: Good.

CHAIRMAN MELIUS: Other comments or questions?

MEMBER BEACH: This is Josie. I

don't have anything right now.

CHAIRMAN MELIUS: Arjun, or anyone else on SC&A?

DR. MAKHIJANI: Can you hear me?

CHAIRMAN MELIUS: Yes, we can.

DR. MAKHIJANI: Okay. No, I agreed with your last comment. I think it's a good next step.

CHAIRMAN MELIUS: So at least for now, maybe we'll change our mind after talking about OPOS. But for now, I think the next step would be Jim would sort of develop a mini-proposal or plan and circulate that to the Board. Is that correct, Jim?

DR. NETON: That's my understanding.

CHAIRMAN MELIUS: Okay. And we will then go on from there. And I do agree, even with some caveats, I think it would be helpful to do and help us understand this issue better.

And I think it's probably more important than trying to figure out all the permutations of internal dose issues, because we could spend a long time doing that and probably get more confused, not less confused. Good. Okay.

Why don't we move on to the OPOS report. Who is presenting that? We got a set of slides this morning.

MR. STIVER: This is John Stiver. Harry basically did the heavy lifting on the OPOS report and so I'm going to have him actually do the presentation. You all should have gotten a copy of our report. I think it was sent out on the 22nd of February.

And the title of course is -- let me bring this up -- Staff Review of the Proposed One Person-One Sample (OPOS) Approach to Coworker Modeling. Barton, Chmelynski, Lipsztein and Stiver are the authors here.

And let me go ahead and share the slide and then I will turn the reins over to Dr. Chmelynksi. Let's see here. Okay, can everybody see that?

MEMBER ROESSLER: I can.

DR. NETON: I think you need to expand it.

MR. STIVER: Do you need it a little bit bigger?

DR. NETON: You can expand it to full screen. Upper right hand corner, see that little box?

MR. STIVER: Right up here? Okay. There we go.

DR. NETON: No, I think it's all the way at the top.

MR. STIVER: Okay, does that work there? I think it's expanded as far as it can go.

MR. KATZ: John, look top right, currently sharing. There you go.

MR. STIVER: Okay. Is that

better? Can everybody see that?

MEMBER BEACH: That's fine.

MR. STIVER: Okay, Harry, would you like to go ahead and get started?

DR. CHMELYNSKI: Sure. There's a quick road map here as to what we're going to be talking about this afternoon. And basically it's the definition of what is OPOS and then why is it different from earlier procedures that were used to develop the coworker models? What are some of the reasons for using OPOS? And how extensive is the problem that it's going to fix?

And, finally, we get into more technical questions, which is how the mean excretion rate, which is what OPOS is trying to measure, is related to the intake itself. And also how well does OPOS estimate that mean excretion rate? And then we'll finish up with some problems with implementations that we noted.

So the first, the next slide

basically defines what we mean by OPOS. And I like to use the term one person-one statistic, because OPOS is the arithmetic average of some results during the time period, which is a statistic. And it therefore has uncertainty, which we will get to near the end of this discussion.

NIOSH has introduced OPOS because of problems which were noted during the use of statistical test procedures to compare different strata.

And the two types of problems were termed data dominance and correlation. And we're going to talk more about these in the next couple of slides. We looked at the problem both from a theoretical point of view and also from a practical point of view when you apply it at two different sites, at SRS and at Fernald.

So the next slide, let me make sure I have the next slide here in front of me. Yes, okay. Before OPOS was introduced

there were several analyses that explain how one should do coworker modeling. And basically it started off with the first two lines here that say take the results from the group of workers -- we assume that all the results are log-normally distributed.

And in the old days what we did was we took the results from all the workers and sorted them from high to low and then applied the next three steps, which is then termed regression on order statistics.

Basically it's a procedure for doing regression on the ranked data in order to find the geometric mean and geometric standard deviation of the data set, not much unlike what people did 50 years ago when you could plot on a normal probability paper to get a straight line that said this is what the normal distribution looks like.

Now we do it on a computer and we do it with the logarithms of the data, and it's the same procedure though. And when

we're done here what we end up with are two data sets. We have the 50th percentile and the 84th percentile.

And those numbers have to be run then in order to determine what the intakes are. And we end up with intakes at the 50th percentile and at the 84th percentile. When OPOS was introduced, the procedures stayed -- that's on the next slide -- the procedures stayed very much the same.

The only difference in the second and third steps, where instead of taking all the data over a time period what we are suggested to do is to average all of the results into one value for each worker. There are some complicating issues about when you have censored data exactly how you compute the average, and we'll get into that at the end of the paper.

But in the simplest case it was just the average of the values. And then instead of using all of the samples for a

worker, we used that one value and then sort them and proceed as we did before and did a distribution for the coworker model.

And, again, that's elaborated in the next slide, which shows it pictorially. The bottom parts of the slide are pretty much the same. The first box is where the big difference is. Do you take all the results from all the workers in the time period of interest or should you average them all, and in particular over a one year period?

Once you decide to average you have to decide what period you want to do it over. So NIOSH has suggested we should do this averaging over a period of one year and then use one value per worker in the analyses that follow. Again, that would differ from what was done previously for the coworker model.

Now, in terms of why these were introduced is on the next slide, on Slide 7.

There are two problems here. Data dominance, which we define as that the large fraction of the samples are being submitted by a small fraction of the individuals.

Now, usually we think that means if they had a lot of samples that they probably had high numbers. And it was repeated sampling for a reason. Although that's not always the case. In some cases there was just some health physicist who decided to test themselves frequently and they end up with a lot of samples, not necessarily high ones. But, again, it may be that a large fraction of the samples in a time period were submitted by one or two individuals when that happens.

The second issue is the correlation issue, which becomes more important when you do the hypothesis testing as to -- the assumptions of the hypothesis test assume that we're going to have independent and identically distributed

samples from each group. But when we have an incident and there are a lot of samples from one person they tend to be highly correlated, and that introduces a complication in interpreting the statistical tests.

So we took it on ourselves to decide, first off, how much of a problem these problems were when they were applied at both Savannah River and at Fernald. And after doing that, and also some theoretical thinking about it, we ended up with the following conclusion. It's on Slide 8.

Now, it's always risky to give your conclusion before you introduce why you got to that point. So I'll go ahead and say what our conclusion was, but I'm not sure we should start discussing that conclusion until we get into some of the more substantive issues that led us to that conclusion.

Basically what we're saying here

is that we think that, yes, there are problems with using pooled data. The problems are of the type that we just described, the data dominance and there is some correlation there.

But we don=t see that OPOS is going to solve these problems in a good way, except in a particular case where we do have a lot of samples taken from an individual after an exposure and it=s clear that's what happened. And then in that case we would agree that we should use OPOS to reduce that data down to one value for that worker for that time period.

On the other hand, in most of the cases we find that there's not a whole lot of them and there's not clear evidence of data dominance. And in those cases we're not sure why there's any reason to use OPOS.

The second issue here is that if you do use OPOS you have to account for uncertainty in the estimate. It is a

statistic and it will be influenced by a lot of things that should be taken into account under the general term of uncertainty.

If we don't do that we're going to end up, I think, with a standard deviation and a 84th percentile run for the intakes that may be too low to really reflect the variability and the uncertainty in the data.

There may be many people who want to argue with these conclusions now, but maybe we should reserve that argument until when we're finished here and then we'll come back to Slide 8 and see how maybe this applies or doesn't.

So the first issue then we're going to talk about that led us to that conclusion is the data dominance problem. Certainly it does occur in the data. There are cases where there is a large number of incident-related samples taken from a few workers.

And if you throw them in all together in a collection, say you have 50 from a worker of that type and then you have another 100 workers and they all have one or two samples, then you will have this problem of data dominance.

