
From: Nelson, Evan C. <evan.nelson@tuckerellis.com>
Sent: Wednesday, March 05, 2008 2:15 AM
To: PValberg@gradientcorp.com
Subject: New Project - Tobacco Smoke Causes Mesothelioma
Attachments: Martell 1983.pdf; Ishikawa.pdf; Andersson.pdf; van Kaick.pdf; Travis_Lois_B.pdf

Dr. Valberg,

I really need to know that you will allow me to be your handler, that all future retentions will go through me and what your time commitments will be to act as a national expert in asbestos litigation. We can collaborate to publish several key, revolutionary articles that you will see unfold as I present this stuff to you. It is amazing that no one has put this together before me, but I am confident that you will agree it is solid science that proves tobacco smoke causes mesothelioma - you just have to look at the tissue through the proper lense.

I have attached what are really the key articles necessary for this next generation science. And, here it is in a nutshell.

We know that 90% (80% to 90% at least) of all lung cancers worldwide are caused by tobacco smoke, so it doesn;t make any sense that cancer of the lining of the lung - mesothelioma - would not have any relationship to tobacco smoke. The epidemiology that looks at tobacco smoke and meso is unclear but there are a lot of confounding factors involved and problems with the studies. So we want to take a new look from another angle.

We know that radiation exposure causes mesothelioma from looking at radiotherapy, Thorotrast, and nuclear worker studies. We also know that tobacco smoke deposits radioactive particles in the lungs of smokers. (Harvard, Winters & DiFranza, even the EPA discusses it) So, lets look at the Thorotrast studies where radioactive particles were deposited in human subjects and resulted in large increases in mesothelioma risks, then see if a comparison to the radioactive particles deposited from tobacco smoke can be made.

Andersson, van Kaick, Travis and Ishikawa (all attached) are the key Thorotrast studies. Ishikawa holds all of the necessary information for our analysis - though I will provide some additional materials to you later. Open Ishikawa and mark it up. The chart on the first page gives us the numbers from the Danish (Andersson), German (van Kaick) and Japanese (Ishikawa) Thorotrast studies. Add up cases and controls and we get 15 mesos in 3299 cases matched against 1 meso in 4441 controls. My math yields a RR for meso of 20+. Now lets find what dose of deposited alpha radiation to the relevant organ is that yields that risk. Ishikawa estimates 2 cGy/year to the liver (for peritoneal meso), and a mean of 27 years from injection of Thorotrast to death. Van Kaick discusses higher doses (as does another primary source document that I will get to you) and it also discusses the concept of wasted dose - radiation dose after tumor initiation. It is generally accepted that a meso originates 10-15 years prior to diagnosis and we can assume a 1 year period from diagnosis to death. This means that the wasted dose is 11 to 16 years, and the deposited alpha radiation dose that created the RR of 20+ for meso is about 22 to 32 rad ((27-11 to 27-16) times 2 cGy or rad). Again, I think that we should moderate this by looking at the dose estimates stated in van Kaick and the other primary source document for organ dose estimates for Thorotrast injection. But, this is an enormous risk for relatively low radiation, even if we jump an order of magnitude to 220 to 320 rad or use the linear-no threshold model to extrapolate down with a slope of 1 to get 2.0+ RR for 22 to 32 rad.

So, how does this compare to radioactive particles in the lungs of smokers? Now we turn to Martell. Just jump to the last page of his report for now and we see an estimate that a 1 pack per day smoker gets about 30-60 rad of deposited alpha dose to "hot spots" in the lung around the radioactive particles and a 2 pack per day smoker gets basically twice that, 60-120 rad of deposited alpha dose. Application of our risk model from the Thorotrast experience to this data would clearly show a RR of meso above 2.0 for heavy smokers (1 ppd or more) due to deposited alpha radiation decay products (Po-210 and Ra) from insoluble Pb-210 particles (22 year half life). Martell also discusses how 1,000,000 cells around the deposited radioactive particle are at extreme cancer induction risk due to the constant bombardment by the alpha radiation decay products.

I will also send you a 1980 report from the ICRP that has two key pieces to this puzzle. First, it has pictures of rat lungs after inhaled radioactive particles - this is a great demonstrative that shows the alpha radiation tracks in lung


tissue. Second, it clearly states that the pleura receives substantial radiation dose from inhaled radioactive particles. There are a plethora of animal studies, mice, rats and dogs that show large meso increases from inhaled radiation dose. You need to talk to Tony Brooks and get the info re Roger McClellan's Lovelace Inhalation Toxicology data (January 1994 or 1995, I think he said) where he found mesos in the beagle dogs with inhaled radiation and none in the controls. There are lots of published studies as well.

