U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES
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 WORKGROUP

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FRIDAY
JANUARY 24, 2014

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The Work Group convened via teleconference at 11:00 a.m., Eastern Daylight Time, James M. Melius, Chairman, presiding

PRESENT:

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

ALSO PRESENT:

TED KATZ, Designated Federal Official
BOB BARTON, SC&A
HARRY CHMELYNSKI, SC&A
ARJUN MAKHIJANI, SC&A
JOYCE LIPSZTEIN, SC&A
JOHN MAURO, SC&A
JAMES NETON, DCAS
MICHAEL RAFKY, HHS
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

(11:00 a.m.)

CHAIRMAN MELIUS: Okay. Thanks, Ted. Welcome, everybody. I appreciate you taking the time. I believe this will be a relatively brief meeting. It's mostly to get prepared for the Board Meeting next week and sort of decide where we are on sort of dealing with the SEC review group that's been looking at the whole issue, along with working with NIOSH and others on ORAU and SC&A on this issue of sufficient accuracy. And just wanted to get an update prior to the meeting and then decide what, if anything, about this topic we want to discuss at the meeting next Tuesday.

So I think our first order of business is sort of get an update from where NIOSH is. And, Jim?

DR. NETON: Okay. Thank you, Dr. Melius. I have a couple brief documents that I can share with you as to our progress

in two areas that we were agreed to look into at the last Working Group Meeting.

And that has to do with what I'll call the 100 millirem experiment where we're going to add 100 millirem to some NOCTS cases and see how that affected PC outcome. And then a little bit on where I am at with the -- I committed that we would start to draft an implementation guide for coworker models. And I've made some progress on that, but honestly I have more questions than answers at this point.

Regarding the first issue, I've just got a brief presentation here about the practical significant dose evaluation. And just this slide -- can everybody see my slide, by the way?

MEMBER ROESSLER: You know, this is amazing. This is Gen. I got this invitation this week to get on this live stuff on the computer and I've been fussing with it for a whole day. Ted just sent the

information, I got on and I see it. This is great.

DR. NETON: Excellent. That's Gen. Everybody else, too?

MEMBER BEACH: Yeah, I do.

MEMBER ZIEMER: Yes, I see it, but it's not centered. Can I do something about this or can you close the left side of your screen?

MEMBER BEACH: No, you can center it, Paul. I did.

MEMBER ROESSLER: Well, how do you do it?

MEMBER BEACH: Down at the bottom of your screen.

MEMBER ROESSLER: Yeah, you should be able to click on slideshow and do it, but that doesn't work.

MEMBER BEACH: There's a bar at the bottom.

DR. NETON: Well, I did slideshow but it's too big, so I kind of left it in

this mode.

MEMBER ROESSLER: Okay, I've got it centered now.

DR. NETON: Just so it can all fit on the screen. I only have -- this is my only slide. So we don't have to labor too much.

MEMBER ROESSLER: You have a bunch of neophytes here.

DR. NETON: Yes.

MEMBER ZIEMER: Yeah, it's too big for my screen for some reason.

DR. NETON: This is the only one and all I want to do is just summarize what we said we were going to do, and then get into another document that gives us some preliminary results.

MEMBER ZIEMER: Okay.

DR. NETON: So just bear with me on these four bullets here. Just to refresh your memory, we had proposed to evaluate the significance -- to attempt to start to

evaluate the significance of what dose really makes a practical difference in a dose reconstruction.

We agreed to look at a bunch of NOCTS claims, and the idea was to identify NOCTS claims with a single cancer that had a Probability of Causation between 45 and 50 percent. And those, by definition, are best estimates, because over 45 percent we're required to do a best estimate. And we also felt, if you recall, that anything below 45 percent would be unlikely to be changed by addition of 100 millirem.

And we also -- in the protocol that we established, we're going to insert a zero millirem exposure line for each case, and then do 30 IREP runs of 10,000 iterations for each NOCTS case and calculate the average PC of all those cases.

Between 45 and 50, this is standard protocol. We're required to do 30 runs of 10,000 because it minimizes the

uncertainty in the estimate. And then we were going to change that zero millirem exposure to 100 millirem, and this is going to be external dose only, and do the same thing, do the 30 IREP runs and calculate the average PC.

Well, we selected the cases and it turns out that, at the end of the day, we ended up with 175 cases out of about 38,000 claims that had been dose reconstructed that met our selection criteria.

So we went about doing exactly what I just outlined here, and it took a lot of computer horsepower. We moved a lot of electrons around doing this analysis, and these are preliminary results because honestly we just got them a few days ago.

And so all I'm going to be able to present here is sort of a brief sketch of what we ended up seeing. And, of course, there's a lot analysis to do here on these data sets, but I wanted to give you a flavor

for where we are at this point.

First table here just sort of summarizes what -- it does summarize the frequency distribution of the cancers that came out of that 174 or 175 case set.

What surprised me is about half the cases -- almost half the cases were either lung cancers or non-melanoma basal cell carcinomas, which really surprised me. I thought it would be more of an even distribution, or more likely I thought the leukemias would be in that category, but they weren't. There was only three leukemias, excluding chronic lymphocytic leukemia, that met the criteria.

So, anyway, this is a distribution of the cancers that we saw. If anybody has any questions, please chime in, because again this is very preliminary and I'm kind of looking at this only for the second time myself.

