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NUCLEAR REGULATORY COMMISSION

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188TH MEETING

ADVISORY COMMITTEE ON NUCLEAR WASTE AND MATERIALS

(ACNW&M)

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WEDNESDAY

APRIL 9TH, 2008

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ROCKVILLE, MARYLAND

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The Advisory Committee met at the Nuclear Regulatory Commission, Two White Flint North, Room T2B3, 11545 Rockville Pike, at 8:30 a.m., Dr. Michael Ryan, Chairman, presiding.

COMMITTEE MEMBERS:

MICHAEL T. RYAN, Chairman

ALLEN G. CROFT, Vice-Chairman

JAMES H. CLARKE, Member

RUTH F. WEINER, Member

PANEL MEMBERS PRESENT:

MARY HELEN BARCELLOS-HOFF,
Lawrence Berkeley Laboratory

BERNARD LE GUEN, Electricite de France

JAMES K. HAMMITT,
Harvard School of Public Health

VINCENT HOLAHAN, NRC RES

CHARLES LAND, National Cancer Institute

KENNETH MOSSMAN, AZ State Laboratory

JEROME PUSKIN, EPA

THOMAS TENFORDE, NCRD

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

8:38 a.m.

CHAIRMAN RYAN: I'll go ahead and get started, please, so the meeting will come to order. This is the second day of the 188th meeting of the Advisory Committee on Nuclear Waste and Materials. During today's meeting, the Committee will continue with the working group on the effects of low radiation doses. At the end of the day the Committee will consider and discuss ACNNW letter reports on other topics.

This meeting is being conducted in accordance with the provisions of the Federal Advisory Committee Act. Neil Coleman is the designated federal official for today's session. We have received no written comments or requests for time to make oral statements from members of the public regarding today's sessions. Should anyone wish to address the Committee, please, make your wishes known to one of the Committee staff.

I believe we have the bridge line open, Mr. Brown? So the bridge line is open if callers want to call in. We'll have them announce as they arrive.

It's requested that speakers use one of

the microphones, identify themselves, and speak with sufficient clarity and volume so they can be readily heard. It's also requested that if you have cell phones or pagers that you kindly turn them off at this time.

Feedback forms are available at the back of the room for anyone who would like to provide us with his or comments about the meeting.

Thank you all very much.

Our session today will build on the activities that we had yesterday. We have three presentations schedule. One, first, by Professor James Hammitt, from the Harvard School of Public Health, on an economic perspective on regulatory decision making, benefit versus cost on the linear and nonlinear models. We're interested in that topic.

Dr. Jerry Puskin, from the United States Environmental Protection Agency, will give the U.S. EPA perspectives. And Dr. Vince Holahan, from the U.S. Nuclear Regulatory Commission staff, will off the NRC staff perspectives. That will be the morning session.

We will have a lunch break and then a panel discussion among all participants from both days for a time and then some time is allotted for any

stakeholder's views, comments, or perspectives that will be offered at the end of the day. Then we'll close somewhere around 4:00.

So, without further ado, let me turn the microphone over to you, Professor Hammitt. Welcome and thanks for being with us.

PROFESSOR HAMMITT: Thank you.

CHAIRMAN RYAN: I guess we can get you right up front.

PROFESSOR HAMMITT: Up here?

CHAIRMAN RYAN: Yes, that's fine.

PROFESSOR HAMMITT: I'm glad to be here and disappointed to have missed yesterday's discussions. I was hoping to learn a lot from that.

So what I'm going to do today is talk about sort of an introduction, and for many of you a review, of the basic economic perspective on decision making with regard to risks. And then I'm going to illustrate with several contexts for the discussion, building up from the very simple case where we're making decisions for a single individual and we know the exposure response function to the more complicated situations where we're making decisions for a population and we don't know the exposure response function, which is, of course, more realistic, and

then illustrate with a simple example involving radon and drinking water.

The objective of economic decision making, our economics assumes the objective of decision making is to maximize well being, and individual well being depends, of course, on health, but on other things we care about, education, housing, food, entertainment, many others. The objective from an economic perspective in setting exposure level, for example to radiation or something else, is both to minimize the harm and/or maximize health benefit and also to minimize control costs.

So this requires inherently that we're making tradeoffs between smaller risk of harm and greater control costs so you have to face up to the tradeoff of what incremental control costs justifies what level of reduction in health risks. You have to compare the benefits of better health to lower health risks with the costs of control.

And the way this is done is to put a monetary value on risk production or health improvement, and that monetary value is often described as willingness to pay for the improvement and it is defined as if somebody pays money to have a smaller health risk, that's money he could have

otherwise used for other purposes so he's foregoing other things he cares about, that are housing or whatever, and so the maximum value of those foregone alternatives is the willingness to pay for the health improvement.

In choosing regulation for population, the general framework is to try and maximize the sum of benefits minus costs where the health benefit can be calculated as the product of the number of people affected by the regulation times their average willingness to pay for the individual risk reduction each faces. And often this is done in a short hand of the expected reduction in the number of cases of cancer or premature fatality multiplied by the value per statistical case.

So if willingness to pay is proportional to the reduction in the probability of harm, as it should be under most theories, then you can have either many people paying a small amount for a small risk reduction or you can -- mathematically that's the same thing as a value for each case avoided times a large value for each case.

What I'm going to do just to focus ideas is focus mostly on the contrast between a linear no-threshold model and hormetic dose response exposure

response function. And the thing that's really critical here is if, as in the usual case, we have data on exposures at some relatively high level and we measure harm or probability of harm at that relatively high level, over on the right hand side of the screen, and we know that at no exposure there would be no harm. So we have an interpolation problem, but we can't observe harm or probability of harm in the range we care about.

And then on the hormetic function, I want to define two points, what I call e_0. e_0 is the exposure level where there's zero effect or the same health effect as there would be at zero exposure. And then e_M is the exposure level at which the health effect is minimized. And then of course a threshold exposure response function could be very similar to this hormetic line over this range and then simply flat over this interval.

But what I wanted to say is, if this is the case where we observe harm at this relatively high exposure level, are interpolating down to 00, then it must be the case for the hormetic exposure response function or a threshold response function the exposure response function is steeper in some range of exposures than the linear, and, of course, flatter

than the linear in other ranges of exposure.

So now the optimal exposure for an individual in the very simple case where we know exactly the exposure response functions just to fix ideas. In the linear case, I have in mind e_U as the uncontrolled exposure level. So at this level there is no control costs because we're doing nothing to control exposure, and there is some harm or probability of harm, and I'm measuring this in monetary units.

If we think of reducing exposure, the costs of control will rise and typically rise at an increase rate of the convex function of the exposure reduction, and the harm or probability of harm will fall at a linear rate under this linear model. So what we want to do is minimize the sum of control costs and expected harm, that's this line, and the exposure level that does that is what I've called e_L*, which is the minimum of this curved line.

With the hormetic exposure as Fonds function, the analysis is the same. It's the same cost function, a different exposure response function. If you sum those and find the minimum cost plus health harm point, it's this level eH*. And then if I combine those two graphs just for comparison, you can

see the optimal control level is different under the two exposure response functions, logically enough.

In this case, the linear no-threshold model suggests more exposure reduction, a lower optimal exposure level than the hormetic response function, but that doesn't follow necessarily. It's just true in this illustration.

Another way to do this analysis is to think in terms of marginal or incremental benefits, meaning incremental reduction in health risk and increment cost. But here, again, now I have this marginal, think of derivative. The comments always say marginal when they mean incremental or derivative or slope, marginal harm, marginal cost and exposure.

So starting at the uncontrolled exposure level again, there is zero cost of control, and because the cost function was becoming increasingly steep as we reduced exposure more and more, the incremental cost of more stringent control is rising. And in a linear model, the incremental benefit of reducing exposure is constant. The linear exposure response function has a constant slope.

So if you start out here at the uncontrolled level, the incremental benefit from reducing exposure a little bit is much larger than the

incremental cost. So it would be a good idea to reduce exposure until you get to some point where they're about equal or exactly equal. If you go beyond that point, the incremental cost incurred through more stringent control exceeds the incremental benefit in terms of reduced risk, and so that would be excessive control. So, again, the way to identify this optimal exposure level is where the marginal benefit and marginal cost curves intersect.

Same analysis for the hormetic response function. And here, you see this is higher than in the linear case because, remember, at the high exposure levels the exposure response function has to be steeper than the linear curve. At some point, I guess this is what I called e_M before, the slope of the hormetic exposure response function is zero. So the marginal benefit of incrementally reducing exposure around this level is about zero. Down in this region, this is where the exposure response is downward sloping. So reductions in exposure would be harmful in a health perspective.

And so the optimal exposure levels where marginal benefit and marginal cost intersect here, and put these together on the same graph, and, again, you see eH at a higher exposure level than e_L*. For this

example, if I keep the exposure response functions exactly as shown here, but assume the cost and control and the marginal costs and control are higher, this dash line, now the optimal control level under the linear model is here, e_L*, the optimal exposure level under the hormetic model is here, eH1*, and so you see the hormetic response function calls for more stringent regulation, larger exposure reductions than the linear model and that is because this is a situation where the incremental costs of control are pretty high so it's only worth controlling a little more when the incremental benefits are pretty.

And in this high exposure region the incremental benefits control are steeper under the hormetic than the linear model because the hormetic exposure response function, and similarly a threshold response function, are steeper at these high exposure levels.

CHAIRMAN RYAN: Just a second, Dr. Hammitt. My apologizes for interrupting, but we need to announce the caller.

Could the caller identify who you are, please?

MR. EHRLE: Lynn Howard Ehrle.

CHAIRMAN RYAN: I'm sorry. Say again?

MR. EHRLE: Lynn Howard Ehrle.

CHAIRMAN RYAN: Good morning. Thanks for joining us. Dr. Hammitt?

PROFESSOR HAMMITT: Thank you. So now let's go to a slightly harder and slightly more realistic problem. A decision again for an individual, but we don't know exactly what the exposure response function is. And here the standard economic decision theoretic perspective would be to assign probabilities to the different possible truths about what the exposure response function is, and then use that to calculate expected harm, so the harm conditional -- here, let's assume the exposure response function might be either the linear or the specific hormetic function I showed in the previous graphs, we think there's a probability p that the linear model is most accurate. A complimentary probability, the hormetic model, is most appropriate.

The expected harm is just p times the harm if the linear model is right, plus 1 minus p times the harm fits the hormetic model is right. Obviously, estimating these probabilities is not easy, but, conceptually, this is what one would want to do and there are practical methods for estimating these kinds of probabilities.

The expected marginal benefit is just p times the expected marginal benefit in the linear case, and so forth. And then the optimal exposure level will be between the linear and hormetic solutions. It's going to be some sort of a weighted average of the two. The weight obviously depends on what the probabilities are assigned to the two exposure models and, also, the marginal harms of the alternative models.

So here is the graph I already showed with the marginal benefit of exposure reduction under the hormetic and linear models, the marginal costs, and the optimal exposure levels conditional on each model being accurate. This line, now, is the expected marginal harm in the case where we assign probability 0.3 to the linear model being correct and probability 0.7 to the hormetic model being correct.

So this line is always between the two and it'll be roughly twice as far from the linear model as the hormetic model for this value of p. And so the point where the expected marginal benefits are equal to the marginal costs is e* between the two models, the two exposure levels that are optimal in the case where we know exposure response function for sure.

So as that last graph shows, what's really

critical is the slope of the exposure response function, the marginal benefit, the marginal health risk reduction associated with reducing exposure. So the question is, how similar is the slope of either a threshold or a hormetic exposure response function to the linear model?

Well, we don't know in general, but one thing we can say is that think of the average slope of the hormetic exposure response function -- I mean threshold function between the uncontrolled level and this level e_0, which is either the threshold or the level at which there is no harm under the hormetic model. And the average slope of the hormetic function will be equal to the slope of the linear model divided by this number.

So think about if e_0 is very, very small compared with the uncontrolled level e_U, this fraction is close to zero, so we're dividing by something close to one, so the average slopes will be roughly equal. And in that situation, uncertainty about whether there's a threshold or not doesn't really matter because it doesn't affect the slope of the exposure response function in the region that may be condition on costs being high enough such that the optimal control level is in this region higher than e_0.

Contrast if e_0 is pretty large, compared with the uncontrolled level, this fraction can never be bigger than one, but it could approach one. And so we would be dividing by one minus something close to one, and so the average slope of the hormetic response function would be much steeper than of the linear response function. And then it might, uncertain about which exposure response function is accurate, could have a big effect on the implied optimal degree of exposure.

And then, of course, if the exposure is smaller than e_0, then with a threshold case we're on the flat of the curve; with a hormetic case we may be in an area where reducing exposure is even harmful to people. In that region, knowing which exposure response function is accurate is clearly critical to knowing what exposure level is appropriate.

So the real problem we have is a population level decision where both the exposure levels and the exposure response functions may differ between individuals. Also, they are uncertain. We don't know exactly the exposure response function. We don't know exactly any individual's exposure.

And one implication of this is we can't write a rule that will ensure the optimal exposure for

every person. Now, the social choice problem of balancing benefits to some people against harms are foregone benefits that we could have provided to other people instead.

Under a standard economic perspective, economists assume there is no objective way to compare changes in well being between people, so we can't say objectively who suffers more from a certain disease or, you know, who bears more pain. So the kind of minimal idea that's accepted is the idea of Pareto improvement. If we can have a policy change that helps some people and hurts no people, that's defined as a Pareto improvement and we, more or less, all agree that that's a good thing.

The caveat there would be it could increase inequality. So something that improves the well being of the very wealthiest, something that improves the well being of Bill Gates had has no effect on anybody else in the country would count as a Paredo improvement even though lots of people in the country might think that's a bad thing socially.

(Laughter.)

So that doesn't get us far. We're rarely in a situation where we can help some people and at least forego helping others instead.

So benefit cost analysis tries to identify what are called potential Paredo improvements. And a potential Paredo improvement is defined as a situation where the people who benefit benefit enough such that they could, in principle, pay monetary compensation to the people who are harmed. And after the compensation was paid everybody would consider themselves better off with the policy change and the compensation paid or received then without.

And so we talk about the Kaldor-Hicks compensation test as just the test for whether a change is a potential Paredo improvement, and the way this is done is you add the monetary value of the benefits across the people who benefit from a change, add the monetary value of the harms across the people who are harmed; if total benefits exceed total costs, then, in principle, compensation could be paid such that everybody would perceive themself as being better off. So that's the logic behind the benefit cost test.

Why is that a reasonable thing to do when this compensation is purely hypothetical; we're not suggesting it be paid? Well, there are two arguments.

One argument is that if we make many decisions over time using principles like this, the

people who gain in each particular case will not be the same. And so, in the long run, we, as a society, will all be better off making decisions on this basis rather than some other basis. And there's hand waving here because what is the alternative basis on which we'd make these decisions? It's not clear.

One thing to say is benefit cost analysis at least counts the preferences of everybody in the population. So, in that sense, it's more populous and egalitarian than something where just some elite decides or the classic politicians in the smoke-filled room decide in their own interests.

A better argument, I think, is that redistribution of resources can be handled more efficiently, more directly through means other than setting health regulations at a non-optimal level, things like tax programs, social transfers, and the like.

What I want to say here is, in calculating the population effect of some reduction in exposure, under the linear no-threshold model, we don't have to know anything about anybody's background exposure level because the incremental benefit of reducing exposure is the same regardless of the exposure level at which one starts. We know if we reduce everybody's

exposure by x, everybody will get the same incremental benefit.

Under the hormetic model, because the slope depends on your total exposure level, it's much more complicated. People who are at high exposure, if we reduce their exposure a little bit, will benefit. People who are at very low exposure, if we reduce their exposure, will either not benefit; conceivably, they will even be harmed. So we need to know how the exposure reduction correlates with the baseline exposure across the population.

Let me illustrate now with an example, just very simplified, doing violence to lots of detail. But I developed this example because there was a regulatory assessment published, a draft regulatory assessment, published by EPA associated with regulating radon in drinking water. And here, as I'm sure probably all of you know, the primary exposure pathway is that radon volatilizes from the water into the air and is then inhaled. That's a more important exposure source than drinking the water apparently. And then this was a good example for me because Ken Bogen had published a couple of articles in which he estimated hormetic exposure response functions for radon and air and the risk of lung

cancer.

So here the policy alternatives EPA was considering was to set a maximum contaminant level, or MCL, for community water systems. To estimate the benefits of different MCLs, what they did is estimated the distribution of radon levels in drinking water, calculate the reduction in radon in drinking water as a function of whichever MCL they chose, and then they estimated the change in indoor air concentration as 10,000-fold smaller than the change in water concentration based on models and measurements of how, essentially, the effect of drinking water volatilizing into the air and then being breathed in.

So in this table, what I'm showing here is potential maximum contaminant levels and pCi/l, 4,000, 2,0000, all the way down to zero. The population of people service by water systems with radon levels higher than each threshold, so 77,000 people, have drinking water with higher than 4,0000 pCi/l.

The population average concentration of radon is something higher than 4,000. I made up this 5,000 actually. But what this table shows you is that average radon concentration for the people above each concentration level. So you see, for the people above the highest concentration level, the average radon

concentration is quite high. For the people with any radon in their water, the average concentration is very low because most of the people have very low radon concentration in their water.

And then this shows the incremental reduction on average radon concentration water as a function of the MCL chosen. So for these high MCLs, there's a big reduction in exposure to the small number of people affected. For the lower MCLs, there's an, on average, small reduction, but applying to many, many more people. That is just obviously the distribution of radon drinking water is highly skewed.

This illustrates a graph from one of Ken Bogen's papers where this is his estimate of a hormetic exposure response function. I've superimposed his threshold exposure response function on that, and this is linear exposure response function with which he compared.

You see here the lowest point on the hormetic function is at a level of about 5 pCi/l. This is indoor air concentration now. It's a relative risk of lung cancer.

Now it turns out that only five percent of household levels have radon levels indoor exceeding the EPA action level of 4 pCi/l. Distribution of

radon in indoor air, residentially, is roughly lognormal, geometric mean, geometric standard deviation, 98th percentile six-and-a-half. So almost everybody is in this region where their exposure level is close to 5, maybe even below 5. So under that specific hormetic exposure response function reducing exposure would be reducing a beneficial effect to these people.

And under the threshold function, reducing exposure would have no benefits to these people. So that, of course, makes the policy decision very simple if we believe either of those exposure response functions that no regulation would be justified because we're doing essentially no benefit and incurring costs.

So to make a more interesting problem I imagined some community with very high background radon in their air and, specifically, I'm assuming 25 percent of the people have only 2 pCi/l, 25 percent have 5, 25 percent have 10, 25 percent have 15. And then relative slope of the hormetic exposure response function relative to that for the linear no-threshold model is for people at roughly the 5 exposure level, the hormetic function is flat, zero slope. People at lower exposure have a negative slope, so reducing

their exposure would be harmful. And then for people at high exposure, this function is steeper than the linear model, and the average is about 2. So on average where just seeing exposure to this population would help some people a lot, have no effect on others, hurt some people some, on average the total risk reduction would be twice as large as it would be under the linear model.

Then here I'm plotting -- should have reversed the X-axis on this -- but here, going from left to right, is increasing regulatory stringency reducing the MCL and the black curve is the costs. These increase at an increasing rate as expected. It turns out here the benefits under the linear model, the blue, and under the threshold model, the green, are almost exactly equal and that comes about, I guess you can see it here, under the threshold model this -2.8 becomes a zero. So we're averaging 001.8 and 2.4 and the average of that is pretty close to 1 it turns out. And so that's why we get the linear no-threshold and the threshold model having roughly equal benefits of exposure reduction in this case.

Under the hormetic model, we have lower benefits because reducing exposure helps some people, but is harming others. So on that it's doing less

good.

This is here the total benefits under each model and the net benefits, benefits minus costs. And then I've highlighted the optimal control levels under the different models. Under the linear no-threshold model, a 1,000 pCi/l would be the optimal MCL. Under the hormetic function is a little bit less stringent. Under the threshold it happens to be a little more stringent.

Obviously, there's some kind of jumpiness in this because I just have different increments of control level. You'd want to do this better by having a more continuous function of the MCL.

Now, to deal with uncertainty about which exposure response function is correct, I said before what we want to do is calculate the expected benefits as the sum of the probability that each exposure response function is accurate times the harm if that response function is accurate. So here, for example, I'll put probability 0.6 on the linear model, probability 0.4 on the hormetic model, and probability zero on the threshold.

And there, again, we have total benefits, benefits minus costs under each model, so the linear no-threshold and the hormetic are the same as in that

pervious charge, and then the expected benefits, the weighted average of these two, is here, and turns out in this case the optimal regulation would be the same as under the hormetic, the 2,000 pCi/l plus stringent and under the linear.

So just to conclude, the first point is economic evaluation can accommodate non-linear exposure response functions. There's no difficulty in principle. It's harder in practice because the incremental benefit of reducing exposure depends on the background exposure level of the people whose exposure is reduced. So you have to know the co-variation of background exposure and exposure reduction due to the regulation. Whereas, under the linear model, you don't need to know that.

Uncertainty about exposure response functions can be accommodated in principle by saying any of these might be true, and we assign probabilities which are a numerical statement of degree of belief in the truth of the model in this case to each and calculate the expected benefits.

So in a way that's just a generalization. When we say, you know, there's a risk of getting lung cancer from radon or something, in fact, an individual will either get lung cancer from radon or will not.

So already we're dealing with that probability. And at the individual level maybe this is stochastic, maybe this is deterministic, who knows.

When we back up a level and say, well, we're not sure exactly what the slope of the exposure response function is or even what the shape of it is, that's just kind of another level of uncertainty that we can assign probabilities to the different potential outcomes and aggregate in that way.

And then, finally, the last point is while many people think that threshold and hormetic exposure response functions necessarily imply that less stringent regulation is appropriate than the linear model, if decisions are made on the basis of maximizing benefits minus costs, that is not necessarily true because these alternative anomaly models will tend to be steeper in some parts of the exposure region than a linear model. And in that region it will be appropriate to reduce exposure more than would be appropriate under the linear model.