And we do think that is going to be a problem. So that's why we say that, yes, when you do have that problem then you should use OPOS. How frequently would that happen? Well, we've looked at, for instance, at SRS for plutonium sampling and the table on Slide 10 shows the results we found.

And basically what we said was let's look in every quarter and see how many workers have so many samples in that quarter. And the number of samples is on the left of the table. And the number of counts we made are in the next column, and then there's a cumulative percentage.

And then we did the same exercise

again by year rather than by quarter. We said how many samples did they have in that year? And we counted up the number of the people that had one, the number of people that had two and we put them in this table, and again showed the cumulative on the rightmost column.

And basically what this table says is that 99 percent of the time there's no more than three samples in a quarter. And 95 percent of the time there's no more than four samples in a year. So what we're dealing with then is relatively rare cases, which are down near the bottom of the table.

The ones that really cause data dominance, there's a handful of them basically. If you think about it, on an annual basis there might be 100 out of 10,000 where they have more than, just say, eight. But I think generally when we think about data dominance we're talking greater than ten and maybe even larger, that there

was repeated sampling for an individual.

And that occurs very infrequently it seems. So we'll come back to this slide again later on in the talk. And, again, I have to admit we only looked at this at SRS in that particular table. So it's not clear that the same results would be found elsewhere for plutonium and it's not clear -- and our report does discuss other isotopes at Savannah River.

And we find that there are very similar patterns of frequencies. Uranium tends to have the highest number of samples. And the percentages are a little different for uranium. Where you might see 95 percent of the samples that workers have them for or less, that might be 90 percent instead of 95 when you do uranium.

We also looked at this question of data dominance at Fernald but we did it in a different fashion. And I was hoping maybe Bob could say some words about what we

looked at at Fernald, if he's on the line.

MR. BARTON: Sure, Harry. This is Bob. You know, one of the things we tried to look at is how many of these type samples where it's an incident sample or a special sample where you would have sort of an off-normal sampling protocol.

For example, if you had a special project or if there was an incident. And these are characterized at Fernald by their particular sample coatings. I don't want to get too far down into the weeds here, but the special samples were type 50s and incident samples were labeled as a type 40.

So one of the things that we took a look at was how many of these type samples did you have in a given year and what effect did they actually have on eventually the derived intake rates? So in other words what you would kind of expect to see is that if you had a year where you had a significant portion of special or incident-

related samples, then you would think that the derived intake rates or the excretion patterns would go up because you would have a data dominance problem.

And when we actually got down to it, we really didn't see that sort of pattern. We didn't see the causal relationship between the addition of these incident samples or increased incident samples versus what ultimately becomes the derived intake rate for the claimant.

So we didn't see the opposite either, and there were certain years where, yes, that did appear to be the case. But there were other years where you would have a decrease in these, you know, data dominance type samples but you really didn't observe any sort of change in the derived intake rate.

So that was kind of specific to Fernald. Is Joyce on the line? Do you have anything to add on to that?

DR. LIPSZTEIN: Hi, I'm on the line. I think everybody -- I don't know if it was well-explained. Just one thing. The Revision 1 was done with the older methodology with OTIB-0019. And the Revision 2 was using the OPOS methodology. I don't know if people understood that. That's why we were comparing the two, Revision 1 with Revision 2. That's it.

MR. BARTON: I guess sort of our conclusion there was that we didn't see that causal relationship between the number or percentage of incident or special sampling that was in the distribution versus what you actually got with the intake rates. And we didn't see that relationship.

So I guess, you know, from our end we weren't really convinced it was that much of a problem, at least in the case of Fernald. And, again, that's very specific to that site. But we really didn't see data dominance as an issue per se in what we

looked at there.

DR. LIPSZTEIN: And one question that was always stood to us is whether -- or we want to know whether the OPOS methodology was claimant-favorable. If it was claimant-favorable it would always give us an intake rate that is higher than in the other method.

So we compared the intake rates from the two revisions, and for some years one of the revisions had the higher intake rate, for other years there was another intake rate, the Revision 1 was higher. In other years the Revision 2 had higher intake rates.

So neither methodology had the systemic bias that will always yield a higher intake rate. So there is no claimant-favorability in either of the two methods.

MR. STIVER: Yeah, this is Stiver. I want to just add one thing. We

looked at Fernald and Savannah River because those were the only two sites for which the OPOS methodology had actually been implemented at the time that we did our paper.

And I'll just reiterate what Joyce said, that at Fernald the use of OPOS versus not using it, or the number of incidents or special type 50 code samples really did not have any impact on the ultimate derived intake in either case. So there doesn't appear to be any correlation from those variables in either data set.

Anyway, Harry, if you would like to go ahead and continue.

DR. CHMELYNSKI: Okay. I guess we're on Slide 12 now. And this is on correlation. I looked at some of these examples of workers with many samples over a short period, presumably following incidents.

And to tell you the truth,

there's not as much correlation in them as you might expect to see. They jump around an awful lot. But there are some examples in our report that show that there is a pattern there where, of course, as time goes on the urine excretion concentrations fall off.

But you might see one at zero right after the incident and another one a week later and then in between there's some high ones. So there's very strange patterns of results following an incident. It's not always as clear cut as one might think to even find the incidents.

And certainly just because a worker had a lot of samples doesn't necessarily mean they're correlated. We would like to see some evidence of correlation other than the fact that there are just a lot of samples there.

The issue of correlation also was raised in some other cases where exposures

tend to drag out -- if there are exposures, the results of those exposures may drag out for periods longer than a year even. And there is, again, in this sense, a correlation that may stretch beyond the one year period due to that single incident.

Those issues are more important, I think, when you're doing strata comparison than when we're just talking about how to estimate a coworker model. But they are something we should consider when we do any strata comparisons, that these workers with a high number of correlated samples should certainly be -- well, according to our recommendation, OPOS should be used in those cases before we do these strata comparisons.

Now, when we think about OPOS for building a coworker model and for building a comparison, a hypothesis test that compares strata, we're talking at sort of a high level about it. Now, what we're going to do now in the rest of the paper here, the rest

of these slides, is look at OPOS at a more micro level, for a single worker, and how well does that value allow us to determine his intake?

And clearly we're going to be doing this for lots of workers and later on we're going to take all those values and throw them together on a curve. But right now we're just looking at the process of getting a single OPOS value for a worker.

And one of the concerns we have here is that -- I'm sorry, I'm on Slide 13 at this point, frequency of monitoring. And there's a lot of words on this slide, but it's a very simple concept.

If there's an incident in November and we have ten samples taken following up on that incident on one worker and again ten samples taken again on a different worker, well, that's good. We've measured what happened after the incident.

But now let's say one of the

workers had routinely been tested for every month before the incident. Well, he'd have ten more samples than the other one. And let's say the other one didn't have those monthly tests.

They both have the same exposure in the last two months or sometime in November, say. But yet in one case we're going to mix together all the 20 for one worker and assign him a dose that's only about half of what we assigned the other worker simply because one of them had more sampling done before the incident occurred than the other one did.

So one of our problems, then, with OPOS is that it is highly dependent on how many samples the worker had and the relative timing of those samples with respect to his actual exposure.

Now, if the exposures are continuous that may not be so much of a problem. But when you're talking about

exposures after incidents and trying to reduce it down to a single number for that worker that's reflective of what he got in the incident, it's disturbing to see that you get two different answers for two workers who may have a previous history of monitoring that differ.

And if you extrapolate that line of thought into the process of comparing two groups of workers, we think that's sufficient reason that they should have both been tested with the same sampling protocol. Both groups. If not, then it's possible for instance that the non-construction workers were routinely tested and over a whole long period and they were given lots of samples compared to construction workers who only had a few samples. Even if people have the same exposure at some point in an incident then we would see different numbers --

(Electronic interference.)

