JIFSAN SYMPOSIUM

ASBESTOS IN TALC

MAIN SESSION

Conducted by Catherine Sheehan

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C O N T E N T S

P R O C E E D I N G S

CATHERINE SHEEHAN: Good morning everybody. Since we are -- I have 15 minutes to introduce -- welcome everybody. Please bear in mind that we have a webinar aspect of this meeting as well. So in the interest of time, I would like everybody in the meeting room to take their seats, please, so we can commence with the meeting.

So welcome, everybody. My name is Catherine Sheehan, and I've been given the honor of doing the opening and closing remarks. So can I have quiet, please? Thank you.

We do have a webinar component, so we need to keep that in mind as well.

So as part of the introduction, the symposium, as you all may know -- okay. All right. The symposium is organized by the JIFSAN Symposium Committee. Who are the stakeholders supporting this meeting? For those of you that want to know, funding is through a cooperative agreement between JIFSAN and FDA.

The purpose of this symposium is to develop a standard and methodology for analysis and testing of asbestos, and hopefully we'll be able to achieve that goal here today or at least tackle it in some form or fashion in that we are providing a forum for experts. We have an audience from regulators, industry, and academia, so I think we are well-equipped here to hopefully move this discussion along.

I see some folks in the audience as well that I know of to work with the United States Pharmacopeia. So we also -- if you don't know, the United States Pharmacopeia also have a standard for talc; and we, also, are very interested in the work that is going on today. Of course, we will share knowledge and come to a consensus on future testing approaches and adequately analyzing talc containing products for the presence of asbestos fibers; and this symposium will include presentations and, most importantly, the concurrent breakout sessions on test methods, characterization, and interpretation of data.

So that's kind of a lineup in terms of what our purpose and goals are. Let me see if I can get this thing moving.

Tim, help. It's not moving. Technical

difficulties here. It doesn't seem to want to move. All right.

So morning session -- briefly, we have divided the morning session into three key areas: definitions and mineral fibers, test methods, and a break, and then followed by two sessions of presentations on the interpretation of data obtained from microscopy measurements.

The afternoon session, the breakout sessions, you can see here we have -- Sessions A, B, and C will be repeated to allow each attendee to have a chance to participate in two of the three planned sessions.

Session A, test methods for analysis of talc and mineral fibers in cosmetics; and Session B, measurement criteria for identification and fiber counting; and then Session 3 will be the interpretation of the testing data.

So after that -- some important information here in terms of housekeeping and how we're going to handle the breakout. Co-moderators will pose questions and record input from the audience using flip charts, computers, and other audio/visual aids. In addition to that, notetakers are available among participants, and they may use recording devices. Also, transcriptionist will be on site. And then immediately after the breakout session, there will be a break during which the co-moderators will review the input from the audience and draft their summary to report out to the larger group.

So after the break -- after the breakout sessions, all attendees will reconvene for the record out session; and then each pair of the session co-moderators will give time to deliver an oral summary of the input to attendees.

During the symposium, most importantly, there will be time for Q&As and if all questions are not answered, they will be posted on the JIFSAN website, and a summary of the meeting will be available shortly after the meeting. And so the date that I have here is that the moderator/speaker will present the summary of the presentation or results by January 5th. So you won't get anything before that date.

So any questions on that? One more thing, the restrooms are directly behind the registration desk.

That's it. So --

AUDIENCE MEMBER 1: Where will the breakout sessions go? Where are the breakout sessions?

CATHERINE SHEEHAN: Good question, Marty. Very good question.

Help, JIFSAN.

TIM: They are two corridors down behind us. So if you got out of the elevators, you just go straight.

CATHERINE SHEEHAN: Okay. I'm sure we will get more information. I'll go and find out and get everybody familiar with the three certain breakouts. Okay.

AUDIENCE MEMBER 2: Catherine?

CATHERINE SHEEHAN: Yes.

AUDIENCE MEMBER 2: Could you explain a little bit about the webinar and what it is and where it's going and --

CATHERINE SHEEHAN: Good question as well. The webinar has just been communicated to me by Tim. So my understanding is that we have this webinar going on, and we are recording this as well.

Tim can -- I think that's all we know about now in terms of they're listening to our presentations.

AUDIENCE MEMBER 2: Who is they?

CATHERINE SHEEHAN: Anybody that was invited to this JIFSAN meeting that cannot attend in person --

AUDIENCE MEMBER 2: Okay.

CATHERINE SHEEHAN: -- has the ability to join by webinar, so --

TIM: I do believe there's only like five or six people.

CATHERINE SHEEHAN: Okay. Thank you, Tim.

All right. So with that, we'll move on.

AUDIENCE MEMBER 2: Is there Wi-Fi access in this room?

TIM: Yes. I can come around and talk to you.

CATHERINE SHEEHAN: Okay.

AUDIENCE MEMBER 3: Just for technical difficulties, I had -- I'm getting a message from somebody that's on the webinar, but they can't hear anything. They can see the screen, but they're unable to do that. I don't know. Is there a way for them to contact help for that?

CATHERINE SHEEHAN: I see.

TIM: I am -- I'm actually listening to the webinar, and it's being broadcast just fine.

AUDIENCE MEMBER 3: Okay.

TIM: So --

AUDIENCE MEMBER 3: Do you have, like, an e-mail or something that I can have him reach out to you to --

TIM: Yes.

AUDIENCE MEMBER 3: -- get help?

CATHERINE SHEEHAN: Yeah, that would be good. Yeah.

TIM: Just Tshaffer@dodwu.

Who needed the Wi-Fi?

CATHERINE SHEEHAN: Right. Yeah. If they had an e-mail just in case they have any questions. Okay.

So in the interest of time, let's move on, and then I'll navigate through this.

TIM: Okay.

CATHERINE SHEEHAN: Okay. So our first speaker this morning -- very briefly introduce Brad Van Gosen. He's a research geologist at the U.S.

Geological Survey, and he began his work with asbestos in 2000, so if Brad could come up to the podium.

BRADLEY VAN GOSEN: First of all, I want to thank the JIFSAN committee for the opportunity and the invitation to speak here today. It's very much appreciated.

I'm hoping that my product will just provide a context for the rest of the day, and that is to just describe to you the elongate mineral fibers, particles that we're even going to need to think about in terms of commercial talc deposits. And I'm going to do this and -- these minerals will be some of the amphibole mineral group as well as the one type of deposit that's relatively spatially associated with Chrysotile, the serpentine mineral group.

The amphiboles and serpentine that are associated with talc deposits of mineable commercial size are dependent entirely on the geologic environment, the geologic conditions that form that type of deposit. I'll describe four basic types of geologic settings and conditions that form talc deposits -- not all are created the same -- and give you a little geology.

I thought I'd provide just a quick background on the current talc production. In the United States there are three companies producing from three different states, and these include the American Talc Company, which operates several pits in the Allamore District, which is in far western Texas. Most of their product is being used in paints is my understanding. Barretts Minerals operates two large open pit mines in southwestern Montana, and then Imerys operates the Yellowstone Mine also in southwest Montana and another mine here in Ludlow, Vermont.

The photo there is a distant view of the Yellow stone Mine, which is the largest talc producer in the U.S. for several years now. By state, production is largest from the Montana deposits followed by Texas and then Vermont.

Just a little background on our most recent domestic talc production and uses. This is information from our USGS National Minerals Information Center. In 2017, the last data that's been published, U.S. production was estimated about 540,000 metric tons, valuated at about 108 million dollars. And at least during 2017, the talc that we [the U.S.] produced and sold was used mainly, as you can see, in ceramics, paint, paper; followed by plastics, rubber, refractories, roofing; and just about 3 percent was used in cosmetics.

We [the U.S.] export about 210,000 metric tons per year. We also import an estimated 380,000 metric tons of talc, as compared to 540,000 metric tons that we produce commercially. So talc is actually one of the rare mineral commodities in the U.S. these days that we produced more than we import, but it's still a considerable amount of import. By decreasing the amount by tonnage, about three-fourths of our imported talc was used in cosmetics, paint and plastics. So if you include imported talc and domestic production, the primary uses are plastics, ceramics, paint, paper, roofing, rubber; and cosmetics is a distant end of the spectrum.

According to our Minerals Information Center, the main import sources in recent years have been Pakistan (35%), Canada (28%), and China (26%), and a small amount of processed talc coming from Japan (5%).

Just the very basics to get you started. Talc is a magnesium silicate mineral. As you've heard, it's probably -- it's number one on the Mohs hardness scale, meaning, it's used as the example of the soft mineral. It has perfect cleavage on the 001 plane, basically meaning that it's very platy, usually; but as we will see, and as you know, there are fibrous varieties of talc.

There are very weak lines between the layers, so they're easily sliding past each other. It gives talc its greasy and slippery feel and its very low hardness. Well-developed, sort of, gem-quality crystals of talc are extremely rare; and common impurities include nickel, iron, aluminum, calcium, sodium, and some excess water, iron probably being the most common impurity to ideal composition of talc.

This is the amphibole group of the regulated amphibole minerals we all know and love, if they occur and when they occur in the asbestiform habit, which will be discussed much today. Of these, principally, the minerals -- amphiboles that we're going to find in the commercial scales talc deposits are anthophyllite, actinolite, and tremolite. There is and, of course, has to be always an exception in geology. There is some manganese variety of cummingtonite in the New York deposits that's also been reported and well documented, but for the most part, we're gonna -- I'll show you examples of different deposit types, and we're gonna find that anthophyllite is very common. Tremolite's very common, and occasionally, as part of the actinolite/tremolite series, we'll find some actinolites in deposits.

We also -- as I said, spatially, in one deposit type I'll show you. Chrysotile is associated in the -- abounding in wall rock, country rock; and chrysotile, being of the amphibole -- or I mean -- I'm sorry -- of the serpentine mineral group. But if you'll notice the formula for anthophyllite, chrysotile and, if I back up to the other amphiboles, magnesium, silica, and water hydroxyls are the critical elements to form all of these -- the regulated asbestos minerals. And also, if you notice, talc is, again, a magnesium silica hydroxyl formula. So the same chemistry involved in the formation of the amphiboles is also the same chemistry in the -- or critical elements that form talc, so it's not unusual to find the amphiboles in a talc deposit, at least based on the chemical components of the systems.

Talc is a replacement mineral. For example, it doesn't form, you know, straight from a magma like mag minerals. It's replacing a preexisting magnesium-rich mineral with preexisting magnesium-rich host rock, and these would include either a dolostone -- you've heard of dolomite, a magnesium calcium carbonate rock -- or replacing an ultramafic rock, which is a magnesium iron-rich metamorphic rock. So you have the magnesium in the host rock already available, and then, if heated, core fluids, usually waters, carrying silica in solution, react with the host rock to provide the elements to form talc. And these processes can be driven by regional metamorphism, tectonic scale, and a regional scale, heat and pressure, whereby, contact metamorphism where igneous intrusion of magma intruded directly into the host rock or the -- by the circulation of magnetic hydrothermal fluids. Those are heated fluids, heated by magma that's at depth that didn't come in direct contact with the host rock, but I'll show you examples in the United States of each of these.

Probably our best example of regional metamorphism in this case is -- cold stone magnesium calcium carbonate is a good -- our best example of a regional metamorphic talc deposit. These were mined on really for the first time on a larger scale mainly underground mining, but a lot made smaller open pits starting in 1948, shown by the red squares; and then the open pit -- larger open pit operations were from 1974 till about 2008 when the mines closed, shown by the hot pink ovals.

The conditions that form these deposits over a billion years ago, again, were from regional metamorphism shortening the depression of the crust in that region over a large area; and this drove the fluids, under high heat and pressure, from the silica being gathered from silica-rich rocks beneath and then probably accessing fault and fracture systems, moving the silica in fluids up into the dolomite, massively replacing portions of the dolomite by talc and amphiboles.

This is -- take you back to chemistry a little bit, but these were -- progressive reactions from top to bottom go from highest heat and pressure down to the lower portions of heat and pressure in the system as the system start to relax and heat also decreased.

First we take dolomite in the presence of the invasion of that silica in fluids to form tremolite and calcite. Carbon dioxide can easily leave the system. Now we have tremolite in the presence of the remaining dolomite, again, with waters involved can form anthophyllite and calcite; and as the heat and pressure decreased even further, that new anthophyllite in the presence of siliceous waters, again, forms talc. This is a progressive stepwise occurrence that are in this metamorphic system, starting with a dolomite -- a magnesium calcium source rock.

Most of the tremolite in these deposits is described as, I would say, prismatic in shape. They're elongate but certainly not clearly fibers. But then you have this fibrous talc, which is the replacement of the anthophyllite, formed during phase 2, if you will;

and the talc has, occasionally, partially to completely replaced the fibrous anthophyllite; and this gives the -- the terms fibrous talc or tremolitic talc have been used to describe the Gouverneur talcs, and this shows you a map of why.

And then we also have quite a few of these transitional fibers, which are the partial and sometimes complete replacement of the preexisting anthophyllite by talc, so it can get very complex.

Our next deposit type to consider are these amphibole. They're tremolite. They're in talc deposits in the southern Death Valley region. I started studying these about 15 to 16 years ago, just curious to see what the morphology of the tremolite within these deposits looked like under high magnification. They're -- well, I should go back a little.

There are 43 talc deposits that were either mined or prospected in the Death Valley region, including a couple dozen within Death Valley National Park itself. These became part of Death Valley National Park. They are now property of the national park when the national monument was converted to national park status in 1988. There's still a couple dozen other talc deposits outside of the realm of the national park boundaries which lie on a mixture of mined claims and federal lands. These talcs were used primarily in ceramics, especially ceramic tiles, as an -- and as an extender within paints. This is an example of some of the mines outside of the national park. As I said, there's quite a few. They're easy to spot from long distance. White piles against the gray dark background of the region. I'm getting hot looking at this again. (Audience laughs.) It was 110 that day. There are a combination of open pits and underground mines that are actually not deep underground mines. They're just added straight into the talc tremolite ore bodies.

This is a schematic diagram from Warren Wright's very fine descriptive report on the Death Valley deposits. He has a description of each one of those 43 deposits in the region. It's more of a general geology discussion. He did not have the use of microbeam technology to look at very fine fibers at that time, but it's a very good guide to where these occur in their basic geology.

And, essentially, what you have is that gabbro soil is the magma that intruded into the tridy (ph) dolomite, which is a term being silica; and it's a silica magnesium carbonate-rich host rock providing the magnesium for this reaction; and this reaction formed a talc-tremolite orebodies which can be generally around 50 feet in thickness. So the heat drove this reaction. Warren has suggested, and it seems reasonable, these sediments may have actually been -- or this dolomite might have actually been a sediment -- part of a sediment sitting on the shallow ocean floor when it was intruded by the magna; and this could accomplish some of the sodium we find in a little bit of the mineralogy in here. So in the end, this reaction formed talc -- a mixture of talc, tremolite, calcite, dolomite, and quartz. So these were not considered, therefore, a high-purity talc; but they are very suitable for use in ceramics and paint.

This is just a good view of the system I just showed schematically. The gabbro soil magma that intruded into the tridy dolomite -- the silk magnesium-rich host rock -- and the reactions on the talc tremolite rock would be the ore itself; and it has very sharp contact between the intrusion and the talc tremolite rock, the replacement of the dolomite. You put your finger on that. And forgive me, I'm a geologist, I got to show some of these details; but they're very layered sometimes, and it's very crumbly. The advantage of mining talc is that it generally doesn't require blasting. Heavy equipment can easily -- you're talking about the softest rock, and if you find a talc rock that's even the least bit hard, that means it has a fair amount of quartz or calcite in it. There's a little rock number for -- scale number on the side there.

So what we see, via scanning electron microscope, is a wide variety of shapes and morphologies within the tremolite in the Death Valley talc. For the most part, what I describe as "prismatic" is the most common form; but we do find these circular needle-like particles of tremolite and some that are very characteristic of the stuff it formed. For example, we find fiber bundles of tremolite mixed with the clay you tab (ph), or if the analysis was by electron dispersive spectrometer that is, of course, part of our SEM, so -- and we do find these -- most of these are dust, dabbed from the inside of the plastic sample bag; so these would represent dust that easily release here in the sample, but we did find plenty of individual fibers in the dust and little -- again, fiber bundles. The Smith liner is east of the park, and I've been told that there is a company that in recent years has been looking -- or has been excavating former stockpiles of talc, and I'm not sure it's being shipped to a paid factory or not, but this is something I think should be kept in mind.

We also found scattered particles with a sodic composition. Again, this is from electron dispersive spectroscopy, which would not be considered a precise method; but they're clearly a sodic-calcium amphibole, and the best fit would -- from our work is the amphibole winchite. And, again, we find some fibers and fibrous bundles that fit another sodic-calcic amphibole being richterite.

So my point here is these Death Valley talc deposits formed by contact metamorphism where the magma protruded directly into the host rock I think need to be considered if you -- oh, we hear of activity of re-mining these deposits and the dust that can be created.

Our third category of talc-forming environments include the replacement of ultramafic rocks. These are magnesium iron-rich rocks formed by either metamorphism and alteration of an olivine-rich rock, a pyroxene-rich rock or an amphibole-rich rock; and these alter to form a rock called serpentinite, which is a serpentine-rich mineral -- or serpentine-rich rock; and these can, of course, as we know on many instances, contain chrysotile and occasionally and sometimes anthophyllite and tremolite.

This is a very cartoonish diagram of work by Rick Sanford in 1982, his long article in the American Journal of Science, which is basically a summary of his Harvard PhD study. And first of all, he determined, at the bottom there, these reactions occurred at very high temperatures, very high pressures; and this would be -- it's hard to generalize a complex system, but this would be the general zonation of what would be visible at the Vermont talc deposits, for instance. And on the left, they're replacing an ultramafic rock, that magnesium-rich, serpentine-rich; and those can, certainly locally, contain chrysotile, tremolite, actinolite, and anthophyllite.

You move inward towards the talc ore, you have a talc carbonate rock, a talc with magnesite -- magnesium carbonate unit, which contain lesser amounts of dolomite and calcite, and evidence of talc replacing apophyllite. And we move into the talc zone, which it is often described as a high-purity talc, meaning it really has a little courser clay or calcite. It's not gritty. It's a very soft, relatively pure talc.

The occurrence of anthophyllite mentioned or actinolite or tremolite fibers within this talc were still a matter of some debate. I, personally, unfortunately, have not been able to look at any of the raw ore, but I welcome samples or an opportunity to sample.

This is bounded by an actinolite fluoride-rich rock. There's evidence of talc replacing actinolite to minor amounts. Perhaps much of this is actually tremolite. Rick did not have the benefit of microbeam analysis at the time.

Then we move outward to the altered country rock, which is the country rock being a metamorphic silica-rich rock or gneiss; and some of the metamorphic texture remains, and you have some prismatic classic amphiboles and then outward to the unaltered gneiss on the opposite side of the system. So you're getting this silica sourced by the country rock and the magnesium clearly sourced by the ultramafic rock, and it's a complex system that occurred under very high heat and pressure.

But the good news, not all talc is created equal. There are another type of talc deposit. These are formed like the upward circulation of hot silica-rich fluids that are heated by igneous intrusion that lies at depth. It's not coming in direct contact with the host rock, and these can form very large talc deposits by the massive replacement of that dolostone and magnesium-rich marble; and in this system no amphiboles or serpentine are created. And they're relatively simple reaction on a stone, like, again, heated silica -- or heated fluids would carry silica, forming talc calcite and carbon dioxide.

This is a very cartoonish depiction of that, but you have the magma rising through the crust heating any fluids, core fluids or even if groundwaters exist in the system. The black lines representing fault and fracture systems which surely help to plum the heated waters upward through silica-rich metamorphic sedentary rocks that can provide the silica and then massively replacing parts of the magnesium-rich marble above. The edges of the deposit can have considerable quarts, calcite, and dolomite, and pockets within the talc body; but for much of the talc body, more than 90 percent of it is platy talc. There's a -- of -- deposits of this type in a quarter -- we're in southwestern Montana -- are very large deposits, and these may be -- this may -- probably represents the largest talc district mill in the United States; and they all form from the replacement of those dolomitic marbles, intrusions at depth; and this includes the

Treasure Mines and the Regal Mines of Barrett Minerals and the Yellowstone Mine of Imerys.

This slide and the next I credit to Childs Geoscience, consulted out of Bozeman, who published one of his PowerPoint presentations. This is a generalized geologic map of the Yellowstone Mine area, the Yellowstone deposit. The blue being the marbles that have been replaced. The red is the talc -- the talc or body which is about a half a mile in length north and south, and all the black lines being fault systems which surely helped plumb the -- in the plumbing system for the heated silica-rich fluids that moved up and invaded and replaced the dolomite.

That Burlington northern pit up at the north was another large talc deposit mined many years ago, and that pit has been reclaimed.

The Yellowstone talc mine itself, it's very large. It's the largest known talc deposit in the United States. I'm not here -- I want to make it clear, I'm not here to endorse the deposits of southwest Montana. I'm just making the point that not all talc deposits are created equal. Some can lack amphiboles we plan to discuss, but it -- my work has led me to show that the geologic conditions that came to form the talc deposit directly impact whether amphiboles or serpentine, in one case, exist at all to discuss.

And as a lead into Greg's talk, again, I want to emphasize that even within one talc district, or even within one talc deposit, you can get a wide range of mineral morphologies; and these may not be obvious or visible without microbeam analysis. So I think we need to -- well, this will be discussed all day long hereafter; but there will -- to get down to the scales that clearly show this variation, it may require things beyond standard microscope work.

And with that, thank you for your time; and hope we can -- well, you'll hear a lot more in discussion today about -- that led to the identification of this type of variation. Thank you.

(Applause)

CATHERINE SHEEHAN: Thank you, Brad.

I think we can move along and get Greg up, and then we have time for Q&A.

So introducing Greg, he's a research scientist specializing in the characterization of fibers and asbestiform minerals. Greg worked as a mineralogist and geologist in the U.S. Geological Survey for 23 years before his retirement from federal service; and in 2009, Greg served as a member of the National Academy of Science Institute of Medicine Committee to review the NIOSH program for asbestos research.

Greg, thank you.

GREGORY MEEKER: Good morning. Catherine, thank you for the introduction.

I'd like to thank JIFSAN for inviting me here today to give this talk. It's good to be back in the mix. I've been retired now for six years and enjoying it, but it's good to see a lot of my old friends here.

I want to put up this -- oh, and Nora --I want to thank Nora so much for all the hard work she's done. She's really put this together, and thank you very much. I never see her in the room.

I guess I need to put up this disclosure here. I have done a little bit of consulting since I retired from USGS, but mostly I've been enjoying summers in

Colorado and winters in Florida.

So the question today is: Has anything really changed in the last 15 years? And I chose 15 years because I'm going to use a presentation that was put out 15 years ago, and I think we're still having some of the same arguments today that we were then.

This is going back a little farther to 1981. Well-known and important mineralogists from University of Minnesota, and he wrote a paper, and he wanted to -- said, "Asbestos is one of the most durable [sic] industrial minerals because it possesses an unusual combination of exploitable properties, such as long fibrous shape, high tensile strength, and flexibility, both thermo and electric conductivity, high absorbency, high chemical and mechanical durability and incombustibility." And then he says, "Ironically, industrial desirable properties of asbestos also appear to be responsible for carcinogenicity."