MEMBER ROESSLER: This is kind of

-- I remember talking about this at the meeting, but all of a sudden now having to think about it and things are flashing around on my screen, which you're probably doing.

DR. NETON: Yes.

MEMBER ROESSLER: What does that mean, that only 175 out of 38,000?

DR. NETON: There were only 175 cases of all the cases that we did dose reconstruction that had a Probability of Causation between 45 and 50 percent, or less than --

MEMBER ROESSLER: Oh, okay. I get it. Okay, I see what you're saying. So those are the ones then that you will test --

DR. NETON: Exactly.

MEMBER ROESSLER: Really what you're asking is what does 100 millirem do to the PC?

DR. NETON: Exactly.

MEMBER ROESSLER: Okay, I got it.

DR. NETON: And this is just for general interest, you know, which cancers comprise the 174, 175 cases. And you can see that about half were between -- 54 out of those were for lung and 30 were for non-melanoma BCC.

The rest were fairly evenly distributed. You have, I guess, all male genitalia and colon cancer represented, next two highest number of cases. That's sort of telling us --

DR. MAURO: Jim, this is John. I'm sorry to interrupt, I also have a question of the nature that Gen just asked.

DR. NETON: Yes.

DR. MAURO: So you've got this group that falls into the category of 45 to 50 percent. And the process you went through, you lost me a little bit on when you described the zeros and 100 a little. Conceptually, what I'm seeing is you've got

these cases and you're adding 100 millirem to the totality of the external dose, or is that 100 millirem per year?

DR. NETON: No, to the totality. It's 100 millirem increase in the total dose.

DR. MAURO: Okay. So whatever the dose was reconstructed using your standard protocols, including the non-detects, including the coworker models, and everything else that went into these realistic dose reconstructions for all these cases, you just went ahead and said, okay, I'm going to add another 100 millirem at some point in time.

DR. NETON: Right.

DR. MAURO: Because we are covering, I guess, multiple years. I guess you just pick some time, a given year, and say I'm just going to add in to that year?

DR. NETON: Actually, we thought about this some, and it was in the protocol,

I didn't go over it, but we decided to pick, since it was external exposure, we added it to the first year of employment, that it would maximize the latency.

DR. MAURO: Got you.

DR. NETON: We didn't want to put it too close in time.

DR. MAURO: Okay, so you picked that year. I'm with you. Okay.

DR. NETON: We did a slightly different adjustment for leukemia because leukemias have a shorter latency.

DR. MAURO: Yeah, two years on that one. Yeah.

DR. NETON: And I forget where we put it, I think we put it at five years out, the exposure, because that was the maximum credit that would be given.

Now, it might be a little confusing why we added -- since we already had the runs, why did we add a zero line?

Well, what happens is, you know,

we reset the zero and put the line in and reran it, and then when we added the 100 we reran the same cases with the same random number seeds so that we could truly look at the difference between adding 100 millirem, and sort of isolate the variability that is due to just the uncertainty in the Monte Carlo calculation.

So, what I'm going to be presenting, not to be confusing, is I've got three comparisons. I'll have the original PC value, I'll have the recalculated value with zero added, and the recalculated value with 100 millirem added. And you'll see there are differences.

DR. MAURO: Got you.

DR. NETON: And the main difference that you're going to see is that, if you compare the original run with 100 millirem added, there's more variability there because they're run on two different random sets of number seeds and that shows

the inherent variability of the IREP calculation itself.

DR. MAURO: Good.

DR. NETON: We're still looking into this, so, again, a lot of this is going to have to go through the gristmill before we --

DR. MAURO: I understand what you said. Very good, thank you.

DR. NETON: All right. And in fact this next slide shows exactly that.

MEMBER ROESSLER: My picture went away, did I hit something?

MEMBER ZIEMER: Mine went away also. My Live Meeting says nothing is currently shared.

DR. NETON: Well, I've got something on my screen here, which is interesting.

MEMBER BEACH: Yeah, I've got nothing, too.

DR. NETON: Okay, well, maybe it

timed out or something. Let me try it again. I have Paul Ziemer's desktop showing being shared.

MEMBER ROESSLER: Uh oh.

MEMBER ZIEMER: Well, maybe I took you over, but I didn't know I was sharing anything.

DR. NETON: No, you took me over I think. Let me –

MEMBER ZIEMER: How do I undo that?

DR. NETON: I'm going to do it myself here. Okay, now I'm going to go back to share and share my desktop.

MR. KATZ: All right, that worked.

DR. NETON: Is that back?

MEMBER ROESSLER: Yes. That's back.

MEMBER ZIEMER: Okay. I'm seeing a chart, is that what you're showing?

DR. NETON: Yeah, now I'm looking

at the second table here which is titled "variable."

MEMBER ROESSLER: Okay, very good. I've got it.

DR. NETON: It has a minimum, medium, and maximum.

MEMBER ROESSLER: Mm-hmm.

DR. NETON: Okay. This particular graph, table, shows the direct comparison. The average PC of the original 174 cases you see a minimum, median, mean, and maximum.

So the mean value of the original cases, of all the cases added up, the PC was 47.37 percent. When we added the zero dose the mean value of all the cases when we reran them with a different random number seed, was also 47.37, which was good. We would hope that would be the case.

When we added 100 millirem dose to all 174 cases, the median value of all the cases rose to 47.43. In other words, a

0.06 percent increase. So not much, which was kind of interesting.