DR. CHMELYNSKI: Is there a problem or --

DR. MAURO: It went away.

DR. CHMELYNSKI: Oh, good. Let's not worry about what it was and hope it doesn't come back. Okay, so that was the frequency of monitoring problem.

Now, on Slide 13, the title here is kind of cryptic. But what we're talking about is how well does OPOS characterize the data for a worker and how well does OPOS characterize the intake that worker had given the data that we see?

Those are two separate questions. And one of them, which is the relationship on the right between OPOS and intake, one of them NIOSH has a long discussion about, which basically says that if there is a series of assumptions made about the use of weighted least squares and what the weight should be, that if you go through this long analysis you will end up with the answer

that the mean excretion rate is indeed proportional to the intake that the worker had. Then this result has been used by many people in the field to summarize the exposure following incidents.

A second question that we looked at is the arrows between the data and the OPOS, which is how well does OPOS estimate the mean excretion rate for a worker?

And it may sound like an obvious answer, that, well, you're taking the average and therefore it's the mean. But since it's a statistic, the question is how well does it estimate the mean excretion rate?

When we looked into the question of the least squares regression approach to relating the intake to the mean excretion rate, we find that both NCRP and the IMBA manual itself state -- I'm not going to read this whole thing. But if you look at the fourth line of the NCRP 164 quote in bold,

it says the formulas assume only one intake.

And that's the first problem that we run into here. It's not clear that OPOS can be used except in those situations. It could certainly be used, but this proportional relationship that is claimed between OPOS and the intake isn't necessarily valid if we're talking about cases where those assumptions the weighted least squares regression analysis are based on, when those assumptions don't hold.

And we listed some of these assumptions and when they don't hold on the next page. The thing in the box is actually a quote that's out of the manual that says least squares can be used only in cases of a single intake with explicit air values on each data point and a single bioassay quantity.

Well, the real important part is the single intake. When they have multiple intakes the equations are going to look

different and there's not necessarily the proportional relationship no matter what type of assumptions one makes about the weights for the regression.

DR. NETON: This is Jim. I hate to butt in. But I just want to make one quick comment.

DR. CHMELYNSKI: Yes.

DR. NETON: Single intake can also be a single chronic intake.

DR. CHMELYNSKI: Yes, I agree.

DR. NETON: So that's a big difference between what we're comparing. Just trying to point that out, because we're assuming chronic intakes here.

DR. CHMELYNSKI: Well, then we'll have to look at these. What we're finding is that the intakes -- first off, that the excretion results should only be after the intake. And, again, that was an incident-related intake. And that the urine activities shouldn't be lumped together, the

ones after the intake and the ones before the intake, to do a single computation of the OPOS value.

Finally, in particular, we don't want to see cases where there are no intakes lumped together with periods where there are intakes.

DR. LIPSZTEIN: Harry, this is Joyce. Should I answer Jim now or would it be better to --

DR. CHMELYNSKI: Yes, I'm sorry. Since we started here I should have given you an opportunity to respond. Yes, go ahead.

DR. LIPSZTEIN: Jim, it doesn't matter what you assume, if it's chronic intake or a non-chronic intake, after you get the 50th percentile of the whole distribution. It doesn't matter what the assumption was.

The problem is that you have some urine excretion samples that come from a

single intake and then all those that are incident-related, they came from the same incident, could be either a chronic or a single intake. But it was a unique intake and you cannot mix them with -- what I mean mix is from these excretion rates from no intakes and then try to get the intakes from this. It's not proportional anymore.

DR. NETON: We'll talk after on that.

DR. LIPSZTEIN: Okay, okay. We'll talk about that at the end. Okay.

DR. CHMELYNSKI: The Slide 17, and we have several points where we might come back here, I think. But to finish the discussion, we're going to look at next, starting on Slide 17, how well OPOS performs in terms of estimating the mean excretion rate.

And here we're not talking about how the OPOS relates to the intake, but simply a matter of, well, we samples at a

couple points in time for a quantity which varies over time, which is the excretion rate. And the time ordering is an essential part of the calculation when you look at what the mean value is over the period.

And we'll see why that happens pretty soon. But in particular, we're looking at what we call the time-weighted average urine concentration over a time period.

And one way of thinking about this is if all the urine were excreted during the year were collected in one container and then we analyzed what the concentration in that container was, assuming this is a long-lived nuclide. That would be what we call the mean, the time-weighted average urine concentration.

And I think it's the one we do want to use when we do the intake calculation. Now, weighted least squares ignores the ordering of these observations

in time, and so does OPOS. So what we did was we did an analysis of what happens when you do look at how it varies over the year, how the excretion rate varies over the year.

And on Slide 18 we have just a hypothetical case where there was some exposure near the beginning of a year and the excretion rates fall off as the year goes on. And in this particular case we're going to assume that, well, we did a good sampling of eight samples regularly spaced along that curve.

And when you do that, we see that we get a good approximation to what the integral under the curve is. Now, why do we want the integral under the curve? Well, the mean value theorem says that if I take that integral and divide it by the time period found at the bottom of the page, the end of the graph here, then that will give me the mean value of the function.

And since the time period we're

covering here is one year and we've decided to use that units of one year, then it's just divide the integral by one and you get the mean value. So the integral is equal to the mean value in these examples.

And in this case, it's a cubic that I picked. So I can calculate the true mean. And we see that if you go back to calculus you can approximate that true integral fairly easily by doing equally spaced sections. And that=s what=s called the Riemann sum, which also turned out to be the same answer you get when you do OPOS.

That example is based on equally spaced observations in time. But usually that's not what happens. And we've looked at that also at SRS for the plutonium data that showed up on Slide 10. And we looked at the number of days between successive bioassays for a worker and we ended up with this interesting plot on Slide 19.

And what this shows is that, yes,

there are a lot of workers who were tested every 90 days or quarterly. And there was a little less, but a lot who were tested semi-annually. And it looks like there's a lot who were only tested once a year.

And if you look out there at 720 you see even there's some that were tested every two years. But in general it's hard to pin down exactly what frequency the testing was done at any particular time during this period at SRS.

So what we started thinking about was, well, when you look at the data and you look at the times of the year when the data were done, a lot of them tend to look pretty random. Maybe a sampling program came on and they decided they had to start doing some testing or maybe they were selecting people at random for testing.

But I'm not quite sure. I didn't see any of the kind of evidence of systematic, quarterly testing that one might

expect. So what we looked at then was how would OPOS work if you did have random times during the year and take samples at those times?

And here we have an example where I took eight random times, two of them ended up being pretty close together, actually at both ends of the spectrum here. And in between they are roughly equally spaced, but not really so. And the point here is we really don't know what the curve is doing in between these sampling points.

So there is some uncertainty as to what the area under the curve really is. In this case I worked it out and OPOS came out to be lower than the true mean, partly because we had too many samples in the low ends, on those two ends, than in the middle, in this example. But more importantly, the confidence bounds are quite broad. They stretch pretty much from the lowest observation, not quite up to the highest.

But again I had eight samples here and it's very rare that we get that many.

It's very easy to make this example jump up over the highest sample when you look at the confidence interval on the mean. If you do the specific calculation, it's informative because, as we know that the sampling distribution of the mean follows the Student t-distribution, and the confidence intervals are calculated from the variance of that distribution. And the variance of that distribution, I have a formula for it here, the degrees of freedom over the degrees of freedom minus two.

And then you say, well, if it's two then you get DOF over zero and what does that mean? Well, that's why we say the degrees of freedom have to be greater than two before we can actually build a confidence interval on the mean.

But since the degrees of freedom is n-1, what we're really asking then is

that we have at least four samples before we can compute the variance of the estimate. And going back to Slide 10, we find that in 95 percent of the cases, we don't have four -- I'm sorry, in 90 percent of the cases we don't have four samples.