I'm gonna come back to this at the end of the talk, but I just wanted to put that out at the beginning because it -- I think it kind of frames the whole discussion.

So I think the questions for us here today -- it was hard for me to know quite what to talk about, but I -- is it possible to protect human health without regulating everything? Is regulated asbestos the only health hazard? Is commercial-grade asbestos the only health hazard? Not necessarily the same thing. And what have we learned over the last 15 years about asbestiform and related minerals? Most important question is: What does the human lung or the human body know about all of this?

Now, traditional analytical methods may not be adequate for characterizing natural-occurring asbestos or contaminated materials. Most of the methods we use today were developed for the analysis of commercial asbestos. It's when you've got asbestos in ceiling tiles and floor tiles or asbestos in the siding and you want to go in and find out if that material is still there after a clearance or if workers are being exposed in production. So you're dealing with a known -- you're dealing with a commercial-grade material, and the methods -- most of them -- were developed to look at that -- the EPA 600, an analysis of asbestos in building materials.

There are very -- there's so much nomenclature and definition -- issues with definitions to talk about that we could have a meeting like this for two weeks and just begin to get into the issues, so it's -- one of the issues is the name of an amphibole and how well can we identify an amphibole. Some are listed in the ranks, others are not. Actinolite and tremolite are listed in the government regulations; magnesiohornblende is not; richterite is not; winchite is not; and the analytical methods we have to identify these different amphiboles, because they're based on chemistry, is -- it's not easy to do.

And this is an electron probe microanalysis of a -- probably an actinolite particle, and it was done in an electron microprobe on a bulk sample -- polished bulk sample. It's probably the most accurate chemical analysis you can get on a micron or two micron spot, and according to Leake, if you look at this --

MAN: I can't see it.

GREGORY MEEKER: -- the pointer -- if you look at the diamond right here, if you use the method in

Leake 97 to identify what this mineral is, you get that point right on the line between actinolite and magnesium -- magnesiohornblende. If you change the way you calculate the analysis, if, for instance, you use all ferric iron, or all ferrous iron, to make the calculation, because an instrument cannot tell the difference, you could end up with a point up here or a point down here and other ways of calculating the analysis will fall in between these two lines.

So the point is that even the best analysis you can get on a very tiny spot does not -- you've got air barns (ph) here. You don't really know if you're looking at actinolite or magnesium -- magnesiohornblende.

I'm not gonna talk anymore about chemistry because I think the issue here today is morphology, and that's because the amphiboles that you find in talc are fairly easy to identify chemically on a TEM with crystal structure. So the chemistry is not as big an issue with the -- usually with the minerals you find in talc, except for the -- the few that Brad talked about -- the richterites and winchites.

So let's talk about morphology. Traditional thinking, I think, uses an in-member (ph) approach. In-member is a term that enterologists are familiar with. It's an in-member approach with no solid solution, which means you either have one solution at one end and the other and nothing in between. I think this is a way to look at it is stove piping. So you either have commercial-grade asbestos over here or you have everything else, which really, over the last about 30 years, have incorrectly been termed "cleavage fragments." Some of them are; some of them are not; but it's just all been kind of dumped into this one bin that everyone seems to call cleavage fragments. So it's either the bad stuff -- whoops. Sorry. It's either the bad stuff over here on the right or the stuff that doesn't hurt you on the left.

Well, there are a lot of definitions for cleavage fragments; and I mean, I can't read all of this, but they're really all saying the same thing. And the summary, I think, is that cleavage fragment is not any particle that does not meet some specific definition of asbestos, and there are a lot of definitions of asbestos also. Cleavage particles must be particles broken from larger crystal, along specific crystallographic point. So it's not only a broken particle, it's broken in a certain way related to the crystal structure in the mineral.

EMP. Why people don't like the term "EMP." EMP is a general term for any elongate mineral particle. It could be a cleavage particle. It could be an acicular crystal. It could be an asbestiform particle. The term was meant to be used for research, not for regulation.

Cleavage fragments, over the years, in my opinion, have become the proverbial get-out-of-jail-free card; and that's due to misuse and misunderstanding of the terms: asbestos, asbestiform, cleavage fragment, and a whole bunch of others. The term "EMP" is not meant to be used in place of specific mineralogical nomenclature when the correct terms are known and when they are properly used. A lot of these terms are misused, and that's a problem.

I want to go into this presentation. I think at least one of the primary authors is here, Ann Wylie.

I don't know if Kelly Bailey is here, but I want to use this. There's a lot of good information in here. I want to say that at the beginning, and there's a lot of good health information that I'm not going to get into; and we need another meeting like this to deal with that, but I want to use this to illustrate some of the points that I feel important.

The introduction says, "Despite this attention, a clear understanding of what asbestos actually is remains a source of confusion to many," and that's very true; but that's also talking about commercial-grade asbestos. "No federal regulatory agency treats elongated nonasbestiform particles as asbestos, yet some in the regulatory and health community believe they should. These individuals mistakenly believe that the essential differences between nonasbestiform minerals and asbestos is not significant," and that's getting back to the first slide I showed from Zoltai from 1981. And I think a lot of people here would agree with this, and I think there are a lot of people who would not.

"Health researchers who fail to understand these differences can assign and have attributed the carcinogist -- carcinogenic" -- excuse me -- "effects of asbestos exposure to nonasbestiform minerals."

And so here is an example from that presentation showing what asbestos should look like, and again, I think this is a good example of good quality commercial-grade asbestos, particularly serpentine; but it says the single most important morphological characteristic of the asbestiform habit is the fibrous polyfilamentous characteristic.

This is an example that I think shows what that drawing -- previous drawing was trying to show. You can see these features -- very thin fibers, parallels, maybe some curvature there. This is tremolite from Death Valley. I think Brad had this image or took this image. It's from the USGS website -- on the microprobe website.

This is the diagram showing the nonasbestiform particles, and nonasbestiform crystal growth tend not to grow -- excuse me -- not to grow with parallel alignment. They form multidirectional growth patterns instead. I guess they're saying that crystals are strong, but crystals grow in a cluster like that. And then it says that when pressure is applied, they easily break apart and form the particles that you see over on the right with stair-steps on the surface and -- so if we tried to find one that looked like this, maybe this one would be a good example. This is an amphibole particle. The -- let me get this pointer. You can see these stair-step patterns on the edge. Maybe if we look a little closer, I think this looks very much like this guy over on the right here; but you've got these steps on the side, kind of a flat top. Things look like they might be breaking off or partially broken off on the side.

So what is this that we're looking at? This is UICC crocidolite, and you know what? Ore mag looks like this. There are a lot of particles that look like this, and maybe some people would call those cleavage fragments, and then here's the particle we looked at earlier.

Another publication that came out in '77 from the Bureau of Mines. This one's showing massive anthophyllite here and massive actinolite over here and then saying that this is not asbestos. Anthophyllite asbestos looks like this. Actinolite asbestos looks like this.

I'd like to show you some other images of a similar theme. Here's a massive gem part richterite. This sample is very hard. If you hit it with a hammer, it will crack. You can't just peel it apart like we used to do in mineralogy class decades ago. And then if you look at -- down here there's some little particles, and if you look at those particles, if you can just kind of brush off the surface, that's what they'd look like.

Here's another one. El Dorado Hills tremolite. Again, it's a massive-looking rock here. Hit it with a hammer, it's hard, it will crack; but it sheds particles, and this is what those particles look like under the SEM.

Here's Libby. This is a very hard rock. I spent a lot of time beating on these rocks. (Audience laughs.) And believe me, they are hard, and -- but this stuff just flakes off the surface. If you look at it under the microscope, that's what you get. This is from USGS publication on El Dorado Hills from 2006. And this curve on the left is from camera 77 showing the aspect ratio versus frequency for particles that they classified as cleavage fragments, and you can see they're all down here with a very low aspect ratio.

They also did asbestos particles. I can't remember what they used, but this curve for asbestos is hard to see; and I apologize, but if you follow the pointer, it goes way out here, and the aspect ratios can be very high.

Well, the material from El Dorado Hills, California, falls in between. It's not here, and it's not under this -- similar to this asbestos curve. It's in between. These are not from a single deposit. These are particles that were gathered over a wide area that come from a range of sources, but still, they're in the dust that people are breathing in the park in El Dorado Hills.

This is Libby showing kind of the same thing. There's asbestiform material. There's stuff pretty much everybody would call cleavage fragments, a lot of stuff in between. Here's the asbestiform cleavage fragments, but I've looked at a lot of this material, and most of it looks like this. What do you call that?

Again, here's another Libby particle. It's got a little bit of everything. There's very long, very thin things breaking off up here. There are things breaking off that look like cleavage fragments. Top of the slab, you've got structures like you see here. What do you say about this? I say it's very difficult to say what this is, but I think a lot of people here would agree that there are hazardous particles here.

AUDIENCE MEMBER 4: It's not respirable.

GREGORY MEEKER: Pardon me?

AUDIENCE MEMBER 4: The particle you showed is not respirable.

GREGORY MEEKER: This big one isn't, but this one over here, which looks like it's fallen over, it is.

AUDIENCE MEMBER 4: I understand. Yes.

GREGORY MEEKER: So for years the toxicity of asbestos has been attributed to the special properties of commercial-grade asbestos -- tensile strength --

when aspect ratio, curvature, and chemistry of these properties really only by an aspect ratio have been clearly demonstrating to correlate with toxicity.

We're working on this instrument now, and I hope to get it operational soon. (Audience laughs.)

So let's go back to that Zoltai paper, and this has been referenced numerous times over the years by many, many people; and we already looked at the first page, and this is a very long paper. It's 39-pages long. So when I first found this, I thought, oh, great, this is really gonna explain the difference between asbestiform and nonasbestiform particles. Well, you read the paper, and 39 pages later, this is all that is said -- (audience laughs) -- in that paper about the difference between why you need those properties for toxicity. That's the end of the paper. It references this Stanton and Layard. It's the NBS special publication 506. And you go to heating, there's nothing here either. I mean, this is all you get. If you heat it up high enough, it's not as toxic.

AUDIENCE MEMBER 5: It's not asbestos then. It's another mineral.

GREGORY MEEKER: That's right. So here's the slide I stole from Aubrey Miller. I think it kind of sums up what we're talking about here. You've got the total respirable material. You've got the regulated asbestiform material here, and then you've got all this other stuff that's not regulated. It's not commercial-grade asbestos. What do you do with it?A lot of people believe that -- this and that and so can any doctor or toxicologist but believe that these things here are a problem. What does the lung know?What does the body know? I think that's the real question we're dealing with here, and I think as we move forward in any kind of effort to put together a statement or a summary for this, we have to keep this in mind.

So that's all I have. Thank you very much.

(Applause)

CATHERINE SHEEHAN: So next up I would like to introduce professor Martin Rutstein. He's a retired professor of mineralogy, teaching and research interests in: mineralogy, metamorphic petrology, optical mineralogy and environmental geology, especially particulates and toxic chemicals; and presently co-chairs the U.S. Pharmacopeia Expert Panel on talc and asbestos in pharmaceuticals and is an expert witness in state and federal courts on asbestos and lead-based paints, so --

MARTIN RUTSTEIN: I guess I don't get to go for a bathroom break. (Audience laughs.) That's a lot to ask for. Let me just set the timer. Are we ready?

It's -- no, like this. We're just saying. I know where the mic is.

CATHERINE SHEEHAN: Okay.

MARTIN RUTSTEIN: There's going to be a -- she got me all set. We'll go back to that. Okay.

When I got the call, "Would you talk? Would you like to talk?" oh, yeah. Sure, I would love to talk. (Audience laughs.) They said, "This is what you're going to talk about," four things, which injected a tremendous --

You gonna fix this thing?

-- which injected --

TIM: Yes.

(Background noise)

TIM: Will you test it?

MARTIN RUTSTEIN: Okay.

MAN: Sure.

TIM: All right.

MARTIN RUTSTEIN: Here we are. Okay.

Which injected, immediately, controversy over limitations, damages. Mickey was beside himself. If you're there, Mickey, on the webinar, ha-ha-ha. (Audience laughs.) I took -- I listened, to you honest.

So I'll tell you how I picked the topics. I didn't even know who I'd be talking to. It started off, is it going to be done with regulators? Would it be people who are wizards in this? Some division -- I had no idea. It wasn't until just a few days ago that I finally got a handle on who would be in the audience. I've been working on this for some time. I think I've tailored it in a way that you'll all get something out of it.

My life has largely been teaching students and also out in the real world where somebody does something about asbestos, in terms of containment. I dare say to Brad, I probably spent more time in containment than him and anybody in this room. It's a different world out there from the laboratory. I also headed up a NVLAP/ELAP lab, so I know my way around a laboratory.

So how do we measure and characterize the elongated stump? Before Brad jumps up and down on this one, we never use "elongated." Beat that into him. It's elongate particles. So we're really looking at these things that are longer, and let's talk -- I'll talk about those. I've got a lot of stuff to do, a short time to do it, so let's get on it.

First, there's some really smart people that I've had the honor to work with -- the USP panel. The first one, I put it on the reference list, the first stimuli article. It's really worth looking at. Five years of heavy intense work from really bright people.

The second panel, many of you are here. I thank you. It's because of you if I seem further, it's because I've stood on their shoulders; and some of them people are so darn smart when it comes to analytical work that I find it scary, and they were fortunate.

They have some of the best instrumentation going. I'm talking as an individual, not on behalf of USP. They drill into us every meeting we have that the meetings are confidential, they're works in progress, it's where we're going; and I think probably three years into this -- or two and a half years -- and were able to get a stimuli article on methodology published. At the beginning I said we had a certain amount of time to do it in.

Okay. Their idea, the first one. Mineralogists, it's like the cowboys and the cow have been in this sprint for decades on whose language, whose words we use. There are thousands of minerals, and mineralogists have their own cult, in terms of understanding the words we use and then often not the same that the regulatory community uses or that biologists use.

We go at minerals to identify them, and we characterize them. We do it on the basis of structure and composition. And probably, if you're interested in this two-page summary from Micky's and Gabby Diers's (ph) book, 2008, it's posted as a reference;

and it's really worth reading if you want to understand the side of the geological and mineralogical community. Not all of them. We all differ. We disagree. We argue. It's a pretty good summary on how we identify minerals.

However, asbestos is also defined as the regulatory six. We all know those. We dream about them. We eat, sleep and -- we know them so well. I like the sum that Brad just did on -- or Greg did on the chemistry. In one version of this presentation, I got over 50 tremolite mineralogical cousins based upon the Leake classification -- name after name after name after name, and it really is messy.

We have the regulated six, and I'm working off those. That's what's in the regulations that we have to live with -- chemistry and usage, also shape and size. The standard five microns long, bla, bla, for the long asbestos fibers. You don't regulate the short asbestos fibers, but they're out there. They're at one end, and then we've got the cleavage fragments at the other end and this EMP thing that we'll talk -- I'll talk about in a little bit too.

We also define asbestos medically and bioreactivity. I've come a long way over the decades. I've looked at this. I did my first asbestos inspection in 1972, before many of your parents were even born. I looked at this stuff in the field, I've look at it in the lab, and more and more I'm evolving toward: What's respirable? What gets into the body? What can cause harm? But we have to live within the rules of what's regulated.

We also have this characteristic of a motion. I can empty a building by saying, "Asbestos is falling down from the ceiling." People have been convinced -- it's almost a religious thing, good versus evil -- asbestos is bad. There's very little debate out in the public area, and I think that one of reasons the jury, say, in St. Louis are coming down so hard against Johnson & Johnson is because they hear the word "asbestos" and right away the bell goes off -- bad, death, evil, punish somebody.

I put together these several pictures of different materials: talc ore; talc powder, the products; and then, from Brad, some of the stuff from

Death Valley; and the calcium amphiboles. In 2007, Dodson came up with 30 different analytical methods for asbestos. The number's even larger now. If you do a search and you spend the time -- is Ella (ph) here? Ella, is she at break?

AUDIENCE MEMBER 6: Yes.

MARTIN RUTSTEIN: Thank her. You know, you put together that list on the definition of "pride." It was you, wasn't it? Or was it Lee (ph). It was Lee. Sorry, Lee.

AUDIENCE MEMBER 6: Go get after him.

MARTIN RUTSTEIN: Get after him for all of us. (Audience laughs.)

But the list goes on. Hey, I got -- Friday one person says, "Well, I've got asbestos." Another person says, "I don't have asbestos." They used two different methods, and they're not communicating; and I hope to convince you that that's one of the really important goals that we have to come up with is a definition that we agree on.

The big issues, as I see it, are these elongate particles, the so-called EMPs: talc, tremolite, anthophyllite. Chrysotile, I worry less about because I think it's so easily identifiable. I can just put it on the side.

I don't even put actinolite up because I think that's just a slightly ironness tremolite. There's also a lot of other minerals, especially sepiolite; and one of Mickey's grad students, Marian Buzon, finds really neat fibrous sepiolite in some of the Montana mines which could mimic talc, which would mimic, maybe, anthophyllite.

The three categories of materials: the cleavage fragments, from a mineralogist, they're broken crystals. They start as big things and you break them, it's a cleavage fragment. How do we break them? A plate or weakness. That's all another source. It's just a broken fragment. The shape, acircular and prismatic. They're just shapes. We used to talk about them as just a morphology. That was a generalization: tall, short, fat -- I guess it's fat shape -- thin, whatever. Thin shape is so much later, but they're just general terms, and they've taken on to some as very important regulatory criteria. Talc (inaudible).

Then there's asbestiform minerals, fibers formed by crystal growth. I won't even touch getting into the finding of fiber. There are dozens of different definitions of that all depending upon the method that is being used.

So we've got to worry about cleavage, shape, and asbestiform materials. I've stopped talking about asbestiform talc, fibrous talc, because the word "asbestiform" immediately connotates something really bad and regulatable.

A couple of time symbols. What you see depends upon what you're looking from. There's a human bias on this. It's real. This is very important. I call it environmental outcome. If you change the way you look at things, the things you look at change. It's one thing to have it in hand sample where we can identify it; it's another thing to go through the microscope, another thing to go in an electron microscopy. Pretty soon you've got really good measurements at both ends of the spectrum but you're coming up with very different answers. What we find in most rocks is something elongated. It just happens, the way it breaks. So it's a level of how much of something is something of concern.

Take a look at doctor's papers and Mary's (ph) papers, especially sepiolite on that one. He summarizes in a pre-notation to SME 2016 all the different deposits, and one of the things you should recognize is that the three categories: the regional metamorphic, the ultrabasic, and the -- the basic, the metamorphic and the --

AUDIENCE MEMBER 6: (Inaudible).

MARTIN RUTSTEIN: -- gabbro, the Death Valley types. Death Valley type, a single heating event. The regional metamorphic, multiple heating events changing of the character of the rock and real effects are water and carbon dioxide during their formation. So it's like boxing around when one mineral forms, and you really have to take that into account, along with the ultramafic rocks. In Vermont, they produce raisins -- I mean prunes -- prunes are even a better for you now that you're a senior citizen -- mixed into a dough and then the dough is kneaded, and these individual masses -- the prunes and the raisins -- get cooked differently and they represent a different composition. So you go to one deposit and you find one thing. You go to another deposit, you find something else, and the producer is mixing stuff from each deposit.

I thought it was critical. I loved Gouverneur Talc at one level. They were very kind to me over the years, letting me into their mines with my students; but the stuff over at talc mill was very different from the stuff at the iron pit; and for many years, without knowing this, I think was the case, they were mixing stuff in the talc fill. I went there one year, and I think -- actually, they were draining the pit; and I could see fibers blowing in the breeze. I went down and said, "You really don't want to start mining that stuff. Just cover it up." Some of the work that's been done on South Hill has been through surface samples. The stuff at depth in the literature is very, very different. They were bodies that were largely fibers of anthophyllite, contrary to what's on -- they use mining at the surface.

Building materials, I think, are really relatively simple. We put the stuff in. We have a criteria of 1 percent, which was only adopted because most of the stuff is 10, 20, 30 percent asbestos. You can see it in the sample.

When I mentioned irrespirable, I thought of a funny sketch that I was doing in school where the student was sitting inside a pipe that had a magnesium block filler with cristobalite; and the student was spending the class time, not listening to the teacher, pulling out the blue fibers and going -- (blowing) -- in the air. (Blowing) I had closed the room. It was very inadept.

So building materials -- I would say that mineralogists, who's into asbestos, can identify a hand sample easily 80 to 90 percent of the asbestos that he sees just by a hand sample. Pharmaceuticals, much more complicated -- much more. If there's anything there, it wasn't put there deliberately or it was put there inadvertently, and it's much smaller, and you can't really see it most of the time in a hand sample.

So the definition of conundrums, as I characterize stana (ph), are mineralogical, industrial, regulatory, and legal. We have to agree upon some method that gives us an answer that discriminates asbestos from nonasbestos particles, and you heard Brad and Greg pretty much address this issue. We got these things. What are they as we start to look at them with finer and finer analytical techniques?

Take a look, if you haven't seen it already, the papers by Gordon et al. against versus R.J. Lee and Drew Van Orden. I slugged through these papers, and at first, this guy is right. This guy said, "No. He's wrong." And this guy seems right. This guy says, "No. You're lying. You're wrong," and it goes back and forth. Have a bottle of Advil right beside you as you go through it. (Audience laughs.) That illustrates to me some of the profound questions are trying to come up with the answer for the property owner, a building manager, a miner, and a government regulator.

So which method is best? Go to all types or tab asbestos four. The alphabet soup, for anyone who's into this -- and I'll explain one of them -- each has individual and corrective advantages. Each one is unique in its own way. Here's a -- fundamentally, in geology and mineralogy we teach students to identify hand samples. Mickey, in that chapter 19 introduction, says that's really -- if I understood it right, not completely adequate. You need more sophisticated data, chemistry, and structure. I think that a large part of traditional mineralogy and probably part of the core arm of this disagreement with some of the regulators and biologists has been that geologists will take something that they know is fibers -- you can see it. You can roll it between your fingers. You can take a torch or a barbecue lighter, try to burn it. A really convenient field method -- we do it all the time in the field -- is to take building material, hit it with a flame; and if there's something left over that we can rub and ball up, it's almost certainly going to be asbestos.

I'm looking over here at some fibrous talc. It's that picture that is -- whether it's anthophyllite, asbestiform going to talc, as some believe, or nonasbestiform anthophyllite going to asbestiform or fibrous talc, as others believe, is really the heart and soul in this. I look at this under the microscope. I look at the images that others have taken with TEM, and boy, some of them really walk and talk like anthophyllite being asbestiform.

Then there's this stereo zoom microscope. Remember in '79 arguing with the people who were writing the original RE's book on methods for hand sample analysis building materials. Saying, "Look at it with a stereo zoom scope. You can see so much. Even for some of the talc products you can see them prismatic. You can see light coming up at you from a prismatic fragment," and I am going to move more and more toward: If you have anything, you're probably going to have aggravation. So maybe that's the goal is to find products that don't have any amphiboles.