Thank you.

CHAIRMAN RYAN: Thank you. Any questions or comments from the panel members?

(No response.)

DR. TENFORDE: May I ask, do you have any

opinions about the Cohen research on radon where he did county by county modeling of concentrations and concluded there was some apparent hormetic effect?

PROFESSOR HAMMITT: Yes. No, I don't want to put myself forward as having any great experience in the epidemiology or the estimation of these exposure response functions. My interest here was in showing if you know or if you thought you knew what the exposure response function was, what you would do with that in terms of decision making.

MR. MOSSMAN: Dr. Hammitt, you mentioned with the LNT theory that you really didn't have to know the total background exposure. It was incremental exposure that was important. And I'm assuming that that's based on your assumption that the origin 00 is a measured point and that you were interpolating. But, in fact, we don't know what 00 is, and the reason why we don't know 00 is because we don't know the proportion of cancer incidents or cancer mortality that's attributable to natural background and natural background radiation is irreducible.

So, in fact, whatever you add, and particularly when you get at very, very small doses where the incremental dose is some significant

percentage of the natural background, becomes very difficult to identify what that value is. I understand what you are doing, but it may be a picky technical point, but the idea is is that 00 is not a truly measured point because you can't eliminate natural background to determine what actually is the cancer rate in the absence of radiation altogether.

PROFESSOR HAMMITT: Yes, but can we handle that by defining my axes as the origin is the natural exposure and cancer rate given the natural background exposure? And then I'm just talking about increasing the exposure of both natural background and increases in cancer risks above what it would be at the natural background.

MR. MOSSMAN: I suppose you could do that, but it doesn't completely eliminate the fundamental problem of understanding what the cancer rate is in the absence of radiation.

PROFESSOR HAMMITT: Right, right.

MR. MOSSMAN: I mean when we talk about -- you know, frequently LNT is interpreted when I look at zero, I'm looking at the cancer rate in the absence of radiation, when, in fact, you're not. You're looking at cancer rate in the presence of whatever the natural background rate is.

PROFESSOR HAMMITT: Right. And also in the presence of many other things that cause cancer.

MR. MOSSMAN: Right. And other things, right. But for smoking and other kinds of things, you can --

PROFESSOR HAMMITT: You can eliminate exposure.

MR. MOSSMAN: You can account for that.

PROFESSOR HAMMITT: Right, right.

MR. LE GUEN: This is a question about all compounding factors that you can have.

PROFESSOR HAMMITT: Yes. So doing the epidemiology and estimating these things is very difficult, I agree.

MR. LE GUEN: Yes.

MR. EHRLE: Mr. Chairman, I have a question for the doctor.

CHAIRMAN RYAN: Okay.

MR. EHRLE: And it is for the whole Committee. Why has this conference omitted a model that has been written about since 1990 and identified in Gofman's impressive book on low dose radiation that was compared favorably with BEIR V, and that is the super linear model. Ken Mossman skipped right over it in his delineation and citing of several models. He

omitted it. And now the conference has elevated the hormesis thesis to the same level as LNT and it's been subjected to numerous --

CHAIRMAN RYAN: Mr. Ehrle, that's a comment, not a question. Do you have a question?

MR. EHRLE: The question is, is there any way that you can deal with, objectively, the super linear or biphasic model?

CHAIRMAN RYAN: Okay. Does anybody want to answer that question?

PROFESSOR HAMMITT: I would say that in terms of economic analysis that can certainly be accommodated just like any other non-linear exposure response function. If you have a function and if you're willing to give some probability that it's valid, you would calculate the marginal benefits of exposure reduction under that function just as per all the other non-linear functions I showed.

MR. EHRLE: The reason I raise the issue --

CHAIRMAN RYAN: Mr. Ehrle --

MR. EHRLE: -- an opportunity to hear Tom Hay from Columbia who made this presentation at Mayo Clinic --

CHAIRMAN RYAN: Mr. Ehrle?

MR. EHRLE: -- to be up there --

CHAIRMAN RYAN: Mr. Ehrle?

MR. EHRLE: Yes.

CHAIRMAN RYAN: I'm sorry, but I'm going to have to ask you to hold your comments until the comment period later on, if you don't mind?

MR. EHRLE: Well, I doubt if I'll be here at that comment that and that's why I appreciate the opportunities to submit this query.

CHAIRMAN RYAN: Now is not the best time. If we have some time later in the morning, I'll certainly give you that time to make comments. But we need to press on to other questions.

MR. EHRLE: Okay. Thank you.

CHAIRMAN RYAN: Dr. Weiner, have you got a question?

DR. WEINER: Thank you. First, a comment. I don't know if you're aware of there is a recent paper by Thompson et. al. in I believe it's the next to last issue of *Health Physics* where he actually demonstrates the hormetic effect. It would be interesting to compare your thing.

PROFESSOR HAMMITT: Yes.

DR. WEINER: But my question is, how does the notion of perceived harm figure into this, and

when you have perceived harm, then the effect and the costs are no longer independent, or could be no longer independent?

PROFESSOR HAMMITT: Yes. Well, that is I think the central problem of health and environmental decision making and decision making under uncertainty. So from the economic perspective, well being is defined and assessed by individuals. So you can't tell me that in my preferences over health states and health risks should be determinative in principle.

But there is huge amounts of evidence that all of us don't understand probabilities very well, make all kinds of inconsistent decisions in the face of probability and risk. So some of those inconsistencies are clearly just mistakes, and if you point that out to me, I will say, you're right, I'm making a mistake, I was confused, you know, framing effects, things like that.

Some of them may not be mistakes, and sorting out which is which is critical. So in terms of -- I didn't really talk about this, but valuing health risk, we talked about value per statistical life and things like that. In principle, there's no reason why I could not have, for myself, a different value of statistical life or a different willingness

to pay for a probability reduction associated with different causes of death, you know, car crash, radiation exposure, terrorist incident, all kinds of things. There's nothing incoherent about that because those ways of dying are different and that might matter to me. I might be willing to spend more money to reduce one risk than another.

But, because we're not very good at dealing with probabilities and small probabilities and numbers in general, when you do surveys of willingness to pay and you ask maybe two different sets of people, what would you pay to reduce your chance of dying this year by 1:10,000, in a different group, what would you pay by 2:10,000, in theory you should get numbers that differ by a factor of 2 or very, very close to that.

Often you'll get numbers that differ by not at all or by 1.3, or something like that. So if you take those as valid responses, that says people would be willing to pay something for a 1:10,000 risk reduction but much less for another 1:10,000 risk reduction.

Do people really believe that? I don't think so. I think that's confusion.

Another version of that is we tend to like the idea that we could eliminate a risk, we could

eliminate the risk of lung cancer from radiation, let's say. But given that we have faced many other risks, why is it important to drive this one all the way to zero as opposed to reducing some others more?

So I think it's very important to focus on the probability of reduction and harm and reflect on that and help people reflect on that and how much they really care about these other attributes, whether it's radiation or a car crash, or something else.

DR. WEINER: How do you extend that to a population? Because if you looked at the Tengs report of some years ago, the differing cost --

PROFESSOR HAMMITT: -- life saving?

DR. WEINER: Yes.

PROFESSOR HAMMITT: So I think, by and large, because we're not good at dealing with numbers, we often don't even know the numbers. We base our judgments much more on the things we can understand, things like perceived control ability and voluntariness, and dread factor large in people's judgments about risks. But if people reflect more, I think those factors become less important and the quantitative probability becomes more important.

DR. WEINER: Thank you.

CHAIRMAN RYAN: Dr. Clarke?

DR. CLARKE: Nothing at this time.

CHAIRMAN RYAN: Dr. Land?

DR. LAND: I love this stuff that you're giving. I was just wondering, how does it sell as a way of influencing public opinion, public regulatory behavior, and so forth? Is it accepted?

PROFESSOR HAMMITT: Well, yes and no. So often when people learn a little bit about it, I mean it's basically common sense, right? We're making tradeoffs all the time whether we buy something, how much do we think it will give us pleasure, or whatever; what are we giving up by buying this instead of something else? So that's easily accepted.

In the U.S. government you probably know when many agencies write regulations they have to have a formal regulatory impact assessment, a regulatory assessment, which is basically doing this stuff. That's required by executive orders going back a couple of decades now.

There is certainly a community of activists and of scholars who reject a lot of this, but they don't, in my view, have any very compelling way to tell us what to do, how to make decisions other than this. They tend to talk about, well, let's have more discussion and things like that, which, you know,

certainly could be helpful. I think it's pretty accepted, but, as you know better than I probably, real decisions are based on many, many factors, including some narrower political things. So how much effect this really has is hard to know.

MR. MOSSMAN: It would seem to me that, following up on Dr. Land's comment, that an important consideration is this notion that we have the capacity to do something. In other words, if you look at the history of radon regulation, you know the 4 pCi/l, where did that come from? It didn't come from a systematic evaluation of risk. It was before that.

And where it really came from was from the Colorado plateau and a determination of what was technically feasible, what could we get down to and it wouldn't cost an arm and a leg to do it. And so we just select 4 pCi/l, and so now we're scrambling around to be able to defend that in a scientific and an epidemiologic sense, which is fine, but it was always curious to me that that seems to be a major driver.

Why, in waste management, are we always trying to get down to zero? Because we've got the technical capacity to do it. And, you know, that, to me, is a major issue and it goes to the heart I think

of a lot of what you're talking about that sometimes these decisions are not done with any systematic, rational kind of way that, you know, if we can do it, then we ought to do it.

CHAIRMAN RYAN: Ken, there's another good example if I could add to the question, and that is that very often we regulate real dose, obviously, and we also regulate the potential for a dose. Waste management is a real good example where we're regulating and setting requirements based on the possibility of some dose to some people at some distant future time without any realization of that risk.

So could you talk a little bit about how do you weight or value future risk versus real risk today? I mean smoking and radon will be a real risk today. Whereas, some of these other things where there's a potential for a dose, a hundred, or a thousand, or ten thousand or more years in the future, we're weighing that as well.

PROFESSOR HAMMITT: Let me separate a couple of things. The real risk from the possible risk, to me there's not really any bright line there. Everything can be quantified by probability, and while you take as a real risk means you and the

scientific community think there's a very, very high probability close to one that this exposure may cause cancer under these circumstances, or whatever. Or it's a possible risk like the idea that there is stored waste and it will only harm people conditional on getting out and people getting exposed to it.

This is a little bit more complicated to causal pathway. First, there has to be a release or people have to get into the site, or something, and then they might get exposed and then they might be harmed. So there's no real conceptual difference there I think that's important. The timing is -- so the question if it's a current risk is, what will people give up now in terms of foregone other benefits to reduce this risk to them or to people now?

In the future risk, what will people give up now in terms of reducing the risk to some future generation maybe far, far off in the future? And that I guess what economics could tell you is that in thinking about that question, you should think of all the things we can do that will affect the well being of these future generations and how effective is controlling radioactive waste relative to many other things and let's weigh the whole portfolio of them.

In terms of how much we should care about

future people, economics probably doesn't have very much to say except most economists would sort of say, well, treat people equally. The fact that this is another generation has no real moral content relative to it being the current generation. And so I'll leave it at that.

It's sort of apropos Dr. Mossman's point. I think the really critical thing the economic perspective brings that we all know, but often overlook, is that it's tradeoffs. You can always reduce some risks more. Some risks you can even eliminate. It's just by doing that you're spending your time and your resources that you could have used on other things that might have provided a larger total gain in mortality risk reduction or other things we care about.

DR. MOSSMAN: On that matter, if you look at countervailing risks, in other words, I apply some risk management strategy to the target risk, but at the same time I'm now introducing some new, perhaps unrelated risk. Is it simply a matter of again probabilities and cost analysis, as you've gone through, to include the possibility of a countervailing risk?

PROFESSOR HAMMITT: Yes, I think it is and

that's an important point. The way our brains work, we kind of segment things and we identify some risk as of concern and we forget about all the other risks we could control and the countervailing risks. So if you think of the precautionary principle, the precautionary principle says when we're uncertain about the harm, we should be more cautious about it. So that's fine.

But what if actions to reduce this one harm increase the risk of other harms? Being precautionary against one entails, by necessity, being less precautionary against the countervailing risk. So which one do we take the precaution against?

CHAIRMAN RYAN: Anything else?

PROFESSOR HAMMITT: I think the only answer to that is kind of tradeoffs. How much do you think you're gaining in reducing one risk, increasing another? Is it worth it?

CHAIRMAN RYAN: And I think the judgment ultimately ends up on the certainty or uncertainty of what you know, what you're think you know.

PROFESSOR HAMMITT: Right. Just caution, I agree, but certainty and uncertainty are more of a continuous variable than a discrete one to me.

CHAIRMAN RYAN: Sure. With that, we're on

the schedule for a short break until 9:45. So, Dr. Hammitt, thank you for being with us today and we'll look forward to your participation for the rest of the day. We'll take a short break and reconvene at 9:45.

(Whereupon, the foregoing matter went off the record at 9:35 a.m. and went back on the record at 9:50 a.m.)

CHAIRMAN RYAN: All right. If we could come to order, please, we'll begin our next presentation. Dr. Jerry Puskin from the Environmental Protection Agency. Good morning.

DR. PUSKIN: My talk is entitled EPA Perspective, but some of it of it's going to be my perspective I guess based on the work I do, which is --

MR. COCHRAN: This is Tom Cochran phoning in. Thank you.

CHAIRMAN RYAN: Good morning, Tom.

DR. PUSKIN: -- assessing health risk from ionizing radiation and I try to track all the literature and epidemiology and the radiation biology that bear on this. Let's go to the next.

The first slide is definitely EPA point of view though, why we use LNTs.

(Laughter.)

DR. PUSKIN: First very good reason is it's the default assumption for EPA and for the federal government generally that this is something that is a carcinogen, that's clear, and it is also a mutagen. So it's guidance for the agency, for I believe IARC. It is OSTP guidance going back to the Reagan administration. It says when something's a mutagen and it's a carcinogen through that type of mechanism, that use in linear no-threshold. Also, that we have guidance from NCRP and ICRP and National Academy that specifically ionizing radiation to use LNT.

Well, right now, of course, we have to have some sort of model for extrapolating because the epidemiological studies have insufficient statistical power to test LNT down at the low doses we're interested in, which for EPA it's really usually your near background levels. And so far the biological research has not filled this gap, so we need to have some sort of model for extrapolating, and, as I said, we have this advice.

Now, I would particularly highlight the last one that the National Academy has said that the scientific weight of evidence still favors LNT.

Previous National Academy reports and NCRP reports, they always kind of hedge; they say, well, if LNT is not inconsistent with the data or something like that. In this report, since we're spending so much money on it, we decided, well, we want more information now. We're want to say, given all the -- we know how far the epidemiology can take you, how far down it can take you.

What we want to know is, in light of the scientific evidence, what is the best way of extrapolating risk? Not from a policy standpoint, just, scientifically, in the judgment of this expert committee, what is the best scientific evidence? And they said, unequivocally, LNT. Now, that's a very powerful reason to use it at this point until that changes.

Scientific basis. First of all, both animal and human data on cancer generally is consistent with LNT. That is, as you reduce the dose, the incidence of cancer goes down linearly, whether you do animal studies or human studies, as far down as you can go until the statistical power is gone. So that's one reason.

Another is there is a scientific basis in the idea that there's a mechanism that electrons cause

ionizations in the cell leading to damage of the DNA and that there's a good chance that some of this DNA will not be repaired properly. And we also, knowing the monoclonal origin of cancer, that a single mutation in a cell will increase the probability the cell will become malignant. Not that a single mutation is sufficient, but that it's one step in a process, but you increase the number of cells that can be transformed.

Now, this is a picture from Dudley Goodhead showing the pattern of ionizations. I'm going to talk mostly about low LET radiation because I think that's where the main interest is here and there's even more evidence I think for LNT for high LET.

But for low LET, while there's a -- on average the ionizations are further apart. When you get down to the ends of the electrons, as the electrons slow down, they produce clusters of ionization, and this is shown on a scale here, with where you see it, the distant, how they're distributed typically at the end of these tracks and with the same scale the DNA molecule. And you can see that this can produce rather complex damage: double strand breaks, which you see there in red, or green will be single

strand breaks; then you can get base damages, that sort of thing. So it's often possible to get a double strand break and -- or, two double strand breaks close together, a double strand break and a base change, this is not something that easily can happen with chemicals.

So there's the fact that this damage can be clustered creates much more complex damages, more difficult to repair, and that's why a threshold is very much less likely for ionized radiation. I know Dr. Le Guen said yesterday that this type of damage won't be repaired, cells just die, and I think in many cases that would occur. But I think this is generally thought to be the mechanism and I would say that for low LET radiation a substantial fraction of the energy is deposited at the ends of tracks like this.

What do we mean by a threshold? Normally, I guess strictly speaking, a threshold's defined as the radiation dose or dose rate below which you have no harm to anybody, even the most sensitive individual and the risk would be absolutely zero to everybody.

That's perhaps very unlikely. I'm going to relax the definition here and talk about a practical threshold, which means, really, just that LNT -- below some level of dose LNT greatly

overestimates risk, that maybe there are just some sensitive people or maybe it's linear, but with a much lower slope than what we would extrapolate based on epidemiology. That might affect our regulations.

Or you might imagine that we could have something like hormesis, that below some dose, beneficial effects, you might still get some cancers caused by radiation, but maybe the radiation prevents more cancers than it causes or it prevents many more heart attacks than it does cancers, or whatever, but that the net health benefit might be beneficial.

Is there a low dose threshold? Epidemiology is generally, generally sensitive down to about 100 mGy low LET. People could argue a factor of 2 up or down from that based on the A-bomb survivor data. You can't really get much lower than that because the risk is just too small and you don't ever have enough people.

Well, you can recognize that from natural background radiation you get, over a life time, about 75 mGy of low LET radiation, and we get additional exposures from medical and so for. So in terms of life time dose, there's really not much of an extrapolation. It's just 100 mGy that -- if we get 75 mGy from natural background and we know there's a

risk at 75 plus 100, since the A-bomb survivors got 75 plus 100, you know there's a risk at 175, we're interested in is there a risk at 75. That's not much of an extrapolation.

If that were the case I guess we'd be done. The fact is there is a big extrapolation because the difference is that in life span study, the A-bomb survivors received all their dose, essentially, instantaneously, or at least over a few minutes. So they got about 100 tracks per cell nucleus in a very short period of time. And we're interested in natural background rates, which is one or two tracks per cell nucleus per year. So in that sense there is a huge extrapolation.

If there is a threshold, it's most likely one dose rate, or the way I'd like to think about it more is some dose increment over some critical time period. So it might be, let's say, the time for DNA repair is typically a few hours. So what matters is how can you, as long as it's there, you get more than a certain amount of dose in that time period there could be a threshold let's say. Maybe that's the wrong time period. Maybe what matters is time for cell division, which would be weeks maybe, depending on the type of cells.

Right now we know that there's these various low dose phenomena which might modulate the risk at low doses and normally you -- these were already described by Dr. Le Guen and Dr. Barcellos-Hoff. Some of these could be beneficial. Some of them could be harmful. I guess I would even -- I've indicated that by with a plus that this is potentially protective. Normally you would think of the adaptive response that way as being protective, but it's not -- some of these aren't too clear.

Let's take the bystander effect. There's a case where we -- presumably, when you get up to doses where all the cells are hit, the bystander effect is going to be less important than those direct hits. That's at least the theory. Below that, the bystander effects might be dominate. But the bystander effect would be either harmful by causing a mutation in a nearby cell, or it could be protective either by inducing the adaptive responses in a neighboring cell or killing off transformed cells as there is some data to suggest.

Genomic instability, I said, is harmful. Actually, I'm not even sure that's the case necessarily. It could be -- it's really more a matter of which of these mechanisms are operative at very low

doses as compared to higher doses. So, in fact, I guess genomic instability, while it's a bad thing to happen, I guess if it happens at high does, not low does you could think of it as protective -- not protective, but it would give you a hormetic dose response.

The same for low dose hypersensitivity, we know that at very low doses cells are more readily killed. That could be a good thing if it kills off cells that are transformed. It could be a bad thing if it leads to mutations.

Another thing, though, is there are types of hormesis that aren't even covered here, like just kind of a general effect, you know. I think of exercise. If you exercise, you know, you go out and you use all kinds of free radicals, tear down your macromolecules and all this kind of thing, and, yet, the general effect on the body is beneficial.

Now, you might think, well, maybe radiation works that way too, you know, kind of just an overall stimulus to your system? I think I would argue that's unlikely, but I think some people are thinking in those terms. Or it could stimulate an immune response let's say again, perhaps unlikely, but possible.

Well, one thing I would say, which radiation biologists maybe don't like the sound of this, epidemiology trumps radiobiology. Where we actually have the epidemiology data, I mean you've got to think, well, no matter what the experiments on cells show, if increased radiation leads to increased rates of cancer, you've got to think that takes precedence.

Or putting it another way is that if we show that there's these kind of protective effects in tissues, and so forth, before we would want to apply it to human risk estimation, I think we'd want to show that these mechanisms would operate in humans in a way that would actually modulate the risk. So, yes, you might not be able to -- as I say, you probably can never get down to -- you can never do an epidemiological study at natural background levels and see an excess risk I don't think, or it's going to be very, very hard.

However, you might be able to, if you understood the mechanism well enough based on cells, you might be able to look for some kinds of changes in the cells of people to say, yes, we can see all the damage is repaired or we can actually see these beneficial changes in the tissues, so we can really

have confidence that radiation risks are lower than would be projected from epidemiology. So I think we would need that step before we could make the changes.

Well, contrary to a lot of assertions you see, there is epidemiological evidence for risks below 100 mSv or 100 mGy low LET. And Dr. Mossman nicely summarized the first one yesterday that prenatal x-rays at about 5 or 10 mGy led to increases in childhood cancer. Now, I had some of the same problems with it as Ken does. I mean this is one very small part of the population, so, even if it's true, it doesn't really affect the population risks very much.