The last piece is then to look at some of the smoking/meso epidemiology in this new light, and we can take at least four of these studies now and find that they show this 2.0 RR of meso for heavy smokers.

We can add a sound policy reason for publishing this info. Winters & DiFranza, pathologists who published re increased radioactive particles in smokers' lungs, state that smokers are more likely to quit when educated about the fact that they are inhaling radioactive particles. I think that if you add to this the risk of meso - a terrible form of cancer - that we can send a powerful message.

Intrigued? I see at least four or five solid articles in here, and it will be an extremely important scientific work.

Regards,
Evan



TUCKER ELLIS & WEST LLP
ATTORNEYS AT LAW

Evan C. Nelson
Attorney

135 Main Street · Suite 700 · San Francisco, CA 94105
phone 415.617.2216 · facsimile 415.617.2409
Evan.Nelson@tuckerellis.com

CLEVELAND · COLUMBUS · LOS ANGELES · SAN FRANCISCO

From: Nelson, Evan C. <evan.nelson@tuckerellis.com>
Sent: Wednesday, March 05, 2008 1:09 PM
To: PVALBERG@gradientcorp.com
Subject: Re: New Project - Tobacco Smoke Causes Mesothelioma

Thank you. I will confirm with Jim Scadden that this arrangement is acceptable to him, and I am confident that he will see it as a beneficial way to handle things, and to ensure that our clients are protected.

I am hopeful that Roberts will go away and give us some time to look at this new project.

----- Original Message -----

From: Peter Valberg <PVALBERG@gradientcorp.com>
To: Nelson, Evan C.
Cc: Peter Valberg <PVALBERG@gradientcorp.com>
Sent: Wed Mar 05 12:15:44 2008
Subject: RE: New Project - Tobacco Smoke Causes Mesothelioma

Evan --

Thank you for the materials you sent, and your thoughts on ionizing radiation risks relative to a role in mesotheliomas.

With regard to your question "I really need to know that you will allow me to be your handler", I am pleased with your interest in using the services of myself and Gradient Corporation, and I can see that this would work fine in an informal way. However, important facts in this matter are that (1) I have past and ongoing projects involving asbestos litigation (although none of them, aside from the Jim Scadden work, have ionizing radiation as the issue), and (2) I am part of the Gradient Corporation consulting group and don't have the ability to give away "handling rights," without full consent of the other Principals and President of the company, and (3) I have numerous other non-asbestos, health-risk assessment clients to whom I need to continue providing expert services. That being said, I see that the "role of ionizing radiation in lung cancer / mesothelioma risk for individuals also potentially exposed to asbestos" is a unique consulting niche, and I am happy to have you as my sole entre to that area (assuming Jim Scadden is OK with that idea).

I agree that the articles we've identified, pointing to the role of ionizing radiation in increasing cancer risk, and specifically mesothelioma risk and lung cancer risk, are very intriguing, and deserve to be pulled together into a coherent whole. Specifically, the calculations you provided in the e-mail below are very provocative. In fact, since you mention that this analysis may be quite important, scientifically, we may want to think about having Dr. Julie Goodman here at Gradient, who is our resident statistician / epidemiologist help out on this task. I've attached her CV for your perusal.

For the cigarette smokers, what we may need to address with regard to the role of alpha-radiation is the fact that the Martell paper talks about "hot spots" at bronchial bifurcations, as caused, not by the cigarette smoke itself, but by accompanying radon daughter products that the smoke has picked up. Moreover, Martell calculates the alpha-particle dose to the bronchial basal cells at the bifurcation of airways, but this location would get a dose much different from the dose to the pleural epithelium, the location where one would expect that mesothelioma arises.

-- Best regards,
-- Peter

From: Nelson, Evan C. [<mailto:evan.nelson@tuckerellis.com>]
Sent: Wednesday, March 05, 2008 2:15 AM
To: Peter Valberg
Subject: New Project - Tobacco Smoke Causes Mesothelioma

Dr. Valberg,

I really need to know that you will allow me to be your handler, that all future retentions will go through me and what your time commitments will be to act as a national expert in asbestos litigation. We can collaborate to publish several key, revolutionary articles that you will see unfold as I present this stuff to you. It is amazing that no one has put this together before me, but I am confident that you will agree it is solid science that proves tobacco smoke causes mesothelioma - you just have to look at the tissue through the proper lense.

I have attached what are really the key articles necessary for this next generation science. And, here it is in a nutshell.