And if you look at the minimum and maximum values, of course the original value had a minimum of 44.9 and a maximum of 49.87. In the cases where we added either zero or 0.1, none of the cases exceeded 50 percent, which is interesting.

So, you know, you have a lot of cases here that were very close to 50 percent. And, again, we reran all 174 and not one of them moved over the 50 percentile, or 50 percent of the 99th percentile. So that was kind of interesting itself.

And so the difference of 0.06 is pretty small. I expected more, actually. So we tried to -- you know, Daniel Stancescu did these comparisons, so I'll give him the credit here, but, you know, we had a few days to look at this so we tried to do a few little breakouts here.

And here we, the next table that you'll see that has "cancer type" in the title, shows a comparison of what the results look like with leukemia cancers versus solid cancers. And you really don't see a huge difference. I thought there might be because leukemias tend to be more radiosensitive and it might move more with 100 millirem added, but not necessarily.

There was an uptick. If you look at the average value right here, the average PC to add 100 millirem dose, you got 47.67. The average for the solid was a little bit lower. So there was a little bit higher increase there, but nothing really that stuck out in my mind as super significant.

Moving on to the next table, this is just what I really kind of just said on the original slide. The mean value changed 0.06 percent for all the cases. Now, you will see that the spread of differences is much greater in the add 100 millirem to the

original versus 100 millirem added to the zero dose added.

You'll see the minimum value was minus-0.43 and the maximum change was 0.67, so quite a spread versus zero when we compare the ones that were run with the same random number seed to a maximum of 0.34.

And what that really reflects is the inherent variability in the random number seed generation of the Monte Carlo calculation. Because the second line comparison here removes that degree of uncertainty because we ran them with the same random number seed.

So, moving on, I have another comparison here of leukemias and nothing really -- again, there's a slightly higher difference in the mean values, but nothing of substance that I think is of note at this point.

Again, further comparisons, cancer type, not much there.

Just on a last note, we just looked at the frequency of changes. That is, how many went up and how many went down and we did the comparisons. And if you compare the average change from the values when we -- the original to the 100 millirem dose, compared those two values, the frequency was 64, went down -- is that right? Four had no change and 106 went up.

That represents, I think, the uncertainty of the Monte Carlo calculation itself. And that's something we might want to look into when we're talking about significant dose, is maybe what degree of dose is required to show a statistical significant difference in the result above and beyond the Monte Carlo uncertainty.

And this last slide I have just shows that when you compare the two that were run with the same random number seed, 173 went up and 2 had no change. None went down.

So, I think that's all I want to say about that. That's all we can really get right now. But to me the big item is that none of the cases went over 50 percent by adding 100 millirem.

MEMBER ROESSLER: Will we get a copy of this data when we get to the meeting?

DR. NETON: When you get to the meeting?

MEMBER ROESSLER: Yeah, or --

DR. NETON: Well, I don't know. I mean, that's -- we're going to decide that I guess during this call, what we want to do with this. These are very preliminary. Again, you know, we just got these done. I don't know how much time I'm going to have to clean them up before the meeting.

MEMBER ROESSLER: Okay. Well, I think at some point it would be --

DR. NETON: Oh, yeah, sure.

CHAIRMAN MELIUS: At some point

it should be a report.

DR. NETON: Yes, exactly. This was just to give you a heads up as a completed analysis and here's where we are right now.

CHAIRMAN MELIUS: Yes.

DR. NETON: But, yeah, we need to have a complete analysis and report of this all.

CHAIRMAN MELIUS: Yes. I think the question may be is -- before we, you know -- before you write your report or before we meet, are there other analyses that we want done?

You know, do we want to look at whether adding in a larger amount -- remember we're trying to sort of figure out what -- how -- I don't know what the right word would be, but how much variability or how much, you know, sensitivity is there to error in some of the comparisons we're making on coworker analyses and so forth.

And it doesn't appear that 100 millirem, you know, makes that much difference.

DR. NETON: Yeah, and I think this may have, actually, more importance down the line in looking at the residual contamination reconstructions.

CHAIRMAN MELIUS: Yeah.

DR. NETON: But I'm still not -- it's still out whether it really makes a big difference in the overall dose reconstruction.

CHAIRMAN MELIUS: Right, yeah. And I don't want to try to push you, you know, into conclusions, you know, without giving you a chance to review the data and sit down and talk to it. But I would say that we, you know, do that -- and maybe the first step is to get at least, you know, give you a little bit more time to review this and pull it together and then, you know, either keep it as a presentation and

do it at another Work Group meeting or, you know, do it as a report and --

DR. NETON: Yeah. We're going to look at this and I think I already sort of hinted that we might try to look at the comparison of the uncertainty of the Monte Carlo calculation itself versus the addition of the dose and --

CHAIRMAN MELIUS: Yeah.

MEMBER ZIEMER: Yeah, Jim, this is Ziemer. I think that issue is probably important to pin down in any event, the uncertainty being the Monte Carlo itself.

DR. NETON: Right. And, you know, I'm trying to tease out here are there big differences in different cancer models and stuff. And we're not really seeing that. You know, I thought maybe for certain cancers it would, you know, be totally different.

Because each cancer has, of course, its own radiosensitivity to dose and

certain latency adjustments and such, but from this first analysis, at least with external dose, it doesn't seem -- it seems sort of spread around pretty evenly.