Secondly, it's not seen in the atomic bomb survivors where you might have expected to see it, and it's a rather small effect. But I would point out that the dose -- but you do see a positive dose response, which is one of the very strongest evidence that it's a real effect, and the other thing I'd say is these are x-rays rather than gamma rays.

What's the difference? Well, for gamma rays, as I said before, at 100 mGy, we were seeing around 100 tracks per cell nucleus. Here, because they're x-rays, they're actually fewer electron tracks for a given dose. So it turns out that 5 mGy of

x-rays, you're really getting down to very close to about one or two tracks per cell, and so we really have evidence here for a finite risk down to nearly one track per cell.

If you believe this resolve, if you're going to look for a threshold, we're only going to have to look between natural background and one track per cell. So that's going to be a very special mechanism. It doesn't work -- it doesn't occur one track per cell, but it's occurring below that.

Two other examples, though, are ones where -- by the way, why is that you can see this? I just said that you couldn't get down below 100 mGy. The reason you can here is this is a very large population, and the other thing is that you're looking at childhood cancers, which are very rare. So you have a lot of more statistical power than you could for just whole body radiation of the population.

For two other populations, we have data where the individual doses are very small. As I said, I thought what really matters is probably the dose over a short time period. We have two groups of patients who were followed in their treatments, tuberculosis patients. They were fluoroscoped periodically every couple of weeks or so. Scoliosis

patients, their treatment was being monitored to see the changes in their spine.

And we're particularly interested in hearing the female patients who received fractionated doses, that is, so at any one time they only received a few mGy, less than 10 mGy, but they received repeated, up to 100 or so fractions. So the total dose was large enough to cause a measurable increase in cancer even though the individual doses were very small.

In both these groups they saw an increase in breast cancer. Now, again, breast cancer rate is a special case. It's possible, but it's certainly a very important one since we have a lot of young women who might be susceptible. It appears that, again, just a few tracks per cell nucleus could -- this provides evidence that that can cause breast cancer.

And then still in other cases, tinea capitis group who were irradiated for ring worm in Israel and they got slightly higher dose, 17 mGy, which is still pretty low, and that saw an increase in thyroid cancer in that group. So that's another type of cancer.

But, again, both these cancers are hormonal. We can't say that it applies to everything,

but this is pretty strong evidence that -- one other thing, not only did these tuberculosis patients get breast cancer, they got it at about -- the risk per unit dose about the same as in the A-bomb survivors. So that would say that LNT, even, goes down to the -- not only is there not a threshold, but LNT works pretty well down to this type dose.

DR. BARCELLOS-HOFF: But that's cumulative, right?

DR. PUSKIN: What?

DR. BARCELLOS-HOFF: You required a cumulative dose?

DR. PUSKIN: Yes, right. But these individual tracks somehow caused cancer.

DR. BARCELLOS-HOFF: Were added --

DR. PUSKIN: Yes.

Well, can we go lower still? And I think there's some chance by looking at epidemiological studies of chronically exposed individuals where, again, you have to have enough total dose to see a cancer, but the dose over a day, a week, can be even smaller than what we saw in the fractionated dose.

Here are some populations that are chronically exposed. The nuclear workers is the one that immediately comes to mind and it's questionable

whether this does have the statistical power because the doses are pretty low and there's potential confounding.

I would say what we really have out of the nuclear workers' study so far is that the risks that we're estimating for chronic radiation are not way low. We know that the LNT is not greatly under predicting the risk. You know, if the risks were ten times higher than what we project, I think you would have seen something, nuclear workers or some other studies. You'd probably also see increases of leukemia in Colorado and the rest of the country and things like that.

Some of these studies may not be useful. They all have problems. So far the first population hasn't really shown any clear indication of increased risk. The Mayak workers probably are not going to be very informative just because their doses are so high that even one day they get what those TB patients got, and they've got additional doses from medical, so their doses are extremely high of the order of 10 mGy a day.

The Semipalatinsk gives another one that's -- I don't want to discuss that one. But the two of them that are probably the most promising I think are

the Techa River cohort and the occupants of the cobalt 60 contaminated buildings in Taiwan, but both are -- you know, they're still working out the dosimetry. The cobalt 60 population, the epidemiological followup is very short.

Interestingly, both of these studies show a statistically -- at this point, at least based on the current followup and the current dosimetry, both these studies show a statistically significant increase in both solid tumor cancer and leukemia. Again, this is probably down well below 1 mGy per day perhaps. I don't know. It's not too clear because the Taiwanese, for example, there's a big range of doses and they really haven't broken it down, dose rates.

And Techa River, there is also quite a range of doses, so more needs to be done. But the preliminary results suggest about the same risk per unit dose as the A-bomb survivors, suggesting the DDREF is not very super high, not ten or more, or something like that, and that there's not a threshold. Now, that's sort of to the side.

But the risk principles I'd like to talk a little bit about how we apply these to standards. I don't know, from the introduction I got yesterday,

maybe this is less interesting than policy here. I think risk protection standards need to account for uncertainty, and, particularly as Dr. Land talked about yesterday, we have to ensure that we are not greatly underestimating the risk.

So if there is a reasonable probability, even if we think there is likely to be a threshold, even if there is a substantial probability there is not and that LNT is correct, even it were to say one chance in three, we would probably not be able to change our regulations. We would have to -- in order to protect, to make sure that everyone is -- that the bulk of the population is at a low risk level, we would still have to regulate radiation fairly stringently.

If we did get new signs and were really convinced -- or there was pretty good evidence that there was a threshold or hormesis, or something like that, at these very low dose levels, would we change our regulations?

Well, one thing, is suppose the risks went up substantially, a super linear dose response, based on past history, regulations are likely to get tightened if that were a very significant increase. If the opposite were true, if let's say we had strong

evidence that there was a practical threshold, not a strict threshold, but let's say we've said, oh, risks are really ten times lower, 50 times lower at least, would we change the regulations?

The answer is maybe, maybe not. It would depend. It depends whether the statute would permit it and you would also have to say that there's a need. Some people would say, oh, let's take the drinking water rates. Somebody might say, well, these are too stringent; the risks are really 50 times lower. Well, people would say, but everybody's meeting them; what's the compelling need to change them? So that would be the --

Before rejecting LNT I would say that EPA would want a scientific consensus as reflected in these kind of reports from National Academy, UNSCEAR, NCRP, and so forth, that we want a concurrence from our science advisory board. In fact, right now we are revising our risk estimates based on BIER VII primarily, and our changes are subject to science advisory board review. And they've already talked, weighed in a little bit on this issue. They wanted us to go beyond BEIR VII to some extent and acknowledge more of the uncertainty about the risk at low doses. Tony Brooks was on our advisory committee.

We'd want acceptance from the other federal agencies I think, you know, try to -- I think we want as much consistency across the federal government as we can have. And we would also want a transparent, public process that people from the public would have a chance to criticize what we're doing and that we would have to consider and we would want our advisory board to consider any evidence that people would want to, at least make it clear that we do consider all the evidence from everywhere.

Well, if we did think there was a threshold, let's say, how might that affect regulations?

First of all, if the threshold is below natural background, it's not going to have any effect. I mean nobody really cares if, okay, we get as I say 1 mGy per year. If there's a threshold of 0.1 mGy per year, it doesn't really matter. That's not going to have any -- and remember, in case of radon, we're actually in this situation that for radon we already know that levels that people get from natural -- in their homes, indoor levels of radon that a lot of people get, has been shown with epidemiological studies that there's a increase in lung cancer.

Now, if there was a practical threshold

above background, they could perhaps change some regulations that are based directly on risk. One is the soil clean-up levels potentially. Another is the drinking water MCLs. I talked about the MCLS, about the compelling need.

But even more so, there's also a provision in the Safe Drinking Water Act amendments that says what they call no backsliding, that if you have a regulation and it's working and you now -- you cannot make the regulation more stringent -- less stringent, sorry, you cannot relax it unless, let's say you said, oh, it's really a strict threshold and there's no risk, in that case you could.

If it was a practical threshold, I think it's a gray area. I think if the risks were below 1:1,000,000, which is where EPA normally doesn't regular below 1:1,000,000 maybe, but if the risk went from 10^{-4} to 10^{-5}, no backsliding regulation would say you really can't do anything about it. Now it might be that at that point Congress would say change that no backsliding regulation.

This is important because a lot of clean-up levels and things relating to waste disposal are tied to the Safe Drinking Water Act in terms of the MCLs for drinking water.

Well, issues in setting a threshold based standard, well, obviously, would be magnitude of the threshold dose or dose rate. The uncertainty and where that dose is, the uncertainty and how big the risk is below that level would have to be considered.

You would have to consider sensitive subpopulations. It's a threshold for most people, but what about people with let's say they're missing some repair enzyme or something or they have less of it. And you have consider multiple sources. Say, for example, and there's no epidemiology that rules this out, let's say that that there's a threshold for chronic radiation at 10 mSv/y, 10 mGy/y has no risk, okay, so no one would be harmed by this dose.

Well, you still, for an individual source, you would still want to set the level lower than that because people are exposed to radiation from multiple sources. So it might be that if there were a threshold of 10 mSv/y you might still have an individual source limit that was 1 or 2 mSv/y. This is along the same lines where, for example, ICRP recommends that, from all sources combined, you can receive 1 mSv/y. Then they have individual source constraints I guess they call them that are 25 or 30 percent I think of that.

Well, what are the down sides of LNT? I think we've heard a lot about that already the last couple of days. You've spent too much money obviously. That actions taken to reduce these very low risks may not be warranted from a cost benefit standpoint. We're spending more money than we'd like to.

The other is probably more important. I think more people are disturbed by this. That this perception of the risk of low doses cause people to either oppose beneficial nuclear technologies or to potentially shun advisable medical procedures like mammograms. I don't think actually think the latter occurs so much, but those people trust their doctors so much. But it could and I think this is a problem, and I can't say that I've got the solution to it.

How do we live with this? The obvious answer is education and I think a lot of people are frustrated. We've tried hard at this and had very limited success. I suggest you try to help the public put the risk into perspective and to balance the risks and benefits and to make clear to them that you cannot -- life has risks and some risk is unavoidable.

The thing about LNT though is it says that low dose's risks are very low. That's what LNT,

that's the message is that risks decrease as the dose decreases. I guess I've spoke up several times already. I think that if we try to say that, well, we're not really sure there is a risk, so let's just not say there is one. I think it's going to damage the credibility and work against the trusted scientific community and the radiation protection community in particular.

So to summarize, radiation protection is based on LNT and that's consistent with current science, and the recent Academy recommendations. We would really need a consensus of these kind of scientific bodies before we would adopt a threshold. If you could show there's a threshold, yes, it could change regulations conceivably. However, you'd have to worry about things like safety factors, sensitive subgroups, and multiple sources.

That's all I have.

CHAIRMAN RYAN: Thank you very much. Questions? Dr. Mossman, then Dr. Tenforde, then Dr. Le Guen.

DR. MOSSMAN: On your last slide, what do you mean by a change in standards? To me the whole problem about thresholds and the like is not about the dose limit, it's about how you apply ALARA. In other

words, I don't think any of this discussion has anything to do with dose limits because what radiation protection is all about is a top down approach in which the dose limit is the ceiling, you use ALARA to reduce the dose as low as reasonably achievable.

The question about a threshold then becomes how far do you take the ALARA down? Because once you reduce the dose, if you're down below threshold, then, of course, you're not getting any more incremental benefit for additional costs of dose reduction. So, to me, the whole issue is not so much the dose limit, it's how you apply ALARA. Could you comment on that?

DR. PUSKIN: Well, I would say this, that, first of all, you can think of regulation -- I don't know that it always works this way, but I think this is the way it was envisioned and to some extent, great environmental regulations work this way, but, unfortunately, they don't entirely. It's to set a level of acceptable risk, okay -- or, unacceptable, and above that we're going to regulate, and that might be a 10^{-4} risk or something like that. And then below that we look at cost benefit and we try to reduce it further as if it's cost effective.

As far as I know, it's almost always

decided by the first, that it's almost never cost effective to go lower than what you're already doing with this risk. Now that may be not true in the occupational setting. I don't know. But environmental, you set the standard.

Let's say it's 15 millirem per year, whatever. They never say, oh, wow, let's calculate whether we can go down to 1 millirem and it's still effective. It won't be. Probably the 15 wasn't effective in terms of if you put a reasonable value on human life, are risks avoided is a better way to say that. You probably wouldn't have reduced it to 15. But we've decided that 15 was -- that above that was unacceptable, or 15 and lower was acceptable. So that's usually the driving point.

I know when we set the standards for the Clean Air Act, it was more looking at how many people were in different risk ranges and it was decided that taking the overall picture, again, that roughly 10 millirems, which is about 10^{-4} risk, was about as -- didn't want to go lower than that, but there was -- in fact there was a court case which kind of said that the risks should be not much above the 10^{-4}, something 10^{-4} range, and at times EPA has said 10^{-4} ranges means three times 10^{-4} or two times 10^{-4}. It's sometimes

higher than one times 10^{-4}.

So things are generally thought -- usually staying in that -- not going above that is usually the driving thing. Now, the exception could be in the Safe Drinking Water Act where sometimes there are carcinogens out there that, you know, can easily be regulated down to 1:1,000,000, you know, they're not there and so it's possible to do.

I hope that answers your question.

DR. MOSSMAN: Managing chemical risks is an entirely different game than radiation risks. I mean chemical risks, you're quite right, it's a bottom up approach. With ionizing radiation, it's a top down approach. So there's a different philosophy. Now I can't tell you whether one's better than the other. It's just from historical --

DR. PUSKIN: Also, I'd say that, for example -- maybe Mike could speak to this. The NRC operates more on this top down approach, that here's a limit and we really try to go lower than that. EPA sets the limit pretty low and say, if you can meet that, you're done, you know, kind of thing.

CHAIRMAN RYAN: Anybody else? Tom, you had a question.

DR. TENFORDE: I just wanted to make a

comment. You were talking about the ICRP 1 mSv/y public dose limit, which is the same as NCRPs, and you mentioned that for a single source under the control of a single operator or group of operators, they recommend three-tenths of a mSV. But I wanted to remind you in 1984 NCRP wrote a statement at the request of EPA when they were beginning to develop the CERCLA regulations recommending 0.25 mSv/y --

DR. PUSKIN: That's where I got confused.

DR. TENFORDE: --for any single source given that the other exposures of an individual exposed that source may be unknown. And, therefore, the idea was you might have as many as four such sources contributing up to 1 mSv/y.

But 0.25 was conservative and there was huge debate about that in terms of shielding for medical facilities and so for. And, in fact, in 2004, NCRP published statement 10 reaffirming the public dose limits and the applications of public dose limits, and reconfirmed that this was, you know, not an unrealistic or unreasonable limit, and in a 70 year life span will get you a risk of more than 10^{-4} of cancer, more like 10^{-3}. But it's still a very low risk compared to natively occurring natural cancers, or cancer caused by other sources associated with life

style, you know, smoking, whatever, or, for that matter, radon at a higher level anyway.

I just wanted to reconfirm that that single source limit is still in place.

CHAIRMAN RYAN: Dr. Le Guen was next.

DR. LE GUEN: Well, I would like to come back on two sides. First side is on the epidemiological studies of chronically exposed cohorts. From my point of view you forgot to mention another study. For example, you remember women workers who painted with radium, watches, and has developed radium osteosarcoma. And in this kind of study they showed also a threshold.

And also about Mayak workers and internal contamination, I think the publication has shown curvilinear. So you remember what I said yesterday, from my point of view there is not only one, but perhaps more than one and perhaps several curves between dose and effects.

And my question about the slide, why didn't you take into account people exposed to all natural background, natural radiation for a risk assessment? Because it is chronic exposure and I think that it would be very good to have epidemiological studies on this population.

DR. PUSKIN: I know Charles could speak to that latter one.

DR. LAND: Well, you know, there are such studies. There's the high background area in China. Personally, I think these studies tend to be disastrous because -- well, if you look at the reports from the Chinese study, every time there's something you see in excess, well, it's because these women have few children, or so forth, and it's just -- we just don't get anything, any good information out of it because it's so difficult to control that the sort of things that might have the same level of effect as the exposure you're studying. I mean maybe in a more regulated world it might be possible.

DR. LE GUEN: Because in China and India, we have begun to have these kind of studies in France and also to associate it with molecular biology because we simply say it's a different dose. From our point of view, if you receive ionized radiation, if you receive from natural background or from external sources, if we assess the dosages, it's the same dose. So from our point of view it would be very interesting to estimate the risk.

DR. PUSKIN: The problem is like if you have -- an example in the case Charles gave, let's say

the level, let's say it's even five times normal, I mean we think that natural background radiation causes roughly three percent of the cancer. So in this other area it might cause 12 percent, 15 percent. So that's 12 percent higher.

I mean the difference between Connecticut and Louisiana is more than that, and here's two separate areas of China, which we don't know that much about, so they could easily differ by that amount. It's hard to -- the potential for confounding is too great.

DR. LE GUEN: Yes, but perhaps what's so interesting about life styles if we have a good control group, because one of the problems that we have at low dose, say, is not only one genetic connection, but there is a lot of them, and perhaps we'll see factors due to life styles. And I think t his kind of study, which can -- of course, I'm sure that it's not because you will have only one study that you will change everything.

But I think we must be open minded and we must continue to work on this field to a lot of different experiment. Because, of course, I said yesterday from my point of view, if we have Hiroshima and Nagasaki just one case, one exposure, we've

neutron and gamma ray and very short exposure, and you can see and you mentioned different studies and cohorts, and we have different sources. We have internal contamination with plutonium. We have external exposure and so on, so different case. Yesterday we mentioned the problem of dose rate, and that's why that it's very difficult. Of course, that's why, today, we are here. It's because it's so sophisticated. Because we have different kind of source, different kind of exposure, and we must take into account all of this. Okay?

DR. PUSKIN: Yes. I would say the radium dial painters, I don't get into that much because that's a high LET situation, but there is -- not everyone thinks that that is convincing the threshold.

For example, there risk study where they have injected radium in patients where -- radium-induced bone cancer where it's certainly consistent with linear no-threshold. And the radium dial painters is very high dose. What's clear is it takes a lot of dose to see an excess of bone cancer and it's a very high dose. The damage to the bone tissue is very high, so we're not really looking at the kind of low dose kind of a phenomenon.

CHAIRMAN RYAN: Jerry, just a follow-up

question if I may. In some of the other studies that are in your list, the Techa River cohort, it's reconstructed doses, and you commented on some of the issues that that's tough. That's real tough, I mean, you know, the fuel cycles, and how they processed fuel, and when they processed fuel all contribute to the short lived component.

I guess I'm not picking on that so much as saying that I think -- I don't know whether it's a background study or high background study, or a real exposure case, or a mixed exposure case with alpha and gamma. Every study has good points and bad points in how you can extract the data.

DR. PUSKIN: It's a question of how well you can do that. I mean it's whether -- I don't know what you'll end up with.

CHAIRMAN RYAN: Well, what my point is I think -- the point I would offer is that all of them probably have some value and all of them probably have some flaws. So try to pull all the evidence together rather than just setting one aside for whatever reason.

DR. PUSKIN: I guess I would maybe retreat a little bit. When I was saying that the epidemiology takes is trumps, if you have an epidemiological study

which is positive and you have a strong radiobiology indicating that it can't be positive, you should look at the weaknesses of that epidemiology study and see whether you can reconcile it. I mean that's part of -- - I mean it's not --

DR. LE GUEN: But you know just an example about nuclear workers, you know that for a different study we observed an LC effect, and the LC effect, there are two reasons. Perhaps we have a natural selection about workers and we follow those works. That's one of the reasons, also, for the moment if I take into a French cohort, I say yesterday, because this cohort is too young. And we need time, also, and that's why for this kind of epidemiological studies, I say it's not only one research that changes something. We need to be very serious, but we must take everything into account, not only one point.

CHAIRMAN RYAN: If I may, I think we want to make sure we get Dr. Holahan's presentation in this morning, and we can certainly continue this discussion after lunch in our roundtable. So, with that, let's hear our second presentation and we'll go from there.

DR. HOLAHAN: Good morning. I'm Vince Holahan. I'm a senior level advisor for health effects research programs in our office of Nuclear

Regulatory Research.

I'd like to, first, apologize or account for Dr. Cool. Dr. Cool would loved to have been here. He's my counterpart in our materials office. Unfortunately, he's part of a drafting session in Vienna, and I guess Vienna in April versus Washington in April, he made the decision to do some traveling.

I'd also like to express the thanks of the health effects group, as well as our environmental and rad transport group. We appreciate the guidance that you've provided to our groups up on the ninth floor over the past years, and I hope even in an advisory status with the ACRS that you'll be able to give us very valuable input.

With that said, what I would like to do today is provide what we would call a staff perspective on the low dose work and some of the changes that have gone on in the literature for the past 15, 17 years. This is a staff perspective, because as we've previously briefed the ACNW, the staff is looking at some of the materials that have been produced. We're looking at our regulations, part 20, part 30, part 50, part 62, to see whether or not we should make a wholesale change to part or all of this.

My role is to look at the technical basis for those reviews. Options will be prepared and we're hoping to send to the commission a staff requirements memorandum at the end of this year. Therefore, if this meeting were held approximately a year from now, I'd love to tell you exactly what the Agency was going to do.

It's a staff perspective because I've been specifically told, try not to get ahead of our commission on what we think might happen because we really don't know what's going to happen. So with that in mind, what I'd like to do is discuss some of the biology through the rose-colored glasses that I wear as a regulator.

I'm appreciative to Dr. Puskin for providing the science, but I'm not going to get into the damage of the DNA double strand break, and I hope not to get into too much detail on the epidemiological studies. But how does this information affect our regulations and where we should change? I'll talk about some of the technical basis information that we look at, where we think the science might be today, and how it's going to impact our regulations.

First off, you have to understand we've got three basic fundamentals in our radiation

protection system. (1) You must have justification from any exposure to radiation. We don't permit licensees to have unauthorized or frivolous exposures to radiation. (2) We have a limitation on the exposure, whether it be occupational or public. And, (3), optimization, and our regulations would call that ALARA.