If you look on Slide 10 for the annual data, three or less, 90 percent of the workers. So what that says is that most of the time we won't even know what the sampling variance of OPOS is, or how accurate it is or how uncertain it is. It's unbounded.

And that, to me, raises some big questions. Why would we use OPOS if indeed it could give us a number that's smaller than the smallest number, higher than the highest number in terms of a confidence interval? So our answer was how well does it estimate, OPOS? It doesn't seem to estimate it very well.

I'm sorry. How well does it

estimate the mean excretion rate, and OPOS, as an arithmetic average, doesn't do it very well when you're only talking samples of size three or less. Now, maybe when you get up to four or five, ten, you at least have a confidence bound where you can start thinking of OPOS as a meaningful number.

But, again, that relates back to why we said it's okay to do it when you actually have a lot of samples following an incident, because then it seems to make sense and you can actually get an estimate that means something.

So, finally, while we were looking at these issues we discovered there were some problems in the way OPOS was implemented in the past. I'm not sure if this is currently being done in the newer reports, but what we said at the beginning of the discussion was that when you do a calculation of the arithmetic average to compute OPOS you run into a problem when you

have censored data, or non-detects is a common word for that situation.

You can't compute the average. So NIOSH has proposed to use a slightly different calculation called the maximum possible mean. And in this, the idea is to use the censoring level, or the MDA, whichever one you call it, for data that are reported as less than MDA.

Now, this is something that has often been done in the past where you just use the detection limit as the value rather than trying to say it's half of the detection limit or zero or whatever. It seems safe and that's why it's called the maximum possible mean.

It seems safe to use the censoring level as the value that that measurement represents because we know it's below that, and therefore it seems claimant-favorable if we use the censoring level for that data point. Now, if we do that for all

the censored data it might turn out that all of them now are censored data, and in that case you still -- in that case you would be computing the mean of all the censored, of all the MDAs.

And that's probably the best you can do. But we admit, in that case, the answer is that it's a censored value, it's a non-detect. Even OPOS is a non-detect in that case.

And then, finally, if there is at least one that was not a non-detect, if there was one detect, then we would go ahead and compute MPM the way that the algorithm says, which is to take it as a simple average. Most of them might be the detection limits that are thrown in that average.

But there will be at least one uncensored value, and therefore we will treat that answer as an uncensored result for that person. This is the way that the

procedure for maximum possible mean was described, but when we looked at it in practice it turns out it's not that simple, it becomes a question of what is the censored value?

Is it a value that's not written down? Or is it a value when it's written down, does that count as a value even if it's less than the detection limit or doesn't it? And that's what this question boiled down to. What we found was in a lot of cases as long as there was an explicit value written there, it was used in the calculation of the maximum possible mean, even though it might have been below the censored value and even though it might even have been negative.

If it was reported then it was included in the calculation. We found that this was not following the instructions for how the maximum possible mean should be computed and suggested that that procedure

should be made clear to workers, to the workers at NIOSH, that when you look at these you should not use any entry below the censoring level to compute the maximum possible mean.

And I guess that was the last slide. Yes, okay. Now, like I said, it's on the last slide, questions?

CHAIRMAN MELIUS: Why don't we start, Jim, Jim Neton, do you or NIOSH have questions?

DR. NETON: Where do I begin? I don't have so many questions as I have some comments.

CHAIRMAN MELIUS: Okay. That's fine.

DR. NETON: Okay. I think probably about the only place that I could say we 100 percent agree with SC&A on their analysis is that individual worker intakes should be used to reconstruct doses, if possible. And we've discussed that once

before, why we don't do that.

What I would say is the coworker model is a distribution of worker exposures, not bioassay results, which is sort of where SC&A is suggesting that we go back to. And in my mind, a simple example, maybe not an exact example, would be is if I was trying estimate the average height of the Advisory Board and I had one measurement for everybody but had ten measurements for Bill Field, SC&A would appear to suggest that I should use ten Bill Field measurements into the 25 data set to calculate the average height of the Advisory Board.

And that just seems intuitively wrong to me. Again, it's not exact, but that's really what I'm hearing them saying, because really the best representation of the worker's intake is some statistical evaluation of his bioassay data during a given time period.

I'm very willing to discuss

tweaks to our approach regarding representativeness of the mean or incorporation of variance in the model. Those are all on the table. But I really fundamentally object to the idea that I would have to ignore the fact that an individual coworker model should be based on a distribution of samples as a pooled set of data.

I mean, that's the first point, I guess. You know, I don't know if we stop there or I can keep going, but --

DR. CHMELYNSKI: Well, I would like to answer one question, which is what if every worker had four samples, one a quarter?

DR. NETON: That would be fine. You would take the average of the four --

DR. CHMELYNSKI: Yeah, but why would you have to?

DR. NETON: Because they may vary. They're going to go up and down.

DR. CHMELYNSKI: I understand they may vary. But why would you have to take -- you know, they're all equally weighted, they all have four samples. Why not just calculate the distribution?

DR. NETON: In that unique situation it probably would end up at the same place. But what I'm saying is the estimate of his total excretion is the mean value of those samples times 365 days. That would be the true estimate of his excretion, not the four samples put into a data set. In some cases you have four, some cases you have more.

I'd like to address this idea of incident samples as well. We have, since this program began, gone under the fundamental premise that a chronic coworker exposure model, a chronic exposure model in general, is bounding for workers who have incident-related samples.

We went through this with

Mallinckrodt many times. We vetted IG-002, which is the basis for this. And it's no different for coworker models. So if there is an incident sample embedded, or a series of incident samples embedded in a routine coworker model, we're going to assume that those represent a chronic exposure scenario.

And if there was one value in that monitored period, a year for example, we would assume his excretion during the year was that incident sample times 365 days. This is a bounding technique that we've applied across the board to all dose reconstructions and also our coworker models.

So the fact that there were incident samples in there with changing retention fractions, such as indicated in Slide 18, really don't matter. We are assuming a chronic exposure scenario for this coworker model.

DR. LIPSZTEIN: May I try to

answer you, Jim?

DR. NETON: Yes.

DR. LIPSZTEIN: Is it possible for someone to put, you know, from our draft paper, on Page 41 there is a table.

DR. CHMELYNSKI: In our paper, Joyce?

DR. LIPSZTEIN: On Page 41 of our draft. Jim, we are not talking about not using an average for -- using all points from an incident as different points in the table. What we are talking about is that once you have an incident and then you have related excretion rate that is related to that incident.

So if you take the average of the excretion rates that were taken just for that period of time after the incident, and you take the average as one of the points of the worker, then you can use the old approach as you always have used before, because what was happening is some types of

incidents or special work were not taken into account on the old methodology.

But what you cannot do is when you take the average you are mixing periods of no intake with periods of intake. So let's see. If you look at this first table here, I measured ten workers -- that my calculation was just of ten workers, okay.

And suppose there was an accident in November and December and the workers were monitored regularly, but there was no exposure from January to October. So you measure the excretion rate and it was always equal to the minimum detection activity, which was one, for example.

And then suddenly in November you had a high excretion rate and in December you had a high excretion rate. When you do the OPOS for the year you take into account the period of non-exposure mixed with the period of exposure. So you get OPOS that are 10, 10, 11, 11, 10, 11, 9, 9, 8, 8 for

this population of ten workers, right?

So the geometric means for those OPOS would be 9.6. Then you are going to apply a chronic intake to this geometric mean of 9.6. Now, what happens if the workers were not regularly monitored? Then you have the next table.

Suppose the workers were only monitored in November and December, only when the incident happened. Then you would have the same exposure but the OPOS would be much higher and the geometric mean of the OPOS would be 53 instead of 9.6.