CHAIRMAN MELIUS: Yeah, but you also have different exposure patterns for people and so there's probably a fair amount of noise in these calculations within a given type of cancer.

DR. NETON: Yeah, and I think it's -- to be honest with you, it's probably somewhat fortuitous that none of them went over 50 percent. I think that, you know, I can't guarantee that if we didn't do 200 comparisons, one or two wouldn't come over.

CHAIRMAN MELIUS: Yeah. No, and I think that's why we got to be a little careful jumping to --

DR. NETON: Right. I'm not jumping to any --

CHAIRMAN MELIUS: -- conclusions and, you know, sort of what is -- does this

help us to –- or where do we think sufficient accuracy is?

DR. NETON: Yeah. You know, it doesn't say much to me right now except, in my mind, 100 millirem doesn't mean a heck of a lot.

CHAIRMAN MELIUS: Yeah, yeah.

DR. NETON: That's about all I can say.

DR. MAKHIJANI: Dr. Melius, this is Arjun Makhijani.

CHAIRMAN MELIUS: Yes?

DR. MAKHIJANI: It seems to me that maybe instead of, you know, inserting some other number into the same calculation it might be useful to deliberate a little bit on what are the uncertainties in coworker doses, for instance, and whether they are different for internal exposure and external exposure. And then to do a sensitivity analysis based on that.

Of course, you know, it's

difficult to know what the uncertainties are in many cases, but I think that may be a more fruitful approach because then you are actually dealing with, you know, where the margins of your analysis lie and how many people might be pushed over if you use a different percentile and so on.

So, you know, there's a difference between the 84 percentile and the 95 percentile, for instance, and that will vary from one coworker model to another and one set of data to another. And maybe it might be useful to get a glance at what those numbers are, especially for internal dose, because external we don't have as many difficulties in terms of estimation.

CHAIRMAN MELIUS: Yeah, though I think we -- I understand what you're saying and I think it can be helpful. I'm not sure I would want to make that step before, you know, understanding these data a little bit better. Because I think we still end up in

a problem, if we go directly to coworker of, you know, how much difference, you know, is too much or, you know, what's an appropriate difference. What kind of difference are we looking for or can we tolerate on these?

DR. MAKHIJANI: Yes, right.

MEMBER ZIEMER: Yes, this is Ziemer. I think though if we went through a group situation versus the individual.

CHAIRMAN MELIUS: Yeah.

DR. NETON: This is Jim. I think -- I agree that we maybe flush this out a little more and then when we get a handle on how much difference we're willing to tolerate, if I can use that word.

CHAIRMAN MELIUS: Yes.

DR. NETON: Then I think we can go and look at a couple internal coworker models as a test case and take it all the way through, because up till now all we've been saying is we're comparing the 50th or the 84th percentiles and saying are they

different statistically, but you really need to carry it through the entire intake calculation, as I pointed out several times.

And given that there's going to be ups and downs on a year-by-year basis, you fit both sets and determine how do those come out and compare. That, to me, is the ultimate test.

Now, we would prefer not to do that for every single coworker model, but we might be able to do some sort of proof of principle on a test case or two.

CHAIRMAN MELIUS: Yeah. If you remember our plan out of the last Work Group meeting was to, you know, try to determine, you know, how much of a difference we can tolerate, or whatever you want to -- however we want to refer to that.

And, secondly, then see how that would -- apply that to external dose models, simply because they were less complicated than the internal -- and then go to the

internal.

DR. NETON: Right.

CHAIRMAN MELIUS: And I'm a little hesitant to change that pathway at this point in time.

Paul, or Gen, or Josie, any comments or questions?

MEMBER ROESSLER: This is pretty fascinating.

CHAIRMAN MELIUS: Yeah.

MEMBER ROESSLER: Good work.

MEMBER BEACH: I don't have any.

DR. MAURO: Jim, what was the highest case again? The 49 point what?

DR. NETON: The highest result?

DR. MAURO: Yeah, of all the cases you looked at, there was one that had the highest PoC.

DR. NETON: Right there, I think it's 49.87.

DR. MAURO: So you're at 49.87, you then take 100 millirem and you add it

into the year that you think would have the greatest effect given latency for that particular cancer?

DR. NETON: Right.

DR. MAURO: And you still didn't move over 50 percent?

DR. NETON: Correct.

DR. MAURO: Okay, thank you.

DR. NETON: And you can see the average difference is 0.06, so that kind of falls in that that must of had a somewhat average increase, because there's others with higher increase.

DR. MAURO: Yes.

DR. NETON: I have a suspicion that the higher the dose the less it makes -- the less difference it makes because it's not a linear --

DR. MAURO: Sure.

DR. NETON: -- seen as a linear, so, you know, maybe the ones with the lower doses had the most increase. That's the

kind of stuff we need to be looking at.

DR. MAURO: Yeah.

DR. NETON: But, yeah, you're right, John, that's exactly what happened.

CHAIRMAN MELIUS: Any other discussion on this? What I'd like to do, just get a quick update from SC&A on where they are, and then come back to decide what are our next steps and what do we do, if anything, at the Board meeting next week.

DR. NETON: Okay.

CHAIRMAN MELIUS: So, John, or -- I don't know who's running the show at SC&A. Sounds like no one.

MR. STIVER: This is John Stiver, I was just getting back on line here.