Optical microscopy. Two major methods: the PCM and the PLM. PCM industrial site. Their samples gave us lethargy and as Dan Prey (ph) always says to me and to colleagues when we're talking: This is what's regulated by Government -- the federal five, the 3 to 1. PLM, this is a really useful technique from building materials -- polarized light microscopy. This one you actually get some clue from structure decomposition. This one clearly is interference by defect -- right interference defect where you just see shapes. So the way I might go with this with you is that I'll march through the different methods -- PLM, polarized light microscopy -- and let's talk about advantages and then quote something more than disadvantage. The big thing about light microscopy, PLM, it's coded. We have rules, and it's wide spread. Any lab who's doing asbestos has the PLM, and sometimes they have people who have been trained with courses in polarized light microscopy. Other times we're taking a shake and bake. Unfortunately, in the geologist community more and more universities are getting rid of light microscopy as a course saying instead let's go to the TEM, the SEM. Let's go to more sophisticated techniques because this is an old fashioned technique, but boy, it really works. It's especially good for building materials. So I give it, on the scale, a really high grade. It's up in the green. It's a pretty good technique.

Then instead of just disadvantages or limitations, I describe it as issues along with disadvantages. One of the big criticisms on PLM has been its magnification limit -- 400. If the wind is blowing right, maybe you can get up to 450 and hope you see something; but there's really anything to me beyond 3'-350 you go easily in the wind. However, that quantification is improvable by techniques such as sieving quality nitration and you can probably -- as someone told me, they can get down to a detection with 100 parts per billion on polarized light microscopy which is really pretty good because 100 ppm or something probably doesn't have a whole big effect on human health. At least I would gladly be exposed to 100 ppm if I had to. It just doesn't concern me when I look at the regulatory limits of what we can have in an industrial workplace.

So I'm not going to talk about all these things. Look at them. I showed them to you. There on the notes that I posted, and if you're into PLM, we can talk about these at great length; but the big thing to me are the disadvantages -- its supposed limitation. So I give it not so good a score. This is Dancing with the Stars kind of thing. You moving over but you can correctly bring it back if you do this.

Then we get to high-tech instrumentation or the stuff that's out there now and clearly unamazing. We have x-ray diffraction from structural fingerprint, and we have electron microscopy that will give us structure and chemical analysis all of which has to be done right. The advantages are extra. It's fast. I'm getting -- I'm trying to convince Carlisa (ph). The minute you get a sample in, the first things you do is look at a PLM and while you're looking up there trying to make up your mind, do a scan, do an XRD scan of a certain portion of the spectrum -- of the angular region of interest and look at both of these states together.

So it's fast. It gives you gross ID. You get much of the minerals that are present, and you can improve it again by concentrating the sample and adjusting the scan speed. So we'll give it a good grade from XRD.

The disadvantages, there's a lot of aggravation if you have an X-ray machine: radiation protocols, you need to the calibrate the machine to the standards, etc., and it gives you very poor shape information. Back when the pre hero rules were being written, X-ray was really omitted. Why? Because it didn't tell you anything about shape, so people just pushed it aside, and it lost a lot of its relevance. I think it's coming back now because it gives you a quick answer in the case of talcs over whether there are other minerals concerning them.

The two issues that I'll talk about are overactive beats and detection levels, and they are really both the same which will allow us to raise the negative score to something that's better.

So here is a measuring fractured scale taken at (inaudible), and the critical point is right about here. There's an amphibole at 2 degrees -- two category, 2 degrees to fail, and it's very hard to see because the talc peak is masking it. So the way you can get around that is just to do a slow scan -- the talc peak stands out and the amphibole peak right here on the shoulder is identifiable at 10.2. So you can see if you've got amphibole in your system, but right away we've got two techniques that work very, very quickly and independently of one another: the PLM to see whether you have any fibers. You push it in and out when you measure and the inside (inaudible), and if you've got amphiboles, they know you have aggravations. Then you can immediately decide: How far do I push the envelope on this before rejecting the material as a product?

SEM. SEM is another one that is our very history. When we first started in the '70s looking at this, people loved SEM. It was a great machine. You could see the shape beautifully. You could get analytical information, and I gave it a high score. However, SEM, because it had no structural capability, when AHERA came out, it was pushed to the side because AHERA and TEM. TEM was perceived gold standard. That's the one we should use. So I don't argue that SEM has a very important place just seeing what's actually in there. It's just increasing the magnification from PLM, and you get a quick answer if you have any fibers or elongate mineral particles. So the negative score is because the perceived conflict with TEM under a hill.

TEM. We can get great prevention from morphology, chemistry, and structure. We distinguish the amphiboles species if done right, and it's perceived as the AHERA gold standard. Remember that TEM, under a hill, was designed for asbestos abatement or remediation projects. It was designed to look at the particles that would be left over, if at all, in the air from the removal of asbestos. It didn't open up the water to look at any EMP. The rules were codified to look for residual asbestos to signify that the cleanup was not going accurately. So it has a really good story. However, there were disadvantages too. And the disadvantages are endurance of the interpretation of the shapes. You saw that a few moments ago with the tossup thing. What is this elongate thing? The population, is it detected? Is it confirmed? What does milling do to it? How do you change it from the product as it was put out for sale versus what we do in the laboratory? And very importantly, this talc versus anthophyllite -- that kinky talc. I wanted to get up here with red kinky boots to put up there, but I thought that would be pushing the issue too much.

Kinky talc is twisted talc. And there's a reference that I will call to your attention. I don't have it here. There's a reference that I will call to your attention in a few moments by Jim Millette where in his last -- the last page of it, he defaults on twisted talc 25. I think this is a real concern, and it's generated a lot of controversy between people who agree with him, people who don't agree with him. So let's look at that one.

If you have a single fiber or just two fibers, how many fibers are too many? How many fibers are acceptable? How do we deal with just a few fibers compared to looking at something you can hold in your hand and you know it is definitely asbestos because you can look at all the classical products. It's likely to be asbestos on the basis of these factors. The aspect ratio, whether it's 3 to 1 -- which I don't like, but I understand it. Going out as the others shown, you really need 20 to 1 or greater. You need a large population. You can't just look at one.

Now, in a PLM, you've got a whole bunch of fibers, a whole field of viewers. We're on step. It's just not a problem. If you're looking at otomicroscopy then we have a few fibers down here, then it becomes an issue. The geometry, the power of size, determination, the end; and some of these come down to just judgment, as you saw -- as I mentioned a few moments ago. Truly a judgment on whether it's a cleavage fragment, whether it's asbestiform.

And then there's nomenclature. Nobody saw leaky at all with the multiple divisions are amphibole nomenclature. We have so many things out there in nature and rocks that would fit as being cousins to tremolite or even some of the amosite minerals, but I'll stay with tremolite because -- and anthophyllite because we're into calcium-rich systems.

Litigation is driving a large part of this. The realities to me seems to be that if you got law cases being won with huge sums of money being awarded, people will start to say, you know, I'm gonna get in on the business -- like bad people. John? (Audience laughs.) But you know, they're going down the road saying, "This is what I asked to show," and sometimes the evidence gets interpreted based upon pride and reception. We scientists like to think we're pure and good, but sometimes bias does creep into it.

The chemistry issues and -- the reason for the crazy fuzziness there is that they switched them back from PC. If you look at anthophyllite talc and tremolite, tremolite is really easily distinguishable because it has calcium. Calcium is a talc and anthophyllite is infinitive. You've got all this calcium. So if you're seeing calcium on the spectrum, you can be pretty sure that it's going to be tremolite if it fits the other criteria. Anthophyllite and talc, however, are a little bit of a problem. The ratio between calcium and magnesium for both of these is very, very similar. So there are some talcs which could appear both logically like anthophyllite and the chemistry seems to be the same, and this was the problem that I saw with Merlet. So it takes real work to distinguish anthophyllite from talc.

Take a look, if you're at all plugged into this. It's only to read a paragraph on -- let's -- page 17, fibers with kinks. That if it has this twisted characteristic -- and Garret's arm is showing you a lot of pictures of twisted fiber. We're calling it -- he's calling them "rivets," and they twist; and if you look at them, they can turn out to have a different interpretation unless you connect the dots right. So the issue is this 5.27, 5.27, 5.28 dimension.

In a deposition once I got hammered by a lawyer saying, "What about the 5.28?" 5.3 I think is what he was saying. It's required to be able to identify the asbestos, and that's down 5.3. I know. I said so. "I really don't know what you're talking about." (Audience laughs.) And he went back and looked it up and scope with a gun to about this long in back. "What type of now?" It was like a golden eagle on this --

AUDIENCE MEMBER 7: It's as easy as ABC, right? (Audience laughs.)

MARTIN RUTSTEIN: Yeah, ABC. Easiest -- and the ABC, by the way, of the dimensions. We don't talk about knock down sideways. We talk about ABC unless we go into reciprocal space, and then it's XYZ, but you guys -- you don't have no problem here.

So it's how you connect the dots in this twists talc, and it's not always correct to use just the 5.27. On this part too, here's a crystal structure. You'll get a tab, and here's one of anthophyllite and tremolite.

(Phone ringing.)

MAN: You’re 30 minutes.

MARTIN RUSTEIN: Shut up. Go away. Stop.

On talc, same dimension. Same dimension. So you need two dimensions and one angle for the correct identification. And Matt and RJ Lee have published on this one, and this will clarify if done right on largely ambiguity.

So summary. There are limitations and advantages of a single map. There's no one size-fits-all. What we're trying to do is prove the absence of relevant amphiboles and chrysotile. That should be the overarching goal for us. We need a full spectrum of analytical tools to put together in this crossword puzzle. We need to be able to look at them with a common analyte definition. If we don't agree, on what we're looking for, then the measurements become highly mental. One side is saying, "You're doing the wrong thing. Blah, blah, blah."

PLM will remain the primary technique, given its simplicity, and part of what we're doing is to find something for industry that they can really go with instead of having a whole separate analytical vat.

I think SEM will start to come back. SIB, especially useful. It's fast, down and dirty. You go through there with only about 5 degrees of stamp, and you're getting answer about amphiboles. TEM, likely to be the ultimate tool, but only, only if we can agree on the definition of making irrelevant shapes.

Prior to the meeting, the speaker sent in questions. I asked one question. Can we agree on some kind of definition? And the sponsors, the conveners of this, their answer was pretty much, "We don't think so, not in this short time." And if we want out of here and we don't agree, then we're going to continue the debate. Remember that under TEM (inaudible), you can use ambiguous in a determinant. This cartoon, three nights worth, I don't know. Throw the problem up to management. Throw the problem to those who are deciding whether to use the product or not. It may be that our analytical techniques aren't good enough yet to decide what these things are. It takes it out of a whole realm of aggravation.

So going down with guard free and our patriots to the Wizard of Oz, the Emerald City as we seek the perfect method and we chase after analytical zeros because I can always measure it better. I can look at it smaller. I can do better, da-da, da-da. Make sure you remember as we go to utopia, we're looking at commercial progress. We're looking at minerals and they both vary in physical and chemical properties, what we're trying to measure. Watching what we did and watching what we're going. We're inheriting the wind, so to speak, because I'll get you because you didn't define asbestos clearly enough. This is a joke. (Audience laughs.) We all remember the wicked witch and she's out to get us, and we didn't define it right because we were looking at stuff. We were looking at schools where stuff was falling down from the ceiling. We were looking at building environments where workers were exposed. You can see the clouds of asbestos in a workplace, and I've been there and done that. I understand that, but I'm not so sure about these trace amounts, whether they really held any flag in trying to protect human health.

So looking back, which you get to do after you get older and you go an Social Security, you get to think a little bit about this life. You can't tell how deep a puddle is until you step into it. If asbestos is really as dangerous as many perceive, if it's ultimately the killer rock that they are asbestos, is it logical or bias that leads us to be concerned about EMPs? This is philosophical, but it's profound. Why are we looking at EMPs? Do we have the health data? Do we have evidence that this is something that should be of concern?

When I started with this decades ago, I should have paid attention to this part. I didn't, and I got trapped in asbestos muck in a mine, and I had to beg for people to pull me out. Now I look at the younger people now and I say, "You got to solve this problem because you've been handed really not a good plate of material." And somebody somewhere has to be able to say, "Let's back up. Let's define what it is we're looking at and what we're measuring."

I'm urging some colleagues I'm working with now to say, "This is what we're going to take, yeah." Other people may disagree with that, but this is the rule. This is the regulation that we're looking at.

So any questions? (Applause) Thank you.

AUDIENCE MEMBER 8: I'm new to this and learned a lot. The question I have is which of these methods is quantitative?

MARTIN RUTSTEIN: Quantitative?

AUDIENCE MEMBER 8: Yeah, because that's -- you know, TMS, CM --

MARTIN RUTSTEIN: They're all quantitative. You can make them all quantitative. You can make PLM easily quantitative by doing point counting, looking at the number particles in the field of view, whether you were looking at four slides or two 400 points or 200 points or 100 points. You can quantitate very easily with optical microscopy.

SEM, I don't think so. TEM, it depends on the number of points you count. Do you count or do you see something? The XRD is easily quantified. You can set up standards and go with that and Gary may want to talk with you. He might be out. Gary? Gary has done some really fine work on quantitation with metrics.

Anything else? Yes, sir.

AUDIENCE MEMBER 9: When you say that that's -- I'm sorry. Thank you very much for the talk and the document about Canada.

MARTIN RUTSTEIN: Thank you. Hey.

AUDIENCE MEMBER 9: I'm sorry?

MARTIN RUTSTEIN: I was talking to me.

(Audience laughs.)

AUDIENCE MEMBER 9: Oh, okay. When you say that TEM is essentially the world standard, PLM it will probably be the primary technique, I guess the part that we struggle with is that the two are not necessarily looking at the same thing with both, so --

MARTIN RUTSTEIN: It was PLM and what?

AUDIENCE MEMBER 9: Well, using PLM while I was sad for TEM. You're not necessarily getting the same results with both, so --

MARTIN RUTSTEIN: Right. Because you can't -- it's environmental alchemy. It's when you change the magnification, you're seeing something that it wasn't before. When you look at a hand sample, when you look at the chrysotile under a back light on fedra (ph), you don't see fibers. It can be 7-meters long and you can just ball it up. If you get out of your car, you can make a snow ball out of it and throw it, but when you look at electron microscopy, you're only seeing individual fragments, small; and I think we fail to see the disconnect between the two, so we have to be very careful, in my view, of how we interpret the TEM. The PLM is relatively easy.

AUDIENCE MEMBER 9: Well, because what we found is -- one of the huge challenges that we've found is something -- a sample that looks like it's really out, there's no asbestos whatsoever. You use PLM, all of a sudden you see and now there's lots of it.

MARTIN RUTSTEIN: And the crazy days around I hear are starting. The city of my kids, I walked in New York City. Shut down their water supply. They were taking it from the Hudson River and they said, "There's asbestos in the intake in the water." And it turned out that what they were calling asbestos in the water was actually pond mar, which is no longer a mineral, but it's a common tern. It's the black amphibole; and it was coming out of the iron ducts and it wasn't a health hazard but they were measuring it with TEM, and that's just part of the issue. What are we looking at, and is it something that we have to be here starting with exposure to human health? I think that's the bottom line. That's where I'm coming around, personally, on these EMPs in terms of -- where's Ray? No, I was -- when he said, "What does the lung see?" I thought that was very profound. What is the body seeing on this one that makes it a problem?

So I -- just let me -- just get out there. Mark? Is this Mark? Hi, Mark. Okay. Thank you. (Applause)

CATHERINE SHEEHAN: Okay, Markey. We're doing pretty good on time, so --

So next up is Dr. Martin Harper, and he has a BS and MS in geological sciences and a PhD in occupational health in the London School of Hygiene &

Topical Medicine. He's a fellow of the Royal Society of Chemistry and the American Industrial Hygiene Association. He recently retired from the NIOSH after completing many projects and publications related to asbestos and other mineral particles, including being a co-author of the NIOSH roadmap.

So let's get you started here.

MARTIN HARPER: You know, I'm following on from I would estimate to be about 100 years of accumulated wisdom in the first three speakers. So if I sort of stall or stutter a little bit, it's because I'm already getting the I'm-not-worthy feeling. But, yeah, again, I'd like to thank, particularly, Nora for all her hard work; the JIFSAN organization for inviting me; and I hope I have something worthwhile to contribute.

As I said, most -- as I was introduced, most of the work that I've done regarding asbestos -- practically all of it was done while I was at NIOSH, but I have now retired from NIOSH, and so -- why isn't this working? All right. So I got to put up this disclaimer. It says I am no longer speaking on behalf of NIOSH or any other part of the Federal Government; and also, in full disclosure, I have never participated in any legal action with respect to asbestos or mineral products.

Now, the general characterization issues, as we've already heard, are the nature of some. I mean, we have so many different samples that we have to analyze for asbestos or other elongate mineral particles; and we're looking at those media with different purposes and different requirements, and so we often have to use different techniques that are appropriate to coming up with the answer that they're looking for; and so we need to ask questions like: How much of the sample is representative of the whole sample? So, for example, how many samples do you need to take in a talc mine to establish the absence of asbestos throughout the mine? You have, you know, veins of minerals that go through different properties.

I remember at one point I was going to look at a taconite mine, and I was told, "Oh, there's a vein of amosite going right through it." "Oh, yeah, but we avoid that." Really? Wow. Okay.

And there's a lot of different laboratories out there, and they don't all come up with the same answer all the time. How can we resolve that variation? When we're looking at particles, what's the minimum number we need for accurate characterization? And there are all kinds of issues of analytical calibration, proficiency testing, and reference materials; and this is all a bit of interest to me out of my analytical chemistry background. We can, again, as been noted, examine materials of different levels of magnification; and all of these have their own issues, different purposes and, therefore, also different kinds of quality assurance.

Looking at I4 and handlets, it's difficult sometimes to characterize things in the field. This is a serpentine outcrop in California, and as you start to look at it in a little more detail, you start to see things that are prismatic and even fibrous up here; and it's pretty clear that there's a range of morphologies spanning different fibrosities.

So what is the appropriate sample to determine asbestos component? Because even commercially exploited asbestos partially include some material that might not be considered asbestiform. So we need to come up with some kind of sampling protocol. At least in the prior example you can see that some of the material is composed of elongate mineral particles and some receive an asbestiform, but as we've -- it's shown there are rock types that you can hit with a hammer and you don't necessarily know that they're composed of fibers.

How many particles do we need to examine? Well, it was reported at a Johnson conference a few years ago that even though UICCB, Chrysler power reference material was examined to the extent of 20,000 fibers, that trace tremolite and amosite could be found -- tremolite at .045 percent and amosite at .003 percent. Because it's a Johnson conference, I can't give you a reference. I can't tell you who said it, but it was there.

And how many particles do we need to measure a reproducible distribution? Well, I would say the bare minimum is 300, but really you need to measure about a thousand particles. It's kind of tough to do that on

TEM, especially when a lot of particles actually are longer than the field of view and they get outside the field of view. And for accurate chemistry? You know, I see people reporting at formulae two-three significant figures based on one EDS analysis. Are you kidding me? And with no attribute of uncertainty to that formula. Wow. You'd be dropped out of the analytical chemistry class for this, but I see it all the time.

So we also have this notion of fibrosity, and this has been popularized by Eric Chatfield (ph) and others to compare fiber dimensions of materials; but the -- you know, the preparation procedure is absolutely critical to the result that you get. What did you do to it? Jaw crush it? Did you grind it in a mortar and pestle? Did you put it in a jet mill? Did you sonicate it? All of these things will end up giving you a different distribution from the same starting material, and none of us really studied this to any great extent. But we have this comment, which I think was very appropriate, from -- from Sterling (ph) in 2010.

So if we're going to report fibrosity measurements, we really need to have a standard procedure to prepare the material prior to making those measurements. So this absolutely calls out for an ASTM Standard. Please, Frank, put it on the agenda. We've got to have this.

Now, there are existing reference materials; and this is the bulk of my talk now is the talk about reference materials and quality assurance, and there are some problems even with the existing materials. Take a careful look at the Wittenoom actinolite here, which is very nice and clean, and this UICC chrysolite here, which I refer to as a lollipop stick of gems. Little particles stuck to it, and all of this material that I've looked at from the UICC -- the amosite, the crocidolite, the anthophyllite -- kind of looks like this; and I thought, well, how come no one's noticed this before? So I went back to the original papers describing UICC material, and it dawned on me, they didn't have SEM. All those pictures are just under optical microscopy. You can't see this effect, but what's happened is because they jet milled it, some of these longer fibers fragmented into tiny little pieces that then adhered, probably by electrostatic attraction, to longer fibers.

And you know, when you look at the Addison-Davis tremolite that was used in those experiments, they're all clean, just like this Wittenoom fiber here, because they didn't jet mill; and we know this because we also had a tremolite reference material, and we tried jet milling it, and guess what? It ended up looking just like this.

So NIOSH has a roadmap goal, a reference material repository for minerals; and I was working on that for a while, and ISO defines a reference material as "a material sufficiently homogeneous and stable with respect to one or more specified properties which has been established to be fit for its intended use in a measurment process." That's not -- sounds like gibberish.

And NIOSH has some reference materials of its own that were prepared many years ago by Fitree (ph). Not very many -- not very much of it left, and it's over in the Minerals and Materials Branch at the

Pittsburgh Mining Research Division now. And then there are some UICC reference materials still out there, but most of the remaining material got landfilled a few years ago. It all got transferred to the South Africa NIOH, and when they stopped receiving requests for it, they didn't want to keep it anymore, and so it's now down at the bottom of the landfill. They have a little bit left; however, you're the ones that are gonna have to figure out how to get it out of South Africa. They're still willing to give it away.

And then, of course, you know, there's been a lot of complaints that nice, common and uncommon materials, are no longer available; and indeed they weren't all -- all of them weren't all that good either. I mean, this is a photomicrograph of the nice tremolite asbestos, which has been criticized heavily for not being very asbestiform; and I'm comparing this with the tremolite asbestos that is the reference material of the Health and Safety Laboratory in the UK, and this is about the same magnification. So you can see there is a tremendous difference here.

The UK reference materials -- the Health and

Safety Executive, HSE, is the parent body of the HSA -- of the Power for Safety Laboratory -- are described in a publication, and we wanted to see if we could get a hold of some of that. So we wanted to know where the tremolite asbestos came from, but the company person who donated the material to the HSE died, and the company had changed hands, and they had no record of it as well. All we knew was from this description that it came from the Salt Woods mine in southern California, and we couldn't find that in the gazetteer. We eventually found it. Brad Van Gosen was a great help in this because we identified it as coming from this Macaroy (ph) property, and here's the mine. I know several of you have visited it. I don't think there's very much left of this thing. Most of it's been taken out, and it was in the past sold to the Powhatton (ph) Company in Maryland for lab-grade asbestos, all of that stuff that you used to buy in the big jars from Baker and Mallinckrodt and so forth. And it's a very nice tremolite asbestos, and it's available from NIOSH. If you ask them nicely, they'll direct you to RTI who holds it, and RTI will give it to you. You have to pay shipping I think, and that's a lot, like 50 grams. If I had known that somebody was selling the UICC stuff for $1,000 a gram, I would have kept hold of it. It could have been my retirement. (Audience laughs.)

And like I said, this is what it looks like; but if you're jetting it, this is what it looks like. So be careful what you do with this stuff.