For all intents and purposes, it's a dose based system. We've heard a little of the differences between EPA and NRC, that is to say it's observationally based. We look at effects in human, animal systems and we start setting dose limits below that. And then we use a series of constraints, if you will, in some cases to worry about source specific items.

There are a number of assumptions. We assume in our regulations that there's a linear no-threshold response for stochastic effects, primarily cancer hereditary effects. Our regulations are gender averaged and age averaged. And right now we protect the most exposed individual. EPA is looking at differences such as looking at the most sensitive individual, but that's a discussion that's going to probably go on with their science advisory board for at least a number of months.

Dr. Cool wanted me to put in that our system of protection in the U.S., at least with the NRC, is supposed to be coherent as well as predictable. That doesn't necessarily mean it's comprehensive or consistent. The reason I say that is many of our regulations are based on regulations from the ICRP, 2, 26. We actually have 60 involved. And there are many things that we're doing today that are consistent with the recommendations in report 103.

But it's been a period of time since we've done a major revision. That was some 17 years ago. That revision was the product of many years of work by the staff. I guess the question is, and this is a question that will come up next week at the NCRP meeting on the low dose radiation as a topic that Dr. Lipoti as specifically asked on the second day, what would it take to prompt a change in the NRC regulations?

First and foremost, we'll have to go back to 10 CFR Part 50. That's our backfit rule. That is to say a revision would have to prompt a substantial increase in the overall protection of public health and safety, and that increase is going to have to keep in mind both the direct and indirect costs associated with that change.

In 1991 we had great difficulty demonstrating that significant increase in public health and safety, with ICRP 60 and many of the changes that proceeded that. Even though we had DS86 changes in the risk coefficients, that wasn't sufficient to prompt a change because of backfit. But the Commission has the ability to waive that.

What other things might we consider? Well, clearly, updated scientific information. Obviously, there have been many changes that we'll talk about in a couple of minutes. Possibly reduction in burden, risk informed regulation, and the last item here that Jerry also eluded to that would be new for the Commission is inner agency alignment. Clearly, none of our federal agencies are on the same page. This might be a reason to prompt a change in our regulations.

So what do we do? Obviously we look at the basic research. This includes the DOE low does radiation program. That's a 10-year, $17.5 million program. For all intents and purposes it dwarfs much of what NIH is doing. We also look at much of the work that's done in the EC with Neil Kelly. That program is on the order of about $30 million euros, and given the difference between the euro and the

dollar, it's a very significant program.

We take a look at peer-reviewed publications, as well as unreviewed publications. We find that many of the states will do epidemiological studies for cohorts around various facilities. Those aren't necessarily in the journals, but we'll take a look at those. There was a recent report in Germany about childhood leukemia I believe it was in proximity to their power plants. That has not necessarily been peer reviewed and published per se. I think it's more of an agency report, although it's got their own internal procedures.

Literature reviews, this is one of the areas that we, as an Agency, get very much involved in. We were one of four sponsors of the BEIR VII report where we looked to established, balanced technical review committees to survey the literature, put together a review and recommendations on future research. I'd have put up here the French National Academy review, but I didn't have a copy of the page to insert in.

(Laughter.)

DR. HOLAHAN: The other item here is UNSCEAR, the United Nations Scientific Committee on the Effects of Atomic Research. They actively are

engaged in looking at both radiation sources, looking exposures, and evaluating the impact of those exposures.

We have a number of bodies that will look at all of this information, both the summary reports and the individual reports, generally, again, focusing on the peer review publications, make some summary recommendations in terms of radiation protection, whether it be the ICRP or the NCRP. We fund both organizations to provide their guidance. And all of this, again, all of it impacts both the regulations here in the U.S., in one case it's our 10 CFR series, as well as the international series, that's the basic safety standards.

Well, needless to say, in 17 years there has been a substantial amount of work that's gone on. We were and continue to be participant at the DOE workshops. We were at workshop I, and, quite frankly, myself and some of the other regulators tried to articulate to the investigators what low does is, trying to explain to them in regulatory space we're interested in mSv exposures or several mSv exposures and we're talking to investigators that have been working in gray type of exposures.

I know that when we worked with Dr. Upton

we defined for LNT. We were interested in low dose. That low dose was 20 rads. And at that junction the question was, is, well, there's no information there. Well, the reason there wasn't a lot of information there is we didn't have the tools. And, fortunately, by articulating to a low dose program that we were interested in exposure of 10 rad, 10 centigrade or less, it's prompted a lot of research to develop tools so we can examine some of the effects of the very low doses.

JCCRER has been a program that this Agency has been very much involved with for over 10 years. Now, Dr. Puskin mentioned he was little concerned about the doses that the workers are receiving, but we view those as intermediate doses that are between the atomic bomb survivors and some of the very low dose studies. But, more importantly, there is a huge cohort of female workers that were exposed either externally or internally to help us ferret out some of the gender differences, and we're hoping to see some of that come out of that data.

Just in the last year or two we have had some significant information out of the RERF. A revision of the dosimetry system, DSO2, a re-analysis of the mortality data, which basically reaffirmed that

the estimates that were in ICRP 60 are very relevant and valid today. But, more importantly, last year we got some information on cancer incidents, and that is going to be of more value to us than probably the mortality data because of the advances in various countries on treatment of cancer. The mortality data tells very little if we're dealing with exposure to radioiodine.

UNSCEAR, the last major compilation of data was put out in 2000; inheritable effects in 2001. There are at least five reports that should have been out last month. These reports are going to be dealing with the epigenetic work. We've got non-cancer data that's going to be presented in a separate annex. We're looking at a review of the Chernobyl. So we're hoping in the next couple of months we'll have a series of reports out of UNSCEAR. Not only coming out this year, but we have at least four more annexes that we're looking at this year for finalization for next year.

BEIR V, BEIR VII, the French National Academy report's come out, again, it will be very interesting to get a group of folks together to find out why two groups can look at virtually the same data and come up with diametrically opposed conclusions.

In ICRP over the last 17 years has come out with some 43 reports, possibly 44 reports, and the question we'll have to ask is, as an agency, do we want to look at ICRP 60 recommendations or do we want to make a jump all the way to 103 and see if we can entice our sister agencies to make the same type of change.

I put this up here very briefly. I think we've got pretty much consensus if we're looking at epidemiology, and if we're looking at excess relative risk, it can be fit with a linear curve, maybe a linear quadratic curve. Maybe the limit of the data is down to about 100 mSv. We had a sponsors' briefing in 2005. I asked the epidemiologist on the group, Dr. Gilbert, what the lower limit of their sensitivity was, and she was 100 mSv, that's it. I asked the same thing of Dr. Bill Dewey, the molecular biologist on the group. He said 1 centigrade.

Dr. Puskin indicated that there are a number of studies that seem to be pushing these limits a bit. I could be the recent mortality morbidity study from RERF. With the trends analysis they think they might be able to go down to about 10 mSv. But there's some question there. You can force the fit of that curve to actually show that you could possibly have a practical threshold of maybe 60 mSv.

The Techa River data is down into the 10s of mSv. But, again, as we've discussed over the last day or so, there's a lot of question, and not only the cancer incidence, but the certainty we have on the dose estimates.

And the workers' studies. Dr. Cardice is indicating that there's an increase at very low doses to radiation exposure occupationally. Much of that was driven by the Canadian data. However, there was a problem with the Canadian data. They underestimated the exposures to the workers.

In the 1970s they set up a national database for radiation exposure. At Chalk River they zeroed all the workers out, so any of the prior exposures to those workers prior to 1974/1975 was not included. When you include that data, there shouldn't be an excess increase in the Canadian workers.

That information is prepublication, but the Ministry of Health up in Canada is working to get that out. Therefore, when I extrapolate from 10 rem to 1 rem, 100 mSv to 10 mSv, I'll put that in as a dash line. The cellular data, depending on the source, is primarily out of BEIR VII, would take this down to about 1 rem, again, showing dicentrics, acentrics, increased mutation frequencies at these low

doses.

But still, even with this information, we have to put a dash line in assuming LNT. Because, quite frankly, we don't know what's going on here. And our concern, whether it be DOE, EPA, or the NRC, is it's this very low dose region right down here that we're concerned for regulatory purposes.

We've seen these phenomena over the last day, day-and-a-half now. The question is, what impact may, could, should, will that have on our regulations? With bystander effects, this was considered by the BEIR VII committee; temporarily discounted. This has got a huge impact on LNT and target theory.

What is the size of target when we talk about radiation exposure? Is it the nucleus? Is it the whole cell? Is it a group of cells? What impact does that have on the surrounding tissue? What impact does that have on the organ? Keeping in mind that type of information might help us understand what's going on, but it doesn't necessarily change the epidemiology.

Genomic instability, is this real? Can we actually induce damage in cells that will perpetuate to the daughter cells, to future daughter cells, to future daughter cells? We heard that there might be

some information for that. Maybe apoptosis takes care of that.

In either case, as an agency, what I'm interested in is to see if this type of information can be repeated from laboratory to laboratory. One of the problems that they've had with investigators in the DOE program is getting results to repeat between different laboratories.

Adaptive response, priming dose required to some reduced sensitivity to a following challenge dose. Those priming doses are greater than our public dose lines. We're not going to use that for public protection.

What about emergency responders? We're not going to allow our emergency responders to receive more than 25 to 50 rem, 250 to 500 mSv. Chances are we're not going to do an adaptive response. We're going to control the exposure of those individuals.

Hyper-radiation sensitivity, I've actually seen it in the tissue culture. Haven't reported on it. I thought it was an artifact where at very low doses, for some reason, you'll see a dip from let's say 95 to 90 percent surviving fraction.

Now, the question is, does that incur in organs and tissues? Have we observed this in the

clinic? Have we observed with conventional radiotherapy a 10 percent breakdown in surrounding tissue to where we've got a targeted region? So I guess the question would be with hyper-radio sensitivity, do we see this in vivo?

What issues might prompt a change? Well, here are several of them. What is the real threshold for lens opacification? ICRP 60 say 5 Sv. Dr. Wortle last year, prior to his passing away in February, in *Radiation Research* published an article on lens opacification for the Chernobyl liquidators suggesting that it might be on the order of about 700 mSv for a threshold, not 5 Sv.

Can that be reduced in other studies? That might be important because that might prompt a change on our regulations ocular exposures.

Non-cancer diseases, RERF is starting to report that there might be an occurrence of cardiovascular diseases, possibly the same type of thing in some of the Chernobyl workers. The problem we have with non-cancer diseases is the induction of those type of diseases is about one-tenth the excess risk than radiation, very low levels.

The second problem that you run into is, what is the impact of socio-economic effects on those

individuals? And I'll cite the Russian liquidators as an example. You have a group of individuals that smoke, high alcohol consumption, diet is very fatty. They've had a decrease in the life span of the Russian males. It's currently about 57 years of age compared to surrounding populations where we're talking late 60s, early 70s.

How do you account for all of those confounding factors and then make judgments about non-cancer diseases? It appears to be a deterministic effect. But if it is, what's the threshold?

Gender sensitivity, our regulations are gender averaged. Is there a real difference between males and females to 1 Gy exposures? We don't know. Should it be something that we need to tease out? It would be something that would be after consideration. Age sensitivity, children, with children, should they be protected because they might be three to five times more sensitive than adults? Should we take that into consideration in our regulations? And, finally, should our regulations reflect us protecting the most sensitive individual as opposed to the most exposed?

Dr. Puskin mentioned we've got statutes that limit what we can do, and this is a big one right here, Johnson Controls Act. In this particular

situation, Johnson Controls prevented women from working in areas where they could be exposed to lead, and the rationale was is that if they became pregnant, the embryo fetus might incorporate the lead, would have developmental problems. You know, the are workers sued basically contending that the woman had the right to choose whether she wanted to work in that environment and accept the economic benefits of working there or protect the fetus, and the Supreme Court sided with the woman's right to choose based on Title VII of the Civil Rights Act.

So what impact does that have now if there's a gender difference? Most likely none because we're limited from doing anything.

Would we be able to also discriminate based on age? Are older workers more sensitive than younger workers? Steve Wing has expressed some concerns about that. We may not have anything we can do. That would be discrimination based on age now. So there are going to be certain limitations that we as an agency, we as a federal government can do without changes in the statutes and court decisions.

So let's go back to our curve here where we've nominally expressed some biological effect as dose. On the solid line I've got what we believe are

the actual effects. We'll call it linear. And we've got this postulated linear extrapolation.

And just for exercise, let's say there's a practical threshold. Now I've set this, if that's a logscale, probably around 20 or 30 mSv. We heard yesterday, Dr. Le Guen said that if there was a practical threshold it might be between 10 and 60. So for purposes of illustration, this could be fairly close. What does that mean to NRC from a regulatory standpoint?

Well, a practical threshold might say, well, we've got efficient repair below that level. Either efficient or maybe there are mechanisms, like apoptosis, that can take care of air prone type of situations, and above it we saturated the repair processes or we've induced some sort of air prone repair process.

What impact might that have on our regulations? Well, as it was expressed earlier this morning, we're going to have to consider what exposures now do we have to monitor and record?

Right now we monitor and record the occupational exposures. But what about differences in background radiation? Clearly, if there's a practical threshold, we're going to be concerned with monitoring

medical exposures for each of those workers.

What about a frequent flyer? Should be put the additional cosmic radiation exposure into that to see whether or not we are below or above a practical threshold? Is there a single threshold or are there multiple practice thresholds? Do men and women have the same practical threshold? Do children have a different practical threshold? Are there other groups in the population that could have a different threshold? If there are different thresholds, now which one do we regulate to?

Dr. Weiner, you were asking about the fourth point there, that history exposure. Does it fade? Is that an annual practical threshold or is a lifetime practical threshold? If I receive a mrem today, and a mrem next year, and mrem the third year, is that a total of three years or a total of one? We don't know.

Then the last point would be is, how do I deal with different workers that have different exposure histories? That is to say I have two workers, one's above the practical threshold, one's below. Do I try to not give any additional exposure to the worker that's above the threshold and assign a task to one below it, or not? Can I do that? How do

I regulate that?

Well, let's go back, maybe do some case study if you will with our practical threshold here. First thing to keep in mind, and this comes out of a case study back in 1975, that just because there's a practical threshold or we have a lack of adverse effects of any substance, it does not generally mean that being below that threshold is safe.

Because of that, we're going to have to regulate our non-threshold, or deterministic effect if you will, with a series of safety factors. We see this in ocular hazards, acoustic hazards, exposures to heavy metals, exposures to organophosphates.

Safety factors, well, they can be a number of things. First and foremost, what's the type of data that we have in animals? Do we have consistent information on rats, mice, dogs? If not, we have to throw a safety factor in, anywhere from three to ten. What about variation between humans? Again, in some cases that'll be a variation of three to ten. How confident were in the exposure? How confident were you with the duration of exposure? Each of those could have safety factors of ten. EPA, in fact, has something on the order of I think six different classes of safety factors to consider.

Note that when Dr. Puskin mentioned something about statutory authority to look at practical thresholds, carcinogens are explicitly excluded from consideration in the system. FDA, when they're looking at food and drug, typically their safety factors are anywhere from 200 to 2,000. In 1996 the Food Quality Protection Act set even tougher standards for children. They said another safety factor of ten would have to be put into this.

So what's that do with our curves? Well, we could have a series of safety factors for just illustrative purposes that might reduce our observable concerns from let's say 100 mSv down to 1 mSv, or a factor of maybe 20 or 30 below that practical threshold.

Do we have sensitive groups we have to deal with? And, finally, what about constraints? We're talking about multiple sources now. We're not talking about a single source of exposure.

The point I bring here is a practical threshold may not necessarily give us any regulatory relief. We're basically back in the same system where we have right now.

This was a toxicity profile that was conducted by the Agency for Toxic Substance and

Disease Registry. It was done in September of '99. This is required as part of CERCLA. And in that assessment for ionizing radiation, they tried to derive an estimate of what the minimum risk level should be for ionizing radiation. The minimum risk level would be is what type of radiation can you receive on a daily basis so you won't have an adverse effect.

The no-observable adverse effect level they selected was 360 mrem/y, background radiation. Now, why did they select it?

(1) It represents the U.S. population. It's representative.

(2) It considers radon. This particular level is not associated with an adverse effect. I think everybody's pretty much in agreement there that we don't think we have any adverse effects there, and it is below some of the levels where we might see some deterministic effects in the embryo fetus. They corrected this value for an uncertainty factor of three because of variability between individuals, and with that they came up with an MRL of 100 mrem/y, or in today's parlance 1 mSv, which is our public dose limit.

Things they didn't consider, however, back

in '99 is, could the human variability be higher where we factor in gender differences? There is no uncertainty factor considered for children, which has been an issue, and it doesn't consider source constraints. But what we might find is, is we've got an MRl something less than 1 mSv/y potentially.

With all this in mind, what I'd like to sum up with is a couple of statements. (1) Without a doubt, it's my firm belief, it's a staff belief, our regulations, our standards are adequately protecting public health and safety. That does not necessarily mean that we wouldn't be convinced that we need to take a look at our regulations for consistency purposes if nothing else.

Adoption of the new biokinetic models, risk coefficients, and weighting factors will not significantly improve public health and safety. We mentioned this committee when we were looking through the ICRP recommendations that was a bottom line, we're adequately protected. Does that mean we would still not do it? No.

For some of the other considerations I mentioned earlier, the better science, we know that we'll probably get some burden relief by just adopting the ICRP 66 lung model. And on a case by case basis

we allow many of our nuclear fuel cycle licensees to do just that. So it's possible, especially if we want to talk about consistency, getting EPA, OSHA who's back in ICRP 2, DOE that's not going to ICRP 60, and our Agency on the same thing, we'd consider that.

And for my standpoint, based on some of the things that we've seen and where we're concerned, we right now don't see any radical developments in the science that are going to have a significant impact, at least in the near future, on our regulations.

With that said, does that mean DOE should not continue their program? No. We're firm advocates of that, firm advocates of the EC program because this is our basic research program that, even though they might not have a near term practical application in the regulatory community, there are other things that might come out of these programs, a better understanding of the cell and molecular biology that might have applications in the clinic, and, as such, I would firmly endorse continuing those programs.

Thank you.

CHAIRMAN RYAN: Thank you, Vince. Just a quick question. Could you back up to your slide? Let's see, one more. You know, I kind of focused on 360 because that number's been around for a long time,

and I recall last year's NCRP meeting when 360 may not be the best number to represent the background or distribution of the various components of the background. What would happen if it were 600, the medical and radon and everything else being considered? What do we do then?

DR. HOLAHAN: Well, keep in mind 360 is the 1999 ATSDR number.

CHAIRMAN RYAN: Sure.

DR. HOLAHAN: So keeping that in mind. Let's say we adjust it and we say that the background is something higher because, obviously, 360, it includes radon, it's industrial sources, other commercial sources, and medical. And let us assume that the medical goes to something on the order of 3, 3.2, 3.5 mSv, whatever the final number is going to come out. So, yes, it's going to go up to 600 or 6 mSv a year. Fine.

Now the question I would have is, is they used an uncertainty factor of three. Typically they use ten. When we look at inner human variation in EPA and FDA space, that's going to wipe out --

CHAIRMAN RYAN: But you could actually argue the other way, that because of the NCRP report, the uncertainty has perhaps been at least the same or

reduced by further update. I just throw that in to think that these numbers aren't necessarily fixed in stone and they have a two-way impact. One is, what do you with a different number, higher or lower, either way? And then, you know, how does that factor into any kind of derived standard or requirement that falls out of that? So it can be a complicated question.

DR. HOLAHAN: The other issue that you're going to run into is there are deterministic end points, and one of the concerns in another analysis would be reduction IQ. And if you look at a single acute exposure of reduction IQ, we're down into the several Sv level. So it's not going to be a whole lot difference.

And, really, the point I have is I wouldn't chase decimals on any of these discussions here. It's just illustrative that our system of radiological protection that we have right now, that those limits that we've established, the optimization in the ALARA programs that we've done, the constraints that we have on some sources are protected, and if we were to have a practical threshold, quite frankly, I think we're going to end up in the same place we're already at now.

CHAIRMAN RYAN: One other practical thing

I think in your next slide on harmonization that's important to think about is just within the NRC that's everything from ICRP 2 to support reactor --

DR. HOLAHAN: Exactly.

CHAIRMAN RYAN: -- calculations right on up to the ability to use the most recent recommendations for models and those calculations, and so forth, and then you mentioned a broader issue that across other agencies is a wide variation of what underpins various regulations, so that's a bigger issue than just the NRC's.

Have you talked to other agencies at this point? Do you have any insights about the inner agency task force on what their thinking is?

DR. HOLAHAN: We actually brought this topic up two weeks ago. We have an inner agency steering committee subpanel report federal guidance subcommittee and this is one of the topics that we brought up. The question is is what is each agency going to do, and, of course, I was specifically said we are going to put NRC on the hot seat, and they directed the question to me, and my response was pretty much what I said about 30 minutes ago, pass me an ear because we're going to have to bring this up to the Commission and get Commission direction.

But, quite frankly, across the board, the other agencies are just starting to think about it. Impacts as simple as we're not going to anything this year because it's an election year. That was one of the responses and that's just, welcome to D.C.

Unfortunately, the rule making processes, they take time. We need for our agency to get guidance from the Commission because, quite frankly, we're talking about a huge investment financially in technical basis. We're looking at Fed guidance 11, Fed guidance 12, Fed guidance 13. Updating and changing all of the annual limits on intake; derive air concentrations, that's in appendix B; that's a lot of work that has to be done and it's going to take some contract dollars.

That, plus any time you manage that program or get into rule making space, we're talking full time equivalents and staff time. And, quite frankly, none of this is budgeted in even our 2010 budget. And if we have a flat budget, the Commission's going to have to make a decision, if we put resources there, where are going to take resources away from.

CHAIRMAN RYAN: If I could impose one more second on your plan? You're actually going to produce

a Commission paper at the end of 2008?

DR. HOLAHAN: At the end of 2008 a paper will be prepared laying out a series of options with resource requirements, costs if you will, for the Commission to consider.