CHAIRMAN MELIUS: Okay, I'm sorry.

MR. STIVER: Yeah, we had a -- we're very close to producing our paper on the kind of consolidation of all of our positions on OPOS. And it looks like it's

probably -- before we get cleared and everything else and have it your hands, it would be probably another couple weeks.

So, I tried to ask Harry to put together some fundamental kind of 10,000-foot view slides of kind of highlighting our position on some of these various issues. Mainly, as a courtesy to NIOSH, to let them know where we stand, what's coming and to inform you all before the meeting next week.

Harry, do you have access to Live Meeting or would you like me to run through, just flip the slides for you?

DR. CHMELYNSKI: That would be better if you could do that.

MR. STIVER: Okay, let me try to take over here. Okay, can everybody see that?

MEMBER ROESSLER: Yes, I can see it.

MR. STIVER: Okay.

MEMBER ZIEMER: We also have

these slides, you distributed them.

MR. STIVER: Right. Yeah, we could do that. I thought it might be a little easier for some of us who are on Live Meeting to do it this way.

MEMBER ZIEMER: Right.

MR. STIVER: Either way is fine.

MR. STIVER: As long as you have them you can follow along. So, anyway, Harry, we're going to Slide 2 here.

DR. CHMELYNSKI: All right. We've been preparing a review on what is known as the OPOS methodology, and up till now it's usually taken to mean “one person, one sample.” But that's a little confusing because each person has lots of samples and what we're really talking about is one person, one statistic derived from those samples.

And, in the simple case, the statistic we're talking about is just the average if there's no non-detects. Now,

OPOS was introduced by NIOSH to address two main problems that they introduced called data dominance, where a large number of samples from a few workers may skew the distributions. And there's also a problem with correlation. If there are a lot of samples taken one after each other, they would be correlated.

So we examined this problem and how extensive they were at the two sites where OPOS has been applied, which is Savannah River and Fernald. I'm moving on now to the next page.

And when there are non-detects, OPOS is to be calculated using what was called the maximum possible mean. And this algorithm that I put here, “Step 1-2-3,” is taken out of one of the documents that is used by the analyst to construct the OPOS values for the sites where the methodology is being applied now.

And the Step 1 says that we're

going to use the MDA for all data that's reported less than the MDA.

Step 2 says if all of the samples for a worker are below the MDA, censored, in other words, then we have to treat the answer, the mean, for OPOS as a censored value.

And Step 3, if any of the data are uncensored then we do the same calculation, but we treat the mean as a measured value.

This is probably the most convenient way to define what OPOS is. When we looked into how this procedure was implemented, though, we found some problems, particularly in Step 1. What we found was, a lot of cases, they don't explicitly have the entry as less than some number.

They may have a zero there or they may have a negative number, or they may actually have a number which, if you look down the column, they all say 0.1 and the

rest of them are all less than 0.1, but this one nobody put the less than next to.

So there's lots of ways that data can be censored in the database, although sometimes not explicitly censored. And what we found is that unless there was actually a notation that said less than 0.3, or something like that, the number was actually taken at face value and used in the calculation for the maximum possible mean.

And this happened both at SRS and at Fernald, on occasions, so we're concerned that this can lead to some very strange answers, including negative answers, which, according to the algorithm, probably should be computed as non-detects.

But sometimes these numbers have remained in the calculations all the way through to determining what the coworker models should be. So that was one of the problems with implementation of the OPOS algorithm.

The second application we were looking at is how OPOS is used to compare groups of workers. And our main concern here still applies.

We had this as a finding in our old report, which is when you're comparing two groups of workers and these workers were monitored using a different monitoring program, trying to use a hypothesis test to compare the two sets of data seems to me not to make much sense.

It's really a case of apples and oranges in a lot of cases here, especially, in particular, the comparison that we concentrate on is comparing onsite workers with contract workers. And a lot of times the contract workers weren't monitored the same way as the onsite workers.

So, this problem remains that we've addressed previously. A new issue, though, that has come up in response to NIOSH's response to our review, is that

there is a justification that they present for why you should use OPOS.

And now we've changed the name, really. OPOS is now -- we're going to refer to it as the mean excretion rate, because that's what we're trying to estimate when we take the average of the results for the period. We're trying to find a mean value.

And NIOSH came up with this argument that says, well, if you do the right regression problem and you use the right weights, you can show that the mean excretion rate should be proportional to the intake.

Of course, we're trying to find the intake from these mean values, or from all the values, however the best way would be, but the answer that they came up with was that we should be able to use just the mean because it is proportional to the intake.

We reviewed the source of this

calculation and we found that there are several problems with it and Joyce will address these later when we get to them.

But, for now, let me just say that both OPOS and the weighted least squares approach ignores the timing of the data during the year. And this sometimes is important and sometimes not. Weighted least squares also ignores the timing of the bioassays. But when we use the word “mean excretion rate,” I think what we're talking about it the time-weighted average year excretion rate over the year for the worker, and that we would think of OPOS as a statistic trying to estimate that mean.

On the next page, then, this is Page 8, there's an example of when OPOS will work well. And here's a curve that's presumably due to some exposure early in the year and it purports to be the concentration in the urine of the worker on each day of the year as you go across the curve.

Now, if we were to monitor this worker, say, eight times during the year at nice, equally spaced intervals and then take the average, the average we get is actually equal to the mean value of this under this curve.