Another material that's going to come out of NIOSH shortly, I hope, is this one, an anthophyllite from the Percival Dunn mines in California that I collected, again, with Brad; and it's also a rather nice anthophyllite; but frankly, I'd rather get after this one, which is my favorite. This is the beekeepers anthophyllite fragments is what I'm talking about. One there. One there.

So then the other issue that we have to deal with is cleavage fragments and fine prismatic crystals, and the work that I've done on this has actually been through PCM of hair samples. And I know that's not of great concern to the audience here except that I think what -- my findings are relatable to PLM analysis, definitely; and the cautionary tale that I'm going to give you is also relevant, I think, to SEM analysis.

And the reason that we were interested in cleavage fragments is because OSHA practices discriminatory counting, even though NIOSH and EPA do not, and there was an ASTM Standard under development D7200 with an attempt to codify discrimination; but the fact is, the procedure for discrimination really needed to be confirmed by an internal laboratory study, so I decided to do an internal laboratory studies. So for that I needed nonasbestiform amphiboles, and that wasn't actually as simple as it sounded. You got onto the mineral dealers, and you say, "Oh, give me, you know, a ton of riebeckite." They say, "What do you want that for? Nobody buys that." And I said, "Yeah." And then we found that things were not always what they claimed to be. So you know, we bought anthophyllite that turned out to be enstatite. We got tremolite that turned out to be inesite. And we ended up with five good minerals: Actinolite, tremolite, grunerite, brookite, and anthophyllite; but all the samples of anthophyllite that we examined contained that fibrous talc, and that's just in the nonasbestiform in Buffalo.

So in the work that we did, we used actinolite from Rockwood, California; NIEHS tremolite, which I believe came from New York; grunerite from Portugal; and riebeckite from Colorado. And these are pictures of them, and while some of them do appear fibrous, the fibers are really nonasbestiform.

And then we have to make cleavage fragments of a respirable size -- a respirable particle size. Well, that's not easy, actually. There's a sense that I get from people that as soon as you hit a massive amphibole with a hammer, you're gonna generate tons and tons of respirable sized cleavage fragments, and that's not actually the case. Most of the particles that are produced by Krishi, Megapee -- actually, eCORP -- and the fiber-like ones are pretty rare, I mean, about 1 percent or so. And if I grind up the material where only 1 percent is my material of interest, I can't use that for tests. It's ridiculous.

So with RTI, we worked out a procedure to concentrate the fiber-like fracture; and RTI was able to make the 100- to 150-milligram qualities of these materials containing about 50 percent federal fibers. I hate that word, that expression, but it saves me having to describe it further.

And so we used the tremolite, actinolite, grunerite, and riebeckite for the PCM round robin that we did; but tremolite and riebeckite cleavage fragments are also being used in toxicity tests at NIOSH right now; and I really hope that the results from those tests will settle some of the discussions that we've been having.

So this is an artificial creation of mind. The slides that we sent around to the different labs were dosed with different levels of asbestos fibers and the equivalent of cleavage fragments. So this is a photograph of the crocidolite and the riebeckite, and you can see sometimes it's pretty clear that that's an asbestos fiber. It's pretty clear that that's a cleavage fragment, but you know, what's this? I don't know. Is it a cleavage fragment or is it a show of part of them? No idea. Can't tell through PCM.

Now, the procedure for discrimination involved a subjective evaluation of morphology, and that was one of the things that we wanted to test. So we sent these examples out to 11 laboratories, all of which, except mine, were accredited by the American Industrial Hygiene Association for asbestos analysis; and we asked them -- gave the set of slides to indicate all those particles which they thought met the morphological criteria for asbestos and which not. And this is the 100 percent asbestos fiber slide, and this is the zero percent asbestos slide. These were all cleavage fragments, and you can see that the -- yeah, the results are all over the place. Here, we've got one lab that correctly identified 96 percent of the asbestos fibers as asbestos but; look here, two percent; and same with cleavage fragments. You know, we have labs that correctly identified, you know, zero or near zero asbestos particles in the cleavage fragments; but here, look at this level. So you know, it was very subjective. It could not be done, in my opinion.

What we did find is if we looked at width distributions, a rather good discrimination, at around about 1 micron -- it was actually about .85 micron -- gave us the best discrimination between our fragments and our fibers. Now, you know, these were artificial creations, okay? So I don't know how this reflects the real world except that I believe Ann's gonna show similar data later on, and so I don't think it's far off.

And we found the labs could actually do a very good separation by width. In fact, it was about as good at 1 micron as it was at .85 micron. You know, I just like round numbers. And so this standard, which, by the way, is applicable to my two quarries only, it does currently include this width criteria of 1 micron, which does a pretty reasonable job of ensuring that we count asbestos. We can't completely clear the cleavage fragments of -- you know, out of this; but you know, we can err on the side of caution, which is always, you know, good public health practice.

Okay. There's some other proficiency tests out there. There's the NVLAP, the AIHA's bulk asbestos testing, and there's also the Health and Safety Laboratory Asbestos in Material Scheme, or AIMS, which I'd like to bring to your attention. It's asbestos in building materials, generally targeted to identification and qualification greater than 1 percent; but occasionally you get samples of interest to the folks here, I believe, such as round 62, which included a sample with .1 percent chrysotile and .1 percent amosite; and these were not detected by several laboratories in the scheme. And that round also had a crushed marble containing wollastonite when many saw asbestos. Twenty-three of the labs, by PLM only, identified the wollastonite as asbestos, and even six with electron microscopy identified the wollastonite as asbestos.

There's another scheme that comes out of the Health and Safety Laboratory called the Low Asbestos Content Scheme, which I think would also be of interest to people here. And round two was a sample of talc containing wollastonite with no asbestos, and 18 percent of the labs incorrectly reported the presence of asbestos.

Now, if you're a lab and you want to join these schemes, there's a little benefit to that. You can purchase the HSL reference asbestos samples, otherwise, you can't. They don't have very much of it left, and so they're reserving it only for people that are in their schemes.

So there's some new asbestos standards that are being worked on. I call them "new" because, for example, this one was first initiated in 2010, which is not that new anymore. And this is my understanding of how these methods are, based on the minutes of the last two ASTM Committee meetings. I'm gonna be pretty interested in gathering a round robin here, and also, I'm going to be pretty interested in insurance round robin, which I understand he's going to be presenting it today at conference; is that correct?

AUDIENCE MEMBER 9: I am not certain if I will be or not.

MARTIN HARPER: Okay. These are quotes, by the way, out of the committee minutes of the April committee meeting.

AUDIENCE MEMBER 9: All right. This is ours.

MARTIN HARPER: Okay. So the future work, obviously, is to extend the number of materials available to include other minerals of interest, such as zeolites and clay minerals, and to characterize those that we already have, particularly in NIOSH; make them available as analytical standards; use them in identification round robins. But I want to see them being used for hypothesis-driven toxicological studies to determine if our theories of disease induction and progression are correct, and then we can use the results to derive mineral-specific risk assessments. And as part of that initiative, I've been working, most recently, on fibrous glaucophane from California. This is the Calaveras stand, which some of you know and several of you have visited; and this is the rock at the Calaveras stand, but this rock is not pure glaucophane. It's only about -- I think about 60 percent -- 70 percent glaucophane. There's other minerals, like lawsonite; and it's not that fibrous compared to this material, which I collected with Mark Bailey (ph) from Marin County, California; and it's really nicely fibrous, and it's about 85 percent glaucophane, and it's really interesting to use as a reference material and also to test our ability to -- toxicity of elongate mineral particles. And you know -- oh, by the way, this is an undatee (ph); and this --

I think, clearly, some of it is definitely asbestiform.

And so this is what we've done to it -- a full mineral characterization. We've hit it with just about everything that we can think of, and I think this is what we need to do. If we really want to know a material well, then one technique; one single SEM analysis; one single EDS result; one single, you know, X-ray is not enough. And so we've done all this to it, and we actually had several disagreements. And I could discuss all this, but the paper has been submitted for publication, including calculating the potential toxicity based on a model from my colleague Alexandre Walteare (ph). And what I need now is for some toxicologists to step up to the plate and come and get some of this stuff to confirm whether the model is accurate or not. Please, please pick up stuff. Come and get it.

And then, you know, just to, you know, clarify that we can't use a single technique, this is a PCM photograph of an air sample from a talc mill; and I don't know what that is or that or that or that. You know, but these were some samples that we were taking while the talc mill was open; and I bought the first set of samples back to the lab, and I prepped them, and I looked at them myself, and I immediately got on the phone to my guys working in the field, and I said, "Don't take off your powered-air purifying respirators. I don't care what they call these things. I just don't want you guys breathing them, please."

And then because it takes a village, I have to acknowledge -- and I -- even after I've written this, I realized I left at least three other people off, you know? And this list is -- and most of these people have worked with me at no cost to me; you know, it just blows my mind that so many people are so interested in this field that they're willing to give up their time and resources to help me in what I've done, so thanks very much.

(Applause)

And I still remember one said, "This is proof that asbestos is still used in construction."

(Audience laughs.)

CATHERINE SHEEHAN: We have plenty of time for questions. So do we have any questions at this point, Greg?

GREGORY MEEKER: Yeah. I'd just like to say the process of making a standard, and you said it either way, is -- it's so difficult. USGS did it, and I never want to do that again. It was a terrible job, and using every technique you can bring to the table to understand what you have is so important. Thank you for setting them.

AUDIENCE MEMBER 10: I really liked the pictures of the fibers that have been jet milled that had on it what you called "Jimmies."

How much of an effect do you think this has on the results we're seeing from toxicology using milled fibers versus --

MARTIN HARPER: Beats me. I'm not a toxicologist. I wouldn't even begin to speculate.

AUDIENCE MEMBER 10: It just struck me though. If we're looking at something that's not necessarily a singular shape, we're making pronouncements about the shape relative to that, we should consider --

MARTIN HARPER: Well, the fact is, we did, you know, 30 years' worth of work on that stuff without really understanding what it was; and that, you know, goes back to exactly Rick's (ph) point, that, you know, we got to know this stuff inside-out, backwards.

AUDIENCE MEMBER 11: Have you used any of the data from the tissue burden studies to evaluate these dariets (ph) you're looking at in terms of toxicity and biological potential?

MARTIN HARPER: I'm not a toxicologist. It's not my field. Other people can do that too. I don't.

AUDIENCE MEMBER 11: Did you know Molly Newhouse (ph)?

MARTIN HARPER: Oh, yeah. She was in the department while I was there.

AUDIENCE MEMBER 11: The golden age.

MARTIN HARPER: Yeah. Oh, it was great. It was amazing. Charles Rossiter (ph) and Cole Coldest (ph). It was great.

AUDIENCE MEMBER 11: You mentioned the UICC samples. UICCs were blends. They were blends from different mines, for example, Chrysler (ph) Town UICC beats Canada.

MARTIN HARPER: Right. Right.

AUDIENCE MEMBER 11: And it's a blend from nine different mines based on the production figures the year that this formulation was --

MARTIN HARPER: Yeah. But I'm not so sure about the others. You know, UICC a Chrysler Power came from --

AUDIENCE MEMBER 11: Rhodesia.

MARTIN HARPER: Rhodesia.

AUDIENCE MEMBER 11: Michelle D. Anderson (ph), yes.

MARTIN HARPER: And I don't know if that came from multiple mines or not. So I -- yeah, definitely B was a blend, but I don't know what the other two is.

AUDIENCE MEMBER 11: Yeah. Chris Bodanic (ph) experimented with the nine separate blends, and he got nine separate biological assets.

MARTIN HARPER: Right. But that -- like I say, they were all jet milled to produce respirable fracture.

AUDIENCE MEMBER 11: Yes. Yes. Jet milling in the introduction of metal particles was also an interesting hypothesis --

GREGORY MEEKER: Excellent.

AUDIENCE MEMBER 11: -- that was raised.

MARTIN HARPER: And also the amosite contamination is in all of them, which means it's probably a carryover from, you know, one batch to the next, I'm sure. But then the Addison-Davis materials, the tremolites, were not jet milled. Those pictures all look nice and clean.

AUDIENCE MEMBER 11: Yes.

MARTIN HARPER: And so, you know, you've got to understand the materials and how they got to be what they are. It's how you use them.

AUDIENCE MEMBER 11: Is the NIOSH study an inhalation study?

MARTIN HARPER: No. You know, 100-150 milligrams, it's not enough for a inhalation study. It's a study of variscite, and there may be a road terminal study. I can't remember now. The NIOSH guys might be able to tell you.

AUDIENCE NUMBER 12: There's nothing specific about jet milling, right? Like probably any milling is coding the fibers with those --

MARTIN HARPER: Well, the way it was done by Addison-Davis was to use a copy trail, you know, the --

AUDIENCE NUMBER 12: Yeah.

MARTIN HARPER: -- the rotary chocolate. Okay.

AUDIENCE NUMBER 12: And any milling. The pictures have me thinking, you know, the effect it's probably having on --

MARTIN HARPER: Well --

AUDIENCE NUMBER 12: -- the energy dispersive spectroscopy too, you know, so --

(Crosstalk)

MARTIN HARPER: The problem with the jet mill is that the fibers end up hitting the walls and breaking up. When we decided to try to reproduce the UICC for the tremolite, we bought a jet mill; and we started off with just glass fiber because we didn't want to contaminate the whole lab, and we wore away the jet mill just with glass fiber. We had to get a specially made silica carbide insert in order to be able to do any jet milling. And then this is what we got out, you know, those lollipops and cheerleaders is what we got out of this.

CATHERINE SHEEHAN: Brad?

BRADLEY VAN GOSEN: I may be getting ahead of the schedule a little bit, but in the talc cosmetic issue right now there's a lot of analysis being done of the product, but how much of the raw ore is being redone?

MARTIN HARPER: I don't --

GREGORY MEEKER: Can you repeat the question?

MARTIN HARPER: Yeah. The question was: How much of the raw ore is being examined in the talc industry? And I would suspect that, you know, people associated with the talc industry would be way better able to answer that than me. So is there anyone that wants to -- I know you --

AUDIENCE MEMBER 13: No. But I'd like to introduce a complicating fact. Most of the pharmaceutical-grade materials are actually blends from different mines, from both foreign and domestic.

MARTIN HARPER: Yeah, I'm not surprised.

AUDIENCE MEMBER 13: So the properties of color, lift, or fragrance, other properties -- skin modification and chemical -- they all play some interest role.

MARTIN HARPER: And I mean, it's one thing if you're in charge of your own mine in the USA, and it's another thing when you're dependent on analyzing some bulk carbo product from some other country and how that varies from day to day, batch to batch, and then so on. I think Matt was going to say something though.

MATT SANCHEZ: Yeah. I can't be too specific. I guess it would depend on the talc mine company, what their internal procedures are; however, it's open to some companies. I know they're not even mining companies. Those that would use talc, get their plastics, ceramics, or cosmetics, it's not unroutine to actually go to the mines independently and do full assessments of the mining properties as well as ongoing quality control of talcs before they're shipped, before they're accepted by companies. But again, it's going to be company-specific how detailed they are. Some are probably not doing anything; others are doing a whole lot. It would really just depend on who the actors are.

BRADLEY VAN GOSEN: Yeah. That was probably where I was going with this important talc. Just curious how much quality control is on every talc.

MARTIN HARPER: Well, you know, the other issue is that you can't prove an absence.

BRADLEY VAN GOSEN: Right.

MARTIN HARPER: Yeah. How many particles do you want to look at? Like I said, with the UICCB, they looked at 20,000 particles and found no amphiboles. By virtue of a pre-concentration technique, this other research finally found .045 percent tremolite. Well, is that acceptable, you know?

If I was a talc producer and somebody came to me and said, "Well, have you got any asbestos in your talc?" and I said, "Well, I've got .045 percent," you know, are they gonna buy it? I mean, what's --

AUDIENCE NUMBER 14: How can you have something that you analyze 20,000 particles and find zero and yet a half of percent of it is another phase?

MARTIN HARPER: Point .045.

AUDIENCE NUMBER 14: Let's say a half a percent for analytics, .45 percent.

MARTIN HARPER: Point zero.
AUDIENCE NUMBER 14: Oh, you're say 0.45?
MARTIN HARPER: Yeah. Yeah.
AUDIENCE NUMBER 14: So they should have found some of it in 20,000.
MARTIN HARPER: Maybe. Maybe --
AUDIENCE NUMBER 14: I mean, if they would have sensed it in the system.
MARTIN HARPER: Maybe. Well, you know -- I don't know because, you know, that study has not been published. So --
CATHERINE SHEEHAN: Hey, Martin, it's yours.
MARTIN RUTSTEIN: When the public pressed on the Johnson & Johnson business, I concluded that one of the reasons the jury has ruled against Johnson & Johnson was because they tried the strategy of diluted the ore. They apparently saw that they had elongate stuff in it, at whatever percent, so they mixed it with a lower concentration, thinking dilution would be the solution to pollution, but it came back to bite them.
I also suggested that maybe the way to look at what's in the ore would be to look at the sediment --

at the runoff from the ore piles from rain and snow melt because the smallest particles would be carried away from the pile, and it would be like sluicing for gold. You would be looking at those, and it would be a down-and-dirty way to see whether it was any percent. I think the answer is, if there's anything in there, nobody wants to buy it.

MARTIN HARPER: What I didn't -- in my original version of my presentation, I had slides, but I took them out, that described the fluidized -- they had a fluidized --

MARTIN RUTSTEIN: (Inaudible).

MARTIN HARPER: -- that's been segregated, which maybe we'll talk about too; and that is a way of releasing respirable fibers from a sample and concentrating them in a way that way you can seriously get down to .000 -- you know, four zero, 1 percent (inaudible). And you know, it's a process that I use to look at soils or ZMI periodine, and it was amazing how low you can go in that world.

MARTIN HARPER: That was published. In fact, there's -- what? -- three publications on the FDAS now.

Anybody that wants one of these, let you know or talk to Ed (ph).

AUDIENCE MEMBER 15: Yeah. You talk to Ed a little about the percent of asbestos or fiber or whatever. Could you describe if that is either -- is it a weight percent are you talking about or a particle count percent or a projected area percent?

MARTIN HARPER: It's basically a particle count that's been converted into a weight percent, and that conversion factor itself is full with uncertainty because you're making certain assumptions about the materials. Yeah. I mean, it's a -- and of course, when people report, you know, material as having, say, 2.4. percent asbestos -- say it's a building material, okay? Did they ever report uncertainty with that value? Any of the labs here report an uncertainty on a weight percentage? Did anybody even try to calculate an uncertainty?

MATT SANCHEZ: Well, I think from accreditations, that they would -- you're supposed to report out a coefficient of variation for ranges, but that's it. It doesn't -- you don't apply those to actually give an uncertainty of the actual measurement reported.

MARTIN HARPER: I think if you actually looked at the true uncertainty of the treatment, yeah. Okay.

MATT SANCHEZ: But the uncertainty is dealing with how the methods that were designed for like building materials quantify. They're either allowing for just simply a visual estimation, which is by definition subjective, yeah. Or you're doing something like a point count where you're only counting like 400 nonempty points, which doesn't give you enough statistical counts to have any real bite, real meaning at any --

(Crosstalk)

MARTIN HARPER: Right. And some people have propose a thousand counts to --

(Crosstalk)

MATT SANCHEZ: You know, it only improves it a little bit.

MARTIN HARPER: Yeah.

MATT SANCHEZ: You really -- to really improve it, you're gonna have to get into the tens of thousands to really get the -- your counts to get a -- to really get a tight measurement on that. But the other thing that can affect the point counts, which is very true, is if you actually go through and do point counting on something that is incredibly fibrous, like a -- just say like a reepa (ph) chrysolite and you compare it to, let's say, a nonasbestos ampha (ph) like tremolite count, the nonasbestos tremolite count is more -- that would be a more accurate estimate than the real fibrous material, because as you go through that area of percentages, those elongated particles -- those asbestiform particles either likes more area -- it creates area by them being so long as part of the count, so they look like they're bigger particles when you're just doing it by areas.

MARTIN HARPER: Yeah. This occurred when I looked at the arenite material that I collected from Rome, and when you crush it and you look at it under the microscope, it looks like it's all fibers, you know; and you -- by point counting you say, "Oh, it's 85-90 percent fibers," but then when you calculate out the size of those fibers versus the size of the glass frames that are in there too, it's suddenly only 30 percent --

MATT SANCHEZ: Yeah.

MARTIN HARPER: -- by weight.

MATT SANCHEZ: And again, the higher the magnification you go on your point count, you minimize some of those effects, but --

MARTIN HARPER: Oh, yeah. Yeah.

MATT SANCHEZ: Because, you know, like -- well, you'll be able to see the two --

(Crosstalk)

MARTIN HARPER: You end up only seeing five -- that's right. Exactly.

MATT SANCHEZ: But the other issue -- point that's important is all these things, because a lot of times people talk about PLM being insensitive, but it's really not. The quantification techniques that are employed are very insensitive, but the ability for PLM to observe something, that's a very sensitive technique. And the real measure of a sensitivity of a method is the ability to see a particle in the total amount of particles analyzed. How many particles can you see when you're analyzing something at 100 decks first then 400 decks, compared to analyzing a bulk sample by TEM where you're at 20,000?

MARTIN HARPER: Yeah.

MATT SANCHEZ: The TEM analysis, in and of itself, for bulk samples, you look at so few particles. It takes so much time to look at so few particles. Then you do these huge extrapolations up. So quantification by TEM, especially in bulk samples, is highly problematic. Again, when you see something is another issue; and then the identification of what you see is separate from this idea of quantification.

MARTIN HARPER: Right. But at the end of the day, if we have targets for trace analysis, we can confirmed that we have met those targets by the use of spike samples and round rock and (inaudible) spike samples. So by whatever technique we can use or whatever multiple techniques we care to use, at the end of the day, we can create samples of 1 percent, .1 percent, .05 percent, .025 percent. We can do that. You know, even though they're not homogenous materials, there's enough experience and expertise in making nonhomogeneous spike materials. We can do that, but just give us a target, and don't ask us for zero -- (audience laughs) -- because there's no such thing.

MATT SANCHEZ: No. You're right.

MARTIN HARPER: A target means that there's a level of acceptability. Well, don't use the word "acceptability." Use the word "tolerability" so we'll tolerate this much. We won't say, "This much asbestos is acceptable."

MATT SANCHEZ: That's true.

MARTIN HARPER: Maybe we can say, "This much asbestos is tolerable in talc because" -- and then what you do is you do a risk assessment --

MATT SANCHEZ: Well, that's right.

(Crosstalk)

MARTIN HARPER: You know, based on that. But I mean, without that information, the analysts amongst are kind of blindly trying -- you know, give you what you want. Figure out what you want; and then the analysts will just take the best technology and best expertise, and we have been, and we can give you what you need or what you want.

MATT SANCHEZ: I think it's important too, if any result -- the result is only within the parameters of the test. You can't extrapolate beyond the parameters of the test.

MARTIN HARPER: Right. That is also true.

MATT SANCHEZ: But -- well, I deal with a world where people say, "Well, it wasn't detected; therefore, it must be very small amounts." And it's like let -- the test doesn't tell us that. All it tells you is what that test is designed for. So if people are looking at that, they have to understand how that data was derived and what the scope of the data is.