So when you calculate the intake rate, the coworker intake rate, for this second population of workers, you are going to calculate the chronic intake rate for an excretion rate of 53 units of activity, while on the other sample of workers, which had the same activity, you are going to calculate a chronic intake rate based on an excretion rate of 9.6.

So that's what I'm saying. You cannot mix periods of no exposure with periods of exposure because they are going to influence the intake rate even if you do a chronic intake rate. So what I'm saying is that what you should do is that the November and December when there was the period of excretion rate related to that incident, then those two should be averaged.

And it would be another point, then that's different. And then when you did the other coworker model, instead of doing it through the whole year you did it by periods of time, so when you look at the periods of time you can see that there was a time period when there was an incident at that installation.

And then the intake rate for that period of time can be higher than when you look at the whole year. So what I'm questioning is the application of this methodology on a year basis instead of using

it on a period basis or a smaller period basis as you did on the other coworker model, on the previous coworker model.

DR. NETON: We rarely do anything less than a year when you have type S material or even type M. It just doesn't change that much.

DR. LIPSZTEIN: Well, I don't know, because you are going to base it -- like in this example, if you have a whole year you would base the chronic intake rate on 9.7 -- 9.6, I'm sorry, on 9.6. But if you did the other samples where workers were not monitored before the incident you are going to base the intake rate, the chronic intake rate for type S -- it doesn't matter -- 153. So you'll get a much higher intake rate.

DR. NETON: But let me finish. I've got a couple of things to say here. One is I think this example is obviously skewed towards the extreme end of the

possibilities. I'm not sure this is going to happen very often, and I can also posit that it would happen where the exposures were in January in February which will counterbalance each other over a large data set.

The second thing is, look at the data set that you generated. If you did not use OPOS, what would be the 95th percentile of the distribution? It would be around 50 dpm per day or 50 units per day, because you've got these high values. And that is wrong.

The average value of excretion during this time period is 9.7 dpm per day times the year, will give you 2,500 dpm exposure per year, which is correct. That's their chronic excretion during that year, not 50 times 2,500. I think you've actually proved our point that OPOS is a better statistic here.

DR. LIPSZTEIN: No, no, no,

because when you have -- you introduced the OPOS to compare regular workers with construction workers. And then you have the people that are not regular employees of institution, and we saw this at Fernald very well, they were measured only when there was a special work or a special incident.

And then they have exactly this, they have like a period of time where they were monitored and they had very high results. And then other periods of time they didn't have any results. So you cannot compare this with the other type of workers.

So what happens, let me put it, what happens, you have one year-round -- I put November and December was on purpose because I did not want to do the correlated samples before. But you have a non-exposure until October and then November and December you have an exposure and it probably would continue on the other year.

So why stop in one year? So the

correlation, it goes from one year to the other. I think the problem with it is that you are taking always a year. If you take by quarter of years like you did before, you would see that in January, February and March there was no exposure in that installation. April, May and June there was no exposure, and then in the last quarter of the year there was an exposure that probably reflects on the next year.

DR. NETON: I would argue, exposures if they go into the next year will bias the model high because we're going to take --

DR. LIPSZTEIN: Yes, yes, of course, yes.

DR. NETON: -- bias it high because we're going to assume that continued excretion in the beginning of the next year, all those samples are going to relate it to chronic exposure during that year.

DR. LIPSZTEIN: Exactly. So what

happens you say that you would assume a higher Probability of Causation and you are not because the next year will correlate with it. So what you have is that -- the problem is the bounding per year because before you didn't have bounding per year.

And now what you do, you not only bound per year but then you have years put together to find the same intake rate for several years in a row. So when you had it before you could see which time periods have the same intake rate and that was correct.

And then if you have an unmonitored worker that worked at an installation in November and December, he had a much higher probability of having --

DR. NETON: I one hundred percent disagree with you. Maybe I need to put this in writing because I'm not getting anywhere.

DR. LIPSZTEIN: Okay.

DR. NETON: This example proves OPOS in my opinion. I would be happy to

discuss in writing.

DR. LIPSZTEIN: Okay, please do.

DR. TAULBEE: This is Tim Taulbee. Can I make a comment please?

CHAIRMAN MELIUS: Yes, go ahead, Tim.

DR. TAULBEE: Okay. In this particular example I agree with Gen here in that I mean effectively you've kind of proved our point. And I know Jim is going to write this up. But just think about this from the construction trades workers in the example that you just gave.

By averaging the regular workers who were monitored throughout the year who are not monitored based upon an incident type of basis, they have a lower overall value from the OPOS standpoint, whereas the subcontractors or construction trades, if you will, end up with a higher bioassay result.

When we did the comparisons from

Savannah River, this is exactly what we were looking at, was people who did not have this large I guess dilution is what you're trying to refer to it as of this monitoring time period versus construction trades that were just monitored after the end of the job or an incident type of scenario.

We didn't see any difference between the two. Based upon your example here we should have we should have seen a large difference where construction trades would have been higher using the OPOS result.

DR. LIPSZTEIN: Yes, but when you go to sample you see it. At Fernald you see this. And --

DR. NETON: Fernald was made an SEC, in my understanding, because of that exact issue. It's incumbent upon NIOSH to demonstrate that the coworker model, the stratified model that is used, is appropriate and for various reasons and we

would do that.

I mean there's caveats associated with that. You're pointing out an example at Fernald that was made an SEC for exactly, valid reason that the construction workers or trades workers were not monitored adequately. It's true. We 100 percent agree with that and we would add a Class if that were true anywhere else.

DR. LIPSZTEIN: Actually, we agreed to discuss next week the rest of it.

DR. NETON: But you understand the Class was added.

DR. LIPSZTEIN: I see, I understand. And I was going to argument a little bit more. But I think as you've told me that you are going to write it, maybe it's better not to bore everybody with the discussion. And when I have the written discussion, then I'll write again. Maybe it's better that way.

DR. NETON: We could talk about

this page for hours.

DR. LIPSZTEIN: Yes, yes, right. I'm okay with that.

DR. MAKHIJANI: This is Arjun. Could I comment on Tim's statement?

CHAIRMAN MELIUS: Yes, please do because if you don't, I will.

DR. MAKHIJANI: The idea that the analysis of NIOSH showed that construction workers and non-construction workers were in the same distribution actually was quite controversial. And when we did the analysis, if you remember our report, and Harry went into it at some length, so Harry please comment if I'm off base or want to augment.

What I think NIOSH showed is that if you use the test that they used, which was basically biased, I'm not using that in a pejorative sense, in the direction of concluding they were the same when the area of ignorance was actually quite big in the

sense that they could have been quite different but the test would still conclude they were the same.

Remember we had all that argument about Type 1 and Type 2 tests. And in the examples that we provided, we showed that the tests would conclude they were the same even when they were very different.

And this was a conclusion that was very dependent on the total number of OPOS samples. And even when there were more than 30 samples, there were sometimes problems. So I wouldn't -- I don't actually agree that NIOSH has shown that the distributions are the same. They have not.

DR. NETON: And I understand what you're saying, Arjun. I think the relevant point is that we need to show that the coworker model that we're using is a valid -- not a coworker model but the stratified model that we're looking at, we can make some reasonable statistical assumptions

from.

And the example that Joyce has put forth, it may be that's not a valid comparison. I'm not arguing that point.

DR. MAKHIJANI: Right. I'm just responding to what Tim said just to set the record straight.

DR. NETON: If you only have two months= worth of, two incident samples on an entire construction workforce that was working the entire year, it may be hard to justify that that model is valid, and we can reconstruct those doses. So I don't disagree with that point.

CHAIRMAN MELIUS: I would just add it's not only it would hard to show that you couldn't reconstruct those doses but you'd really be hard put to justify comparing these, you know, a model based on the construction workers with a model, you know, coworker model based on the strata that's the production workers.