And, in fact, it's probably one of the best known ways of doing an integral, which is to do the Riemann sum and say, ah, that's what you can get when you do the integral.

I've normalized the X axis so that it's all one year. It could be two years in some cases, but as long as you use one year then the area under the curve is equal to the mean.

And in this case you see the actual calculation of the true mean, which is -- this is a cubic function and I was able to do the integral. It comes out very close to what the Riemann sum, or the OPOS calculates.

I'm going to go to the next slide, though. We see that the picture is a lot more complicated than thinking about equally spaced bioassay collections in time.

And what this graph shows is how many days we found between successive bioassays for plutonium for any given worker and the frequency count, basically, of how many of them had 30 days between them, 90 days, et cetera.

And you can see pretty clearly that while there's a tendency to have testing done every 90 days in that first spike, or every 180 days, that's half, two a year. The next one is four a year, and even out there at 720 you can see where sometimes it's every two years. But the point of this slide is that, in general, we don't know that these workers were being sampled on any regular basis.

This is particularly true for the construction-type workers who may be in and

out of the site a lot and may only be tested for a particular reason, if something turns up.

Given, then, that we don't believe that there were these nice, regularly spaced sampling for most workers, we can then think about, well, what is OPOS telling us if it's not telling us the integral under the curve?

Well, there's another way to think about it, which is if they are random sampling times then really what we've done is we've sampled at eight points along a curve and those points are just like taking a Monte Carlo integral to determine what the area under this curve is.

And that kind of calculation, usually you use a lot more than a handful of bioassays, such as we're doing here. Here, I think, you know, eight to ten is about the most you would reasonably see for any worker.

But, still, you can think of it as a Monte Carlo approximation to the integral with just a small number of iterations, maybe eight or even less.

And if you do that, then, you can put some statistical statements on what the precision of your estimate of OPOS is, thinking of it as a Monte Carlo estimate of the integral.

And, of course, as we already know, what you're going to end up with is the Student t-distribution, tells you what the confidence bounds are for that estimate of the mean. And, in particular, it's a Student t-distribution within minus one degrees of freedom, which we always have to keep in mind here because when we're staring to take averages of three or four samples that gets us into problems.

The next page has some formulas for how you do the calculations for the upper bound and the lower bound, so I'm not

going to get into those. But, basically, if you just look at the picture that I drew here with the samples, eight samples, and I did calculate according to these formulas what the confidence bounds were.

If we go back to page, what was that, Page 10. And you see the confidence, the 95 percent confidence bounds almost span the whole range of the data here. Well, not all the way up to the top.

But we have eight samples here. Now, if you only had four, those confidence bounds would go beyond the range of the data. So it just makes me wonder why we put a lot of confidence in this number that we call OPOS, especially, as we're going to see soon, almost 95 percent of the time we're doing it with four or less samples.

At any rate, that was some of the concerns we've had going into this and I think maybe Joyce can start with the rest of these slides and give an overview of what

her concerns were.

DR. LIPSZTEIN: Okay. John, please continue with the slides, I can't do it from here. We are on Slide 13 and I think some of this in this slide Harry already was talking about.

So, OPOS was designed to address the presence of data dominance, which is a large fraction of samples being submitted by a small fraction of individuals, and correlate the date where multiple samples submitted by individuals can be correlated, which greatly complicates the use of statistical tests.

Then we go to Slide 14. And we wanted to know how relevant is the problem of data dominance. And we wanted to know if a large number of incident-related samples from a few workers would skew the distribution use for coworker modeling. And we wanted to know how frequently do we find data dominance in the DOE facilities. So

that's why we looked at SRS and at Fernald.

The next slide, Slide 15, we can see that -- and Harry already told this -- that in over 95 percent of the cases where OPOS would be applied at SRS, the workers have no more than four to twenty bioassays in the period. We did this for all the radionuclides that we examined, and there's very few cases where you would have workers with more than -- we saw a lot of samples with more than four bioassays.

And then we looked at data dominance at Fernald. So at Fernald we have one coworker model that was done in 2012 using the coworker method. And we have the Version 1, which was done in 2010 and was done with the old methodology.

So we could have both of them to compare, and they are relatively new: 2010, 2012. What we found out is that on the Revision 1 samples, code 50, which are samples that were taken on special jobs,

implementations, they were not considered in the Revision 1 2010, but they were considered in the OPOS methodology.

And the accident-related samples, which were codes 40 and 49, were analyzed in both versions of it. And then we compared the 50 percent and the 95th percentiles intake rates derived in Revision 1 and Revision 2, and we wanted to know how the addition of samples code 50 would influence or not these intake rates.

And what we found was that there was no relation. It's not sometimes and some years, the OTIB 2012 had a higher intake rate than the one in 2010, but many times the 2010 had higher intake rates than 2012.

And this was not related at all to the number of samples code 50, and also it was not related to the code 40 and 49, years that had more samples than codes 40 and 49. You couldn't establish a

relationship between those samples.

So then we aimed to see what was the problem of correlations. The fact that some workers have more samples than other workers in a given time period is not itself a basis to establish correlation.

We looked at both coworker models, Revisions 2012 and 2010, and they both cite the main -- the same problem of data dependence. And they explicitly, for example, in the OTIB, the coworker models from 2012, it's explicitly exemplified that they take some -- in order to derive the intakes for 1994-2006 periods.