MARTIN HARPER: True.

MATT SANCHEZ: And you can't go beyond that. The data only tells us what's in the scope of analysis.

MARTIN HARPER: All of these tests are surrogates for actually examining particle by particle every particle that goes into a can of talcum powder. Everything is, you know, a surrogate because of that. That's the whole definition of sampling and a sample, and that adds to the uncertainty of the technique, but uncertainty is inevitable. Of course, try telling that to a judge or a jury. Perhaps the reason I never have testified in front of the jury is because I never want to admit to practicing uncertain science.

(Applause)

CATHERINE SHEEHAN: All right. So we've pretty much caught up, and we are now ready to take a 15-minute break -- maybe 17 -- but we will be back here at 11:00 a.m. In the meantime, I'm gonna find out where the breakout sessions are being held, and I'll also check with the people on the webinar if we received any questions for our speakers.

(A break was taken.)

CATHERINE SHEEHAN: All right. Welcome back, everybody. So if everybody could take their seats, please. So thank you, everybody.

For those of you by webinar, I want to introduce the next speaker who will present on interpretation of data obtained from microscopy measurements. Dr. Taylor Mossman is a distinguished professor of pathology at the University of Vermont College of Medicine, going back a few years actually, has over 30 years of research, service, and training in the field of environmental and occupational lung disease. She has received a career achievement recognition award for her scientific accomplishments from the American Thoracic Society and the Wagner award from the International Mesothelioma Interest Group for historic contributions to mesothelioma research.

And I did get some information on the breakouts. The breakouts will be in this room. It will be partitioned into three, and we will promise individual easels.

BROOKE TAYLOR MOSSMAN: Thank you very much, Catherine, for that introduction.

I am going to talk this morning with one of the bullet points under this session that Ann Wylie and I are doing about mineral-type form inventions, emphasizing on research and others in terms of carcinogenic facts.

So I want to emphasize, in view of all we heard, that there are many properties of minerals that have been recognized by geologists and mineralogists throughout the decades. Most recently, this volume was one that Dr. Gualtieri, a mineralogist, had arranged in terms of a short course on mineral fibers, again, emphasizing that there are a number of properties that are important. This was a short course, and many individuals in this room played a role in teaching this course, as well as sampling the volume.

I think what's important here -- and I'm not getting a really good point here though. You probably can see. I apologize.

The point I want to stress is that in the summary of this pack here, Dr. Gualtieri, myself, and Dr. Roggli was historically looked at fibers in lungs in many individuals with disease show that if one looks at just the mineralogical features of dimension, that's only encompassed on one of these many boxes which Dr. Gualtieri has formulated with a number of minerals, giving them a relative score, in terms of toxicity, and I invite you to read this volume. I think it's very illuminating, and there's a wonderful discussion of all of the other properties other than dimension that are important in the cancer process. Several of these I'll touch upon today, but again, there's a myriad of other ones that have become recognized.

So I'm going to talk about a tumor that we've studied for almost 30 years. It's called mesothelioma. It's associated with exposure to high iron-containing amphiboles, such as amosite and chrysolite asbestos. The point I want to emphasize is that the -- and again, I'm not really getting good feedback on this. But let me just emphasize that we know that in this type of tumor that the affected cells are mesothelial cells. They occur in a contiguous mile layer, which means they're a single layer that has the property largely of fluid dynamics in the pleura in the lung cavity and that tumors arise when long, thin iron-containing asbestos fibers are able to get out to the pleura, and I'll illustrate that for you in a minute.

So this is what happens, and we'll see if these animated slides work, but the point I wanted to make is that the long, narrow amphibole fibers have the capacity of entering through the, primarily, inhalation route through the trachea and then a series of bronchiales that branch into several other smaller bronchiales until they reach, typically, the end or the air sacs of the lung. And here you see what happens as they enter. Again, this emphasizes that the rod-like shape and the dimensions of the amphibole align themselves with the airways that then penetrate through the airways through bronchial tubes to the alveoli of the lung, and you see that here, and then it's important to realize that they eventually need to get out to the pleura to cause disease. And this just shows how these narrow fibers, which because of not only their rigidity but also some of their flexibility in working themselves up to the lung, are known to penetrate through the alveolar sac, and they get out to the pleura, and then emphasizing that the pleura consists of two membrane-like structures with this one pleura and the parietal pleura, and the parietal pleura is where it's thought that tumors exist in man.

It's important to realize that fibers are known to penetrate through the air sacs, through the visceral pleura, into the pleural space, and eventually come in contact with a pliable pleural mesothelioma cells where tumors exist.

It's also been widely studied there are

clearance mechanisms that can take these fibers, not only through cells that are in the alveoli, known as scavengers or macrophages, but also, lymphatics naturally penetrate through and between pleural mesothelial cells and then drain into everything else, and this is what happens. We all got that?

So here you see -- if you look really carefully, you're going to see fibers, and it's known that a few fibers can align themselves and be cleared through lymphatic channel. The problem comes when there's a high-dose exposure, and you can see what happens here is a group of long fibers, that the stomata are occluded, that they build up, and they can actually come in contact with and persist at the site of tumor induction over periods of time, as long as 40 years, which is the average latency of these tumors in man.

On the other hand, there's been a lot of work done with inhalation of short fibers and particles. It's known that they reach the air sacs of the lung effectively. They also are removed by stems or cells called macrophages, completely. And here we see that non-asbestiform fragments are encompassed by macrophages, and if they are nontoxic, they are actually taken up effectively. Some of them are digested. This is known what happens, for example, with magnesium containing chrysotile is that it breaks down within these cells; and so these cells can transport the materials up through the airways; and other particles, as you see, can go through the somatic and drain out to the lymphatic system.

So the point I want to make is that certainly dimensions are important in terms of materials getting to the sites of tumor induction, but there are other properties that become important in terms of reactions that are necessary in the carcinogenic process with mesothelial cells. So our work through the decades has really focused -- thanks to support from the NIH, EPA, Mesothelioma Applied Research Foundation, and most recently, the DOD, we've really focused in our models today using human mesothelial cells on the properties of materials that are important in eliciting cancerous effects; and what we've invariably used in our studies have been crocidolite asbestos samples. We've used the

UICC. We've also used the NIEHS characterized materials as well, and what we've shown is that crocidolite asbestos fibers is the prototype, highly pathogenic type that's been known to cause human mesothelioma, causes a number of triggering events when it comes into contact with mesothelioma cells; and this cascade of events then results in the number of activation of receptors as well as cascades of a number of critical protein pathways that give rise to increased cell division; increase survival, which are hallmarks of cancer; and other stages that are necessary for a normal cell to become a full-blown cancer cell.

I want to emphasize that oxidants are something we focused on as being important and that is a result of crocidolite inhalation as well as interaction with cells in vitro. We've also focused on, most recently, what are called epigenetic effects through things such as microRNAs, which, therefore, affect the DNA to cause many of these cascades into silence a number of critical tumor-suppressive chains.

So what have we learned about asbestos? And again, I consider myself fortunate in that I've been able to interact with many of the geologists in this room in terms of co-authors and supplying me with well-characterized reference samples; and this is just, as you know, a general scheme of the classification of asbestos.

Oh, we actually pointed out in the 1990s to the scientific community that there were actually different types of asbestos with different packages. We have focused because of our interest in oxidants and generation of oxidants as a result of exposure to these pathogenic types. We hide iron-containing materials, again, blue crocidolite, and amosite, which Moscow's studies have reported maybe 20 to 30 percent bulk asbestos.

The other thing I want to emphasize is that there is little experimental work with, especially in vitro, with these other types of asbestos that can contain iron, may not be comparable in terms of charge but certainly had not been studied with regard to many of the models that we've examined.

So the take-home message here is that through the years we've discovered that the crystallite and amosite have a number of different mechanisms that -- and I'll go back to this -- that are important in the persistent release to cells as well as the generation of oxidants by cells themselves. The important point here is that the fibers themselves can generate oxidants by cell-free mechanisms, and they also can generate what's called frustrated phagocytosis and generation of oxidants do the uptake by the cells. So it's been shown that the oxidation state of these materials is important as well as how the cell recognizes them, which at low concentrations is curved by natural production, antioxidants, and high concentrations. We know that these methods are of control or healing are curved, and we see cancer-causing events. All right.

Inflammation. Chronic inflammation is also a feature that we've looked at in our animal experiments that are important in generation of oxidants. So this just emphasized the differences that we've noted through the years, and I'll go into our studies in -- that we've seen, some of the endpoints we've looked at in a few minutes.

Here we see what happens. This happens to be a lung trachea epithelial cell, so this is an event whereby we use whole 3D X-clamps and corollate these studies with inhalation work. We've emphasized in our work that it's the long crocidolite fibers that are unsuccessfully engulfed by cells who perturb and produce excess oxidant release, whereas -- what is seen here by TEM is how effectively short fibers and fragments are taken up or engulfed by cells. If we -- as these advance over periods of several months in our models, you see what happens with long, thin fibers. Here we see -- this is a 3D model, so we see inflammation. We see accumulation of macrophages along the fibers. We also see that the fibers act as matrices for cell division in something called squamous metaplasia, which is a pre-cancerous step in development of tumors.

So in our experiments, we've looked at a number of materials. Initially, we emphasized our work with chrysotile. It's asbestiform, obviously: nature asbestos, crocidolite asbestos, and amosite asbestos;

but we also have gotten from many of our colleagues non-asbestiform preparations -- in this case, antigorite and riebeckite that have been supplied -- and we've looked at comparably in many of our models.

And this is just a listing of the studies that we have done where we have prepared various concentrations of crocidolite asbestos as we -- one type of asbestos that we really emphasize is the high iron-containing and oxidant-generating species and contrasted that with what are called non-asbestos fragments or preparations of riebeckite.

We began in the '80s with preparations of milled material, or ground material, that we received from somebody -- might ring a bell to many of you -- Fred Monten (ph), the U.S. Geological Survey. Others we've received from different sources throughout the years. The point I'd like to make is that in all of our studies, unlike a number of laboratories, we've also done dose responses with all of these materials and have been unable to detect markers of either oxidant generation of what are called genes. These are early responsive genes that are causally related to mesothelioma and the various protein pathways that we've discovered. These have all been demonstrated effectively with crocidolite asbestos but not with riebeckite, and again, our preparations have contained between about 1 to 6 percent of fibers that are greater than 5 micron in the riebeckite species that we did drain them.

This emphasizes, again, historically, where we've proceed with our work. We've looked at cell survivor proteins. We've looked at cell survival as an endpoint of -- in growing response to asbestos. We've looked at cell receptors that simulate many of the protein pass gates that are important in abnormal proliferation and survival.

In addition to the non-asbestos fragment, we've applied -- and I'll talk about this more in detail. We've done studies with the New York State Gouverneur Mine -- talcs which contain 11 to 59 percent fibers. Dr. Wylie and Skinner (ph) have been kind enough to supply us with these materials, and we've also looked at what's called a Derrick Mine platy talc in many of our models. In this case, we've looked at mesothelial cells, and we've looked at ovarian epithelial cells. Have not seen effects of this platy talc in terms of gene expression, which is time-dependent and robust with crocidolite asbestos.

Curiously enough, in our work with mesothelioma, these are all human cells -- mesothelial cells and ovarian epithelial cells. We find ovarian epithelial cells are very resistant to talc as well as crocidolite. That's compared to the human mesothelial cells that are quite sensitive to these materials.

So I just want to emphasize the study we did with Ann in 1997. This I think is important because it addresses some of the material that I knew you would hear about today, thanks to previewing some of the slides by others this morning; but the fact is, in this study, we looked at both NIEHS samples of crocidolite and chrysotile asbestos; and we looked at three samples from New York. Fibrous talcs listed on the previous slide. We looked at changes that signified either increases, meaning increased survival of these cells -- again, mesothelial cells and lung epithelial cells. We also looked at toxicity by looking at the decreases in cell survival of these into colonies, and what we noted here was that only asbestos caused significant increases in cell survival, which is one of the markers that we have looked at in our mesothelial cell systems and not the fibrous materials, despite the fact that these materials contained a very high proportion of talc fibers, of tremolite that is non-asbestiform tremolite fibers, and also 3 percent in one of the samples of anthophyllite. And Dr. Wylie, I'm sure, can comment more on the mineralogy of these materials in her presentation.

So we went on from there to validate our findings, and what we did is we looked at the literature on talc exposures, and these are animal studies. I emphasize here that these studies, historically, were known as the Stanton Study. Many of you are familiar with them, I'm sure; but the take-home message is that regardless of the routes of exposure -- and it's very important that these studies look at fibrous talc. In fact, in the Stanton and Wrench studies, they looked at seven different samples, none of which gave rise to mesotheliomas in their models.

Other studies I've listed here because they look comparatively at asbestos and non-asbestos fragments, and here, again, are more studies done in different species using a variety of methods of administration pointing out that these did not appear to show any response in terms of cancers developing in animals of any species with talc.

It's also important to realize that there are a number of additional negative studies. I refer you to the IARC of 2010. IARC meaning International Agency for Research on Cancer. Their publications summarize a number of the studies that I could not add to these tables.

I also want to emphasize that cell studies are also summarized here, and there have been several laboratories, including the laboratory by Andrew (ph) and Catherine and all that have looked at samples of industrial talcs from Spain, from France, and from Italy that have not been able to show a significant increase in any marker of what's called genotoxicity in vitro in mesothelial cells.

So what did we learn through the decades? And curiously enough, this slide came from a National Party of Science committee that I served on around 1980; and this was one where Dr. Zoltai and a number of prominent geologist, Dr. Lanberg (ph), were highly beneficial in terms of educating biologists on the mineralogy of asbestos; and in a take-home matter, this probably is not anything that's new to any of you; but I would like to emphasize that when one considers a material, one has to consider more than just dimensions; but we have to consider what the cell sees or what the lung sees, and it sees a variety of different crystalline structures, tensile strengths, chemical compositions, certainly the surface area, chemistry. The charge of things such as iron become important, and all of these have really been related to the endpoint, which is endurability of certain types of asbestos and their ability to not only get to the pleural but to be durable there and stimulate changes that occur in cancer development over periods of as long as 40 years in some cases.

So what we learned about mesothelioma in humans as well. Naturally, we compare our results to human studies that emerge over time. We know now that dimensions alone do not explain the ability of a fiber caused mesothelioma. There, in fact, are many more of thin fibers that don't cause mesothelioma in them; and they indeed are different chemically, physically, etc. And crystallography also varies between these and the pathogenic types of asbestos fiber, so we have to take that into account before looking for agents that cause mesothelioma.

And lastly, I just thought I should provide a few suggestions, apologizing that I'm not a mineralogist; but I feel that as a biologist I've interacted with many, and it's really helped me understand that there are different mineral properties that may explain the lack of carcinogenicity of non-asbestiform fragments, such as tremolite, which we've used in our studies.

We also emphasize the importance of dose response in our work. It's very important if you're going to assess standards or test materials in biologic systems that you do dose response of a variety of doses and concentrations and dose parameters, which we had done in the Wylie work; and this is the only way that I think you can really sort out what is happening with these different types of materials.

And lastly, I'd like to emphasize that dose response studies in animals, special inflation studies are extremely rare. We have done them and shown that, in fact, there's striking dose responses to chrysotile and crocidolite asbestos; and lows low age (ph) signatures of cancer are not observed.

So I'd like to end here, and we'll move on to Ann's presentation, which will take these observations into humans and a little more about dimensions.

(Applause)

CATHERINE SHEEHAN: So any questions before we move on and I introduce Dr. Wylie? We have some questions? Okay.

GREGORY MEEKER: Well, it's a comment more than a question. But amongst the materials that I collected for NIOSH, there is a range of rather asbestiform tremolites that vary in iron content from non-detectable up to around 10 percent; and I think that will be a really useful reference set to examine beyond hypothesis further, and I'm just leaving it out there that those materials are prepared NIOSH.

BROOKE TAYLOR MOSSMAN: Yeah. I meant to talk to you about that, and I know we did briefly before the meeting; but I think that your presentation here really has illuminated sources of materials that can be well -- that are well characterized that can be examined by laboratories, and I really appreciate that presentation.

MATT SANCHEZ: And, obviously, a lot of these are commercial properties, which are very happy to measure as a great one too. But surface area is one that's been talked about. Philip Cook (ph) spent a fair amount of time with it. I think it should also be looked at with greater vigor.

Also, I wanted to ask you a bit. As you were looking at inflammation pathway, how important was that inflammation pathway as a precursor to the carcinogenic outcomes or those physiologic changes; and have you looked at, also, the fibrogenics outcome as well?

BROOKE TAYLOR MOSSMAN: Yes. That's the finding from NIEHS and your National Heart, Lung, and

Blood Institute. We have looked at great numbers of asbestosis and have models of asbestosis by inhalation. The difficulty, as you know, is mesotheliomas take the lifespan of an animal to develop, and we have not been able to do those. We go out several months, and we look for early indicators of mesothelial self-proliferation.

Your point is really a very good one in terms of these standpoints. Surface area you brought up, and I think that is something that Ann and I looked at. We actually -- now, I think I've moved the scientific community to -- rather than just adding weights of materials to models, that they actually adjust for comparable surface areas; and you actually get a whole lot of differences between fiber types much easier if you can do comparative surface area on determinations.

MATT SANCHEZ: Thanks.

AUDIENCE MEMBER 1: Have you looked at the Canadian chrysotile and into the Globe, Arizona chrysotile? Because that's essentially pure white.

BROOKE TAYLOR MOSSMAN: Right. I haven't. The only chrysotile that we looked at in Canada was the

UICC reference sample, and when we started these experiments, we used -- UICC was the Canadian and Rhodesian, and we also did crocidolite. Then with the characterization in the NIDHS samples that were characterized by Ann in the camalital (ph) paper, we were able to get enough to do inhalation experiments and dose response studies. So I think --

AUDIENCE MEMBER 1: There was a test of the iron, and the gold stuff is so clean, they used it as a blood filter in World War II for pongee (ph), and of course, every soldier in the Pacific who was wounded liked the old Arizona chrysotile.

BROOKE TAYLOR MOSSMAN: Yeah. I wasn't aware of that, but I think -- I was somewhat disillusioned before coming to this meeting because the NIH of samples no longer exists; and the fact that we can now get samples from NIOSH and different institutions -- we miss samples -- really is going to be very helpful.

AUDIENCE MEMBER 2: Did you look at short chrysotile too?

BROOKE TAYLOR MOSSMAN: Yes. We had sized materials, and we didn't see any effects. We were looking, again, at endpoints of self-proliferation. We did not do inhalation studies with the short.

Yes.

AUDIENCE MEMBER 3: The type of particles that got in through the mesothelial layer in your studies, as you indicate, some of them bound to the surface in some were able to penetrate the cell. Was there a difference in size or composition between those different types of fibers?

BROOKE TAYLOR MOSSMAN: Yes. There was a difference in size. As Bob referred to, we gave our size materials -- chrysotile. We also had different size fiberglass. Preparations of size definitely was an important feature in terms of cell uptake. However, the iron content and the fact that the block made the changes that we saw with antioxidants indicated the importance of chemistry -- iron charged, iron surface availability, for example.

AUDIENCE MEMBER 3: Thank you.

CATHERINE SHEEHAN: Okay. So briefly introduce Dr. Wylie. Currently a professor in the Department of Geology, University of Maryland, College

Park. She holds a BA in geology from Wellesley College and a PhD in economic geology with minor concentrations in mineralogy and petrology, structural mineralogy, and mining engineering from Columbia University; and she joined the faculty of the University of Maryland in 1972 where she taught courses and directed research in geology.

So I'm going to set your presentation up.

ANN WYLIE: Okay. Thank you very much. It's a pleasure to be here, and thank JIFSAN for inviting me and Nora for all her hard work.

I have my name -- only have my name up there because it's sort of an opinion piece, but I wanted to recognize that I have work on (inaudible) Chrisantha (ph). I'm working with Allen Seagreg (ph), and some of the data we have, I will copy that; and some of the work toward the end this fall has benefited from conversations with Andrew Corechefski (ph), Andrew Duane from Chemistry and Industrial Hygiene, and Mark Loutel (ph) from the University of Rochester; and we are working together on some of the things that I'll talk about today.

So the question we have is amphibole. I'm just going to speak about it generally. Is it asbestos? You know, sometimes that question is very easy to answer. Depends on the size of the particle. It can be very easy to answer. It also can be somewhat confusion -- confusing and not so clear on a particle-by-particle basis, and I always deal in populations for that reason.

Is it hazardous? I think that's the basic question. Not so much how it formed in the absolute, but is the material hazardous? What does the lung see, as some people have mentioned? And how do we identify it? And by that I mean something that might be hazardous, and when you have to -- when you're dealing with cosmetic or pharmaceutical talc, which is really the topic here, then we really do need to know how do we identify it.

Now, today I'm really going to talk only about amphiboles. I'm not going to talk about anything else because that's really, I think, the issue that we have here before us. And this is almost the identical slide that Brooke ended with, so I can skip over it very quickly. But we do know that there are certainly more than dimensions. I don't want to assume that that's the only thing. There are many things that impact bio durability, but I'm just going to talk about dimensions and the dimensions of sets of data that are composed of elongated mineral particles; and by that, I mean 3 to 1 particles. So I'm only going to talk about elongated mineral particles. I use the term EMP for that purpose just to describe the data set. And at the end of the talk, I'll come back to the issue of fibrous talc.

I believe it's a good place to look at -- the effect of dimensions in amphiboles because we haven't seen a lot of variability in terms of their retention characteristics other than dimensions in the lung or their solubility or many of the other issues that might impact their clearance or -- and so as a group, they're pretty insoluble and have a lot of characteristics in common, so we can try to isolate dimensions.

Well, if you knew my children, you would know that -- they'd tell you that I never throw anything away; and so when I was being asked to come and talk about amphibole and talc, I literally went into my bathroom closet, and I found a bottle -- this is the god's truth -- I found a bottle of baby powder, and so I brought it to my office, and I made mounds, and I looked at it under the microscope. And sure enough, voila, I found tremolite, and I had no problem finding it. I mount tremolite in an index of refraction oil, 1.578. That makes talc effectively invisible because it's a metal in the index of refraction, and so a quick scan of a large number of particles will show you immediately where you have high index material like amphibole. You can see talc platelets on end. They also stand out because they have a very low index, but this is a very easy distinction to make.

And I think our basic disagreement about things and why we're here is that: Do we accept the counting criteria that are used to assess the magnitude of exposure to asbestos in environments where asbestos is known to occur? We developed a whole methodology for protecting worker and for making sure buildings were clear when we knew asbestos was there. Do we accept those as the definition for asbestos? And that's the crux of the problem.

This is not asbestos. This is just a piece of rock. I mean, you look at it under cross-colors you see that it is a fairly uniform material. It's not composed of fiber bundles. It's not asbestos. It can't even be inhaled. This is 19 by 83 micrometers. You can't inhale it. It's not going to braid up when you put the powder on your body to make a lot of other little particles out of it. So this is not -- to me this is not asbestos, and I don't think I'm gonna get a lot of disagreement about that from anyone in the room.

