activity. The third is plasma membrane permeabilization. The fourth is membrane lipid -- my notes fail me here. Actually, disruption of the membrane lipid structures so as to render the cellular structure of the microbes non-viable. Yes?

DR. EDMISTON: The charge of this Committee is to provide the FDA with guidance in terms of how these devices should be evaluated, and you brought up a point which Mr. Heinbuck actually brought up earlier in terms of the impact of these devices in both a aqueous and dry milieu. Because we're going to be discussing possible performance criteria, do you think as part of the application process there should be documentation by industry in terms of the activity of these devices which will be impregnated in both an aqueous and dry milieu?

MR. PAGE: I do believe that, basically, simulation of conditions of use, if that is your question, is absolutely essential because, otherwise, the testing, whether in vitro or clinical, is simply not a realistic reflection of what the device can do. I mean, the FDA has essentially made that point clear

to us, and we feel that it's absolutely necessary. In other words, what happens in vitro is not necessarily a reflection of what will happen in situ unless aqueous versus dry conditions are simulated. We feel that, yes, that's very important. I don't know if that answers your question.

DR. EDMISTON: It does. Thank you.

CHAIRMAN JARVIS: Are there any other questions?

DR. GORDON: You'll excuse me, as an infectious disease clinician, the skeptical nature of the resistance issue.

MR. PAGE: You'll excuse me as a non-clinician because, you know, I certainly welcome your question as a practitioner.

DR. GORDON: We heard for years and years how vancomycin, also with multiple mechanisms of action, protein synthesis and so forth, would be very difficult, or some people went further than that for it to develop resistance, and now it's a huge issue worldwide for us, and we have vancomycin-resistant not just Enterococci but Staph. aureus.

MR. PAGE: Right.

DR. GORDON: When you guys would take a product like yours where you may not have demonstrated a significant amount of resistance yet, would you take that upon yourself to warn about this issue of resistance developing? Because I really don't think it's going to be a matter of if it's going to happen. It's going to happen. The bacteria are just too many and too adaptive.

MR. PAGE: Okay. First of all, to the extent that it would be an issue, we would certainly agree to warn. We believe, basically, that it's very important not to try to out-market our technology in a way which is irresponsible. So to the extent that that is an issue, you know, we actually would be interested in warning about it. I mean, the experience with this naturally-occurring form of copper, however, is that it remains effective against a wide variety. Basically, every kind of gram-positive and gram-negative bacteria that have been tested against it, it remains effective against. And since it's naturally occurring, it's been around in

the biosphere for as long as it has, I mean, once again, I wish our microbiologists were here to specifically address your question. To the extent it was an issue, I think we would want to address it. And to the extent you're skeptical about the effectiveness, about the resistance issue over time, I mean, we would want to sort of get together with you and demonstrate, essentially, the mechanisms of potential resistance versus tolerance.

It's tough to answer in a vacuum. My understanding being, you know, from our scientific team, is essentially that the likelihood of engendering resistance is extremely low. And we documented that in our written comments to you and to the FDA.

CHAIRMAN JARVIS: Thank you. Are there any other questions? Go ahead.

DR. AZIZ: Is your product or the technology of this product being used in non-medical devices?

MR. PAGE: Yes. Actually, copper oxide has, for decades if not much longer, been used as a

colorant. It's a fabric dye, as well. And before, you know, it's antimicrobial properties were discovered, it was used in that way very widely. And today it's also being used more in the Environmental Protection Agency sphere for a number of sort of fabric protection and odor-control uses.

I should add that some of the mechanisms are similar to silver, which has been looked at. Silver was mentioned earlier, and they're both metals, and some of the mechanisms are similar.

CHAIRMAN JARVIS: Thank you very much. Our next speaker will be Dr. Wava Truscott from Safe Life Corporation. Dr. Truscott?

DR. TRUSCOTT: First of all, I'd like to thank the panel, the FDA, for this opportunity to speak. I'm excited about the interest in antimicrobials and PPE, and I believe that the time is very significant, as the many types of threats, whether it be bioterrorism, whether it be developmental antibiotic-resistant organisms, or just emerging new organisms as we push upon the habitats of our joined existence on the earth with our microbe

fellows.

I am an employee of Safe Life Corporation and, thus, have that bias. The triosyn iodinated resin is incorporated into disposable respirators, but it is also incorporated into many other products, as we'll hit very briefly at the end.

What I'd like to do, since the focus is on respirators at this point in time, is to talk just a moment about air filtration and its appropriateness as far as testing and how you evaluate it with or without an antimicrobial and the important factors, as Dr. Heinbuck was noting as well.

First of all, just looking at a microscopic view of a typical disposable respirator filter media, you can see it has strong bounds around the outside, and on the middle it will have very, very, very fine filter media called meltblown usually, and that particular meltblown is about one-third, each of the fibers, one-third the diameter of a hair, of a human hair. So it's very delicate. It's very important that it be that thin as far as capturing mechanism in a torturous pathway as a mechanical

filter, as we'll start our discussion about. And, of course, the density is going to be very critical as far as the efficiency of the filter.

This first generation is a mechanical filtration first studied in-depth in 1942 during World War II for smoke inhalation for the troops, as well as other particulates on the field and was a truly, if you put a cotton across your face in a particulate-laden area, this would be the type of capture you would have. And it's divided into three forms: gravitation or segmentation, or interception rather. All of these can be applied. But also impaction are for particles that are above .3 microns.