CHAIRMAN RYAN: And just for the folks that might be interested, what would be the public part of the process on reacting to anything you might do or what the Commission might do? What does the public have input?

DR. HOLAHAN: Well, the public will have input on the actual rule making process because we'll solicit information before an advanced proposal is prepared. Public comments will be solicited. There will be public meetings on the topic. Obviously, we'll be going to the advisory committees looking for their input, working with the other federal agencies. Annually, they have a public meeting. I'm sure that will be a topic of discussion there as well.

All of the proposals are put in the Federal Register. Comments are solicited. Undoubtedly, we will receive thousands of comments. And, quite frankly, every one of those comments has to be considered and reconciled.

CHAIRMAN RYAN: Right. I just wanted have

that kind of requirement and everybody here hear it as well. Thank you.

Other questions? Dr. Tenforde first.

DR. TENFORDE: Is ISCORS directly involved in the inner agency dialogue or is that separate?

DR. HOLAHAN: ISCORS is the Interagency Steering Committee on Radiation Standards --

DR. TENFORDE: Right.

DR. HOLAHAN: -- and it's membership includes all of the federal agencies --

DR. TENFORDE: Right.

DR. HOLAHAN: -- to include OSTP, and we have representatives on the federal guidance subcommittee for all of those agencies that have representation with radiation regulations.

DR. TENFORDE: So the inner agency committee reflects the ISCORS composition was my question. That wasn't so clear.

DR. HOLAHAN: Yes.

DR. TENFORDE: I think that's good, and, at the same time, I've been a little discouraged and I think others around the table have written on this that there doesn't seem to be a constructive end point to some of the inner agency dialogues, and I mentioned yesterday one of our reports, which you didn't

mention, 146. I'm looking at the final decommissioning goals of EPA and NRC and I think that's just one example of a number where a little more harmony and constructive dialogue would really be helpful because I do think things need to be looked at, at least periodically, even if no changes are made and I'm glad this is happening.

But I hope that the end goal will be to make whatever changes seem appropriate in view of the exposure to the public, as well as, of course, the occupational setting. So I'd like your sense on that subject.

CHAIRMAN RYAN: Allen?

DR. CROFF: Can you go back to your slide 8, please? If my math is correct, natural background is on the order of 15, 20 rem, and you're showing the region of regulatory interest being well less than one. Maybe I don't understand the scale or something about this graph.

DR. HOLAHAN: Here we're just talking single exposures for all intents and purposes. I'm not talking about cumulative background. I mean if you want to think about it as such, this is the discussion that was earlier this morning. That biological effect isn't zero if you're talking about a

cumulative effect. You've got a mortality rate of 20 to 21 percent. And, clearly, the dose here we're talking about is that addition to background.

Background, if we're talking about the lower LET is what, 1 mSv/y times 70 years. That would, what, 7 mSv. Not 7 mSv, 70 mSv, 7 rem.

(Laughter.)

DR. HOLAHAN: Keep in mind, our regulations, we have rem first and parenthetically we have mSv. Thank you.

DR. CROFF: I guess I understand your response. Let met just let it go at this point.

CHAIRMAN RYAN: Ken?

DR. MOSSMAN: Could you go to your slide 11? I've been interested for a little while on the question of, do we need additional protections for sensitive subpopulations? And it's really interesting that the Commission has been at the forefront of this.

In fact, the Commission essentially preempted the Supreme Court on this decision because we are quite right that in the Johnsons Controls decisions, essentially what the Supreme Court said was it's up to the woman, and that's exactly what the Commission says with regard to pregnancy. You know, in other words, a pregnant woman can declare her

pregnancy; under those circumstances, the employer is obligated to provide additional engineering controls or other kinds of controls, and there's a new dose limit that's established for that person temporarily.

My question is this: if we think of the pregnancy situation as just being a broad model for sensitivity, then if we identify sensitive subpopulations, and there have been estimates anywhere between one percent and ten percent of the U.S. population might be sensitive, that's a very, very rough estimate, then could we adopt a pregnancy-type model and allow workers to say to the employer, yes, I am sensitive, and by doing so, then the employer either educates the worker, assigns new positions, establishes new engineering controls, whatever it is, and just like we have for pregnancy, the worker could also undeclare the sensitivity if they don't happen to like what the employer is going to do for them, or whatever? Are you looking at that, at the sensitivity question that subpopulations in the pregnancy model at all?

DR. HOLAHAN: It hasn't been discussed. It's something I guess we could look at. But I guess the question would be, from a simplicity purpose or point of view, how many different standards do I want

to set for a worker?

DR. MOSSMAN: Well, you already have the pregnancy standard that you've set.

DR. HOLAHAN: But, again, that's voluntary.

DR. MOSSMAN: Right.

DR. HOLAHAN: It's not required. That's in this country. Now, if you go over to the European Union, the fetus has the right of an individual --

DR. MOSSMAN: Right, right.

DR. HOLAHAN: -- and that fetus basically is limited to 1 mSv during the term of the pregnancy and there is no choice about voluntary, involuntary declaration.

DR. MOSSMAN: I'm talking the U.S.

DR. HOLAHAN: And that's one of the concerns or one of the problems we have with adopting the BSS because of those type of considerations.

CHAIRMAN RYAN: Dr. Le Guen, do you want to make a comment on that?

DR. LE GUEN: Well, we have an AEN meeting on this topic and I sat during this topics, but it's not my point of view. It's much more a Europe point of view. No one should be discriminated by gender characters. And when you have a good radiation

protection process, you must process the most sensitive. And as a second point, if you look, if you remember yesterday what I mentioned about the dose received by the nuclear workers, but also true about ideologies. In fact, about nuclear war, the average dose was 1.5 mSv. And for the moment we don't have describe population. We are very sensitive for 1.1 mSv. But, you know, sometimes this is a rule. But sometimes much more complex, the real life is much more complex.

I have a story, as a physician, I remember a few years ago one woman, she had breast cancer and after five years she survived. And she asked me because she wanted to work again, and she was in the hospital and she was a technician for radiography, and she said, well, I would like to work again. And the occupational physician also called me and said, well, I have trouble because I know about radiation, there's a link between radiation and breast cancer. And so what is the solution? And I told him, you know, she survived after first cancer. If you said to her, you cannot work, you will die again, so be careful about that. And I say, well, can we have a work place study? He said, yes, of course. So where the risk is? In fact the risk is when she need to go in

emergency service close to the patient and you must make some radiography. But if she stay in the department behind all protection, she receive no radiation. So I say okay. So she can work, but she will work only in the department and that's all. That's why it's sometimes not so easy.

DR. MOSSMAN: No, no, I certainly didn't mean to imply that it was easy. But, you know, in the case of subpopulations, you may want to consider alternative work environments simply because there is some enhanced sensitivity. There's two ways you can do that. (1) You can have different administrative levels or you can just use some kind of average limit as we are currently doing. There's any number of ways of doing it, but it's an issue that's important. I know that the Nuclear Energy Agency, I was on the committee that Henri Metivier had shared and one of the questions that surfaced was this whole notion of how you deal with sensitive populations, and is it something that we in the international radiation protection community should be concerned about? Is the current system protective of everybody?

And, again, it's a utilitarian philosophy versus one in which, well, no we need to be very specific about how we're going to deal with sensitive

subpopulations. So it's an ongoing debate, but it's very important.

DR. LE GUEN: Yes. About sensitive population, I can one point. In France we are looking for people who have cancer at the moment of treatment. And, of course, we try to have different tests because if they are sensitive to radiation, we will try to have another kind of treatment, chemotherapy for example, much more than the radiotherapy because we are looking for the certain malignant cancer in case of radiotherapy.

But so, all the time it's a problem of dose and, of course, in case of sensitive population, it exists but at very high dose. So you remember what you say yesterday, you believe much more in ALARA process, me too. In this case I think we need to protect everybody and I think this is a most important thing.

DR. MOSSMAN: I agree.

DR. HOLAHAN: What I would suggest that you do is, if you're interested, we have a radiation exposure information reporting system report that the agency puts out on an annual basis. All of the NRC licensees that report into this system we publish exposures for each of several groups of individuals

and break out the ranges where we have the exposures. We find that with our ALARA system, on average, most workers receive zero exposure.

Now, in that type of situation, if you're using ALARA, you're optimizing the exposures, I'm not sure what benefit in an occupational setting a differential, multi-tiered system is going to have because the exposures are so low. We're saying on average most of these workers are received a mSv or less, and that's the average. There are a few that might exceed 2 mSv, but generally that's a fraction of one percent; 99.some percent are below that. And that's the value of, again, the optimization, the ALARA programs that our licensees have because, quite frankly, they want to keep, if nothing else for litiginous purposes, exposures as low as possible.

CHAIRMAN RYAN: That's a great way to finish up, Vince. Thank you for a very informative presentation, and Dr. Puskin, and all our presenters today and yesterday.

I hope that after our lunch break, when we reconvene at 1:00, we can have a rich panel discussion. We'll start with that some question from the members and we'll continue on from there.

Again, thank you all for participating in

what has been a real rich meeting today. Hopefully this afternoon will be even better. Thank you. See you at 1:00.

(Whereupon, the foregoing matter went off the record for lunch at 11:35 a.m. and went back on the record at 1:06 p.m.)

CHAIRMAN RYAN: If I could get everybody to take their seats, please, we'll come to order for our afternoon sessions. We are scheduled for a panel discussion and individual summaries by all of our participants and questions from the committee members and any other questions that might arise and that's going to go on from 1:00 to 3:00.

I've had one request from Mr. Dennis Nelson of the organization SERV to speak for about five minutes and he will be --

(OTR comments)

CHAIRMAN RYAN: As others join the conference call line, we'll have them announce themselves when they do that, so please forgive any interruptions. Dr. Mossman, you started us off yesterday morning. How about starting us off now? And let me set the stage, if I may. We started off yesterday with Commissioner Lyons giving us his

interesting perspectives on an interest in this topic and I guess I'd ask all of you to think about what advice or insights would you share with the Committee as we think about what sort of a letter and what kind of information we might want to convey to the Commission and the Commissioners in particular.

DR. MOSSMAN: Thank you, Mr. Chairman. I sort of summarized my comments yesterday and so I'll just spend just a couple of minutes conveying my thoughts about today. I was particularly grateful to Professor Hammitt for taking time out from his busy schedule to come join us and talk a little bit about some of the economic perspectives which is a perspective that I, for one, don't fully appreciate but realize how very important it is in the grand scheme about how we deal with the science.

You know, we'll be making some decisions or perhaps, in the future there will be some decisions about the nature of the dose response and whether we should continue to use LNT as policy and part of that is going to include the economic considerations and I think Professor Hammitt's overview of some of the basic principles on costs and benefits and the issues about threshold and whether that's really relevant in the end, I think, was very important, so I'm

particularly grateful for Professor Hammitt's perspective on that and I think that whatever we do we need to consider that.

I was also very interested in the comments by Dr. Puskin and Dr. Holahan, differing agencies, but I think we all have the same kinds of issues in mind about linear no-threshold theory and the underlying radiobiology and what this particularly means.

At lunch today, I -- we had a very interesting discussion on future directions and one of the issues that we brought up that we might want to explore later was, would it be useful for the Commission to revisit the Below Regulatory Concern policy, the BRC policy, that was, for lack of a better word, a disaster back in 1988 and `89, primarily because of a -- because it was not -- the concept wasn't marketed well. And I think a lot of people in the public had -- the general public had some concerns about whether safety was being compromised by a BRC kind of proposal.

The interesting thing is from my perspective as a scientist, BRC is really on very solid ground, the notion that there may be risks even though they're non-zero risks nonetheless, they're so low that they don't cause us any heartburn. They're

not anything that we should be concerned about with regard to public health protection and should we be concerned about ratcheting -- or should we be concerned about expending resources to very, very small doses that, in fact, the incremental benefits that you would be expected really aren't very real at all.

So one of the things I'd like to see is a revisit of that and maybe that's something that might be considered for this letter that you want to write.

CHAIRMAN RYAN: That might actually be a little bit beyond the scope of our information gathering --

DR. MOSSMAN: Okay.

CHAIRMAN RYAN: -- for this session. So that certainly could be something that could be considered by somebody down the line but it would be a little bit out of the wheelhouse of gathering information on that topic for this letter.

DR. MOSSMAN: Okay.

CHAIRMAN RYAN: But I can clearly see it's a logical extension of --

DR. MOSSMAN: My -- the reason why it's brought up is the idea of risk communication, how you frame risks, become very important and that was the

failure point, if you will, in the whole evolution of the BRC initiative.

CHAIRMAN RYAN: I understand that and I think what our letter is going to focus on is the appropriate and best way to communicate risk and to characterize risk and to analyze risk.

DR. MOSSMAN: Right.

CHAIRMAN RYAN: And whether it's applied to any one regulatory effort or another, I think that our focus ought to be on the risk aspects that we've heard this time but I appreciate your point.

DR. MOSSMAN: I understand. That's really all I wanted to say.

CHAIRMAN RYAN: Okay, anybody else? Mary Helen.

DR. BARCELLOS-HOFF: Well, I wanted to add -- I thought it was very useful for me as a basic scientist to hear how regulatory decisions are made and the complexity for each agency. It leaves me a little bit to wonder how relevant basic biology is, but I think there is an underlying assumption that I'd like to just bring out and that is essentially that we know the basis for radiation's action as a carcinogen.

I think that's one of the underlying assumptions and thus, you know, radiation is a

mutagen, a poor mutagen. I think that one of the considerations that the basic biology brings to the table is not only the complexity of biological responses but given that that complexity may well be very much dependent upon dose, and that there may be contributing factors at high dose that really augment the carcinogenic potential of that mutagenic effect and that's what we're really trying to bring to the table, is that the non-targeted effects that we have this kind of question, well, these are very interesting biology but what does it mean to us, is that that non-targeted -- those non-targeted processes are the ones that more and more basic biology is focusing on as really the drivers in carcinogenesis and understanding then the dose dependence of those non-target effects become critical to actually saying not only do we have a regulatory model to evaluate risk in a population but we have a good biological understanding what that risk is due to.

I think that allows us to do something that we haven't been able to do before and that is actually think about susceptibility in a different fashion and I can go on about that but I'm not going to.

CHAIRMAN RYAN: Please do. I find this

part of our meeting fascinating because you know, as a physical scientist based person, you know, ergs per gram is just fine and has been for a long time but you know, I'm re-educated over the course of these two days by the details that are so important, well, that's not fine. I mean, it really is energy deposited in what, where, how, when and next to what.

DR. BARCELLOS-HOFF: And the consequences of the --

CHAIRMAN RYAN: And the consequences. So I would appreciate you expanding on that a bit.

DR. BARCELLOS-HOFF: So I guess my -- the thought I'm trying to convey here is that we have, for example, in the presentation -- I'm sorry, I can't read your name from this far away. Vince, and I'm terrible with names as I demonstrated yesterday. It was Peter O'Neal whose name I was trying to remember yesterday.

So in one of your slides you had dose and effect. It was one slide we went back to later and there was the epidemiology and then there was cellular molecular biology and then there was this line and one of the things that the cellular molecular biology you referred to was cytogenetic and clearly we can see cytogenetic effect. But effects, like cytogenetics is

really an assay or really reflects dose and therefore, we think the effect is also associated to the risk and the only -- the main point I'm trying to convey in the biology is that risk is multi-faceted. The process of carcinogenesis is multi-faceted and that what we're really looking at is in cancer incidents is the culmination of this. And that while it's true we see very early effects and that we can track them linearly with dose and there's absolutely no question that there is a linear consequence of radiation exposure at one level, which is generally DNA damage, and that it does have a probability of causing mutation and that mutation has a probability of contributing to carcinogenic process, that it's really a more complicated process and one of the things that allows a tissue to develop a clinical cancer is perturbation in all the other cell types that are not mediated by mechanisms dealing with mutations.

And that's -- but it's a two-part problem. I believe you have to have the genetic change in a cell and that radiation is good at doing that, but I also believe you have to have this perturbation of the system that we referred to and that actually high dose radiation is good at perturbing that system and that's why it's good carcinogen at high doses.

But the question that remains is whether it perturbs the system at low doses and whether it does it in a deleterious fashion. And that's my assessment of the biology and so of cancer as a process. And that's the part I don't see represented when we talk about radiation effects being a damage and then leap to carcinogenesis. There's a big leap there and we see it over and over when we draw these models and I know everybody -- I just wanted to bring that up.

DR. MOSSMAN: Is this a merchant's problem, I mean, you know, where you're looking at individual cells and then extrapolating over to the grosser pathology.

DR. LAND: Is there anything radiation specific about the non-targeted effects?

DR. BARCELLOS-HOFF: Is there anything radiation specific about the non-targeted effects? No. Well, I'm afraid that my -- I don't know anything but radiation. No, so I couldn't compare and contrast it to like a chemical carcinogen. The experiment that I showed you yesterday -- here I can, I can. Okay, so here's a non-targeted effect, right?

The experiment I showed you yesterday, where you have your mouse and you take out the

epithelium from the mammary gland and then you irradiate the mouse, right? This is the experiment I did and then I transplanted in unirradiated epithelial cells and showed that they readily went to cancer even though the host had only been irradiated, right?

And that actually that was a very strong effect, because I could see an increase in cancer, a 30 percent increase in cancer at 10 centigrade. Okay, so that's acting on all of those other processes not on mutagenic load in the target cells. So that experiment has been done with two other chemical carcinogens by colleagues of mine, one with NMU and one with DNBA.

In the case of DNBA, in rats, DNBA in rats or NMU in mice or vice versa, but anyway they're both carcinogens of mammary gland. In the case of NMU, there was no effect via the host. If you treated the host, you didn't change NMU's carcinogenic potential but in DNBA if you treated the host you almost -- it was almost 100 percent of the cytogenetic potential.

So are there other agents that act through additional processes then mutation? Yes. And there are actually a lot of carcinogens that aren't very good mutagens, asbestos. Asbestos actually acts indirectly through the production of reactive oxygen

to generate mutations but not a direct mutagen.

DR. MOSSMAN: Mary Helen, do you want to comment on the school of thought that this guesstimates derived from epidemiologic studies already include consideration of non-targeted effects? I mean, it would have to. Simply, is there anything more -- I mean, so in terms of our understanding of risk, if in fact, linearity holds and it is true, then the risk estimates that we get primarily from studying effects at high doses, say above 200 mSv, 20 rad, then whatever influences, positive or negative, that bystander effects would have and things like that are already accounted for in the risk.

DR. BARCELLOS-HOFF: Well, that's true but that's only true as far as the epidemiology shows an effect.

DR. MOSSMAN: Right, right.

DR. BARCELLOS-HOFF: After that, you're extrapolating based on underlying assumption that you understand the mechanism and that the mechanism isn't linear. And I have a slide. I don't know that we have an AV person, and we don't have a chalkboard. And actually, I'll talk about and try to present this idea next week at the NCRP but if you think about that linear component, and we say it's a two-compartment

problem that you have to have both compartments or both modes of actions, right, I talked about modes of action yesterday. Both modes of action have to occur in order to actually get that effect, that consequence cancer.

So you're linear no-threshold, right, that's targeted effect. So remember one of the things about non-targeted effects is they tend to have a step-function dose response. A very small dose will elicit the response, a larger does doesn't increase it considerably. It's not proportional to dose. It's more like it's a biological process that turns on and once it's on, it's on.

And so then it becomes a question, well, at what dose does those other processes occur? And yo could put your linear no-threshold. You could say, okay, at 10 centigrade, see, I use a completely different set of -- 10 rem, right, that's where it turns on and anything below that all you're going to have is that linear component and it's therefore, not going to be as efficient as a carcinogen because all you've got is the mutagenic potential.

And I think if you go to the chemical toxicology literature, there's a lot of discussion about modes of actions and how they intersect with

each other and how they change as a function of dose. But in radiation biology for some reason we kind of left off that whole other effect that radiation really has and that may well be acting in concert with the mutagenic effect and we don't understand it.

So that's the -- I started off trying to say what we tried to bring to the table is from the science side is what we understand about the biological processes and clearly we understand a lot more about DNA damage than we did 25 years ago and we have an exhaustive amount of information about the mechanisms of damage repair and resolution and cell type specificity and now I think we'd like to have that equal depth of knowledge about these non-target effects, changes in phenotype that have persist on gnomic instability. It's really a phenotype. It's not a mutational -- it's not a train mechanism frequencies consistent with a mechanism mutation. It's a phenotype.

CHAIRMAN RYAN: So the next leg of this chair is to kind of gather that all up at the cellular and now we're going to talk about you know, groups of cells and tissues and organs and organ systems and the whole --

DR. BARCELLOS-HOFF: The systems biology

where we try then to compile all that information in that useful fashion that we begin to predict how -- so when you get back to sensitivities of populations, what I begin to -- what I find very interesting about radiation cancers is that it's not -- there's nothing unique about it. It's no different. You don't induce a particular set of cancers. There's a susceptibility inherent in the population. We seem to be augmenting that susceptibility and whether that susceptibility is lifestyle, in the case of the gastric cancers somebody mentioned yesterday or is it a case of genetic predisposition, it could be that you're actually dealing with an accelerated -- well, you know, I don't want to say that because it gets into very -- but in breast cancer right now, there's a large effort in understanding not only those very strong genotypes that drive familial breast cancers like BfCR1 and 2 which only contribute to -- only account for what is it, five percent of all breast cancers is familial; is that right, Charles, something like that. But the preponderance of breast cancers are actually due to interactions between very weak polymorphisms so there's -- but they're high frequencies so the BrCA1s are very strong but they're very infrequent.

And then you have the genetic component

where you have a lot of weak high frequency polymorphisms and there's an argument right now that a large proportion of those cancers that we distribute across the population actually only occur in a very small portion of the population. This is Bruce Ponder's analysis of polymorphisms in the breast cancer populations.

And I think that's an interesting idea that we should consider in radiation protection is a sensitive population, whether those cancers are really occurring randomly throughout the population or really in a very discrete set of individuals.