DR. NETON: Right. You know, it came up the last time we discussed. And SC&A actually made some mention to it in their report and I'd like to clarify that a little bit.

You know, the use of incident samples in coworker modeling is tough. And I think I said if I had a situation where it was a hundred percent incident-based sampling and there was quite a variable exposure in the work place and not good work place monitoring controls, then I would hard pressed to say that we could do a coworker model.

You have to be careful. I'm not saying you can't. But the burden, it becomes a lot harder burden of proof to demonstrate that model is bounding and is not just bounding-plus. So I think we're on the same page there. I just wanted to make clear on that.

DR. MAURO: Jim, this is John.

During this conversation I heard something very interesting. I think Harry said it. He said that the problem is the averaging time for OPOS that's being employed or considered -- I think it's on the order of one year for each worker, but if it was on the order of a quarter, it would work.

I guess I'm not quite sure why that would be the case. Did I hear that? Is that the essence of really where the dilemma is with OPOS is that you're averaging over too large a time period?

DR. NETON: Well I think Harry's point was that if you take averages over a longer time period it's likely to have some issues with the mean values because, you know, where the samples were collected and that sort of thing.

I mean, I don't think it's necessarily related to the -- it certainly would be better to have quarterly samples. We of course don't have that very often. I

would say that it seems to me that SC&A's concern, at least in my opinion, boiled down to the representativeness of the mean of the OPOS value and the incorporation of variance in the model that's generated from that.

And I think those two things can be dealt with. For example, I'm not 100 percent married to the mean value. Maybe the -- it may make sense that the time-weighted average is a better approach because that gets away from this inadequate or this, you know, unrandom distribution of samples, or random distribution of samples.

And in the variance itself SC&A did an -- I notice you didn't talk about it today in your analysis, but you had this page where you weighted the OPOS statistics based on I believe the number of samples. It's hard to tell what you did there, and came out, and essentially regenerated the general distribution of samples.

DR. CHMELYNSKI: Yes, what I did

in that example was I went, I carried through with the idea that each OPOS statistic had an uncertainty and I used exactly the same logic that was used to justify the proportional relationship of the OPOS value to the intake.

In other words I used weighted least squares and knowing the relative variances I assigned those weights, and lo and behold, when you come up with the answer, it says what the ratio estimator always says. It says you add them all up and divide.

DR. NETON: You assume that the variance is proportional to the number of samples, which I don't think is true. That's something that needs to be verified. We've looked at that and I don't think it's true at all. But that's something we need to look at.

In fact it may be true that the variance is inverse to the proportion of

number of samples because you have people in higher exposure scenarios with variable exposures.

DR. CHMELYNSKI: Yes, but you're using a log-model and that's a variance stabilization which already takes into account what you just said.

DR. NETON: Well, I'm not sure.

DR. CHMELYNSKI: Larger values certainly do have larger variances. But we do the logarithms.

DR. NETON: I don't think that the assumption that you made that the variance is proportional to the number of samples is really valid. You didn't, and you picked a three-year time period which is kind of interesting.

I mean there's a lot of issues I had with that analysis. We would never, you know, you tell us not to use more than one and now you're using three. That tended to incorporate a lot of values where you had

multiple, many multiple samples per person, which kind of skewed the distribution.

If you look at annual doses, that curve would be to the left, to the right or right on the OPOS value. You know, I don't think that's a representative analysis that was done. That's a different issue.

But I do believe -- I do understand that the variance needs to be at least considered somehow in the model. Again, I would say that the abandonment of one person, one value just does not make sense to me.

If it's okay in the extreme case because it really weights it, then it's not necessarily an indication of why it should be ignored in the normal case just because it doesn't make a big difference. That's not clear to me why that follows.

You know, it's either right, the technique is either correct or incorrect. It's not only applicable when you have large

data dominance that makes a huge effect and then, by the way, if you have four samples, you ignore it because it doesn't make a big difference. I just don't follow that logic at all.

DR. CHMELYNSKI: Well, I guess one of the things is, like for instance, if you had -- if we did have analysis on a quarterly basis, if you look at Slide 10, first off almost all the big problems go away because almost everybody only has one or two. And I don't really mind averaging those.

And the ones that have a lot we're going to use OPOS on anyway. So we get them down to one. And we would have one value per quarter for each worker who had any samples in that quarter. And in that case I don't see too much of a problem with OPOS.

But when you keep expanding it over a longer and longer period, it starts

diluting it too much.

DR. NETON: But I'm wondering if the time-weighted average wouldn't be a better estimator.

DR. CHMELYNSKI: Yes, I was thinking of that. But then you have this problem of, you have an additional point and you're not quite sure how much time to assign that one and then you have one at the end, near the end of the period and you're not quite sure what to do with that time.

So you're right, though. I agree that the time-weighted average is the right answer. I wasn't sure how to do it.

DR. NETON: Well, I think, you know, rules can be developed for that. But to me the time-weighted average is an estimator of the total picocuries excreted in the year. That value times the annual, the 365 days gives you the total amount of chronic intake that has been inhaled and excreted during that year.

And it's an overestimate because we agree that carryover happens with long-lived radionuclides. So I think it's a perfect solution. I don't see anything wrong with it. It takes care of a lot of the issues.

And I think we have the data to do it. I think the original count was, well, maybe we're gilding the lily too much because, you know, I can get into it later and we don't have time today, but if you start looking at the coworker models that are fixed, the uncertainties really become larger year to year than within the year itself.

When you start developing chronic exposure models over a period of 20 years and look at the variability in the individual OPOS data points that make up that fit, you have factors of 5 to 7 to 10 differences in the intakes. But I would not argue against the use of a time-weighted

average because to me that's a tried and true -- that's been used for years as a rough indicator of intake for workers, and the average value during that year represents it. I don't know. That's my opinion.

CHAIRMAN MELIUS: Do other, any of the other Board Members have comments?

MEMBER ZIEMER: Well, this is Ziemer. I'm trying to evaluate what the next step is here. Do we need something more formal, a response from NIOSH? I think I'm understanding what Jim is suggesting here and it makes sense to me.

CHAIRMAN MELIUS: I should have pointed out earlier I discussed this with, I guess Jim and I can't remember if Stu was involved in the, Jim and I did is to, in order to sort of expedite this meeting, we sort of skipped the need for a formal response and figured it was easier and in some ways more productive just to do it by

discussion.

My suggestion actually is, where I think part of our problems in discussing this is sort of understanding the procedure that's involved and how the decision is made as to what are, you know, when is it legitimate to look at strata and when is it not, you know, in terms of what kind of monitoring was done.

The issue we just talked about in terms of Savannah River and so forth. And also when you would, when you get concerned about OPOS, use of OPOS or some other, you know, variation of OPOS in a model if it's only a few incidents that are in a very large, you know, sort of chronic intake database, monitoring database I don't think it makes much difference or, like as Harry just said, if you're just having, you know, a couple of samples per person, it probably doesn't make much difference.

And I think we still have some

decision criteria as to when we would be applying this and when is it appropriate and when is it inappropriate and how do we go about determining that? You know, so we're backing up a little bit away from OPOS, but eventually getting to OPOS as one of the ultimate tools that might be used in certain circumstances.

I think it might be more productive, because I think some of the problem we get into, we're having is that we're sort of using extreme examples. And I'm not sure we'd ever get to some of those examples in a practical way or at least I'd like to think that we would, you know, be able to avoid them in terms of our initial evaluation of data sets.

And I think there are also some much more fundamental problems in looking at different strata in terms of, you know, developing coworker models both in terms of how many people were monitored in a given

year. Is there data from preceding or subsequent years?