If it's not asbestos and it meets the 3 to 1 and longer than five, then how do we approach the problem? How does FDA approach this problem? I think that's the crux of the matter here. We need a different definitional characteristic for tremolite if we are going to enable the identification of asbestos or hazardous particles in talc.

I'm hoping this next slide shows up. I've got a new camera, and I'm not so sure. It's okay. Now, this is a sample of tremolite asbestos. Art Langer, you gave this to me, gosh, a zillion years ago. It comes from Metsovo, Greece, where there's a high incidence of mesothelioma and other lung diseases among the residents of four villages in Greece. Art reported on it, and it's tremolite, and it's asbestos; and it's about the same size particle, about 11 micrometers wide and 77 micrometers long. And there's no question that this is asbestos, and even if this is just a -- not as nice as those electron microscopy pictures, when you look at it under the cross-colors, you can see that it's composed of lots and lots of little fibrils, and they break up easily just like spaghetti and have all the characteristics that make asbestos, in my mind, dangerous.

But can we tell these forms apart? And I will grab, there are many variations between this and the one I showed you before in terms of habit but not in terms of relative abundances. Almost all the amphibole that makes up the crust of the earth and in the United States -- I would say that's between 6 and 10 percent of all rock is made of amphibole. Almost all of that is just ordinary garden-variety material that will form cleavage fragments if you break it up. That's just -- it's not uncommon, but it is uncommon -- it is rare in terms of its abundance, and any of the other forms are there also. You can find them. There's nothing out there you can't find, I have learned, but I'll keep going.

So I want to talk about dimensions. I want to talk a little bit about width and length. Where are we going here? So as Brooke I think has well summarized, those particles that are known to cause asbestos-related diseases, where we actually have it in human populations. We have narrow widths on long fibers. It is the narrow width that makes asbestos flexible. You can actually bend any rock if you can make it long and thin enough. That's the truth of the matter. So it's the relative proportion -- the flex, the width -- that gives flexibility and people are so tired. I wrote a whole paper on this, this great mineralogist that was mentioned earlier.

Width and density control the aerodynamic behavior of fibers. Width controls the penetration potential of fibers deep into the lung and access to the pleura, and migration through fluid vessels in the body is controlled primarily by breadth; and when I say very narrow, I'm talking about fiber rates that range from less than .4. I'd say around .35 to .03, which are about the narrowest fibers that I've seen reported in the literature.

Now, length -- again, we look at length and we know that, as Brooke described very clearly, the short fibers are removed by a variety of mechanisms. The long fibers persist, and almost everyone that has studied the issue believes that long fibers are more important in the carcinogenic response than short. We find abundant long fibers in lumber and stumps. The long fibers appear to be preferentially retained in the lungs. The short fibers are removed, and of course, ultimately, for the work I'm going to talk about a little bit later, it's important that our occupational exposure, our risk analysis, all the things that we depend upon to understand the carcinogenicity of mineral fibers are based on exposures to long fibers -- L5. I call them "L5." I got tired of saying "length greater." So L5 fibers, that means longer than five.

And the -- there is, however, a conundrum that we face, and that word was used before. I hope I'm using it properly. Whereas, the long fibers are associated with disease, the short fibers are much more abundant. The mobile fiber lengths for crocidolite, that 1 to 3 micrometers; amosite, 1 to 5; Libby 1 to 4; and so forth. So there's lots and lots and lots of short fibers, but I'm gonna focus on the long ones for all these reasons that I described. I do treat the widths characteristics of long and short fibers differently for that reason.

So in the court cases that are in front of us, the Davis set's been entered in evidence. It's part of the public record. I took it, and I plotted it, so I wanted to see from my own mind what is it exactly that we're talking about in talc.

And so these are L5 elongated mineral parts. They meet 3 to 1. They're longer than five, and they were -- the data was provided by Longo (ph) in 2017; and what we see here is for these long fibers. You see that there's a range in fiber widths. It's actually fairly uniformly divided between .2 is the narrowest fiber recorded. There are no .1 fibers in that data set, and they range the -- I put the mode on there --

it's hardly a mode, but at least it's the highest value -- at .4, but they stand rather regularly over to about 1.2 micrometer, and then there's another bump out there at 1.5. Now, I want you to remember the shape of this curve because I'm gonna come back to it a little bit later.

I know that Metsovo, Greece tremolite asbestos that I showed you, this is the width distribution. I thank you Allen (ph) for these data, and you can see that the mobile width is .175, and this is a very uniform material. It's remarkably uniform. It has virtually no fibers braids, and that's .4. S little tiny bit out there. There's always going to be those things. It's very, very narrow, and it doesn't look at all like that other sample, and I want to show you putting them side by side on the same scales just what I mean when I say they don't appear to be the same at all. And so this material has a wide long range and low abundance of a lot of different material. This material has a very narrow range and a very high abundance -- a small number of widths.

So we have what we know about asbestos as a human carcinogen. Comes from exposure to asbestos in human population, in mine population, industrial workers of all sorts; but I want to look then -- let's look at -- compare what I just showed you to what we actually know about what asbestos is like. And I like this slide very much because these data come from Shedd in 1985, the Bureau Mines. She measured extraordinarily carefully. You had very high magnification. A lot of different crocidolite samples, and the one on the left shows you that there are molds of crocidolite that are very, very tiny -- .03 in width and the one from the Cape there is about .05. You know, mostly, you don't know that that's there because the way we do measurements -- a part of the measurements is we use wide bins when we plot frequency. So this and that, those are exactly the same data. There's no difference in those two data whatsoever. It's just that this is plotted at a very, very narrow bin width, and I wish that we had data like this on amosite. I wish we had it on a lot of things because they -- biological potencies of those very, very narrow fibers, it's like it was rather poorly investigated.

So this -- most of the width distributions that I can show you have bin widths of about .1 micrometers, and so you'll see. If that's there, I don't know. We'll see what I'm going to show. It's like this, but I do want to point out that virtually every fiber in these samples is less than .4 micrometers in width and the abundance of particles is the greatest, less than .1.

Now, it's also very important for us to remember that just because we call something crocidolite or tremolite asbestos or whatever, that does not tell you much about it because mineral samples are location specific. There's no ideal one of any of these things, and these are four different locations where crocidolite asbestos is mined; and the first two, again, these are single individual samples, are from the trans -- I'm sorry -- from the Cape and from Australia, and they have the very narrowest widths, .05. And then when you move into the Transvaal, you can see that the width -- the modo (ph) width is much wider. It's still pretty narrow but much wider. And then when you got to Bolivia, which they are still mining crocidolite down there, by the way, you see a much different kind of distribution.

In 1971 there was an article published in Nature and -- by Timbrell, Grifferson (ph), Pooley, 1971 who -- the title of the article was The Role of Fiber Width in Mesothelioma, and at that time they were looking at mesothelioma among the mine populations in the world, and they didn't find any in the Transvaal. Now, the Transvaal doesn't just mine crocidolite. The major asbestos mine there is amosite, and these widths are a little bit wider than this. But for the Cape and Hamersley that the widths were much wider, and they postulated that it is the width of the fibers in South Africa -- these two locations -- that explain this huge abundance of mesothelioma in the Cape and its lack in the Transvaal. I think they had one case. Somebody might be able to tell me another. Reference that for prep.

And then I'm gonna look again at comparing. I just picked one of these asbestos populations from Hamersley, Australia. Again, this is the Shedd data, and this is data from our lab, and this is the California riebeckite. And I want you to look at the shape of the distribution, a large number of evenly abundant particle sizes and width, a little bit -- another big bump out here a little bit further. This is exactly the profile of those tremolite particles that Belongo (ph) presented as coming from a platy talc.

So let's look at some of the other types of asbestos that we know have a potential to cause asbestos-related disease. This one was characterized, again, by my lab by SEM. I think -- I wish I had done the TEM, but I was young and stupid; and here you can see that we have a mode at about .33, and then there's a shoulder on this width. They may be two independent sets of data there, two modes that are just not clearly defined. There's certainly a couple more as we go out.

Amosite has very fine fodders. I see a .1. Just about 6 or 7 percent in this particular profile, and at .2, there's 15 or 16. So there's a lot of narrow fiber. There's a lot of white fiber. Amosite is very interesting. Mineralogical studies have shown that there is actually -- there are -- other than amphibole minerals that sometimes form between the fibers that tend to glue them together, and there is a structural continuity across fibers; and so I think amosite doesn't break apart quite so readily, but it does indeed have these very, very narrow fibers that are characteristic of asbestos.

Libby. Okay. So mesothelioma is known from a Libby and these data were gathered by MRI in a study that was done a long time ago. They were extracted from the ore, and you see a pattern; and by the way, this pattern looks exactly the same as the pattern of the amphibole in the air around the town of Libby that was collected by EPA not all that long ago. So this is a very stable cross-section, here, frequency diagram. I'm not -- I have numbers of fibrous elements exactly the same. So this is at .34. We have -- we have another bi-modal distribution. Like this beginning to show an amosite, but we can clearly see it here, and then it will kind of lump out further.

This second may be a courser fiber. It may be two different periods of fiber growth that have produced this. It could have broken fragments in there. I'm not totally sure what it is, but that -- this profile is very characteristic.

And we've talked about Italy. So the epithelia, there's mesothelioma among the people who worked in the quarries there. These are data from Paoletti (ph) and Bruny. They published their data in charts, and I copied it, so I'm not totally -- well, I think my arrow copy is .02. So I think these are pretty good representations of what they show, and again, you see kind of the same sort of thing. You see a lot of very narrow fiber -- .25. You see a secondary peak at .5 and another one at .75 and then one a little bit further down.

And finally, this is Pokela , Finland. Asbestos was mined there for, I don't know, hundreds of years, and it stopped production in the year of 1970s. At that time there was no -- and even into the '90s there were no mesotheliomas at all reported from Pokela. The population there has a -- the recent publication where there are some mesotheliomas reported. I don't know what that means since it's been, you know, 40 years since the mine closed; but nonetheless, I'm not sure about the mesothelioma potential for this particular anthophyllite, but I would predict that it should, based on this. You can see it's got very narrow fiber in it. It has this bi-modal distribution, and there's a lot of characteristics that are similar to the ones that we have seen.

So if I were to summarize, what does the width look like in asbestos, I would say that we have one type, which is like crocidolite and that Metsovo tremolite asbestos where we have 50 to 60 percent of the fibers that are longer that 5 micrometers. Now, I'm only talking about longer than 5 micrometers and the percentages are all those particles that start out at least at 3 to 1. 50 to 60 percent are less than .2, and amosite and -- we have the dimensions of crocidolite present, but generally speaking, the width is a bit larger.

We move onto Libby and to Pokela and Italy, we see these bi-modal distributions. We see the presence of these very narrow fibers, in decreasing proportions perhaps, but they do all have particles of width less than .2. So if I'm looking for asbestos, I'm gonna find out -- I'm gonna look for what's always there. It's always less than .2. It's always there, and so if you're gonna call something asbestos, you better have particles in there that are longer than 5 and less than .2.

Now, does all this matter? Does it make any difference whether these particle populations are different? Does it matter? And the only way we know is to look at the patterns of disease among the mining population and mesothelioma mortality. Most of our studies are done from mixed exposures, you know, where you have four different kinds of asbestos or an unknown exposure to asbestos -- workers and that sort of thing. But there are estimates of mesothelioma potency, and the measure which I'm just referring to, they often refer to as RMeso, and that's the percent of all expected deaths per fiber -- per fiber, and that's by -- per fiber. I'm talking about the ones that are measured for occupational exposure, longer than 5 and 3 to 1 expectation, so the sack per fiber, per cc, per year. So that's the measure, and Hodgson and Darnton published some mineral-specific values for RMeso, and Garrett and Castillo (ph) have updated these data. The Journal of Toxicology and Applied Pharmacology has a volume coming out very shortly -- I'd say within the next three weeks -- from a conference that was held on this topic in Virginia a year ago, and this paper is in that volume. So it's something certainly to look for. A lot of them are -- papers are already available online.

And so they published an update on crocidolite and amosite. They added the Libby and the mining populations at Homestake, South Dakota; and Homestake is the largest and oldest active gold mine (inaudible). It's a great place to go to. I like (inaudible), but I like it anymore. But the miners there mine deep underground mines in a rock that's basically made of grunerite and quarts. And so they were exposed to these particles, and we do know that there is -- has been no asbestos related diseases in that population.

I think there will be additional studies come available that we can use. And what do I mean by "being able to use?" Exposures to a single mineral. And what do they show, and I'll show you some real data, but I just want to be sure that the point is clear. They show that for the same occupational exposure as measured in fiber per cc year that there is a great difference in mesothelioma mortalism from location to location, minerals content, and that must be reflected one of these or more characteristics. It has to reflect dimension or durability, composition, and common structure. It should have been right there. It should reflect something that's different from location to location.

So here are the data. These are from Garrett (ph), Brad (ph), and Custor (ph). Asbestos type and location. Now, there's a lot of assumptions should come into some of the data that I'm gonna show you, but these just come right out of the paper. You can read it yourself, and I'm giving you the RMeso for overall crocidolite, and that's from the Cape and Transvaal. So for those two locations the overall -- and they published one for the Cape, and they published one for Hamersley and they -- you know, they have several; but

I averaged these, and they have averaged them, so I'm giving you the average. It's 0.451 and that's the -- 95 percent confidence intervals are shown there.

Amosite in the Transvaal, look how far that drops. It drops way down, 0.09. Winchite and Richterite asbestos from the vermiculite workers of Libby, Montana, 0.028. Drops down. Overall chrysotile 0.0012. I'm going to talk about that, and we're about to be perplexed with some of the things that Brooke talked about. It's a different mineral. We usually can't compare them.

And then fragmented grunerite from Homestake gold mine in Lead, South Dakota. This is not asbestos and there is no excess disease, so they have RMeso at zero.

So what do we do with those data? Well, we need an index for the toxicity of durable mineral fibers. What index can we use that we can compare and try to understand this mineral difference? And I got three up here. There might be a lot of other ones. Litman (ph) has suggested that in order for minerals to produce mesothelioma it has to have a width less than about 0.15. Stanton used 8 micrometers and 0.25 in width, and I dreamed up another one here. Longer than 7 and a width less than 0.4, and I have -- I'm using that one. I'm gonna show you some data from that one because Fred Pooley, in his studies of lung tissue and what particles actually get to the pleura, has shown -- and this paper's coming out in this volume --that these 7 micrometer particles long are sitting right there at the surface of the lung waiting to move into the pleura. And Lance (ph) et al. published their assessment that particles have to be less than 0.4 micrometers to make it to the pleura. Now, we can argue about those. I'm not sure these are the right, but I've got three here, so let's look and see how they work. It could be added that I hope our work, as we go forward, will improve this.

So what we have plotted here is the total fiber in the exposure and what proportion of that fiber meets certain width definitional criteria. So let's just take this first gray triangle there. That is for length greater than 7, width less than 0.4. That's for crocidolite, and I've averaged crocidolite at eight populations, so I'm happy to -- it's a way to gain (inaudible). Anyway, there it is. So it's 58 percent of the crocidolite fiber fall in that category. For amosite, it's about 30 percent. For winchite, richterite asbestos from Libby, it's at 17 or 18; and for Homestake, it's zero. But that is with a simple regression line on there, and put it just right through all those, and so that quotes the percent expected deaths against a dimensional characteristic of a population; and I did that for the length greater than 7, width less than 4. I did it for width less than 0.15. I did it for length greater than 8, width less than 0.25.

So in the fiber per year, this tells you something about what that fiber that they were breathing in actually looks like. It isn't a bunch of particles that are 5 micrometers long and 1 micrometer wide. There are much different from that, and they vary among these native sacks, which I think is a -- the reason why the mesothelioma potential varies. The 0.85 and the 0.15, they almost fall on exactly a straight line. They are very, very similar. The R squares should be something like 98 percent, and they put these when you only have a points. You only need two to get 100 percent now. (Audience laughs.)

So let's try -- can we use this to predict? Can we take a curve like this and predict mesothelioma outcome? So I've taken three samples I'm gonna show you. One is in Metsovo, Greece, where we know there's mesothelioma. One is Pokela, where we're not so sure, but if my medical (inaudible) would see, what would they predict. And then I've taken the data from Italy. What does it predict in terms of -- at home, I don't know how to plot error and square in the Excel. I'm old and really backward about all that, so I asked a friend of mine to do that for me. I have all the errors. I just want to show you what the errors are in these points. So these are one standard deviation in the percental fiber and 95 percent confidence interval. Just want to be sure. We talk about error earlier.

All right. So here are these three curves, and Metsovo, Greece tremolite plots on these three different curves, and it plots at an average of about 0.3 RMeso, so you know, something in there. By all these criteria it should cause mesothelioma. Of course, we know it does. With young Lidia (ph), in Italy, well, that one is around 0.2 expect for the width less than 0.15, and it's way down here in the lower corner. There were no data from that chart I copied of particles that were less than 0.1 micrometers in width, so I'm not 100 percent sure about the quality of that data point. And then Pokela, Finland, they plot at about the same level as well. Just a little less than 0.1.

Okay. So how do we use all that information to help the FDA? That's the question. This, again, is from Metsova; and under PLM, do I have any trouble telling this from that? I don't think so. I don't think anybody would have any problem. This is composed with a zillion fibers that are less than 0.2 micrometers in width. I mean, it is a material that will come apart. If this were in talc and you rubbed it on your body, I'm not sure you wouldn't release a lot of this fiber. You might start with a certain number. You might end up with a lot more. I think when you inhale fiber particles that it's aggravating your lung. So I think there's a lot to be said for the health effects of asbestos because of the habit that it forms, and it certainly is predicted by my analysis that this would be highly carcinogenic. No problem -- this is a PLM. This particle is 18 micrometers wide. It didn't come out from a talc deposit. Here's another particle from that bottle -- my children's baby powder -- and it's not asbestos. It isn't a fiber bundle. It can't disaggregate. It can't be inhaled. Nothing can happen to this that I know of that has any health hazards associate with it whatsoever, none. And there's no confusion about a particle this size, about whether or not it's asbestos, using PLM. By PLM, it is unambiguous.

AUDIENCE MEMBER 1: Did you throw out the bottle?

ANN WYLIE: Pardon?

AUDIENCE MEMBER 1: Did you throw out the bottle or keep using it?

ANN WYLIE: Well, it's -- my children are in their 40s.

Okay. So the analysis issues in cosmetic talc

I think are the crux of the matter. And we ask: Is the amphibole in talc -- is it asbestos? Does the talc contain chrysotile? And how do you distinguish anthophyllite from fibrous talc? So let me just make a few comments on these things.

Okay. You see amphibole asbestiform. Well, the talc that I looked at under my microscope last week or week before -- week before Thanksgiving, actually -- the particles were huge. I mean, we're talking about 70 micrometers. Wow, these are huge. And these talc particles were gigantic. I don't know what I was expecting. Why we would have gone to the TEM, I'm not totally sure. Almost everything that I saw in this bottle was very, very large; and so polarized light microscopy is great for this kind of thing. You can see fiber bundles no problem, and they're going to be there -- I contend that if it's amphibole and it's really asbestos, they're going to be present in these large sized particles. They don't just all break up by themselves. The talc does. Remember talc is the softest mineral known. If it's not breaking up into tiny little particles, I don't know why the tremolite would. But if we go to the electron microscope and we count 3 to 1 long, width 5, what about -- how do we deal with that? How do we look at those data? And I think you have to ask at those data whether or not you've got particles that have widths less than 0.15. Do you have lots of particles that are longer than 8 and less than 0.25? Do you have a lot of particles that are longer than 7, less than 0.4? I mean, are these particles that are asbestos-like present in the sample? If it's chrysotile -- well, I would ask: If there's serpentine found in talc, is chrysotile evident by light microscopy? Chrysotile asbestos is just like amphibole asbestos in the sense that when it occurs as asbestos in veins, it seems you should be able to see this no problem. If it's dispersed -- if it's like a mass fiber deposit, sort of mass fiber -- chrysotile plus talc, you'd have to go with the TEM, but I don't know of any assurances like that. Now, some of the rest of you may. I just am unaware of that occurrence.

I found this in that same bottle of powder that -- I swear it was there. And this is fibrous talc, and I know it's fibrous talc because the indices of refraction are too low for it to be amphibole. They're not even close. It also has an extraordinarily high birefringence. In other words, the indices of refraction parallel and perpendicular to this bundle are vastly different and the material shows up under polarized light microscopy without a problem. It is actually so simple under a PLM to tell fibrous talc from anthophyllite asbestos.

Let me just -- so let's talk about some of these issues because I see this issue all the time. People talk to me about this. Why is it a problem? It appears to me that by chemistry and morphology that the grains of fibrous talc and anthophyllite asbestos look an awful lot alike by SEM (inaudible) 1:14:55.1; and they look very, very different by optical, and the reason for that is that optical microscopy is sensitive to the water content. Water content lowers the density. When you lower the density, the indices of refraction go down. But TEM and SEM are insensitive to the water, and so people confuse them all the time by just looking at chemistry. As I've said before you can easily tell these two apart.

Now, I've talked to a number of TEM microscopists and asked, "Why do you have this problem all the time of fibrous talc being called anthophyllite asbestos?" And they said that in ISO, methodologists that -- not always when you have two minerals in that similar composition that are constantly present, not only do you look at the zone access pads for consistency, whether it's tremolite or anthophyllite, but you also want to evaluate them for inconsistency with the crystal structure of other minerals of similar composition and this is simply not done. It is not evaluated. It used to be that -- just the 5.3. Instant spacing got the definition of anthophyllite, and then we started getting a few zone access patterns, but they are not necessarily specific for anthophyllite. They may be consistent, but they may also be consistent with talc and, therefore, do not provide the necessary distinction. I know this can be done, but I think it is an extremely difficult proposition. And those of you who deal with electron microscopy can comments on that in a little bit more widely.

Well, I was asked weight percent versus particle number. Boy, there's a really different way of looking at things. I don't think you should begin an analysis for asbestos unless you know it's there. I just don't think so, and you can tell that it's there by looking for evidence with fiber bundles, scanning the slides by PLM. You have some indication that you have asbestos present by mechanisms that we know are reliable before you began counting individual particles.

Normally the levels are very low in tremolite, in top material; and that is a consistency -- there's a possibility of then homogeneo (ph); and we had a little earlier discussion. Someone said they looked at 20,000, and there wasn't any; and then someone else did some concentration, which is a very good way to abuse PLM, by the way. I think it could be sample inhomogeneity at those very low levels. But PLM, you can -- particularly if you concentrate, you can get as low of a sensitivity as you want. It just depends on how much material you want. Really? And how much time you want to spend. But 0.1 or .01 percent BLM is pretty easy.

Remember, the mass is in the large particles. It's not in those little tiny particles. They don't have any of the mass. It's in the big particles. We have particles that are 100 micrometers wide, and we are trying to measure the mass of a component with the little particles that are 1 micrometer? The mass is in the big stuff.

Now, fiber number, that is a very complicated approach. I don't think that it is helpful in terms of estimated percentages of anything. I don't -- I think there's a great deal of difficulty and reproducibility. I'm going to leave it to the TEM people to comment on this. What are you going to count? What do you measure? If you use TEM or SEM and you measure fiber number, I would argue that you must record the length and the width of every particle that you measure so that you can evaluate the population for toxicity, and that would be the recommendations that I would have to give you. Thank you.