CHAIRMAN RYAN: Interesting. Thank you very much. Jerry?

DR. PUSKIN: May I respond to that? Maybe my take on it and you can respond to this. If it's correct let's say that radiation causes mutations but then it also causes other things and these other things are necessary in order to get a cancer from this mutation, it would seem like a threshold, a real threshold you're in likely because we already know that whatever processes convert a mutation into a cancer are already occurring in the body without any extra radiation, people get cancer. So if all these cancers kind of rise out of these mutations. So

wouldn't that argue that yes, the dose response could be non-linear below where we can see the epidemiology, sort of the question that Dr. Mossman asked but it could be very non-linear because the relative importance of these different processes, the effect of radiation on these processes could be very different low doses than they are at higher doses. So you might get something that doesn't look like a linear dose response but you still -- radiation should still be able to cause some cancers.

Now, you would say --

CHAIRMAN RYAN: I think the secret there is some, you know, but not all.

DR. PUSKIN: That's right, that's right.

CHAIRMAN RYAN: So that's a little bit of a confounder there.

DR. BARCELLOS-HOFF: And so you could have two parallel curves with a drop in between, right? And so then my question is, yes, there's -- the linear component will always give some kind -- we did talk about this concept of negligible and at some point it does become negligible in a body of, you know, 14 cells, that one mutation and one randomly hit cell.

DR. PUSKIN: Or you can prevent some cancers, you know, and that sort of thing.

DR. BARCELLOS-HOFF: And one of the ideas that comes out of thinking about it, is that you can actually begin to think of ways of reducing the carcinogenic potential of radiation which you can't do with mutations because you don't know what your mutation is. You can't come in and target your p53 or your, you know, whatever, ETFR. It's hit and you don't know what it's going to be but these other processes actually do lead you to other strategies for thinking about carcinogenic risk and it's inevitability.

DR. LE GUEN: We must keep in mind that if we observe cancer due to the edge, it's do to an accumulation of mutation due to the edge and in fact, at high dose we accelerate the process and that's why you know, of course, that after high exposure you have a risk of cancer not next year after the exposure but 15 -- an average of 15 years after high exposure.

It's only time -- the need, time to need -- no, the need to have a second mutation and to have a process and in fact, for us to -- the first exposure is the beginning of the process, this is a first step but you need to have other steps before to have the cancer, the tumor and for sort of tumor it's between 10 and 15 years.

And that's why in fact, I wanted to say this morning we talked about the different non-targeted effect but from my point of view, it's not good to try to compare one non-targeted with another and say this one is good for the body, this one is not good. This is a war reaction of the body and we must take this reaction as a war and particularly, you know, today we know that cells react at very low dose. This is a reaction and it's not a problem. And for people to say, "Well, of we observe a reaction, it's bad".

No. We live under stress and if we are not a reaction of a cell we die. And in fact, this is a reaction and this is normal reaction. Yesterday I said about the evolution and probably because now at this dose we have a lot of different stress. Today we talk about raising radiation, but we must take into account also the other stress. That's why about education on the seven point, I full agree with Ken and also Vincent who says this morning that we must think about which kind of communication we must have with the population.

And if we are talking about risk, we must talk about all the genetic toxic agent because if we want to focus only on one, it's not fair because we

live with other stress and to -- the body is a marvelous device because if we can live under stress it's because we have different mechanisms. The problem is and when you begin to have trouble when we begin to be on the way of the cancer and that's the difficulties that we have. But to have a -- to observe a reaction at low dose, I think it's not bad. It's normal.

CHAIRMAN RYAN: One of the things that, you know, in this whole issue of, you know, accumulating dose and thinking about the natural background and then workplace exposure, there's one part we really haven't talked about and I'd be happy to have any insights, and that's medical exposure. Medical exposure is usually given compared to the workplace or compared to the natural environment, a very high dose rates relatively speaking in very short bursts. So I'm not so sure, you know, fluoroscopy can be 10s or even 100 centigrade over, you know, typically, you know, major portions of the body.

How do we account for what is -- what NCRP has reported last year and hopefully will publish soon an increasing population of folks, now I know not everybody gets, you know, the same level of medical care. Certainly nuclear workers get a level of

medical care that's appropriate for good health and all of that, but how do we deal with that now significant component of what is typically ignored as part of their background exposure?

DR. BARCELLOS-HOFF: I was actually very struck by that comment. Essentially, isn't it doubled almost.

CHAIRMAN RYAN: Yeah, it's more than that actually.

DR. BARCELLOS-HOFF: Yeah, I mean and so I'd characterize it as a schizophrenia, right, because on the one hand we regulate to incredibly small doses. On the other hand there's no regulatory checks other than, you know advisor decision --

CHAIRMAN RYAN: And again, I'm asking this question about the radiation biology and how that would flow into the epidemiology. I realize people judge medical exposure differently than they would workplace and background. I'd just like to leave that on the side.

DR. BARCELLOS-HOFF: Well, how can you treat it differently?

CHAIRMAN RYAN: Well, I mean, very often it's not recorded or known and yet it's double the background if not more in some cases. Some folks have

lots and lots of exposure. Some have very little and some are in this kind of average condition but there's a large fraction of folks who get up into the 50s that have cardiac scans and all the rest. You know, those could be up in the near 100 rad.

DR. BARCELLOS-HOFF: Well, my colleague at DOE always asked the question about the RERF data set and how the population there has been very carefully monitored with radiation and how that doesn't -- that piece of information isn't part of the dose exposures or the cumulative dose is not included in that.

CHAIRMAN RYAN: Can you, Tom, talk a little bit about what the NCRP is finding in this area in terms of the numbers?

DR. TENFORDE: Yes, actually we will be soon putting the draft of the Committee report on our website and that will be publicly available at that point and it will undergo then formal council review. It's about to undergo expert panel review, which we do before the council review but in brief, the average medical exposure per annum for an individual in the United States has increased from about 50 millirem in the early 1980s to a little more than 300 millirems in 2006, a six-fold increase, which is very substantial.

So now in looking at the total exposure

with average values for terrestrial, cosmic, internal body, radon, and minor contributions from occupational, et cetera, adding medical you're up to about something like 6.2 mSv per year. About twice what it was at the time Report 65 was published in 1987.

Now, this introduces in my mind a lot of very interesting questions and complications. When we were talking about average exposures, let's say 20 years ago, we were talking about roughly 300 millirem of which nearly all was chronic exposure, very low rates, like a millirem a day. Now, we're suddenly looking at a background exposure including medical, where about half of the exposure consists of acute exposures to fairly significant, non-trivial doses at higher dose rate, much higher dose rate.

So given the fact that a lot of regulations are built around the idea that exposures are chronic at low dose rates, how do you now compare those regulatory guidelines with the current, if you will, total average amount received by US -- a member of the US population? This is true, by the way, in Europe, Japan and a number of other countries, having looked at this --

CHAIRMAN RYAN: And if we pick up on

Vince's point that the large fraction of the workforce has, you know, low cumulative doses, you know, it really boils down to even in the nuclear workforce, it's really the medical exposure is in excess and at the higher dose rates than the work exposure.

DR. TENFORDE: Right, and the issue, where I was headed on that is that you now have the complexity of comparing low chronic doses delivered at low dose rates with a much higher average annual, if you will, background, including medical --

CHAIRMAN RYAN: Right.

DR. TENFORDE: -- for the population and half of which is delivered at a much higher dose rate.

CHAIRMAN RYAN: And in small bits or in bits across --

DR. TENFORDE: Yeah. And I don't -- this is a very complex issue. In regulatory circles typically, in the past, medical has been set aside, the idea being that this is a beneficial use of radiation and you really need to look at health benefits versus the risk of having radiation administered for medical uses and you know, we've tended to ignore that but the level of medical exposure now is reaching a point where I'm not sure it should be ignored in terms of public or occupational

exposures.

CHAIRMAN RYAN: And just to take the point -- and I don't disagree that that premise is a valid one to think through but the fact that there's now these episodic exposures that are significant compared to the chronic exposure from what we've learned about, you know, these more sophisticated ways to think about the biology, it would seem that the biology could be confounded by these short higher dose rate exposures as well as you know, the question of is there a question of appropriate, you know, requirements for control, et cetera. So am I right there, that that could be a confounder?

DR. BARCELLOS-HOFF: But it would also be compounded by, except in the whole body CT scans, you have very localized radiation and one of the things, I just don't know how to extrapolate is, is whether -- we were talking about this over lunch, your colomated (phonetic) tumor would elicit an immune response, right, even though it was a local volume that was irradiated, but, you know, volumes irradiated also might impact this.

CHAIRMAN RYAN: Oh, sure.

DR. MOSSMAN: Mike, if I could add --

CHAIRMAN RYAN: Yes.

DR. MOSSMAN: -- you know, this problem with medical exposures and the high doses isn't anything new. You can go back better than 20 years and the American College of Radiology and other groups fully recognized even back then that doses were very high for many of these procedures. The problem became very acute within the last four or five years when it was recognized that you had this tremendous increase in number of examinations that were done from three million CT scans in the early 1980s to over 60 million today and so that's the fundamental problem.

It might behoove the Advisory Committee to look at the paper that Amos, et al., published in the Journal of the American College of Radiology back in May or June of last year in which they set up a whole structure of dose reduction, the kinds of issues that they needed to look at that included unnecessary repeat examinations, partnerships between patients, physicians, insurance companies, that were major drivers in elevating the dose.

I mean, there are all sorts of stories about a patient going to his primary care physician. The primary care physician orders a CT exam of the abdomen. That study is done. The patient is then triaged to a gastroenterologist specialist. The

gastroenterologist specialist within two weeks does the exact same exam all over again and why are they doing it, well, in the name of ligation, in the name of whatever philosophy of patient care that they have but it's those kinds of problems.

From a personal standpoint, I think the driver in all of this is not so much the public health impact of the increased radiation dose, but the medical costs. I mean, I think that the major issue is the tremendous costs of doing these CT examinations, but if you look at the ACR White Paper, they have a well-thought out strategy about how to deal with what is ultimately a dose reduction problem. How do you eliminate unnecessary x-rays things of that nature.

CHAIRMAN RYAN: And I appreciate those additional, you know, areas of interest and concern, but again, I'm trying to narrow our --

DR. MOSSMAN: No, no, but in terms of where we're going in terms of it's a dose problem from a radiation protection standpoint, it's how you eliminate the dose and there's all sorts of reasons why you have the high dose.

CHAIRMAN RYAN: Right. No, I appreciate that and not all just because it's more. I mean, I

understand. Thank you.

DR. LE GUEN: I agree, just to moderate but all is true and I agree with everything but one of the increase is also due to the aging of the US population and because in the modern democracy in Europe and in US we have trouble that we have an aging, an important aging of the population. And of course, if you increase the aging, you increase the number of medical examinations and that's why if we are talking about -- as the problem yesterday I mentioned that from my point of view, it's very important to focus on the most sensitive population, so children, pregnant women and so on, much more than other all population because if you are 80 years old or 75 years old, it's not a problem if you have two CT scans but if you are younger, yes, of course, it's much more interesting to take into account.

CHAIRMAN RYAN: It would be interesting to try and figure out how many nuclear workers or radiation workers have medical exposure that exceeds their workplace exposure.

DR. LE GUEN: Yeah, yeah, you're right.

DR. HOLAHAN: Well, I think that information might be available. One of the things hat we haven't seen yet because the report is not out, is

with CT demographics. And it's pretty much equal across the board. The children under age 10 are getting as many CT scans as the geriatric cases in their 70s and 80s.

DR. TENFORDE: Yeah, actually, I have a slide that shows the distribution. It does -- it's sort of bell-shaped with a peak in the 50s, age-wise but it's not a, you know, it's not a huge drop-off between the very young and the very old. It's a very understandable peak because people begin to develop health problems that require nuclear cardiology and CT exams in their late middle age and as they get older, either the problem is cured or they die, you know, or their judged not to be curable. So they don't get more and more exams.

So that's the explanation of the curve, I think.

DR. HOLAHAN: But the issue that I'd go to is those children are also the most sensitive. All you have to do is look at the life span study and the children under three and five are much more sensitive than somebody radiated in their 30s or their 50s and what's going to be interesting to see what happens to those kids 50, 60, 70 years from now, because if you look at the life span study, when did most of the

solid cancer start showing up? It's only been that last 10 or 20 years.

That is to say, it was the folks that were exposed under age 20 at Hiroshima and Nagasaki, so that age dependence is going to be very important.

DR. MOSSMAN: But you know, in that regard, though, the Oxford Childhood Cancer Survey is very -- is very instructive because one of the issues in trying to understand the nature of causality was asking the question, what was the medical reason for the woman to have the exam to begin with. And did that medical status or risk of disease have any impact on the risk calculations?

We can ask the same questions here with regard to CT exposure of children. Why are they having the examinations?

DR. HOLAHAN: Traumatic injury. I mean, traumatic injury won't necessarily be disease.

DR. MOSSMAN: And -- it may not be, but we don't know. I mean, we just -- we don't know whether it's some kind of chronic illness. We don't know if it's, you know, and appendicitis or something like that. Sure you might say that it's an isolated disease, we don't have a problem but we just don't know and all I'm saying is that it's -- that kind of

concern complicates the interpretation of the data in trying to attach some kind of public health impact to CT exams of children and you know, that's the only reason I bring it up is that those kind of issues have been brought up before and it makes the interpretation difficult.

CHAIRMAN RYAN: Jerry.

DR. PUSKIN: Along those lines, another concern is CT scans of infants and that often happens if there's problems, spinal fluid and so forth. There's -- there was a study done by a Swedish group Herr Hall and others that showed that infants who are radiated for birthmarks on their face that years later, it turned out they had lower cognitive ability than controls and the doses weren't that much higher than typical head CT scans.

You know, the total dose was around six rad. You know, if you get a series of three CT scans to the head, you're in that same range. So that's certainly another concern.

DR. LAND: Also true of the tinea Capitis patients.

DR. MOSSMAN: Reduced?

CHAIRMAN RYAN: Well, it's a dimension I think we've kind of heard a number of, you know,

examples of the studies that address this idea that medical exposure is certainly increasing and certainly there's some evidence that say that's part of the overall radiation risk profile for workers or others and as well as background and workplace exposure. That's an interesting observation.

DR. PUSKIN: This is off of medical.

CHAIRMAN RYAN: Please change the subject. That's fine.

DR. PUSKIN: I just wanted to sort of make a final few points along the lines that I made. First of all, I would second what Dr. Holahan said, that you know, that aside even from the question of radiation risk, that we certainly second the support for the low dose program at DOE. I think there are very interesting things coming out of there that I think will have wide implications in terms of understanding carcinogenesis and biology in general. And also we're interested, very glad that DOE and NCI are supporting the Techa River study and other studies of chronically radiated cohorts.

What I've seen here though is that we have these effects, these low dose effects and undoubtedly they are real in some systems at some doses and so forth but what we don't really know is do they have

any significant effect on the US and I think that's really what drove BEIR VII. In Committee they said, yeah, these effects occur but any effect on the reask at this point is highly speculative.

You know, in looking at it, we don't see why it would necessarily have a big effect and given also that as far down as we can look, there's no indication of a strong deviation from LNT. And as I tried to bring out, I think we're going down pretty far. You know, it's true, it's not as far as we need to go, but and we don't see that.

So right now, I think the effect on risk is at least highly speculative and given that, I don't think there's really an alternative to LNT either for risk assessment and especially, I think Dr. Holahan made the point stronger than I did but on regulation. That we're really not going to be able to relax the risk estimates in the -- or relax regulations based on these kinds of studies any time really soon.

And I guess that's really what I was --

DR. BARCELLOS-HOFF: And good I just add as the biologist here --

CHAIRMAN RYAN: Yes, please.

DR. BARCELLOS-HOFF: -- that as a citizen, I hope you don't. The precautionary appearance of

ALARA all those things hold. What we're trying on the basic biology side is really to understand radiation's action as a carcinogen. It is the only known human carcinogen that we have to understand this process better. I often speak to cancer biologists who go in and mutate that and then make a mouse that's all mutated or you know, and say this oncogene drives all of carcinogenesis and I say, "But does that tell you anything about spontaneous cancer or does it tell you about exposures in terms of how we think about human populations". And it's very hard to get them to come to that, you know, "Oh, well, radiation is spontaneous DNA damage, it would cause this mutation one out of 10^{14} times, you know.

And you could do those calculations. So it's really important just to understand that radiation is very interesting as a biological -- in terms of the biology it elicits. And what we're trying to understand better is, is that biology and you're absolutely right, some of these effects may be just that, effects, transient. And one of the goals if the DOE program is to make sure that people try to take that biology and link -- make the next linkage which is does that effect have a consequence that fits into this model of cancer?

And it's easy to do with DNA damage. But it's going to be much easier to do in the next 10 years with the biology that's coming out now to link all these so-called non-targeted effects. I just want the radiation biology community to be aware of them and to be thinking about how that might impact the way they consider radiation's action as a carcinogen. But it's actually true, we're not done.

DR. MOSSMAN: Mary Helen, do you see in the future moving away from cellular radiobiology studies all together and focusing on tissue and organ effects in a system biology approach recognizing as -- we see that cellular effects are fine but they are very limited in terms of what it is that they can tell us about cancer as a tissue and as a multi-cellular organism phenomenon. Do you see a general shift in the kinds of models that you will be using that --

DR. BARCELLOS-HOFF: That's one of the big emphasis in the DOE program against a fair amount of resistance if a portion of the radiobiology community because it is easier to look at things that you can have a flat on a dish, you know. There's a lot of technical advantages to that when you're trying to control variables.

As we get into more complicated models

it's more difficult to control variables and to attribute. And actually, you know, it's very hard in the United States right now and I think even worse in Europe to do an animal study.

DR. MOSSMAN: Yeah, that's true.

DR. BARCELLOS-HOFF: But it's -- you know, to put all those pieces together, I think requires a slightly different framework that we brought up earlier.

DR. MOSSMAN: Right, right.

DR. LE GUEN: If we have a -- just to complete because that's an interesting point. I believe in that. You know, if you have a look on the story, during the `60s I was too young but a research was -- worked on the protein and after the discovery of the molecular biology and we begin to work on the genome, and after the genome, perhaps it's interesting to look on the function of the genome, so we have the transfetom (phonetic).

Now, we are talking about proteinic so about the protein again, because it's only a part of the answer, the gene. After it's very important to have the function into the cell and after into the cell, into the tissue and into the body. And we have a lot of disease about that just -- I don't know who I

was talking to yesterday about that to say, when we have a higher radiation, we don't --

DR. BARCELLOS-HOFF: We were talking about that, multi-organ failure.

DR. LE GUEN: Yeah, absolutely. In fact, this is a reaction, this is a reaction of the body. We die at the end due to an important inflammation. And the reaction is too strong and we know that. That's very important after we observe physical evidence but yesterday I say it's important to know what will be the outcome, what will be the consequence. And as a consequence we must take into account the tissue reaction and the body reaction.

So that's very important to all of this. And one of the problem, and I full agree with you Mary Helen, it's that today it's very hard to work on animals, that's true. And you remember yesterday I mentioned that it's very hard to extrapolate from a model to the body because we miss something and of course, it's very important to have this link between the observation and the consequences as label, in 3-D in the body, not only in vitro experiment.

DR. TENFORDE: Let me add one thing, I don't know whether this has been said yet or not but in my own mind, the very important research that's

being done with low dose radiation effects to me it is important for more than one reason, more than just understanding low dose effects in the context of policy, practices and regulations. To me it's basic science that will undoubtedly eventually pay off in terms of medicine. I think there's no question about that.

We know that localized insults to tissue propagate. I mean, this has been known for many years, I mean, in terms like abscopal effects, you know, and that the more we understand about response of integrated tissues to localized radiation effects, the more we will be able to put that knowledge to work in terms of treating disease not only at the tissue level but you know, a major issue that's still being dealt with, we deal with it at NCRP and ICRU as well, is what happens outside the treatment volume because we know there is scattered radiation and there are certain norms for how much that can be for various types of radiation and we know that this is an appreciable amount of radiation compared to the amount that people are getting from natural background or other sources.

So I think that a lot of this basic knowledge will ultimately translate into the medical

arena and lead to some enlightened decisions on either proactively or retrospectively treating secondary effects of disease or treatment of disease.

DR. MOSSMAN: I wanted to add that --

CHAIRMAN RYAN: Vince, did we skip over you, Vince? Did you have --

DR. MOSSMAN: Yeah, I need to leave and I just wanted to make one comment --

CHAIRMAN RYAN: Oh, please, okay, all right, sure.

DR. MOSSMAN: -- on Dr. Tenforde's comment. I agree with you 100 percent. I think that the more we get to know about a system or systems and understand their behaviors, the better off we are in managing it. But on the flip side of the coin, it's interesting to note that historically all of the major treatment strategies for radiotherapy in cancer back in the 1910s, 1920s, 1930s were done and understood and in place before we ever understood the concept of radiation repair or anything like that.

We learned about fractionation and all of that stuff and the benefits of doing that before we ever understood one single thing about cellular basis of ionizing radiation repair and the like. So the flip side is interesting but I concur with you 100

percent that we need to learn more about these things in order to be able to develop new therapies like clevat (phonetic) for the treatment of CML that only came about because of findings in molecular biology in the nature of the ABL oncogene and things like that. I mean, I think that that was absolutely critical and is a perfect example. And with that, I excuse -- I need to excuse myself, Mr. Chairman. Thank you.

CHAIRMAN RYAN: Thank you very much.

DR. MOSSMAN: Good to see everyone, thank you.

CHAIRMAN RYAN: Vince?

DR. HOLAHAN: I guess my thought might be to Mary Helen and actually Dr. Mossman is we have to be very careful with the information technology and availability of information. That is to say many of the young investigators know the internet and nothing else. And here's my point; back in the `60s and `70s Al Klein (phonetic) was doing experiments in sub-lethal damage repair and potentially lethal damage repair.