Information we have or don't have on changes in production or process or something that would give us more or less confidence in the development of the model. And I think those are much more likely to come up and I think, I'm not sure those have ever been written down.

In fact, I'm pretty sure they haven't been at least for internal models.

MEMBER ZIEMER: Yes, of course I think I heard some agreement between SC&A and NIOSH on the time-weighted average issue. It's not clear to me that the questions that Joyce raised were, if she fully understood what Jim was saying or is there some additional information that needs to be generated on that matter.

CHAIRMAN MELIUS: I think Jim offered a written response there. I tended to agree with Joyce, but I didn't quite

understand what Jim's response was. So that may just be me.

MEMBER ZIEMER: I understood Jim's response. But I think we need to make sure that SC&A is sort of aboard or if the objection still holds, to make sure we understand clearly what the difference remains to be.

CHAIRMAN MELIUS: I think we could all benefit from that. I agree.

DR. LIPSZTEIN: I just want to make one point that when we compared the uranium intake type S for Fernald from the OTIB that you used the coworker model that was done before, that was Revision 1 of OTIB-78 and then we compared the intake rates for 78, Revision 2.

And there are years where the 95th percentile and the 5th percentiles were double or more than double ones from the other. So really, it makes a difference which way you do the coworker model. It's

not something that you'll get similar results.

So this issue has to be resolved. One of those has to be the correct one. Like for example in the 59 and 60, the 95th percentiles for the Revision 2 was 28 micrograms per day intake while the 95th percentile intakes from Revision 1 was 47.

So you have values that you have a large difference not only here but also on the 5th percentile intake rates. So this is a very, it's not something that, you know, just a few results and doesn't make a difference. It's a completely different approach of doing coworker model that has to be solved because big difference probably important when you do the PoC.

DR. MAURO: Jim, I have a question for you. It just hit me. When you do this experiment that we talked about earlier where you do these two distributions, one for the strata and one

for the full set, you're going to process some bioassay data to get these two distributions. When you process that --

DR. NETON: Not necessarily, John. I mean I think we'll use already in place values.

DR. MAURO: Okay. So you're going to use the -- that was my question. So you're going to --

DR. NETON: It really doesn't matter. I don't think we have to go from de novo bioassay data to come up with the doses. I think we need to be mindful of what the distributions are.

DR. MAURO: Okay. I guess my question is, you're going to get these two distributions. Are you going to get them working from OPOS, working from real reconstructed intakes using the classic method with IMBA or are you going to use it using pooled data to get the distributions?

You can do it from three

different approaches.

DR. NETON: Well, no, but I think you're connecting the analysis of the coworker individual annual doses versus how we compare distributions.

DR. MAURO: Yes. I am, maybe --

DR. NETON: I think you can compare the distributions without going back to the raw data. I think you --

DR. MAURO: So what distributions will you be comparing?

DR. NETON: I think what I'm comparing is if you took a 95th percentile value and then you can calculate what the distribution, the full distribution would have to be. Well you'd have to start with a distribution. I don't know yet, John. I guess I'll have to comment on that.

DR. MAURO: You see why I asked the question?

DR. NETON: I wasn't thinking about going back to raw data.

DR. MAURO: I didn't say you should, I just wanted to know, right now it sounds like you're still thinking about how you'd come at the problem.

DR. NETON: It may have ended being OPOS data. I don't know. But I would like to go back a step and see if I can get some kind of agreement that, since this is a coworker model, a worker model not a sample model, that somehow under some format we would use one exposure value per person per evaluated time period.

To me I just don't understand why that isn't true. And like I said before, SC&A has agreed in the extreme case that it's valid. I don't know why it's not valid in the normal case.

And their argument seemed to be that you don't have to do it in a normal case because it doesn't make any difference. Well, I would say if it's valid in the extreme it's valid in normal and then just

use that as the default.

They've already agreed that if you had equally spaced bioassay samples, it's a perfectly valid approach. If we end up using a time-weighted average for not equally spaced bioassay samples, you'd end up with a much better estimate of the annual intake and excretion.

I just think, I just don't understand why one can argue that it's a coworker model, not a bioassay sample model and you shouldn't use individual values. Agreed that the variance somehow needs to be dealt with. I mean, I'll agree to that.

CHAIRMAN MELIUS: Jim, this is Jim. Yes, but I think that is the fundamental concern about it. And I think that's -- it doesn't mean that it's not in certain situations a concern that can be ignored or doesn't make, you know, any practical difference.

But I think we have to sort of

understand sort of the situations where it does or doesn't make a difference. And I think that's sort of what we're struggling with. And I think that's your, so your discussion with, interchange with Joyce was about that. Where does it make a difference, where doesn't it?

DR. NETON: No, well, maybe. I think --

DR. LIPSZTEIN: Jim, can we go to page 88 of our draft?

DR. NETON: Sure.

DR. LIPSZTEIN: There's a table, C-3.

DR. NETON: Okay.

DR. LIPSZTEIN: Okay. Can you see it? It's Page 88.

DR. NETON: Yes, I got it.

DR. LIPSZTEIN: Got it, okay. You have, for example, for 54 you have the 95th percentile is 45,000 micrograms per day. And the 95th percentile for 54 on

Revision 1 is 91,658, while the 5th percentile is the same rate. One is double the other.

And you have no differences, the same number of samples, the same samples that were used. So it's just the same, the difference is on the statistics or how you use it. It's just the methodology.

So this has to be taken into account. It's not only the number of samples that are repeated or that are correlated because you have this big difference when you have a lot of samples like, for example, the samples related to 50 are the ones that you had the same worker repeated many times.

So in 59, 60 period of time, you have a difference, but you had 4,573 samples by 50 that were used in Revision 2 but were totally ignored on Revision 1. But in 54 were the same samples.

So, you know, the methodology

has, which one is the correct one? And it's very important to have this.

DR. NETON: This gets to a critical evaluation of the samples that are used in the calculation.

DR. LIPSZTEIN: Yes.

DR. NETON: I don't want to get too much talking about --

DR. LIPSZTEIN: Yes, yes, you're right.

DR. NETON: -- but I think --

DR. LIPSZTEIN: I agree.

DR. NETON: -- if you know, for example, that you have a series of incident samples and a person was chelated, I would be the first person to suggest that those samples be removed from the analysis.

DR. LIPSZTEIN: But those, I think those samples that were labeled 50 they were not chelated. But I agree. If they were chelated, no way. And if they had a wound instead of inhalation also you

cannot count that.

DR. NETON: I can tell you from my knowledge that those samples were not routine samples, okay.

DR. LIPSZTEIN: No, no, they were not. That's why they were labeled 50, yes.

DR. NETON: Probably more than likely. So once you have that knowledge then you need to make a conscious decision. Are those valid to put into the coworker model or not?

So what you're getting to is sort of the ground rules of how you analyze the data. That really has nothing to do with OPOS. It has to do with what type of samples are included in the general coworker model itself.

DR. LIPSZTEIN: Yes, but the OPOS was introduced to deal with this: people that had many samples, right?

DR. NETON: Right. But if you have a number, and I don't want to talk

about Fernald specifically, but if you had a number of samples that you knew were totally incident driven in the middle of a routine monitoring program, you might want to, if you could definitely determine that they were incident samples, I would suggest that they don't belong in the coworker model.

I mean, now there are many cases where you just can't tell. And that's the problem. So this gets down into the professional judgment and vetting of the samples, but not so much one person, one statistic or one measurement or one value because to me it's a model for a person not the distribution of bioassay samples.

And again, in the extreme case, it's obvious even to SC&A. But in the general case, I think it equally is applicable. If I have five samples, four samples equally spaced the mean value is a better representation of that guy's total excretion during that evaluation period. It

just is.

To me it's a very simple concept. You know, again the mean of the Advisory Board is not the mean including ten measurements, repeated measurements of Bill Field.