(Applause)

CATHERINE SHEEHAN: Thank you very much.

ANN WYLIE: You're welcome.

CATHERINE SHEEHAN: So any questions? We got questions?

AUDIENCE MEMBER 4: Yes. Often when we're looking at talcs that have these amphiboles in them, what we're seeing aren't necessarily singular structures. We often see bundles, and it's difficult to actually determine what we're going to use for the width in a bundle if you have a bundle that has, say, some fibers that are 0.3 and some fibers that are particles within that bundle that are less than half a micron. How would you address that when you said you should be measuring the aspect ratio of every particle by EM?

ANN WYLIE: All right. I never measure aspect ratio. Aspect ratio is an absolutely useless parameter. It's dimensionless. It has no value.

AUDIENCE MEMBER 4: Wake me up.

ANN WYLIE: So I really -- I feel really strong about that. Well, when you look at all of these distributions, we all had that problem. We have it in every distribution that's ever been done, but in terms of particle -- you just take the width. Just take the width. Whatever it is, take the width. Of the bundle, whatever, take the width; but you should have -- asbestos easily disaggregates by hand pressures. It's one of the definitions. It easily disaggregates, but you're gonna have a lot of the other things in there, and I wouldn't worry about that one bundle. I would worry more and measure more those individual particles that you see which are by far more abundant than the one particle that you're talking about. That's been my experience.

AUDIENCE MEMBER 4: Well, my question was, basically, if a bundle is defined as three or more fibers, parallel each other, separated by less than the width of one fiber and those individual fibers have different widths, how do you determine a width of a particle when you said that ever particle must be measured for its length and width?

ANN WYLIE: I would measure the bundle, as I told you. I mean, all those populations that I've shown you -- all right. There is thousands and thousands and thousands of measurements, and whenever there was a bundle, we measured the width of the bundle. All right? Because the number of those particles that are individual far out -- exceed -- and that's why you always have tails. That's why you always have tails on distributions of asbestos. You don't always just -- it doesn't just end at .1 or .2 micrometers. It's all -- the crocidolite decided it's so readily that you tend to have much shorter tail on crocidolite. All right? For me, I (inaudible) why it's so dangerous because I think it would disaggregate under any circumstances, but the -- you measure whatever you see there, and then -- that's what all of these are based on. We never try to say, well, what about those individuals that make that thing up? Never tried to do that. So all the data that I'm showing you here, it's just every particle however it presents -- bundle, no bundle -- are what makes these data. That's what I've showed you, or that's how we've dealt with it.

AUDIENCE MEMBER 5: Just a comment, actually. Showing up. If you can't do magnification better and better and you keep chasing zeros, you can end up increasing the number of fibrils or fibril masses gone to the individual fibril. Now you've got millions where you only saw one bundle to begin with. The end is sitting right here. Just measure what's there, not the individual separations.

ANN WYLIE: Yeah. Next question.

GREGORY MEEKER: I appreciate what you said at the end about measuring individual by TPM the dimensions, and then you went on and said something I think was wrong.

You said because then you can calculate from that the toxicity, and I guess you were getting it in mass, and mass is really irrelevant in toxicity. It's the number of individual small fibers that are gonna reach the lung. Because as you said earlier, 70 micro-like fiber never going to reach the lung, but it --

ANN WYLIE: Right.

GREGORY MEEKER: -- has a huge mass. It's gonna overwhelm millions of other fibers.

ANN WYLIE: That's right.

GREGORY MEEKER: As Roe (ph) said 40 years ago, .25 percent in talc, it still had billions of fibers.

ANN WYLIE: No. I agree with you. I don't disagree with anything that you said, and I think that you misinterpreted. If you're gonna measure particles, you're not going to be calculating mass. I mean, that would be fiber number, and that's where I think you measure everything; and I think it's a very complicated to extrapolate from TEM print to an entire ball of talc. But nonetheless, I think what you're measuring, measure everything; and then what I met my toxicity, I think that you have to have asbestos-size particles to have asbestos-related disease. Now, that's my opinion, but -- so I would say that if you don't have populations of particles that have widths less than 0.4, then -- and I mean 0.35 measured or less -- usually there's a 0.05 error -- then it's very unlikely that you're going to have the kind of toxicity that we see with amphibole -- of crocidolite. Now, that -- that's my opinion, and you know, it's not something -- and I say it is that based on some of the work that I just showed you why I think that way, because I didn't get to see dose response on those sized particles.

AUDIENCE MEMBER 6: I wanted to put in a good word for aspect ratios. (Audience laughs.) One of the biggest that we found useful with aspect ratios is that as you look up populations of non-asbestos fibers and asbestos fibers, the diameter of the asbestos fibers, the width stays pretty narrow. So as they get longer, the aspect ratio jumps up, and it doesn't happen with non-asbestos fibers. If they get longer, they get fatter, so their aspect ratio goes flat.

ANN WYLIE: My experience has been exactly the opposite. The longer they are, the higher the aspect ratio concluded fibers, and I've got a lot of data published that shows that.

AUDIENCE MEMBER 6: Compared with asbestos?

ANN WYLIE: No.

AUDIENCE MEMBER 6: That's the comparison I'm making.

ANN WYLIE: No. As you -- if you take ordinary tremolite and crush it off, when you look at the smaller particles, the aspect ratios will be last, and it isn't until they get longer does the aspect ratio increase. So I don't like aspect ratio, because when we see populations and you compare two populations up here on aspect ratio, you do not know what the range of length over which those particle populations represent. And so one of them might represent particles from 2 to 100, and one might represent particles from 1 to 20; and that might be very, very different; and we're not comparing apples and apples in that way. Aspect ratio can be very misleading.

AUDIENCE MEMBER 6: We were building the size distribution and then we're comparing the aspect ratios of the two populations, so you know what the lengths are.

ANN WYLIE: As long as you compare aspect ratio over the same length range, then I think it has some validity for comparative purposes; but if you don't have the same length range, then you are not comparing apples and apples.

AUDIENCE MEMBER 6: I agree.

AUDIENCE MEMBER 7: I've got one question along these lines. Has it been determined if someone said reason or bundle, what happens over time to the bundle in the lung? Did they -- are they -- do they come in a case like at Cenegenics? Are they individual fibers? Does anybody know?

ANN WYLIE: Well, maybe, Brooke, you can answer. Most of the data I've seen shows single fibers.

BROOKE TAYLOR MOSSMAN: Yeah. I think a lot of the original work on the fiber breakdown in bundles was done by Bob (ph) a long time ago, in the 1960s; and he did show that even long asbestos fibers in Crocidolite-enticed talc broke in.

AUDIENCE MEMBER 7: Okay.

ANN WYLIE: There was a wonderful study by Coffen (ph) on, apparently, actinolite in rats, and they -- I think they did inflation. I'm pretty sure. And then they killed the rat slowly over a long time, and looked at the populations; and with time, the numbers of fibers in the lungs increased. And that shows you that those bundles were breaking up. So I'm pretty sure that that's my answer.

AUDIENCE MEMBER 7: Uh-hum.

CATHERINE SHEEHAN: Hunthro (ph).

AUDIENCE MEMBER 8: I've had, I guess, a

unique opportunity with my association with Dr. Dodson to have analyzed postal valves and lung tissue samples, and it was interest. Your width is, I think, spot-on is what I see; and I can show you data because we have compiled length and width. Where I would take objection is the greater than five. The vast majority of fibers that I find are actually not less than 0.4 but probably less than 0.25.

ANN WYLIE: In width?

AUDIENCE MEMBER 8: In width. And less than 5 in length.

ANN WYLIE: Yeah, I know. That is the conundrum about length, and I don't understand that; and every population I have ever seen or looked at has the most abundant fiber tests in 5 micrometers or less. So there's no question about that, and that is a problem, a conundrum is something I don't exactly know how to deal with; and I know how Dr. Dodson feels, that this is important; and particularly, I think it's going to be important today; it will be important in inflammation; it will be important in asbestosis; maybe it will be important in lung disease; but for mesothelioma, I'm not so sure.

AUDIENCE MEMBER 8: I could hear him in my head. (Audience laughs.) The question he's asking is: How long does it have to be in there to start the process?

ANN WYLIE: That's a good question. I just use five because all our exposure data is five, and if I'm gonna use data that suggests the variability of your potential to get disease, I have to use it on the basis of fiber, measure, and exposure.

AUDIENCE MEMBER 8: Exactly. That's just on the occupational exposure is all five. So we don't have that data --

ANN WYLIE: Right.

AUDIENCE MEMBER 8: -- to be able to -- you know, the data that I've been able to find shows that, yeah, the majority of the population is less; and it matches very closely what we find -- what I've been finding in human lung tissue.

CATHERINE SHEEHAN: Okay. We're cutting into our lunchtime now, so we can take one more question. I see two hands up. Okay, Aubrey (ph).

AUDIENCE MEMBER 9: Yes. I thought your analysis was really interesting trying to look at the differing sizes and shapes related to mesothelioma, and obviously, at the beginning of that exploration into the arenite populations and other populations --

ANN WYLIE: Yeah.

AUDIENCE MEMBER 9: -- as well; and obviously, the worker populations are selective, so I think that would be commercial asbestos.

Have you also been trying to look at other health influences as well? Lung cancer, fibrogenic, interstitial lung disease, fibrogenic pleural lung disease because they -- there's different sensitivity to different size and shape with respect to the other health influences, and they're just as important as mesothelioma.

ANN WYLIE: Oh, the anthophyllite workers in Pokela margin -- the population was full of asbestosis and lung cancer. And so there's no question in my mind it's -- the certain area of anthophyllite is very high. Timbrell did work on surface area and demonstrate very clear to my satisfaction that he can explain asbestosis on the basis of the high surface area of anthophyllite. So, yes, I absolutely --

AUDIENCE MEMBER 8: We actually do those same kind of analysis.

ANN WYLIE: Absolutely. Now lung cancer is very hard because the data that have been shown by Garret, Brad, (ph) and Castillo (ph), and Hodgson and Darnton show no correlation, no variability that I can call against dimensions. So I don't know. Lung cancer I don't understand. There's a lot of factors there, and it's not just a dimensional argument.

AUDIENCE MEMBER 9: You know, stop and shield or --

ANN WYLIE: Yeah. Yeah. No. You know, I don't.

CATHERINE SHEEHAN: Okay. I hate to break this up, but we have to move on. So lunch is from 1:30 to -- I'm sorry -- 12:30 to 1:30. I see they're setting up the buffet outside, but most importantly, the breakout sessions are going to convene in this room divided into three. Recall that you signed up for two of three sessions, so come back and be prepared to know which of the sessions you have signed up for or we will have chaos.

The co-moderators for Session A on tech methods is now Robyn Ray and Frank Ehrenfeld. The Session B, measurement criteria, the moderators are Ann Wylie and Art Langer; and then the third session on interpretation of testing data is Brooke and Matt Sanchez. So everybody knows where to go after lunch.

(A lunch break was taken.)

CATHERINE SHEEHAN: So what we're gonna do now is if everybody can come back into the main room. We are going to begin with a report-out by session moderators. The report-out will last for 45 minutes, and so we'll do the math. Here, we have three sessions, so we have to stick to our 15-minute time.

So I will begin with Session A, if I could have Frank and Robyn. If they can come up and share their report-out.

When we're done with the three report-outs for Sessions A, B, and C, we will then go into a discussion questions for the moderators; and that will last half an hour, 30 minutes. So we should be out of here -- basically, we should be done by five o'clock; but I will finish off 15 minutes with closing remarks and next steps. So --

FRANK EHRENFELD: Can we have ten minutes to put our ideas together here?

CATHERINE SHEEHAN: Okay. Do you want to go second? Which of the sessions -- A, B, or C? Who wants to go first?

FRANK EHRENFELD: We're just putting our notes together.

CATHERINE SHEEHAN: You're putting your notes together.

FRANK EHRENFELD: I thought we had more time.

CATHERINE SHEEHAN: Yeah, I was given the instructions to get this thing moving, so if you're not done, we don't have any choice.

FRANK EHRENFELD: Okay. Here we go.

CATHERINE SHEEHAN: You're good?

(Background chatter)

FRANK EHRENFELD: We seem to be down a few people. Do you want me to get some more people back in the room once you --

AUDIENCE MEMBER 10: I'll grab them.

FRANK EHRENFELD: We'll do that.

(Background chatter)

Okay. Folks, I think we're ready to go here. I want to summarize for our Session A today. Session A, this is our charge is before you on the screen. Martin added his. And so we were charged with what test method for the analysis of talc and mineral fibers in cosmetics -- it was very specific -- where asbestos is not there and the word "cosmetics" are there. So we sort of specified that as we went through this.

And, again, here we are again. I will tell you that we had a lot of assistance putting these notes together, this presentation, from Robyn Ray who is the special projects manager for asbestos for EMSL; and again, I'm Frank Ehrenfeld. I'm the laboratory director at IATL in New Jersey as well as the chair of ASTMD2207.

We started by asking for a show of hands as to who our audience was, and so we discovered that we did have a number of geologists. We had a number of lab rats that specialize in various traditional technologies and techniques. We had XRD represented several times over, a number of light microscopists and electron microscopists present. We had those who were familiar with some of the medical epidemiological background of the subject as well as a toxicologist in the room. Everybody should have a toxicologist in the room when they're meeting. We also had those who were involved in the regulatory community.

We had a number of things that we wanted to consider, including about the matrix of the material. Some matrix considerations were discussed. We can even look at an overview of that.

Is this something that is a talc deposit, and what analytical methods might be appropriate for that versus what analytical methods and techniques would be appropriate for talc in a product? Obviously, our charge was cosmetic, so a product.

We talked about some of the products themselves, to what extent would they be used. Was it something that was bound in waxy matrix like lipstick or something that, perhaps, was more materially that could be readily airborne like a talc?

We also talked about the lack of reference standards and calibration standards. We talked about all of these various analytical techniques in detail. One of our core conclusions was that no one analytical method shall trump another and that you must have either complimentary or a suite of analytical methods in order to be able to confirm these minerals in those matrices.

Under the term "other," we actually had a couple other things proposed for -- to overcome certain challenges, including SEM OSHA analysis using EDS -- thank you, Greg, for taking me back to my days as a graduate student at Lehigh -- as well as ICP mass spec to look at some of the chemistry of the minerals as well as the matrices.

Under "prep options," we were reminded by Chris Weis, our toxicologist. Careful about prepping your sample. Do not create anything if you can get away with it, and don't diminish or demolish or dilute anything that might already be in there. So careful not altering the material as it is received for a laboratory -- in the laboratory.

We have other takeaways regarding prep options. We talked about various modernization techniques. We talked about the disadvantages of knowing -- and everything you see here on the slide, we talked about it at least in some length.

We also talked a great deal about, okay, once it's under a light microscope or in the XRD or under the SEM or TEM, to what extent are you going to -- I don't want to use the word "limit" an analysis but to extent -- or to tolerate some limit, to put it in Martin's terms. But we thought that the best idea was to analyze everything so the microscopist would never have to put that sample back into a stove and if there's a particle there that can be analyzed and the dimensions recorded and the chemistry measured and the fraction pattern obtained and documented, that you do it right there and then. Don't have to go back and do it.

One of the other filters that we mentioned a couple different times had to do with an unknown or a certain tie it up here. We also asked repeatedly about those who had experience analyzing these materials, and a number of hands went up as well. So the room had a lot of experience in it.

What we said we would learn some of the lessons from the morning sessions, and I proposed that we filter our comments through these couple points that were made by Greg Meeker -- two of these points -- Ann Wylie, Martin Harper, while in the hallway, and others.

Greg said, "Is it possible to protect public health without regulating everything?" So we had to think about that, to what extent. You know, where's your cost-benefit analysis? If you're doing an analysis of material, do you want to analyze everything? Do you want to have that boxcar of an ore deposit pull up and somebody say, "Okay. Tell me what this has or does not have in it" or, "Here's a thimble full of material. We need your analysis to proclaim the asbestos or mineral fiber content of this boxcar of material"? So all that stuff we considered. So to what extent is public health going to be protected without regulating everything?

Another comment that filtered our

conversations had to do with geologists used to own the definition of asbestos, and it has been -- and those definitions have now been turned over, for better or worse, to the legal community.

Greg had another important statement that we used to filter our discussion, which is: "What does the lung know?" So regardless of how you might define a particle or a fiber, what does your lung have to say about it?

Make sure I have all of these out of the way. We were also concerned about it turning into a discussion about asbestos definitions, and we at some point there was at least some murmur of consensus about the fact that the initial definitions of "asbestos" had to do with materials that were intentionally formulated with these minerals for building materials and other such things and if there are other products that might be contaminated with these minerals or coming up out of the ground that they may not -- that we need to maybe create another definition for them. Those are some of the filters.

Again, the main points to take away from our discussion, use multiple techniques and technologies. Make sure that your prep is sound and not either removing anything that you might detect or creating something that you're going to be counting. And also, if you're gonna analyze something, take the time and analyze everything so that 20 years from now they can use that data and not have to reinvent the wheel.

And again, we had a lot of minor points that will eventually come into a summation that we'll submit to JIFSAN.

And any questions before I'm done with your little synopsis there? Yes sir.

AUDIENCE MEMBER 1: Did you discuss a possible combination of these techniques, whether these or some of the others that you mentioned, that could be used as an additional screening process that could -- identifying risk, maybe be a way of identifying talc that was reasonably safe and should be making in our commerce, you know, based upon, you know, what our IHHE or one of the risk assessments we come up, give us some number to hit on; but what I'm looking for here is a screening protocol that might be a little over sensitive, but if it gave false positives, bam, then you go ahead and do the additional confirmatory analysis to get rid of it.

But what I'm looking for is an initial screening protocol that would give us, you know, a high -- relatively high confidence that whatever product got through was safe for the public.

FRANK EHRENFELD: Okay. That's a long question. Let's see if I can get it down to its bare components there. The last thing was like, hey, with this screening protocol, can I have a high confidence? But that may be counterintuitive there -- screening and high confidence, right? However, we did bring up at least the term that: Now, what would you use first? Is there an order you'd use these analytical techniques? Is one better than the other? Can you just go straight to this analytical method? And the answer over and over again was, "No. You need to use a suite or use multiple confirmatory techniques."

Nobody was too confident with using a screening method outside of using light microscopy at least on the ore deposit side of things, only cosmetic products -- finished product side of things. Obviously there would have to be a lot of prep involved, and then, again, you're losing some of the pool --

AUDIENCE MEMBER 1: That's a whole -- that's a whole different.

FRANK EHRENFELD: Yep. I may not have answered your question, but at least some of those elements were discussed. Again, most of the comments that we shared also related to the morning sessions.

Sean.

AUDIENCE MEMBER 2: We discussed XRD and PLM as valid screening pools that have advantages and disadvantages, but I thought we had agreed a group that some form of electron microscopy was needed for final -- or at least quality assurance.

FRANK EHRENFELD: Yeah. And with that, we also discussed measuring the width of various suspect minerals, and so TEM would obviously need to be used for that, with the limitations of light microscopy, in order to collect the data that might have pertinent biological information. TEM would have to be used.

Any other questions? Okay. Thank you very much.

(Applause)

Of course the secret weapon of our session was Art Langer, so we had a wonderful broad-ranging conversation about all sorts of things.

Our goal was to establish concurrence on a morphological criteria for the identification of mineral fibers in cosmetics containing talc, and so the things that I think we did agree on was that the longer than 5, aspect ratio 3 to 1 gives you -- may give you false positives. All right. So although it will patch her what we're interested in, in an analysis, it would necessarily -- or likely give you false positives if both fragments and asbestos was present.

We also noted that 3 micrometers is the limit of respiration for fibers, and so that's an important limit on what should be included if respiration is the method of entry.

Someone asked if you could get talc through the skin. I don't think we were experts enough to answer that, but I think it was raised. We then agreed that particle morphology using this standard method for assessing asbestos exposure will exaggerate, or may exaggerate, asbestos fiber counts.

We agreed that the analysis should look at and focus on particles longer than 5 micrometers, and we do not accept coal without dissent, that it's only long particles that we should be worried about; but what we're looking for is an index and an indication that we have fiber present. And since all of our risk assessment and everything that we know about how these minerals were likely to behave are based on that, that analysis should focus on longer than 5 micrometer particles.

We also believe that the FDA has an opportunity for a method of analysis of a bulk material, that there is no reason to apply a method that was used for air sampling and environments known to contain asbestos to bulk analysis, that that leak is not necessarily warranted; and we urge the FDA to think creatively about what else they could do to try to develop a method in bulk -- criteria for bulk materials.

We agreed that false positives by just simply conventional counting can be enhanced by using more than one type of instrumentation. Polarized light microscopy is an advantage over phase contrast, that electron microscopy gives us another set of data by which we can make the analysis; and so I think we concur with what was discussed earlier. These -- the analysis would benefit significantly in bulk materials by heavy liquid separation, that we should use it. We use light microscopy. It should be polarized light microscopy.

We agree that we need -- if we're using electron microscopy, we need to establish a set of data, a certain number enough to feel that a mode has been established in width. So we measure a large enough population in order to establish a width mode so that that can be compared to known asbestos populations to enhance the certainty of the definition -- of the identification.

We had, I thought one, a very interesting discussion. It was a little bit outside our direct charge, but the question would be: At what level can we tolerate a mineral fiber in talc?

And I think Martin had a really good idea to use some of the risk assessments that have been done at Libby. We know exactly what Libby looks like. There's enough information in that analysis that they establish a safe level and that that might be used to help establish a tolerable limit for analysis, and an analyst has to have a detection limit. They have to have a level below which you can't prove the absents, and so we need something. We need some limit that we work toward in the analytical community no matter what criteria that we apply.

Anything else? Anybody from our group, again? Okay.

(Applause)

MATT SANCHEZ: All right. I'll tell you excuse my computer up here. It's limited space, so I took my notes on here.

I would like to excuse Brooke Mossman. I'm pitching when you can go to her as a co-moderator of one of the sessions, and then Brooke Mossman had to leave to catch a plane, so I'm -- I don't know. I'm just pitching and gone. (Audience laughs.)

The goal that we are given, which I learned about two days ago, was to establish a consensus on the interpretation of microscopy measurements for mineral fibers in cosmetics containing talc. I would -- fellows kind of liked my show. There was a lot of give and take with the participants. I'll do my best to summarize kind of what I thought I said and then also based upon some of the questions for those that were in the other panel -- or in that one meeting.

Before I do that, I would just recommend, if you haven't yet, there have been two stimuli articles published by the USP, the different expert panels working on testing talc for asbestos. I think it was -- the discussions in both of those are very relevant to everything we've discussed today, and it also gives an idea of the talc expert panel, which is working on analytical methods, the direction we're going. There's some information about where we're going with that, and we'll be more forthcoming, too, in the coming year I'm sure.