That's not a new phenomenon. I mean, we knew going back to your four R's of radiotherapy, there is going to be repair, repopulation, reoxygenation, redistribution. Much of this is where

we got our tissue, much of this is where we get our DDRF. And I would go back to the French National Report. That was all discounted. It's there. It's nothing new. The BEIR VII report acknowledged that, yet the French Academy Report pounded them on that issue there.

We know that there are single strand breaks in every cell. It occurs daily. You cannot transcribe and translate information unless you break the DNA, unwind it, transcribe it, wind it back up and like it. It goes on daily. You indicated that there was no repair at the very low dose but you said yourself there's eight double strand breaks a day in every cell. It's metabolic damage depending on the proximity those can be realigned.

You've got non-homologous end joining techniques that can repair them but it might be error prone. But this isn't new, so I would caution you that we've known that different tissues have different sensitivities to radiation. Rapidly population tissues are more sensitive than slowly dividing populations. We know that there aren't 10^{14} sensitive cells. Many of those are internally differentiated, subject to cancer but we hear these things. I mean, I've heard 10^{14} unfortunately at least three times in

the last hour, that's not the case. Not every cell is going to be --

DR. BARCELLOS-HOFF: But in terms of the initial events, those 10^{14} cells get the same thing, and I'm just using it to emphasize that there's a lot of biology.

DR. HOLAHAN: We sit there, we radiate the liver. We have liver functions. If the cells don't divide, you could have all sorts of double strand breaks but you haven't lost any genetic material. Partial hepatectomy, sure you brought that up. What happens? We express that damage, the organ falls apart.

We also know that the immune surveillance we talked about yesterday, that again isn't new either. We go to that palpable one centimeter tumor, 10^{-} cells. The first thing we do in a radiobiology course, we sit there and say, "Given the slope of the radiation survival curve the D sub not, how many Gys of radiation do we have to kill to sterilize that cell"? We're talking 35 Gy? Can't do that in a single exposure because we destroy the normal tissues, so we fractionate it.

Dr. Mossman said, five fractions, two Gy, six weeks, do we sterilize the cell? No, we've got

10^4, 10^5, 10^6 cells still there but it's the normal immune suppression that keeps it in check, ergo we have basically got cancer survivors that are in remission. And we hope the immune system keeps it in check unless it emerges again.

So go back to Hall's book, make sure these kids read this stuff. They're not going to see it on line because too often what we find is we're using new techniques to do that same thing over again. Back in my day we looked at single strand breaks, you gave, you know thousands of rads because the techniques weren't sensitive enough to detect anything else other than that.

Now, gee, you know, we don't use BUDR to look at exchanges. We've got these great probes, antibody probes, beautiful band-aid techniques, much more sensitive and that's where the excitement is going to be, looking at many of the same problems we used to look at 20, 30, 40 years ago, with the new techniques. And I say, DOE keep pushing on that because we'll get a much better understand.

DR. BARCELLOS-HOFF: Well, you can't see this probably from the other side there, but this is my systems biology slide for the old -- you know, what is systems biology? It's linking physiology, cell

biology and molecular biology. It's what we used to call -- physiology is what I want people to think about in terms of radiation biology because we've been down here for so long that we have forgotten all these other levels exist and so my next slide is the oxygenation, repopulation and repair. They're exactly the same levels of organization and that's what I was saying yesterday, radiation biology actually deserves a round of applause. We've always been systems biologists. We've always considered all the way from the molecular to the physiological response to radiation but it's so hard to get people like you say, to move out of their particular box, their favorite Google window and think about what actually is occurring. Did I show you that? Yeah.

So it's the same thing. I think it's you know, just needs a new framework and unfortunately it requires a new word and that's systems biology but it's basically --

DR. LE GUEN: Well, it would be one of the conclusions in your letter to create a science -- the 3-D approach as I said.

CHAIRMAN RYAN: Yeah, it's been a very rich discussion on the biology question and so we appreciate all. And thank you, Vince, for your

emphasis on making sure -- I mean, there is stuff that was discovered before 1970.

DR. BARCELLOS-HOFF: Oh, yeah. And actually I think we're going to go back to the cell membrane, so another 50 years from now.

DR. HOLAHAN: Ron Koss was looking at the microtubule exchange back in the '70s, Bill Dewey's lab, looking at what's being exchanged between cells for hypothermia. And I'm one of the feeder folks. We use feeder cells all the time. Increase survival, two orders of magnitude--

DR. BARCELLOS-HOFF: Bystander effect; right?

DR. RYAN: Dr. Land, you've been quietly taking all this in. What do you think?

DR. LAND: Actually, I--well, okay, I'll say something. I don't think I've heard anything that suggests a need for anything, except the LNT with the DDREF. I think it's the same as it was.

DR. RYAN: I'm sure you say the current biological work is probably saying an interesting and--

[Simultaneous conversation]

DR. LAND: Of course it does. I don't "cue" easily.

DR. HAMMITT: A couple points to make and I'm not sure where they best fit, but one is--this is partly, would have come well after Dr. Puskin's remarks. One is this idea of looking for acceptable risks in ALARA and stuff like that, and it relates to the medical exposures versus occupational and natural background.

And that is, to my mind, there's always this question of how much can we reduce risk and what do we give up to do it. And that's the central question. Talking about acceptable risk is saying there's some level of risk, such that if it was below that, we wouldn't bother to reduce it. So if it was above that, we would reduce it, ignoring whatever we give up to reduce the risk.

And ALARA is basically saying that it's easy to reduce the risk, let's do it, even if we don't reduce it much. If it's hard to reduce the risk, let's not do it, even if it might be very beneficial. So both of those are incomplete because they focus on only one side.

And as a way to think about this, the kind of, the risk of a fatal crash per car trip is something like one in a million. So that's very, very small; right? So from that, I might argue any time

you fasten your seatbelt you're just wasting your time. And this is an acceptable risk. Why do we bother to fasten a seatbelt? Because it's easy. You know, it doesn't hurt us much to fasten it.

Another framing of the same thing is the risk of dying in a traffic crash in the U.S., over the lifetime, is about one percent. That's huge; right? So why don't we ban traffic, ban cars, ban trucks? All because there are a lot of advantages to having them.

Well, why don't we reduce the speed limit to 10 miles an hour. That would eliminate most of these deaths; right? Well, that's very costly in a bunch of ways. So it's kind of always how much benefit you get against how much of what else that you care about do you give up, and any approach to kind of ignore that tradeoff might be a useful heuristic, in many cases might work well, might avoid complicated calculations, but it's an oversimplification that will be misleading, at least some of the time.

The other point has to do with this choice of model. So I think it's very clear that a very low dose is where we can't measure the arm directly, we're always kind of extrapolating, and it seems to me there were comments about--maybe you said two different

groups looked at the same data and came to diametrically opposite conclusions.

I don't know the details of that, but it seems to me that some of what goes on is people kind of have a null hypothesis and then say, well, we can't reject that null, and that low dose risk, so all reasonable nulls are not rejectable. It could be linear null threshold. We can't reject that. There could be some threshold in the lower than EPI range, we can't reject that, and that's not really a useful way to think about the problem.

Most people, when they learn statistics, do learn this kind of frequent as classical style, as a null hypothesis, can you reject it? Failure to reject is not the same as evidence in favor of the hypothesis, of course, although we slip over that a lot of the time, and there's very little power, you can't reject anything reasonable. And so what I think, the way I handle this is to recognize there's a false suite of models or risk levels that might be true. We can't differentiate among them very well.

We just need to acknowledge all these things are possible, and from biological theory and various sorts of evidence and EPI evidence, we maybe able to look, assign kind of rough probabilities to

different models, and then we need to work with expected value over those models in the uncertainty, and then risk over those different models.

DR. RYAN: I mean to borrow some risk language, it sounds like you're talking about see if you can come up with central tendencies, in a range around some central tendency as the real predictor.

DR. HAMMITT: Exactly. You know, we, as humans, are always uncomfortable with uncertainty and tend to be unwilling to admit how much uncertainty there is about anything we care about, and that's just a problem.

DR. RYAN: That's a good point.

DR. HAMMITT: But, you know, to some extent--maybe this example would help. If we think of different models. So what we care about as a person, or a government official, is whether somebody gets cancer or doesn't get cancer. We don't care per se about the probability of cancer. That's not important. It's the outcome that's important.

If I have a .5 risk and I don't get cancer, I have a .1 risk and I don't get cancer, it's all the same to me.

So you can think of these different dose response models as essentially like buckets of balls

where there's some--you know, in this bucket there are two or three black balls and if you draw a black ball you get cancer, and a lot of white balls--or here, there are ten or fifteen black balls and a lot of white balls, and these represent the different dose response functions.

So if we know the dose response function, then we're drawing from this bucket, we know the probability of getting cancer. If we don't know the dose response function, essentially we're saying, you know, I'm drawing from this bucket or this one or this one, and maybe I have some rough probabilities for how likely it is I'm drawing from each.

But in that sense, uncertainty about the model is no different than uncertainty about the outcome. It's just sort of compound. First, there's the lottery, which bucket am I drawing from? which dose response functions; true. Then there's the lottery--which ball do I pick from? So conceptually, it's not really much of a addition, but I think people overemphasize, too much, results conditional on the model and are unwilling to say I'm uncertain about the model, and I can handle that by thinking about it as a risk over which model is actually most accurate.

DR. RYAN: That's a very important

insight, I think, for us to think about. You don't have to pick the, quote, right model. You have to explore all the reasonable probable models, and understand what that means in terms of the overall outcome. Thank you.

DR. HAMMITT: And there are cases where the slopes of these models will be pretty similar, in which case uncertainty about the model doesn't really matter.

DR. RYAN: I think the graphic presentations you gave really explain that well too. Yes. Thank you. I didn't mean to cut you off. Is there anything else? Okay.

Jerry.

DR. PUSKIN: As a response to that, I'm very sympathetic with what you're saying. Let's assume that LNT is correct and the implication of it would be, that really matters, is the collective dose and not maximum individual dose, and the problem, of course, from a regulatory standpoint is that people are--you have the equity as well, that nobody wants--you know, I think part of it is acceptability of risk. People like to feel like, well, my risk is trivial, my kids' risk is trivial, and that's important to them, aside from the fact of what's the expected

number of cancers in the population.

From a public health protection standpoint, you know, we want to minimize the number of cancers, the right thing to do is to minimize collective dose. But we don't do that occupationally. If we can, you know, if we could reduce the collect dose, in some cases is the case, as I understand it, you could reduce the collective dose by allowing a few people to have really higher doses and don't have, you know, allow an individual to stay in there and get five or ten rads at a time, so we don't keep changing, getting a extra dose every time you change--

DR. RYAN: I don't think any of those ALARA strategies have a huge impact on collective dose, anyway.

DR. PUSKIN: Right. But anyway, you can imagine that. The same thing with regard to--well, in the case of environmental exposures. Generally, it's just from a public policy, public perception standpoint, regulating on individual, the maximum individual doses is more palatable, and that's what ICRP's kind of come down that way now too. They said what matters is people's risk. I'm sort of sympathetic to the idea that people don't really die of risk, but they do die of cancer, and what really

matters is what the collective dose is.

DR. HAMMITT: If I could comment on that.

DR. RYAN: Please. Yes.

DR. HAMMITT: I think often, a lot of what happens is we kind of frame things, so you worry about the risk of getting cancer from radiation and you don't like that being distributed unequally within a population. But that risk is pretty small compared with the total risk of dying or dying of cancer, and dying within a year, and I think--you probably know the work of Daniel Kahneman and Amos Tversky, psychologists, who developed this idea of heuristics and biases, which sort of explain the way--heuristics we use to deal with quantities and probabilities and stuff, and, you know, certain attributes can be very salient, and we frame things, we segment stuff.

So, you know, I'd be quite willing to tolerate a cancer radiation risk, I don't know, 10 or a 100 times after than the average, if my risk of heart disease went down 5 percent, cause that's probably a much bigger increase in survival probability or--you know, I'm making up these numbers but you know the point.

And there were proposals kicked around with Superfund cleanups, where there are claims that a

number of sites, the cost of cleanup relative, is very high relative to the health benefit, and it's logical for the community around that site to say, yeah, clean it up.

But what if the responsible parties could go to the community and say, well, look, instead of cleaning this up, we'll give you half as much money as it would cost to clean it up and you can use that money for things that you might actually find more valuable, and it's sort of likely the community would find stuff they'd much rather have than these pretty small risk reductions.

So framing is important in this more comprehensive view, and can protect us sometimes from focusing too much on stuff.

DR. RYAN: Let me see if our members have any questions.

Jim, do you have any questions or comments?

DR. CLARKE: Just a quick comment, if I could. Again, I think it's been another wonderful day, and it's got me thinking about a lot of things. As I mention, I come in from the risk analysis with chemicals and Superfund sites into the radiation arena, and I still think--it kind a pains me when I

hear people say I work with chemicals and I work with radiation. It always seemed to me that there's very fertile ground there, where those intersect.

But I liked your comment. I've been in two very serious automobile accidents. Both times I had my seatbelt on. Both times the air bag came out. I guess I'm glad I did it.

And that's the problem with probabilities. You know, they all go to zero or one, and it's really the outcome that we're interested in. So again this has stimulated a lot of thinking about chemicals, initiators, promoters, radiation.

Vince's chart with the practical threshold. What do we do with that? Well, we probably look at it the same way the EPA looks at chemicals that don't cause cancer. Incorporate some safety factors.

So again I think there's very fertile ground here, and thank you all.

DR. RYAN: Ruth.

DR. WEINER: I too want to thank the panel. This has been really great. But I do have some questions and these are things, these are problems that are of concern in how we apply some of these to, in my case, to environmental impact

assessment, and I'd particularly like to address Dr. Puskin.

You mentioned that the real thing is collective dose. Well, how do you handle the question of the microdoses to mega populations question, especially when, if you continue to multiply, and then multiply your result--if you continue to have a larger and larger population and then you multiply your result by some linear conversion factor to latent cancer fatalities, which is what is done in environmental impact statements, and this is presented, then presented to the public as you have X events and that's going to result in Y cancers.

And what people take away from that is, you know, radiation gives me cancer. They don't look at, oh, the probability is small compared to some other probability.

And there is a certain, I don't know whether to call it misuse or fallacy or what, but the notion--getting back to what Dr. Mossman said yesterday, if the individual isn't harmed, the group isn't harmed.

How do you square that with your statement about collective dose and how do you apply the very small average dose to large populations? How do you

handle the microdose to mega population?

DR. LAND: Can I add something on that? When I present, or my coworkers present the results, or our estimates of risk from, say, fallout in the Bikini tests in the Marshall Islands, one way we can do it is we put this is the excess and this is what you would have without that--what they would have had without that, is what you would predict without that particular thing. So it tends to be a rather small amount, except for the people who really did get an awful lot of dose, and in that case you tend to overestimate the risk an awful lot because we don't know that much about the risk from really high doses.

DR. WEINER: If I could respond to that. Yes, we all present it that way. It's presented that way in every EIS. Oh, the risk of cancer is 25 percent and this raises it to 25.06 or some such number.

I do not think that that conflicts with the message that people--people don't look at the relative size of the probabilities. They look at cancer or no cancer.

Yes, I quite agree with you--the number that you come up compared, with some more realistic number, is always very small, but we're still sending

a message that you have this event, and what happens? You get cancer from it. And I think we've somehow got to send a different message, and if I could get back to something that Dr. Mossman said, and I wish he had been able to stay.

Your slide, Dr. Puskin, your slide 17, which said help the public put risks into perspective. And that's what you're saying. I think we've had 20 years of that and it hasn't worked, to be perfectly frank, blunt, about it. With every talk, we put the risk into perspective, and the perspective is always there, and it's always the same, and we still have--you know, we have whatever "spin" is put on this, it is that you can say it's safe, it's safe, it's safe, but at the same time you say it gives me cancer.

DR. PUSKIN: I have to think of what the actual situation is where you'd have such a large population but--

DR. WEINER: Would you like an actual situation? I'd be happy to provide it right now. But go ahead.

DR. PUSKIN: Well, as I said when I did that slide, that it is a problem, and I don't have a magic solution to it.

But I would say this--and maybe I'm wrong

about this--but what is it that the nuclear industry is not able to do because of this? Sure, there's some resistance, but is it really that large, that it's such a huge problem to our society? Actually, I don't see it. I see a resurgence of nuclear power, people accepting it, I think is one example.

I don't know what to do beyond explaining to you. I think we can do better at explaining what a risk means. For example, ten to the minus four risk is one that we often use. A one in 10,000 risk means that in a city of three-quarters of a million people, that's one case a year.

Now if the murder rate in your city were one case a year, would you really be worried about getting murdered? And one in a million risk is one every 100 years.

I think partly, maybe we need to be more creative in terms of explaining what these risks mean. I know one thing that's true is that oftentimes, the risk is concentrated in the people who are closest by. It's not just a huge--the effect of including everybody doesn't really make that much difference.

DR. WEINER: Let me give you the example that I was thinking of, and this is a real example. In the Yucca Mountain environmental impact statement,

we calculated the risks from routine transportation of spent nuclear fuel from 77 sites around the country to Yucca Mountain.

If you do this in trucks, with four assemblies per truck, this is 53,000 shipments. If you calculate the population dose from that, and multiply by, at the time we used five times ten to the minus four, latent cancer fatalities, which should be latent fatal cancers--but anyway, latent cancer fatalities per rem, you get two cancers.

DR. PUSKIN: Over what time period?

DR. WEINER: Twenty-four years. Now I believe that we can all come to the conclusion that it is very unlikely that there will be two cancers from those 53,000 shipments over 24 years.

You take that number with an EIS that I reviewed recently--

DR. PUSKIN: What do you mean "unlike"?

DR. LAND: How do we come to this agreement that that's very unlikely?

DR. WEINER: I find it hard to believe that taking what is a very small average dose, on the order of ten to the minus eighth, ten to the minus eighth, ten to the minus seventh rem--we did this in rem--taking that and simply multiplying by the number

of people by the side of the road--

DR. RYAN: Part of the problem I think in these scenarios, and this one, in particular, is that there is no central tendency evaluation of what is a likely dose. It's all bounding case.

DR. PUSKIN: I'm assuming the dose--

[Simultaneous conversation]

DR. RYAN: A bounding case masks the real central tendency of the risk. So I think that's part of it.

DR. PUSKIN: I would say there's nothing wrong with the idea of adding up a lot of very small risk--for example, as we've said, ten to the fourteen cells in the body, one of them is going to turn into a cancer cell. So the odds of any one of them is one out of ten to the fourteen, and yet we see finite numbers of cancers.

So you can add up a lot of very small risk to get something finite, and obviously it's not observable.

DR. RYAN: And I think the other point is if there is some estimate--Ruth, excuse me for jumping in--but if there's two cancers that are excess because of an activity, that it's really, the question, the second part of this, Can you distinguish that from the

cancer that will occur in the affected population anyway?

DR. LAND: The fact is you'll never find out.

DR. RYAN: Right. I mean, there could be, you know, three extra cancer deaths in a family of heavy smokers that moved in during the 24 years. So, you know, something else, and it really is well down in the variant rate that's going to occur anyway.

DR. WEINER: As a matter of fact, in the same environmental impact statement, we did a number of traffic fatalities. You compare it with this, you compare it with that, and to a member of the public who wishes to focus on the cancers from ionizing radiation, this doesn't make any difference.

Now let me just carry this one step further--

DR. RYAN: Just one.

DR. WEINER: Just one. This is another real-life environmental impact statement. Instead of 53,000 shipments over 25 years, 24 years, we have something like 150 shipments over larger distances, larger populations along the side of the road, over a period of 40 years, with the result of 1150 cancers.

Now you might be able--and I'm sure that

even those 1150 are a tiny fraction of what you would get anyway. But that's a big number, and if I saw that number in an environmental impact statement, I don't think I would want that project.

DR. RYAN: So what's your question?

DR. WEINER: So my question is, is this an appropriate use of collective dose? I've been hearing, yes, collective dose is fine. But when you just keep multiplying and multiplying, you get a ridiculous number.

DR. LAND: So what's your alternative?

DR. WEINER: The alternative would be to look at the maximally-exposed individual, to look at individual doses rather than collective doses, because multiplying an average dose by the number of people somehow strikes me as not a dose calculation.

DR. RYAN: Ruth, I would point you back to some of the things Dr. Hammitt talked about, that we discussed, and that is that if you can get at a central tendency, and some range of behavior around a central tendency, you're really exploring the risk for what it is. You know, then you can judge it based on those various parameters of risk. A bounding case is misinformed.

DR. WEINER: Yes.

DR. RYAN: They're misinformed, and they mask risk, not--

DR. HAMMITT: That may be useful if we can calculate--

DR. RYAN: In some contexts, quite frankly, you know, the more they use the less I like them, because they really do overestimate, typically, and they miscommunicate reality.

You know, just to give an example, 10 CFR 61 is based on the agricultural and true-to-scenario, that grows his food in radioactive trash, which is plastic tie-back booty shoe covers, shovels and picks. I mean, he has to grind up metal and grow food in them. It's not a realistic scenario.

By the way, nobody that I know grows all their own food.

DR. HAMMITT: Certainly not in soil like that.

DR. RYAN: Certainly not in soil--and by the way, has to be unemployed cause he has to get external radiation exposure for 18 hours a day. And on and on and on down through the scenario.

So, you know, the old thinking of, well, if I bound the problem then, you know, I know I'm better than that in reality, so I'm okay. Well,

that's not a good treatment of risk. That's an engineering type of judgment.

So I get back, to answer your question, at least my view would be to follow, you know, our predecessor in this committee, Dr. Garrick's view, and let's get at, you know, a real treatment of probability and risk.

DR. PUSKIN: I would guess that the exposure's been--the collective dose has been greatly overestimated. It's some sort of upper bound--

DR. WEINER: The dose has been--the dose may be overestimated by a factor of about five or six. But it is true, that other parts of this exposure have been greatly overestimated. And Dr. Ryan's quite right. If you do a central tendency or a more realistic exposure, these things come down and--

DR. RYAN: So you got your answer.

DR. WEINER: I do have my answer, from you. But there is--if you combine collective dose with the conservative estimates, this is what you get--

DR. RYAN: Dr. Hammitt wanted to make a comment.