Early intake rates significantly biased later intake rates for all solubility types of uranium compounds. So the problem of data correlation doesn't end with the use of the OPOS. You still have correlated data whether there is accidents or there is routine exposure, it doesn't matter, you always have data correlation when you have

internal exposure.

Then we went to the problem of using weighted least squares to justify the OPOS. The problem is that if you go from the beginning, in order to justify that it's been -- that the mean excretion rate would be proportional to the mean intake rate, you have to go to least square using weighted least square.

The problem is that the weighted least square is only justified applying when there is one intake. And we have this explicitly said in MCFB 164 2003 13. We also have that explicitly said in IMBA application also.

And it all starts with the equation that you have to calculate the intake, and so in certain special circumstances you can say that the mean excretion rate would be very special circumstance, as you saw in Harry's slides.

You can say that the mean

excretion rate would be proportional to the mean intake, but that's excretion rates that are related to that intake. You cannot take the whole year intakes and take the means because then -- okay, Slide 19 is what IMBA says.

But then you can see you cannot take the mean excretion rate to be proportional to intake when you mix times in the year, times that there were no intakes with times that there were intakes.

What happens if you have a worker or a facility where the monitoring was very heavy so you have frequent monitoring for the workers before the incident or the special job? Then you have a smaller OPOS. If you don't have any monitoring before the incident or the special sample, then the OPOS which would be much higher.

So what happens is that the OPOS, in reality, if it's taken on a year basis, it would be proportional to the frequency of

monitoring. This you can see on Slide 20.

The complication of OPOS for year average urine activities collected from periods of no intakes lumped together with activities from periods with intakes.

The consequences are strong dependence on the frequency of the monitoring, in addition to the number of significant exposures. We did an example that you will see on our paper, we took some people from Fernald that were exposed in the same incident. There was an incident in one of the years that we took as an example, and we compared, there were three workers, one worker was only monitored during the incident, but just one time.

Then there was another worker that was monitored during the incident but he had several monitoring during this incident. And then we had the worker that was monitored many times in the year before the incident.

And so the same worker worked in the same incident and we could find that those workers had similar exposure in this incident. The OPOS of the person that was heavily monitored before the -- routinely monitored before the incident, had the smaller OPOS.

So what I mean with this is that when you average the OPOS over the year there is a dependence on the frequency of monitoring.

And, for the same reason, when you compare two groups of workers, if one group of workers is only monitored when there are some kind of incidents or special jobs and is not monitored before, and then you have a group of workers that's been monitored both routinely and when the special job is done or the incident occurs, then you cannot compare the two. Because in one of them you were just comparing the incident or the special job, and on the other worker you

were taking into account also the routine monitoring from when he was not exposed. So, that's it.

CHAIRMAN MELIUS: Okay. Anybody have questions?

MEMBER ZIEMER: Well, this is Ziemer. I --

CHAIRMAN MELIUS: It is difficult to -- I mean, I'm actually finding it very hard to ask questions. It's very hard to understand this kind of report from a slide presentation.

DR. MAKHIJANI: Dr. Melius?

CHAIRMAN MELIUS: Yes?

DR. MAKHIJANI: It might be helpful maybe if I can give you a bottom line of where our team wound up in regard to OPOS.

MEMBER ROESSLER: That would be helpful.

DR. MAKHIJANI: So, this is still in the final wordsmithing stages, but I

thought it might be helpful if I read you the words that we have in the final draft.

The use of OPOS on an annual or other fixed period basis, the way NIOSH has now constructed it, as a general matter does not appear to be scientifically justified.

The use of pooled, individual bioassay data is recommended despite its known drawbacks. When there's clear evidence of data dominance the samples related to a particular incident may be averaged to provide a single composite data point to be inserted into the distribution of the pooled data.

So, the bottom line from Harry and Joyce have been saying is that there are some times when you would want to combine samples, but you don't combine them on a fixed period or an annual period or any other period when you have incident-related samples that are clearly auto-correlated, then you will combine the samples related to

that incident into one data point because it's really relating one intake.

And then you put that into the distribution of pooled data. And so you have a mixed distribution that consists primarily of individual bioassay samples that would have some data points that are OPOS-like data points, although not as defined by NIOSH.

They'd be one person -- one incident, one statistic, you might say, points inserted into a distribution of bioassay samples. So, that's where we wound up.

CHAIRMAN MELIUS: Okay. Thanks for the summary, Arjun. Any questions or comments, Board Members?

MEMBER ZIEMER: This is Ziemer again. I assume we're going to get the detailed report, as will NIOSH, and then we will have a chance to study it.

CHAIRMAN MELIUS: Yes, that's --

definitely.

MEMBER BEACH: This is a lot to take in. This is Josie.

CHAIRMAN MELIUS: Yeah, yeah. No, I agree.

MEMBER ROESSLER: And I'll echo that. I guess my question is does -- I couldn't understand it all as they went through it. Probably the first part was easier to understand, but if NIOSH understands it and can respond then I think we can evaluate it.

CHAIRMAN MELIUS: Well, I think we need a report to be able to --

MEMBER ROESSLER: Exactly.

MR. STIVER: This is John Stiver. That report should be in your hands within a couple of weeks.

CHAIRMAN MELIUS: Okay.

MR. STIVER: And I agree, it's a lot to try to assimilate, and the report goes into -- well, it's more detailed. It

will be easier to understand once you're able to go through the entire thing.