DR. LIPSZTEIN: No, but that's not the same because when you have a --

DR. NETON: Repeated data on an individual measurement. Yes, it is.

DR. LIPSZTEIN: No, no, no. But when you have an excretion rate, even if you had the mean for them, if you had 30 measurements of that incident or if you just had two measurements of that incident spaced between them, then the OPOS would be different.

But that's why I think that the incident case if they are to be handled by the OPOS they should be handled as one number for that incident because of the number of samples.

DR. NETON: If we don't know it was repeated measures and we don't know it was an incident, we will treat it as a chronic exposure value.

DR. LIPSZTEIN: I'm not discussing this; what I'm discussing is if you have samples that were labeled 50 for example.

DR. NETON: I don't want to talk about the Fernald cases.

DR. LIPSZTEIN: That's the only one we have to make reasons. But anyway, okay, but suppose you have someone that was exposed and he had 50 samples taken in a period of two months. And another person was exposed in the same incident but he had one sample taken just after the accident and at the end of the, after the accident.

So because he had less samples taken, his OPOS would be much less. So what I mean is that for the whole workers of that population of workers would depend on the

frequency of monitoring that the Health Physics has imposed at that installation.

So that's what, what is allowed with this methodology because it depends on how the Health Physics has determined that the number of samples were to be taken.

DR. NETON: The program there that can be used in the incident samples that are unknown to be an incident and be dealt with and treated as if chronic exposure occurred and they will bias the value towards claimant-favorable.

DR. LIPSZTEIN: I don't think so. Do an example. I'll wait for your written response.

DR. NETON: We discussed this five, seven years ago, maybe ten years ago at Mallinckrodt. We went through numerous examples of why a chronic exposure model will bound infinite level samples.

We do this with routine dose reconstructions. If a person has one

bioassay sample two thirds of the way into the year, we will fit a chronic exposure all the way through that so that it goes through his value that was excreted two thirds of the way through the year.

And that's how we assign the dose. That's exactly what we do. That has been vetted through this Board years ago. You can always postulate and speculate on extreme situations where that might not be the case.

But it was decided that in general in an overwhelming majority of cases, it's claimant-favorable and that's what we use. Otherwise you can't do anything. You're hand-tied.

DR. LIPSZTEIN: No, you have been doing it for the whole period until now. You did dozens of coworker models without using it.

DR. NETON: And they're chronic exposure models. That's what I'm saying.

DR. LIPSZTEIN: Yes.

DR. NETON: We're saying that the chronic exposure model now should include some better estimate of the person's annual excretion during that year. And our opinion was that the mean value is better. If the time-weighted value is better, so be it.

But that's what we're trying to say is if you have repeated measures on a person, you're going to say the best estimate of that guy's exposure was the first sample that was taken at the beginning of the year. Now that's not true. It's some average of the samples that were taken throughout the year is a better estimate of his intake.

It's just, what you excrete is what you inhaled. It's directly proportional assuming, as long as you can agree that carryover excretion is going to bias the model high. We're going to assume that he inhaled the chronic exposure during

that year. I don't know any other simpler way to put.

It's, to me, it's technically correct. It's not scientifically undefensible or whatever was said in the first paragraph of SC&A=s slide. I think it's the best way, best we can do given the data that we have.

MEMBER ZIEMER: Mr. Chairman, this is Ziemer. I think we've reached the limit of what we're going to accomplish today. I wonder what our next steps are.

DR. NETON: I agree.

CHAIRMAN MELIUS: Thank you, Paul. Yes, I think we have at least one next step which was Jim was going to write up a proposal and circulate it, on that.

The second next step was that I was asking, and I think we had talked about this at the last sort of in-person Work Group meeting, but maybe my memory is faulty, is that we should, if I'm trying to

still understand sort of the whole criteria that go into the development of these coworker models and the application of one person-one sample and the comparisons -- and I thought you were going to develop a procedure for that. I thought we had talked about that at the first meeting. I think it would be very helpful to have an outline of that at least so we, for discussion because I think that would help to maybe narrow the differences and avoid some of the issues about some of the examples we're dealing with.

DR. NETON: Dr. Melius, I agree with you. And what I really had suggested was I would come up with an implementation guide for coworker models. And I've drafted pieces and parts of that. But unfortunately, you know, my thoughts change as we have our discussions.

CHAIRMAN MELIUS: Okay, I'm sorry.

DR. NETON: That's okay. But I still, my basic tenets haven't changed, but I do agree that certain things maybe need to be shored up and such. But I could probably have, it would be a rough, you know, sort of the premises behind coworker models and maybe not the full details because obviously we're still debating how that goes.

But I can do that. I don't know if it will be before the Board meeting or not, to be honest.

CHAIRMAN MELIUS: Yes, it doesn't have to be before the Board meeting.

DR. NETON: I do agree that is a deliverable that I had offered up.

CHAIRMAN MELIUS: Okay. I thought maybe I had --

DR. NETON: No, no, no. I read all 300 pages of the transcript last week.

CHAIRMAN MELIUS: Wow. I'm impressed. But I think that really would be useful at this point. The more I look at

this issue, the more I get --

DR. NETON: And I think maybe as rough as I have it, I can polish it up a little bit and just put it out for, you know, discussion. It may have some question marks in it and it may have some incomplete, you know, concepts.

But I think the beginning of it, in my mind, is pretty solid. This whole idea of chronic exposure models and, you know, that kind of thing. I think if we could agree to the basic tenets that I put in there or to the extent we can, then we can maybe move forward. I get a sense that maybe some of the basic concepts that I've assumed have been agreed upon maybe are not necessarily so based on some of the feedback.

CHAIRMAN MELIUS: I think the other important point is that, if we're going to be coming up, we're going to look at strata within potential coworker models

is, how are we going to look at incident versus, you know, routine monitoring and how do we take that into account? I think there's also some issues about how, you know, how many people have been monitored, I think, makes a difference in -- say within a given year or something in terms of how these models apply and some of the statistical concerns we may have.

If it's, you know, only one percent of the group that's monitored I think we obviously have a lot more concerns than if it's, you know, 90 percent or something. So if you can, you know, whatever you've done and polish up and give us a basis for discussion of that because I think that would be helpful.

Are there any other sort of deliverables that would be useful for people out of this conversation? Paul, did you have any?

MEMBER ZIEMER: No, I think what

you just described would be satisfactory.

DR. NETON: So just to make sure I have three things on my plate for NIOSH. Sort of the hypothesis, the experiment into how we're going to go about evaluating stratification, differences in strata versus the general model.

CHAIRMAN MELIUS: Right.

DR. NETON: And then a discussion of SC&A's write-up on Page 41 which has to do with this hypothetical coworker or hypothetical exposure cohort. And then the third one is some description of the criteria that go into coworker models, whether it's an annotated outline or what. But I'll just put it out there for people to chew on.

CHAIRMAN MELIUS: Okay, great.

DR. NETON: I'll do that in my spare time.

CHAIRMAN MELIUS: Good, I'm glad you have some.

DR. NETON: Yes, that sounds good.

CHAIRMAN MELIUS: Okay, any other Board Members with comments or questions?

MEMBER BEACH: None here, Jim. This is Josie.

CHAIRMAN MELIUS: Okay.

MEMBER ROESSLER: And I agree getting this in writing will help get us all understanding just what we're doing.

CHAIRMAN MELIUS: Okay. Good. Okay. With that, Ted, do we have anything?

MR. KATZ: No, just thank you. That was a great meeting.

CHAIRMAN MELIUS: Okay.

DR. NETON: All right. Bye.

CHAIRMAN MELIUS: Okay, thanks everybody. Have a good day.

(Whereupon, the above-entitled matter went off the record at 4:02 p.m.)