DR. HAMMITT: I was going to try and add two things. One is first on, back to the linear no-

threshold and so forth--well, imagine, we think there's some chance linear in our threshold is correct, and a much higher chance that there's some threshold that's relevant, such that there's really zero risk.

If we calculate the expected risk, it's going to be the probability that the linear no threshold model's right times whatever risk it suggests.

So if you think there's only a 10 percent chance that LNT is right, that means you've reduced your risk by a factor of ten, but that may not really be enough to actually change any policy or change policy very much, given the wealth of other uncertainties here and what the dose is and everything else.

DR. RYAN: And I mean that's a very important point for us to take away as a complete and thorough treatment of all the components of risk, and the uncertainties in them, is really the right way to get at it.

DR. HAMMITT: And then the other thing was, on this first communication point, is I think a very powerful book by a guy named Howard Margolis, who's at Chicago Public Policy School, called "Dealing

With Risk," I think 1996 or thereabout, and he was sort of proposing, it makes a lot of sense to me, that when people react to risks, what matters a lot is whether there's some activity, whether the benefits and/or the risks of it are on screen, to me, the person making the judgment, and, you know, in the case of people trucking nuclear waste by my doorstep or having a nuclear power plant near me, I tend to not really perceive the benefits. I perceive potential harm to me, I think that's outrageous, and shouldn't have it; right?

Whereas if it's driving a car or something, I perceive the benefits, I perceive the harms as well, and make it a somewhat more reasoned judgment, and there are cases where, you know, I perceive the benefit but I'm putting the risk off on somebody else, then I don't worry about the risk perhaps.

And so you mentioned nuclear power plants. It seems like with climate change, and people worrying about that, that will improve the discussion of our nuclear power because there's a big clear benefit associated with it, and that we're avoiding some other harm that many people care about.

DR. LAND: One thing is would you rather

live next to a nuclear power plant or a coal power plant? And I know the answer.

DR. HAMMITT: But we've known the answer to that for like 30 years--

[Simultaneous conversation]

DR. HAMMITT: --figured that out yet.

DR. WEINER: Nothing has happened.

DR. HAMMITT: But with climate, too, maybe they'll get it.

DR. LAND: Maybe.

DR. RYAN: All right.

DR. LE GUEN: In fact about this, we are exactly the same experience in France. People who are living close to the nuclear power plants work in the nuclear power plant, and live with the nuclear power plants. So there is an economy region.

But when you are talking about waste, you take waste from another place and you put in another place, and people say, well, why we must accept waste from other parts of France, because we have no benefit about that? And so the acceptation's completely different.

DR. PUSKIN: So what do you do then?

DR. LE GUEN: Well--

DR. PUSKIN: Are we able to take it?

DR. LE GUEN: Well, we have, we try to create now an economic region around the west, and we provide money for that, and from the industry we use the waste--and this, now, we have decided to give money, to give grant, and so on, in order to develop a real economy around the waste disposal.

DR. LAND: An economy that depends on having the waste, that it used the waste, or--

DR. LE GUEN: Sorry?

DR. LAND: An economy that depends on the waste, that isn't perceived as sort of a bribe for having to live next to the stuff?

DR. LE GUEN: It's the expectation much more than--that's why I fully agree with James.

DR. LAND: No, but what I mean is that the economy wouldn't be there if it were not for the waste, not just because--

DR. LE GUEN: Absolutely. No, no, no. There was nothing.

DR. LAND: I mean, the economy depends on having the waste there, in more than sort of a bribery sense. That's what--

DR. LE GUEN: Yeah; yeah. Okay.

DR. LAND: Yeah.

DR. LE GUEN: Okay.

DR. RYAN: Any comments?

Neil, you had a comment?

MR. COLEMAN: Neil Coleman, ACNWM staff.

One of the take-aways I have from this meeting is the idea that we might never be able to differentiate the most applicable biological response model in the low dose zone.

And it has some significance on the economic models as well. But I'm going to slightly take issue with that because I think one of the models is directly amenable to testing, can be tested with unsophisticated but somewhat difficult experiments.

Yesterday, Tom Tenforde spoke about the idea of extreme low dose effects, where experiments could be done in very low background environments, the idea being to see if test subjects actually do suffer in the absence of background radiation, which in the U.S. averages about 350 millirem, is this hermetic effect real as some experiments actually do suggest now?

Unlike the other biological response models, you can validate this with controlled experiments. This would help address the unfortunate public perception that each and every ionization event carries a cancer risk, leading some people to fear

even getting a simple diagnostic dental x-ray.

The question is: How could such experiments be done in a credible way with results that the public would believe and accept?

DR. RYAN: So there. Does everybody accept the question? I'm not sure I agree with the question but--

DR. METTING: Mike, can I say something.

DR. RYAN: Sure. Please just come to the microphone and tell us who you are for the record.

DR. METTING: I'm Noelle Metting. I run the low dose program. This is an interesting concept. Of course you know that people have been suggesting that we do that, that we lower the background, and it's been done, preliminary experiments have been done with cells. The cells do look like they're worse off. But I don't even want to get into that.

I wanted to make one comment about the low dose program and just biological, the biological experiments in general, and I think that you may have missed this but what I think is it's giving, the biology is giving us a reason to do the experiment, of ignoring high dose epidemiology. Let's ignore it for a while and see what just the low dose epidemiology tells us. Why don't we take a look at that? Let's

pretend that the A-bombs didn't drop. Let's look at the low dose epidemiology. I think the biology says it might be interesting. So there's an idea.

DR. RYAN: Great. Thank you.

Any other final comments? Questions? We have some other--you've been waiting patiently.

MS. MITCHELL: Jocelyn Mitchell from the Office of Research. I wanted to mention that the NRC and the Commission of European Communities, about ten years ago, attempted to get a group of experts, four from the U.S. and four from Europe, to give likelihoods, degrees of belief, if you will, on possibilities for what would be the low dose response, and it's actually written up in a new reg report, a new Reg CR report.

Unfortunately, the deviation from LNT was so insignificant, that it just didn't exist for all practical purposes. Only one person gave a nine/zero likelihood to something that was not LNT. And I don't know whether we didn't have the right experts, whoever they were, but we did attempt to do that, and I don't know how you would get folks to give you numbers like that.

DR. RYAN: Thank you. Is there anybody on the bridge line? Hello? Nobody else is there. We've

had one request for an individual to make comments. Let's see. It's Mr. Dennis Nelson. Dennis, now is a good time.

DR. NELSON: Right here?

DR. RYAN: Right up there is fine. This is Mr. Dennis Nelson from the organization SERV, S-E-R-V, and he'll tell us a little bit about that and make his comments.

DR. NELSON: Good afternoon. My name is Dennis Nelson. I'm a retired naval officer. I have a PhD in biochemistry. I did biomedical research in the Navy for a number of years, although my research was not specifically in the area of radiation, it was biological. I did work on hemoglobin. I did work on immune function.

But there are a couple of points that I wanted to make, that I think you should try to incorporate in your decision making, and one of those is that--and I also want to follow up on the risk management thing that was mentioned earlier.

Basically, the traditional view of radiation damage in biological systems has been that it damages DNA, and that the DNA damage then reflects a altered protein or a defective protein which then doesn't do what it's supposed to do.

And that's probably still very true. However, some of the recent studies have shown that epigenetic effects may address more, not the integrity of the gene and the protein but the actual turning on and turning off of that gene and protein.

So it's possible that radiation epigenetic effects may cause methylations or alkylations of various control proteins, or substances, which may turn on or turn off tumor suppressor cells or tumor promoter cells. Sorry. Tumor suppressor genes or tumor promoter genes.

And this may be the cause of cancer. It may not be that you have just a defective protein but you just turned on the wrong gene. So that needs to be looked at. It needs to be looked at in terms of dose, dose response.

Also, I think that you need to look at latency, and that's something that's been bugging me for many years. You know, what causes latency?

Now the traditional explanation is that there's a multi-step model of carcinogenesis, that it has to get hit once to cause it to transform, and then another time to promote, and then to transprogress, or whatever. I don't know all the procedures.

But suppose that there's another

explanation, and that other explanation is that latency is caused by a one-time hit, or defect cause in a pluripotential stem cell, one that lies dormant or quiescent for a decade, and then all of a sudden is recruited in the dividing population when the needs are there for repair or for growth or whatever.

So I think you said earlier that maybe there aren't ten to the fourteen cells that are susceptible. Maybe it's only--maybe it's a fraction, one percent, maybe less, and maybe those are the susceptible cells.

So we have to think about that. Maybe it's just a one-time thing and when that cell finally is recruited into the dividing population, it goes berserk.

So there are many alternative, possible models for carcinogenesis, and I think they all need to be looked at.

Then lastly, the risk-benefit thing, I wanted to address that because that I think is the biggest sticking point, and it's a point that you made earlier, that why can't people accept this. It's because the same people don't suffer the risks that get the benefit. And that's precisely why.

For example, we have nuclear medicine

patients that are floating around amongst us, that may sit next to you in an airplane, or in a theater, or on a bus or a train. And they may be emitting 20 milliroentgens per hour, and you're sitting next to them for two hours, you may get 40 millirems. And next week you might go to another plane, and you might sit next to another one, and you get another 20 or 40 millirems. These are not controlled sources. They're just basically random events.

And you yourself have no benefit from them. The benefit is derived by the person who is sitting next to you but not by you. So why should you have any risk whatsoever. So I think that these people need to be controlled and I think that the NRC needs to revisit its policy of allowing these people to leave while they're still very highly radioactive.

And conversely, maybe it's not as big a problem, but these shipments that I talked about earlier, these radiative casks going to Yucca Mountain, and as we get more and more medical procedures, nuclear medicine procedures, as we get more and more shipments, what we're talking about with Yucca Mountain, these casks are going to be a lot more prevalent on the highway.

And how do we know that they're going to

be protected? How do we know that the individual along the road, at the gas station or the truck stop, who goes over and leans on the truck, isn't going to get--well, I won't say a huge dose, but a larger dose than he really deserves, because he's not getting any benefit from that nuclear waste shipment.

So anyway, these are just my observations. That if you want it to be accepted, it's going to have to be fair, and it's going to have to impact or cause risk to the people who benefit from it, not another segment of the population. And that's really all I have to say.

DR. RYAN: Mr. Nelson, thank you very much. Would you mind telling us again what SERV was. You mentioned it to me.

DR. NELSON: SERV. Support and Education for Radiation Victims.

DR. RYAN: All right. Thank you very much.

DR. NELSON: A group that I founded a few years ago. I am also a down-winder. That's why I have this interest in this subject, because my family was affected by the bomb testing in Nevada back in the late '50s, and I have three members of my family that died at very young ages, and seven different kinds of

cancer in five family members. So to me, it's a personal thing. but I'm also a scientist and I want to understand this scientifically. I'll reject things that are not scientific but if it can be explained to me scientifically, and it's defensible, and it's not just, what I sometimes consider politics or propaganda or economics or whatever, then it's a lot easier for me to accept and understand.

DR. RYAN: Well, we appreciate. Hopefully, you've gotten some benefit from the scientific discussion here with a couple days--

DR. NELSON: I have. It was a great--

DR. RYAN: Thank you for sharing your--

DR. NELSON: --couple days and i really enjoyed it, and I got something from every one of you.

DR. RYAN: Well, thank you very much for coming, and thanks for sharing your views as well.

Are there any other comments from anybody?

DR. TENFORDE: I have a question, Mr. Chair.

DR. RYAN: Come on up, Mike.

MR. BOYD: Okay.

DR. RYAN: Yes. And Tom, why don't you ask that question in the meantime.

DR. TENFORDE: Real quick. I had the

impression that the outcome of this discussion would be a letter report from the Advisory Committee to the commissioners.

DR. RYAN: That's correct. Yes. We actually address i to the chairman on behalf of the whole Commission.

DR. TENFORDE: I'm wondering at this stage, before some of us depart, we have some continuing responsibility to review and comment on your letter report?

DR. RYAN: No. What we do is take the record of the transcript, and then we synthesize the information into a letter to the Commission as we see it, and it's not your report to the Commission. It's our report of what information we gathered and our assessment of that information to the Commission.

If you have anything else you want to provide to us, in writing, or additional support information, or you want to make any comments on that key points, and that's--I think we hit some key points about biology and some of the other issues, and modeling, and so forth. From each of you I think we've gotten, you know, rich views and key points, and we'll be faithful to summarize those, and that's the typical scheme for letterwriting here with the ACNW.

And of course once our letter is prepared, we actually read it out in public before it's finalized. Anybody's welcome to come and attend that session, which will be next May, or next month, in May, I forget which week at the moment, and then we finalize the letter, we vote on it as a committee and then that's prepared in final form and sent to the Commission, at which point it's a public letter.

Mike Boyd.

MR. BOYD: Mike Boyd with EPA, and I'm really sorry that Ken Mossman left, because he's the person I wanted to say this to, but I--

DR. RYAN: You can say it and he'll get--

MR. BOYD: I'll say it and it'll get into the record; right. And this is mainly just a little bit of a defense of the risk assessment process at EPA and the risk-based cleanup process as opposed to dose-based, and why I think that the risk-based process that we use, the classic Superfund approach, actually has some real advantages.

And one of the things is that effective dose, as you know, is a surrogate for risk, and it tries to wrap up, and, you know, just a handful of tissue weighting factors and radiation weighting factors, you know, all the risks, biokinetics that we

have over, what, Jerry? 3200 risk coefficients--four risk coefficients for each of over 800 radionuclides. So there's a lot of complexity that we have in our risk coefficients that gets sort of summarized in the effective dose term.

And another thing that we do, when you do--for doing occupational radiation protection, it absolutely makes sense to use dose as your metric. But when you're looking at long, you know, perspective, or retrospective assessments, the risk assessment approach that we use allows you to account for decay. I mean, instead of a committed dose, you actually are looking at a true decaying dose, over time.

So, for example, people say EPA regulates it 15 millirem, which is three times ten to the minus four risk. That's not true. 450 millirem happens to work out, using our risk estimates, to be about three times ten to the minus four risk, but that's assuming a 30 year default exposure, and a myriad of other default exposure factors. So there's a lot that goes into that three times ten to the minus four number.

So to say that say that 15 millirem is three times to the minus four is really not capturing it, by any means. But I just wanted to point out that

when you do a risk--if you were to do a three times ten to the minus four target risk-based cleanup under Superfund, you would come up with target cleanup values that almost, across the board, would be a higher concentration than you would have to clean up to, to achieve NRC's license termination rule at 25 millirems.

So I wanted Ken to know that, really, from my perspective, there is no difference, and I just wanted to say that the risk approach that we use does capture a lot of variables that I think are useful. You can capture, you know, weathering, decay, occupational exposure factors. I'm probably just babbling at this point but--

DR. RYAN: No, no, Mike, I think that's an important point. There is--and you know, you highlighted in that discussion, I think many of the points we've heard today, that you really can't pick one number or one parameter and really understand the whole profile of dose and risk. You have to look at it as a system.

MR. BOYD: System; right.

DR. RYAN: So that's a good point. And even on the--and you're talking about the assessment side and all the things that go into that. So we

appreciate that comment. Thank you.

MR. BOYD: Sure.

DR. RYAN: Anything else?

Going once. Going twice. We are a little bit ahead of schedule but--I'm sorry.

DR. LAND: I was just going to make one last--

DR. RYAN: I'm sorry. I didn't see your hand. Excuse me, Dr. Land.

DR. LAND: The discussion about how do you express risk, I think the one thing you don't do is say that there isn't any risk. Or you say that it's a risk and it's too small to worry about; don't worry about it. That never works.

DR. RYAN: Fair enough. My doctor says don't worry about it. I still worry about it sometimes. I'm with you.

DR. NELSON: There was one thing that i forgot to say, and that is--

DR. RYAN: Yes, please, and just again, just for the record, this is Mr. Nelson again.

DR. NELSON: David Nelson.

DR. RYAN: Just come to the microphone.

DR. NELSON: This is Dennis Nelson from SERV again, and I just wanted to say that if you go

back and look at history, you'll see that there has been a progressive decline in the level, which was seen to be biologically significant over 50 years. Way back when, you know, 50 rads was not much, and then it went down to twenty, and then it went down to ten, then to five. Now we're talking in the one rad range.

I just try to extrapolate that historically and say, well, who knows what's going to happen over the next 15, 20 years. Maybe we'll get down to effect seen at millirads.

DR. RYAN: Thank you. With that, unless there are any other closing remarks--yes? I did. Mr. Early may call back. So I'm going to suggest we take our 15 minute break and come back briefly for 3:15. We do have a call-in time, that other folks may be calling in, so we'll have to honor that obligation for stakeholder input. So if you wouldn't mind, we'll just take a 15 minute short break and reconvene at 3:15 and if there are other comments, we'll take them at that time, and if there are no other comments at that time we'll finish up. Thank you for your patience.

(Whereupon, the meeting went off the record at 3:00 p.m. and continued at 3:19 p.m.)

DR. RYAN: Thank you all for your patience. I know a couple of folks had to duck out. I'd like to reconvene if we could, just for a minute and check. Are there any commentors or members of the public, or stakeholders, that wish to make any comments on the bridge line?

It is the appointed hour for any additional--is there anybody in the room that wants to make any additional comments or observations? Hearing none on either the bridge line or the room, we'll adjourn the meeting, and again I thank you all very, very much for your participation and your information. It's been really enlightening for the committee and I think we'll have a very rich letter to offer to the Commission on these topics and the science involved.

So thank you all very much.

(Whereupon, the meeting went off the record at 3:19 p.m. and went back on the record at 3:43 p.m.)

DR. RYAN: The committee is here. You okay? All right. We have the microphone. You can go ahead and take five minutes or so and make your statement.

MR. EHRLE: Thank you very much. There was much discussion of the problem, the uncertainties

related to dose, and I think those were well-taken. It was a difficult task for Dr. Hammitt to quantify the specifics relative to any kind of dose cost-benefit analysis. It's been very difficult.

I've been conversant with some of those issues over the past several years. But what really peaked my curiosity was the inability of the committee to deal with the superlinear model, and Dr. John Gofman, who of course was former associate director of Lawrence Livermore, I have his 1981 book, and it appears as though that was the first book that ever really looked at this particular issue.

And he used the Land-McGregor RERF study, and analyzed it, and concluded that, indeed, it does show, using the RERF statistics, a superlinear model, and so he explains it at some length there.

But then he goes on and in his 1990 book, which was very favorably reviewed in New England Journal of Medicine, he points out that a single primary ionizing radiation track, operating independently, these tracks from each other, are never innocuous with respect to creating carcinogenic injuries in the cells which they traverse.

Every track, without help from any other track, has a chance of inducing cancer by creating

such injuries. And then he cites a study by Brackenbush and Brady, which is 1988.

"Since most cells repair radiation damage with a characteristic time ranging from a few minutes to a few hours, it is evident that irreparable or misrepaired damage must dominate the low LET radiation effect at low-dose rates."

And then he cites UNSCEAR, 1986, and quotes: "The error-free repair of the DNA, which is the most likely target involved leaves some fraction of the damage unrepaired and the error-prone repair may produce misrepaired sequences in the DNA."

And then he quotes Albrecht Kelleher, who apparently was on the BEIR VII committee and he describes the type of radiation-induced lesion which would be difficult to repair.

A simple example would be two neighboring single-strand breaks on opposing strands of DNA which interfere with excision repairs.

And then he points out that there are nine low-dose studies, human studies, the highest of which is .9 rad, it isn't even a single rad, which would have been of course 10 millisievert. So at that level, he points out that the observation of radiation-induced cancer means that repair is failing

to become flawless, even when it has to cope with the average track frequencies per nucleus of only 12 tracks, only ten, only six, only two, only one track, only .67, and only .29 track. Those of course correspond to the nine studies.

If repair had been flawless, it would have successfully undone every carcinogenic lesion, and so there would have been no excess cancer, at all, in any of the nine studies.

He then discusses the question of unrepaired, unrepairable, or misrepaired carcinogenic injuries which occur at low dose, right down to the lowest conceivable dose, or dose rate. And so here we have evidence, at these very low ranges, and when Dr. Mossman indicated that we don't have any information at low doses, obviously there are numerous studies in the literature, in the peer review literature, which demonstrate, at these very low doses, every significant excess impact.

Unfortunately, the studies that you're using, and that ICRP, NCRP and even NRPB, and the UK, which has now been reorganized, they all use of course the Japanese study. Consequently, they do not deal with internal dose. This is external gamma dose.

It is internal doses which have been

estimated to be at least 20 times more effective in terms of the inhalation into the lungs, and then distribution throughout the other parts and organs in the body, that has the greatest effect, and UNSCEAR has recognized this again. In fact the British National Radiological Protection Board, in 1995, said that it may be argued, and I'm quoting, that a single radiation track, the lowest dose and dose rate possible traversing the nucleus of an appropriate target cell, has a finite probability, albeit low, of generating the specific damage that will result in tumor-initiating mutation.

So I would hope that the members of the committee, and others, would call for some of these experts who have been studying this issue for years, to be involved in future conferences, and that a careful analysis of the superlinear model would be in order, and would hope that the committee will recognize that by elevating the hormesis thesis to the level of LNT is a disservice to the scientific community and to the public at large, because it has been vetted by these committees on numerous occasions and had been found wanting, and obviously, if there is a superlinear effect, and I mentioned earlier the comment, I ran into and got in on a meeting at Mayo

Clinic where Tom Hay from Columbia was giving a talk, and he showed with a diagram how the superlinear model works.

So it's been recognized by persons in the field who have high standing, that indeed, this is worthy of further investigation and hopefully the committee will respond in kind.

Thank you for your time. I appreciate the work that you've done on this particular conference and hope that it will lead to other conferences which will have an expanded scope. Thanks again.

DR. RYAN: Thank you, Mr. Ehrle. We appreciate your comments. Have a good afternoon.

MR. EHRLE: You too.

DR. RYAN: All right. We're done. Thank you.

(Whereupon, the meeting adjourned at 3:50 p.m.)