DR. MAKHIJANI: Well, John, there's going to be a DOE review, so, you know, it's going to take -- it may be a little more than a couple of weeks.

CHAIRMAN MELIUS: Okay.

MR. STIVER: Two weeks is probably, maybe optimistic.

CHAIRMAN MELIUS: Okay.

MR. STIVER: We are kind of captive to how quickly DOE can get to it.

CHAIRMAN MELIUS: Okay. Then you have to give us time to read it. We'll figure out a schedule on that. Jim Neton, do you have anything you want to add?

DR. NETON: No. We discussed this late yesterday like everyone else. So I haven't had time to really think about it too much.

CHAIRMAN MELIUS: Okay. I want to go back to -- well, I guess, first of

all, on this report, this set of slides, I would have severe qualms about using this at the Board meeting, because it -- I would rather put that off until the Work Group has had a chance to review the report.

I don't think it's fair or appropriate and I think it's going to sort of confuse issues until we've had a time to look at it and respond.

I don't know if any of the other Work Group Members feel differently, but --

MEMBER ZIEMER: This is Ziemer. I agree with that completely, and I think the only thing you need to report to the Board is that SC&A is completing a review of the OPOS methodology and we expect a report. That we had preliminary discussion at this meeting, but we expect a report in a few weeks and it'll be analyzed at that point.

CHAIRMAN MELIUS: Yeah, okay. And, Jim Neton, what do you feel comfortable presenting, if anything, at the Board

meeting? I mean, should we just give an update that, you know, you've received, you know, you're progressing on your report and SC&A is, you know, progressing on their deliverable and we're going to, you know, be getting those sometime in the relatively near future and then we'll have a Work Group meeting and then be able to report back?

DR. NETON: Yeah, I would be most comfortable with that.

CHAIRMAN MELIUS: Yeah. As interesting as it is, and it's going to --

DR. NETON: It almost raises more questions than it answers.

CHAIRMAN MELIUS: Well, yeah. That's what I'm concerned, and without having it in a report with, you know, sort of explanation and so forth I think it's hard. And in a Board setting, though, I think that a lot of the other Board Members would be interested.

Paul, Josie, Gen, does that --

MEMBER BEACH: This is Josie. I completely agree with that approach.

MEMBER ROESSLER: I do, too.

MEMBER ZIEMER: Yeah, this is Ziemer. I do, too.

CHAIRMAN MELIUS: Okay. I mean, in some ways it's tempting to move forward, but at the same time I think it's hard to that until NIOSH has had a chance to analyze and we have a chance to review and discuss it and so forth and try to bring these reports together to the extent that we can.

So, maybe -- I can't remember how long we set aside on the agenda. It'll give us a little bit more Board work time, but that may be fine.

So, any other business? Ted, anything we need to --

MR. KATZ: No, this all sounds good. And we only have a half an hour set aside for this anyway, so we can easily cede that back to Board work time.

CHAIRMAN MELIUS: Okay. Good, yeah. Okay, anyway, in that case, I thank everybody for their work and the presentations of the data and we will look forward to seeing everybody, at least a number of you, next week in Kansas City.

MEMBER ROESSLER: That depends on whether the blizzard hits Minnesota again on Monday.

CHAIRMAN MELIUS: Is there another one coming?

MEMBER ROESSLER: Yes. I'm getting kind of tired of this.

CHAIRMAN MELIUS: I confess I looked at the Kansas City weather the other day. It looked like it was going to be cold. I didn't see snow in the forecast.

MEMBER ROESSLER: Well, I thought it looked wonderful.

CHAIRMAN MELIUS: Yeah, we've been, you know, ten below or 20 below the last few days, so some sympathy. But the

snow, our snow ended up in New York City and south entirely. The latest snow storm, anyway. But I cringe every time I hear about what's happening up your way, Gen.

MEMBER ROESSLER: Yeah, but at least we don't have as much snow, but it blows and that's then the problem and it reduces visibility to nothing and it's hard to drive then.

CHAIRMAN MELIUS: Yeah. No, it's hard, and I know, Paul, Indiana's been hit.

MEMBER ZIEMER: Yeah. We're cold and below zero, but we're surviving.

CHAIRMAN MELIUS: Okay, good, everybody. And even down in Atlanta I think it's been cold, Ted.

MR. KATZ: I don't think we get any sympathy though.

CHAIRMAN MELIUS: No, you don't. I had a very irate phone call once when I was working for NIOSH from the State Health Officer in North Dakota who couldn't

understand why nobody was answering their phones at CDC in Atlanta.

And he had looked at the weather and, you know, all they had had was an inch of snow, and he couldn't believe that they were closed down for two days in row. And had no sympathy. He was trying to track down some result from something.

MEMBER ROESSLER: Well, you know, it has to do with the amount of traffic that tries to move, too. In North Dakota there's not that much.

CHAIRMAN MELIUS: Yeah. It's also, I don't know if Atlanta's any better, but my experience down there used to be that they had no snow, you know, equipment at all and no salt to melt the ice and so forth. On top of bad traffic.

MEMBER ZIEMER: Yeah, we'll see how Kansas City does.

CHAIRMAN MELIUS: Yeah, hopefully. So, anyway, we'll look forward

to seeing everybody in Kansas City next week. Thank you all for your time.

(Whereupon, the meeting was concluded at 12:06 p.m.)