We know that 90% (80% to 90% at least) of all lung cancers worldwide are caused by tobacco smoke, so it doesn't make any sense that cancer of the lining of the lung - mesothelioma - would not have any relationship to tobacco smoke. The epidemiology that looks at tobacco smoke and meso is unclear but there are a lot of confounding factors involved and problems with the studies. So we want to take a new look from another angle.

We know that radiation exposure causes mesothelioma from looking at radiotherapy, Thorotrast, and nuclear worker studies. We also know that tobacco smoke deposits radioactive particles in the lungs of smokers. (Harvard, Winters & DiFranza, even the EPA discusses it) So, lets look at the Thorotrast studies where radioactive particles were deposited in human subjects and resulted in large increases in mesothelioma risks, then see if a comparison to the radioactive particles deposited from tobacco smoke can be made.

Andersson, van Kaick, Travis and Ishikawa (all attached) are the key Thorotrast studies. Ishikawa holds all of the necessary information for our analysis - though I will provide some additional materials to you later. Open Ishikawa and mark it up. The chart on the first page gives us the numbers from the Danish (Andersson), German (van Kaick) and Japanese (Ishikawa) Thorotrast studies. Add up cases and controls and we get 15 mesos in 3299 cases matched against 1 meso in 4441 controls. My math yields a RR for meso of 20+. Now lets find what dose of deposited alpha radiation to the relevant organ is that yields that risk. Ishikawa estimates 2 cGy/year to the liver (for peritoneal meso), and a mean of 27 years from injection of Thorotrast to death. Van Kaick discusses higher doses (as does another primary source document that I will get to you) and it also discusses the concept of wasted dose - radiation dose after tumor initiation. It is generally accepted that a meso originates 10-15 years prior to diagnosis and we can assume a 1 year period from diagnosis to death. This means that the wasted dose is 11 to 16 years, and the deposited alpha radiation dose that created the RR of 20+ for meso is about 22 to 32 rad ((27-11 to 27-16) times 2 cGy or rad). Again, I think that we should moderate this by looking at the dose estimates stated in van Kaick and the other primary source document for organ dose estimates for Thorotrast injection. But, this is an enormous risk for relatively low radiation, even if we jump an order of magnitude to 220 to 320 rad or use the linear-no threshold model to extrapolate down with a slope of 1 to get 2.0+ RR for 22 to 32 rad.

So, how does this compare to radioactive particles in the lungs of smokers? Now we turn to Martell. Just jump to the last page of his report for now and we see an estimate that a 1 pack per day smoker gets about 30-60 rad of deposited alpha dose to "hot spots" in the lung around the radioactive particles and a 2 pack per day smoker gets basically twice that, 60-120 rad of deposited alpha dose. Application of our risk model from the Thorotrast experience to this data would clearly show a RR of meso above 2.0 for heavy smokers (1 ppd or more) due to deposited alpha radiation decay products (Po-210 and Ra) from insoluble Pb-210 particles (22 year half life). Martell also discusses how 1,000,000 cells around the deposited radioactive particle are at extreme cancer induction risk due to the constant bombardment by the alpha radiation decay products.

I will also send you a 1980 report from the ICRP that has two key pieces to this puzzle. First, it has pictures of rat lungs after inhaled radioactive particles - this is a great demonstrative that shows the alpha radiation tracks in lung tissue. Second, it clearly states that the pleura receives substantial radiation dose from inhaled radioactive particles. There are a plethora of animal studies, mice, rats and dogs that show large meso increases from inhaled radiation dose. You need to talk to Tony Brooks and get the info re Roger McClellan's Lovelace Inhalation Toxicology data (January 1994 or 1995, I think he said) where he found mesos in the beagle dogs with inhaled radiation and none in the controls. There are lots of published studies as well.

The last piece is then to look at some of the smoking/meso epidemiology in this new light, and we can take at least four of these studies now and find that they show this 2.0 RR of meso for heavy smokers.

We can add a sound policy reason for publishing this info. Winters & DiFranza, pathologists who published re increased radioactive particles in smokers' lungs, state that smokers are more likely to quit when educated about the fact that they are inhaling radioactive particles. I think that if you add to this the risk of meso - a terrible form of cancer - that we can send a powerful message.

Intrigued? I see at least four or five solid articles in here, and it will be an extremely important scientific work.

Regards,
Evan

<<http://www.tuckerellis.com/>>

Evan C. Nelson
Attorney

135 Main Street · Suite 700 · San Francisco, CA 94105
phone 415.617.2216 · facsimile 415.617.2409
Evan.Nelson@tuckerellis.com

CLEVELAND · COLUMBUS · LOS ANGELES · SAN FRANCISCO