One thing that I noticed from the morning sessions is nobody defined a mineral. I found that interesting because in any of the interpretation of microscopy data, or any analytical data dealing with minerals, you need to make sure that you've collected enough data to identify them. So this is a basic working definition of the mineral. This is where you get "a natural occurring solvent." It's going to have a crystal structure. It's crystal in it. It's gonna have a chemical composition. You can measure something that's consistent. So depending on however you're looking at the sample, whatever kind of technique you're using, be it XRD -- XRD's not going to tell you anything about the composition of what you're looking at. It will tell you what crystal and phases are present. When you're looking at PLM, PLM's not going to tell you anything about the composition directly. Based upon refractive indices in the amphibole, you can make some inferences.

There was a lot of -- you know, Ann rightly pointed out that anthophyllite and thallophyte, PLM, that's child's play to tell those apart by refractive index. However, I mean, you move into things like tremolite and anthophyllite, if they're not asbestiform, you're dealing with an extinction-angle difference. You can tell them apart by the distinction angle, otherwise you can't.

When you're dealing with a phase like cummingtonite and actinolite, you're never going to tell those apart only by optical data. So if these specific mineral species of interest are important, the optical data could get you pretty far; but if you're -- you may be assuming something incorrect if you just call it actinolite. There could be something else. And I will say that in historical talcum powders that I've been testing over the past year, we are finding cummingtonites that historically were reported as actinolites and tremolites. So that is a -- from a historical perspective, that is something that is real.

And so just moving on, when you're -- so when you're evaluating data, it's critical to understand what these instruments can and can't do on identification. I spoke -- I'm trying to think it here. So sorry. I'm gonna follow my notes.

One of these -- we were pushing for in the USP expert panel -- maybe I'm speaking for them, but what

I'm trying to push for is the data that's reported with any test report would contain all the information necessary for third parties to be able to independently verify the results. What that means is, if it's the PLM testing, there will be photographs of the particles and plane-polarized light in different directions with the -- so you can see the Becke` lines or dispersion stain colors, however you're doing that, where you have imagines showing what the extinction angle if one was observed was, when you have imagines to see what it looked like, you know, signing and longation, all these different measurements. I require that those things all be reported because through all those pieces of information that an analysis is supposed to be doing, you can then understand what the data actually means and whether there's been misinterpretation on the laboratory side.

The same holds for any kind of a TEM analysis. The different issues with TEM make it much more difficult. They're not more difficult. I know it was said earlier that somehow PLM is not sophisticated, or it seemed to be implied that, and that's just not true.

Minerals are very complicated. The technology and the science and the physics behind polarized light microscopy are also very complicated. They're very robust within their limitations.

The same goes for TEM. TEM has very wonderful things that it can do. Martin Rutstein mentioned this idea of this 5.38 row spacing by, you know, TEM analysis to somehow confirm an amphibole. Talc has that. Sepio has that. There's a -- any bio pyro glass (ph) -- that's a new term for everybody -- will have those 5.38 in row spaces. That does not make them amphiboles. That does not make them asbestos.

So whenever these issues are coming up in TEM data, the SAED data that's collected must be robust enough that you have zone axis to fraction work -- and this is all spelled out in old documents from the EPA. This is also spelled out very precisely and good by the ISO Methods by using TEM, but when you need that zone-axis work -- and then the zone-axis solution needs to be specific to the mineral you're identifying. There are a lot of zone axes for different minerals that will be the same, so unless you have a unique solution, you cannot say you've identified that mineral. A caution -- a cautionary note, that most -- I can't speak -- in my experience, I'll leave it at that, a lot of asbestos testing labs by TEM only have crystal structures provided to them through NVLAP which does not include the crystal structure of talc. So how is the lab supposed to analyze talc for asbestos if they can't differentiate by electronic fraction talc and anthophyllite? I'll just leave it at that.

There was a lot of comments from the audience there. The questions, a lot of them revolved around almost like surrogate techniques to measure for asbestos content or amphibole content. One of the discussions revolved around using, you know, calcium as a tracer for maybe a tremolitic or at least a calcic amphibole. I did my best to try to deal with those issues. You know, talk about using iron. There's just issues if you're trying to do a certain chemical solution for these things, and I hope I explain this well enough that that was clear. I think we're stuck with doing microscopy on individual particles for the most part.

Some of the discussion dealt with the quantification revolving trying to do techniques to concentrate, like, amphibole phases from talc, which can be done in a variety of ways. There's pros and cons to doing that, but I tried my best to discuss what those are; and really, I think from an idea of getting better quantitation, I think there's a lot of merit to doing concentration techniques once you've identified whether something is there to know how much is there.

But you know, for an example, if you take 10 milligrams of talc, put it in a heavy liquid separation and, you know, do your thing and then look at the residues, that's the same as just looking at that 10 milligrams of talc but actually by PLM, which you can do rapidly and quickly. So there -- but from a quantitation perspective, to be able to remove the nonamphibole from those components, you can get a much higher idea of the quantitation, get a much lower -- much more sensitive burden. Accurate quantification is best by using those kind of techniques at the expense of, you know, doing nothing about chrysotile, if it is present or not.

There was a lot of talk about the idea -- especially from the FDA groups, there was an idea of, you know, having a rapid and also reliable testing and screening of these materials. My recommendation was for rapid testing, I think PLM is the best. We can do it on site if you were equipped to do it, but again, I agree with what was said earlier. I think doing multiple approaches is necessary here. There's a lot of -- a lot of nuances, and having other techniques, they complement each other. Where you have contradictions in the data, you need to resolve those contradictions, and a lot of times other techniques will be able to allow you to do that.

There was also some discussion of the cosmetics, and I think Frank Ehrenfeld already mentioned that -- the idea of removing, you know, waxes or binders from them. The amp flows are there. I think that would have to be done before you analyze reliably. Those things could mask and make it difficult to measure pertinent properties of those particles for identification.

I think I -- I think that was all my notes I had. I don't know if anybody that was in the group had anything to add. Did I miss anything important?

AUDIENCE MEMBER 3: Ross (ph)?

MATT SANCHEZ: Yes.

(Crosstalk)

AUDIENCE MEMBER 3: Were you enshrined in doing much with UBSD?

MATT SANCHEZ: Yes, we have.

AUDIENCE MEMBER 3: How is that going?

MATT SANCHEZ: I mentioned UBSD in the session. It's going well sometimes. The beautiful thing about UBSD is it either works right away or it doesn't work at all. The other issue with UBSD techniques is it's very dependent on anything on the surfaces.

AUDIENCE MEMBER 3: Other than just --

MATT SANCHEZ: We've been doing them -- it's best to do them uncoated, so we haven't --

AUDIENCE MEMBER 3: No. I mean the ion sputtered.

MATT SANCHEZ: Oh, we haven't got that sophisticated from that perspective. Most work that

Brian (ph) did for his PhD work was using filter preparations and then using geometry is where they were actually transmitting with the transmission -- it's not back scatter anymore but it was a transmission mode for the diffraction pattern generation. We've been trying to take that into -- what we're doing now, we're isolating individual particles that we see, like, on PLM, removing those, putting them on the SEM, getting the compositional information, then obtaining the diffraction information at UBSD; and we're probably about an 85 percent success rate doing it that way. And we've seen some -- yeah, well, we can talk about that later, but -- so we're having success there.

One of these we're trying to do is actually tie in the UBSD to the automotive analyses on SEM, but we're not doubting much -- we're having difficulties at that. That's far off, I think, before we can merge those technologies.

AUDIENCE MEMBER 4: Have you had success with all the different asbestos types or --

MATT SANCHEZ: No. I would defer to Brian's PhD and publications. Brian Bannon (ph). Sorry. He's a colleague of mine at RDAG Group. From my recollection they -- there's issues with the -- there's a few issues. When you're using the transmission mode, you have much better spatial resolution; but if the individual fibers are very, very fine -- I don't remember where that was, whether it was .1 microns; and then for somewhere, there was just no signal from them -- the UBSD technique.

It does not work at all with crisapa (ph) because of that scrolled structure. It just looks at more of just pretty much IBDSD work, but for, you know, single crystals of amphiboles that are, you know, big enough for the spatial resolution to work, you can usually get that from that, assuming there's no coatings or something on the surfaces.

AUDIENCE MEMBER 5: You mentioned cummingtonite. On the TEM, is that just too complex or too similar to, you know -- can you still do diffraction there to identify them?

MATT SANCHEZ: Well, absolutely. I think the -- cummingtonite, for those that don't know, it's a magnesium amphibole.

AUDIENCE MEMBER 5: So --

MATT SANCHEZ: And the number of the formula would be $Mg_7Si_8O_{22}OH_2$. So compositionally it would be the same, or potentially the same, as any anthophyllite you would encounter. The difference between them is cummingtonite is part of what's called a monoclinic -- it's part of a monoclinic system. It has different -- it has a different crystal structure. Because of that, it has different diffraction properties than anthophyllite. So if you're doing the electron diffraction correctly and understand the differences in the space groups, you can make those distinctions whether it's an orthorhombic amphibole or a monoclinic amphibole. This is not something that is routinely done by any laboratory that I know of in the asbestos-testing world.

AUDIENCE MEMBER 5: Pretty straightforward for anthophyllite. It's orthorhombic. Cummingtonite, its structures collapse because of the iron in it. It has more iron than anthophyllite.

MATT SANCHEZ: What do you mean? Well, you still have to collect data and make the measurements and do the indexing; but the real difference there is -- the important differences are the differences in the space groups between the monoclinic amphiboles and the orthorhombic amphiboles.

AUDIENCE MEMBER 5: That's what defines them.

MATT SANCHEZ: I'm sorry?

AUDIENCE MEMBER 5: Yeah. That's what defines them. That's what differentiates them.

MATT SANCHEZ: Yeah. But the issue is understanding what those are and how those -- and how those result in the diffraction patterns to make the appropriate determination. I think that's beyond my topics here today but --

AUDIENCE MEMBER 5: All I'm saying that there's no cummingtonite asbestos.

MATT SANCHEZ: I don't know. I've never seen it, but cummingtonite is a real -- it's a real amphibole, so --

(Crosstalk)

All right. Anything else? All right.

(Applause)

CATHERINE SHEEHAN: So I think now we can move into the next session, which is questions, discussions for moderators. So I know we don't have chairs here, but moderators now can take questions from the audience.

So any questions, discussion points? Yes, Gary (ph).

GREGORY MEEKER: Did I understand in your group you decided to eliminate any airborne --

ANN WYLIE: No.

GREGORY MEEKER: -- (inaudible)?

ANN WYLIE: In fact, there was discussed -- it was discussed -- we weren't doing the testing methods per se, but it was mentioned by several that aerosolizing the samples might be a useful thing to do.

GREGORY MEEKER: Okay.

ANN WYLIE: Okay. So it wasn't -- but it wasn't our -- that wasn't our charge.

GREGORY MEEKER: Yeah.

AUDIENCE MEMBER 6: So I think we've talked it out, and there's really an uncertainty, problems. I think we discussed this at ASTM and definitely at USP. You have what -- you'll see some of the special, but necessary to keep, certificates. You want a de minimis sample on some of your reference materials, and that's important when you're taking a sample for analysis. Whether you take 10 milligrams or 1 milligram, are they the same? You have to establish that somehow, somewhere that when you take on a semblet (ph), if you don't do duplet, triggerclet (ph), or even for analysis, in order to rule out and analyze it, we have to also approach it from that perspective. And you can say, "Well, it's a fine cosmetic talc or pharmaceutical talc." Okay. Granted that helps in some situations, but if you're looking at maybe the courser talcs, you do have a situation where you have to think about how you're subsampling and what would really be of the de minimis sampling before you put it all on diffraction, PLM, or Tega (ph). So I just think that should be brought out.

CATHERINE SHEEHAN: I'll give you mine just in case.

MARTIN HARPER: Sure. I got a couple of comments. And one is the availability of proficiency test samples. I mentioned the HSE's schemes that they occasionally have talc in -- as the material; and I've mentioned also through ASTM that there's a couple of initiatives to do some inter laboratory studies, but they like you to be one-offs, I imagine. Now, it's perfectly possible to go along to a PT producer in the US and request a PT sample be added to one of their programs. In fact, I'm thinking of the American Industrial Hygiene Association, that bulk asbestos proficiency testing program. It's -- you know, their provider is similar to the, you know, NVLAP provider. I mean, if you wanted a proficiency test sample of talc contaminated with different materials at different levels, these can be put together. I mean, obviously there's a cost involved in the start-up. You know, there's a cost involved in participation in the program too, and American Industrial Hygiene Association, pack, LLC, may be willing to invest money in the creation of the samples, knowing that they'll get it back from the participants later, or there might be, you know, a government agency that would, you know, put a grant together to enable them to get them. I think it's a really, really useful thing to do because labs need to know what their capabilities are -- what their true capabilities are, and you just can't get it by guesswork.

And as it corroborates with that, I also want to ask that if anyone has, you know, an electron microscope with an EDS, please, please calibrate it and calibrate it on the right kind of materials. You know, reference tremolite, reference actinolite, and please check the results of those calibrations because, you know, I've seen results where the actinolite calibration stat, it was off by 20 percent from 30 percent from the reference composition in the missed sample. So you know, this is something that I beg the labs to do.

CATHERINE SHEEHAN: Is it on her?

GREGORY MEEKER: Could I just -- I'll walk through quick. He got EIRONG glass -- EIRONG glass, secondary stick will do for SEM.

AUDIENCE MEMBER 7: Martin, to that point, Session A, we talked about standards as well, on the calibration standards but also reference standards, of course; and our biggest obstacle, perhaps, was the fact that -- can we get standards formulated to match a cosmetic product? We can get Loan Pine. We can go and -- Money Lab's represented here today and others that are at least of that status would, you know, have in their library of standards all these minerals; but I don't necessarily have something that I could call a reference material for a base, foundation, cosmetic, something or another or -- so either can the industry -- so can USP say, "Hey, manufacturer, can you supply the base formulation of this stuff and then can it either be spiked or -- we're looking for that bulk matrix material, not just the mineral fiber itself."

CATHERINE SHEEHAN: Happy birthday. No? Okey-doke.

AUDIENCE MEMBER 8: Regardless of the chemical composition, the various amphiboles and talc and things like that, Matt, I believe you mentioned in our session that there was a study that looked at the general elemental composition of various talcs around the world. Is that the only study available on that subject?

MATT SANCHEZ: I think it's the most inclusive for sure. I know in the -- what is it? The International Agency on Research for Cancer? I don't bet that -- they had -- they had some bold compositions presented in there from citizens from different top areas that produced, but with Marian Dosone (ph) at the Smithsonian Institute, they went to different talc mining areas; and other gentleman researchers was in academics and did a lot of work in talc and assembled a huge collection of talc from all over the world, different mines; and they made a first passthrough that, characterizing those things, bulk composition and some other work using both XRF techniques as well as EPMA or electro microprobe analysis. And they did some cluster analyses in trying to look at some correlations in that paper, but that's the most widespread study I know, gosh, from everywhere, as many locations as possible.

AUDIENCE MEMBER 9: Roughly, what sensitivity do those methods have?

MATT SANCHEZ: I don't know. They did run everything by pattern straight fraction as well to identify the mineral phases, but then they were going through and doing -- it will be sold out for -- the chemical analyses, I don't recall, but they were doing a lot of trace element levels down, parts per million, maybe even parts per billion levels. They were using the Research Institute over at Washington State University of Pullman to do a lot of elemental analysis that way on the bulks.

When they got into doing the microprobe work, it was -- those would have been particle specifics that they would have identified beforehand; but as far as the chemical compositions, that's very precise data of a large suite of both major and minor and then trace elements.

AUDIENCE MEMBER 9: Thank you.

CATHERINE SHEEHAN: All right. Were there questions? No? Going, going, gone. Okay.

So I move to close the session if nobody else has further questions, and we can now go into the closing remarks and next steps.

So these are my closing remarks, not USP's, but my first closing remark is I wanted to thank everybody that has come to this meeting today representing us from industry, regulators, and academia because I think it really did give us that brainstorming at first. There's a lot of themes, definitions, and measurement, structure, composition, shape size. It was a soup of nomenclature, and from that, there was a lot of questions I felt, and I thought they were very fundamental questions. Do we have a definition of what we are testing for? We just heard many, many times, "Define the mineral. Define asbestos. Who owns the definition?" We talked about revising the definition. Perhaps it may need to be revised. Secondly, in terms of definitions: "What are we really looking for? What do we want to test for?" I think these are fundamental as we go into the big task of developing method and limits.

I think the second theme common throughout the morning session speakers and the sessions was that we were really looking for a standardized approach that labs can follow. I think the consensus was that there is a toolbox out there. No one method will suffice, but which ones do we used and for what? We also talked about what is the right reference standard, that that was important as well.

So there were my general closing remarks in terms of what, you know, we discussed both in the morning and afternoon.

So in terms of, I think, next steps -- because I believe there's a lot of unanswered questions of those that I mentioned; but to start the ball rolling, in terms of next steps, I think it's important now that there's a lot of information shared here, a lot of critical discussions that will move us on this journey. But the summary notes definitely, in terms of the moderators and the speakers, the presentations from this morning, the summaries from the breakout sessions, definitely they will need to be posted on the website. My information here is that has to be finalized by January 5th. I do not know when they will post, but January 5th is the deadline for speakers and moderators to get summary breakout sessions to JIFSAN.

Another next steps is to make sure that all slides that were presented in the morning session and also as part of the breakouts that they will be provided on the website.

And then third is kind of an open question. You know, what does the audience think should be a next step? You know, what have you learned from today that could help us move to the next step. So I'm going to leave that as kind of an open question to the audience in terms of next steps because I think it's important to hear it from all stakeholders.

Any thoughts? I think I see one -- one show of hands in the back row. Yes.

STEVE: About PLM. Just a thought and moving into (inaudible). Just a thought that be aware that there are standard development processes currently taking place concurrently and that my belief is that everybody that's involved, and certainly all the folks in this room, ought to provide comment when those -- whenever those standards publish to make sure that we get the best -- ultimately the best standard. So that's just a reminder to be on the lookout when things publish to read them and comment on them.

So that -- thank you, Steve (ph).

And I don't know if anyone's familiar here with the USP Standards that are in process, just to follow up on that comment. We have a public comment period through proposing -- our standards are official, so if we make any changes to these official standards, we have to go public and we have to solicit input comment feedback.

Given the number of stakeholders that are involved and the impact of us revising the USP Standard, my thoughts are that USP could probably convene all stakeholders prior to the publication of this standard so that we could get input before we actually propose it, because it pretty much -- once it goes into the PF, the formal PO forum, you have a 90-day comment period. The expectation is that that will go before the counsel of experts for approval and ballot to become official. It's very difficult when it gets on that track, so I think it's important that we get some feedback as Jeff (ph) said, that we do this publicly and we invite all stakeholders in to give us input on where this revision is going. So --

AUDIENCE MEMBER 11: Kind of getting back to the question about, you know, what to test for and the definition for asbestos. Based on some of the -- what

I've heard here is that there are others compounds that don't presently fall under the asbestos umbrella that have similar toxic and carcinogenic effects and should those compounds be now pitch or clustered underneath the umbrella of asbestos, or do we need to come up with a different term than "asbestos" than what we're using right now? Can it be better descriptive?

CATHERINE SHEEHAN: Martin here? Martin?

MARTIN RUTSTEIN: This is artificial, and I'm speaking for myself, but to avoid this dangerous debate upon what EMP might be out there, I believe that my colleagues are moving in the direction of using regulatory asbestos as the group of materials for which we will have analytical method and that will end that. If we were to invent -- if we were to develop methods for these other materials, which may or may not be hazardous to human health, we would be going into major uncharted territory, and we collectively didn't think it would be prudent at this time.

CATHERINE SHEEHAN: Thank you, Martin.

So any other thoughts? Next steps.

AUDIENCE MEMBER 12: Yeah. I was gonna add to what Martin just said that there was -- that we have been considering that the methodology must develop for the determination of asbestos as currently defined may be applicable to other mineral vipers in mineral counters.

MARTIN RUTSTEIN: I left out one thing. I'm pretty sure in STEM Article 1 we said minerals -- other minerals that have known hazard.

AUDIENCE MEMBER 12: Right.

MARTIN RUTSTEIN: I think we included that one. So that's our ruling. That would be in there if the evidence is pretty good for it. Like winchite (inaudible).

CATHERINE SHEEHAN: I think that's in the STEM article, Martin, right?

MARTIN RUTSTEIN: In the previous STEM articles.

CATHERINE SHEEHAN: I think -- I would advise to -- yeah, to -- that goes into the details.

MARTIN RUTSTEIN: That's posted. They really should read it.

ANN WYLIE: As was pointed out in our session, the tolerable level is a policy decision, not a scientific decision. And we need a tolerable level because an analyst can never prove the absence of something, and a tolerable level gives an analyst a target, designs techniques designed to meet that level; and since that's a policy decision, without that, I think we really have a problem. So that's an -- FDA needs to provide that policy decision on what level the analysts should aim their methodologies.

CATHERINE SHEEHAN: Thank you. Okay.

MARTIN HARPER: If I might just add --

CATHERINE SHEEHAN: Okay.

MARTIN HARPER: -- to that. If I may just add to that that the tolerable level may be different depending on whether we're talking about, you know, bulk talc that's feeding into a product line or a final commercial product. Just a thought kind of.

AUDIENCE MEMBER 12: And then, again, we have to come back to, well, what's detectable and what's tolerable. If we look at the high court of history, when we developed standards in the past, the regulatory agencies have often said, "Anything that's detectable is unacceptable." So if you have a zero-tolerance policy, then you have to define what your detectability is, and that becomes your edge point.

GREGORY MEEKER: I assume we're talking about a tolerable level with respect to health?

AUDIENCE MEMBER 12: Well, that's why we're really here.

GREGORY MEEKER: Is there a tolerable level with respect to impact on industry? Should we consider that also? Because it always seems to fall on the health side, and I don't know.

MARTIN HARPER: That would be more like an OSHA regulatory process where the socioeconomic impact has to be dealt with --

(Crosstalk)

GREGORY MEEKER: No, not worker health. I mean, the impact on the industry.

MARTIN HARPER: Yeah. Well, you know, OSHA's standards are set taking into account what's achievable by industry. So for example, the methylene chloride standard allows a risk above what they would like to have, simply because the furniture refinishing industry wouldn't exist without methylene chloride and it can't really be controlled to the level they'd like to control it. So yeah, I mean, there's definitely precedent for not setting everything entirely on the panel.

AUDIENCE MEMBER 13: From an FDA perspective, we want to thank you for all the thoughts and all of the hard work that went through this morning as well. And there's a lot of food for thought for all of us, not just at the FDA but all through regulatory agencies that are here and a variety of governmental agencies that are present today as well to go back and think about what all of our discussions mean for the products that we all regulate and have some jurisdiction over. That you.

CATHERINE SHEEHAN: Any other comments, suggestions on next steps? No? Okay.

So I believe the meeting is over, but I would like to give a special thanks to -- I'm gonna call out everybody because I think everybody did a really great job. Presenters: Brad, Greg, Martin, Martin, Brooke, and Ann; and then the afternoon session, the co-moderators: Robyn, Frank, Ann, Art, Brooke, and Matt. Thank you so much.

(Applause)

And a final thank you to JIFSAN staff, and a special call-out to Veronica -- sorry -- Nora Petty for the assistance in getting the moderators and speakers together and trying to get this altogether.

(Applause)

Thank you.

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December 9, 2018

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