So if I've got a filter, this is basically what's going to happen. I've really gotten into PowerPoint in the last two years, and this is so much fun. But for the impaction, of course, just as it says, it runs into something. Its inertia is stronger than following it around the curve with the airstream, which would have gone around the fiber or does, thank goodness, or we wouldn't be able to breathe through it, and similar to the air going over the wing of an

airplane, a jet.

Now, the next one is unique. This is diffusion. Diffusion works on things that are smaller than .3 microns. It's like when my child was very young, ADHD, he's got that attention deficit disorder and hyperactivity, as he is beat around all over the place by the different molecules in the air, Brownian motion. And he acts, it acts as a much larger type of particle and is trapped in that way by the different fibers as it tries to get through the torturous pathway. Okay. That is first generation. That is mechanical filtration. Like I said, that was in 1942 studies and has been studied, of course, significantly thereafter.

So what's the hardest to filter particle size for mechanical filtration? In other words, what particle size would penetrate the most readily? The most penetrating size then is right between the two of those. It is .3 microns. It's the most penetrating particle size for mechanical filtration. NIOSH appropriately chose .3 microns for respirator certification based upon this mechanical filtration of

particles. It makes sense. Thus, you really do understand the weaknesses of that particular filter.

Test parameters for an N95 respirator would be .3 microns. Salt particles for 20 minutes at 85 liters per minute, which represents a heavy labor type of inhalation/exhalation activity. Of course, that is an average, and it will reach peaks upwards of two to even sometimes three hundred and peak at active activities, running up the face of a hill and that sort of thing.

However, we have now gone on to second-generation filtration which is adding a static charge to a device or actually to the material that the device is made from. This is a charge-induction machine. It can be done about five different ways with a corona charge or various types of inlaid charges, some of which will be stronger than others, will track better, will hold the microorganism better, and, in other cases, it will actually be less durable and be prone to losing that charge more readily. So you will have variations between different materials with this charge. You can see in this picture, the

enhanced filtration or the filtration, how even little tiny fibers can hold on quite tenaciously.

After the material is charged, its term is actually electric media. It's now utilized by just about all manufacturers and most manufacturers, at least in the United States, for disposable respirators. And there are many methods applying, as we talked about. Some are probably more appropriate than others or stronger than others.

Now, let's go back to our pictures. We still have mechanical filtration. That's already part of it. We're just adding the electrical charge. So here's the electrical charge, and when the particles come, large or small, they are attracted, as you see here, even away from its directed path in the stream of the air current.

Now, looking at this graph or this chart, you can see that we have, at the bottom would be the mechanical filtration with the most penetrating particle at .3 microns, that first generation. Second generation, electric media. You can see that the most difficult to capture, the most penetrating particle,

is actually 0.05 to 0.12 microns by most studies that have been performed. So although it's better at filtering everything when it's got an electric charge, the weakness of the material is at a different size rate. And, unfortunately, that size rate is also the size of viruses and small bacteria, as you see here, that which we are trying with our PPE to protect against. And they are just about, even the viruses, just about everything. I mean, of the viruses, they are practically all smaller than .3 microns.

Okay. Now, should the media, that is both first generation and second generation, so it's electric plus physical, should be tested with .5 to .12 micron particles. The size particles, they behave the same as bacteria. And in a world where you're not looking at antimicrobials, either one should show you about the same performance. About. There are differences in microorganisms: stickiness, slime layers, lost capsules, and things that make it slightly different.

I think it's important to note, look at all of those 2006 articles and 1999 articles, while

all of these are studies that are showing that it should be moving to the .05 to .12, slight variations with each of these studies, that these smaller size range, rather than the .3 microns.

Now, I'm going to come up with a new concept. It says I'm set up for migration and dump. And this is a moisture of an arctic visual. After a respirator has been used for a while, fibers will begin to absorb the moisture from exhalation. That's just a visual of one blow-out. The air that we exhale is full of moisture. Moisture accumulates to form minute droplets within the filter on the fibers. These fibers, the electrostatic charge begins to decay with the moisture. The efficacy of the microbe retention strength is also decreased. Then filtration actually improves for a short while. You've got the bump of the droplets throughout the fiber. It will actually improve the filtration after the slight loss in electrostatic cling just because you've got an extra physical entity there that will capture some of the viruses or bacteria.

And so the journey begins. As we look at

it a little bit more closely, a respirator, as we saw before. And, finally, at the fibers we can see the live organisms are trapped, but they are alive, and that's something we tend to forget on respirators or masks filter materials.

The droplets continue to expand soaking off more and more of the viruses and bacteria already retained on the fibers. Remember they are still alive. And here is the droplet that has formed and is growing. The growing droplets reach a critical mass and are pulled into the air stream rather by exhalation burst or inhalation burst, where they may be either impaled onto another fiber, droplets break apart, which has been studied by Spurney and by Fuchs and also, more recently, by Kowalski. They pushed back into the environment by exhalation or inhaled by the wearer by inhalation.

And if in absorbing out those organisms, obviously they are going to be present in that droplet. If the person is present, where is it going to go? And when we talk about viruses, we talk about low-infectious dose rates.

So how do you ruin an electric charge on filters? Well, I already alluded to one: water and moisture is going to start to decrease its effectiveness, decay it. So will time. So will heat. So will oil-based products: diesel mist, vaporized fatty tissues. So will alcohol. So will most disinfectants. So when we talk about spraying something with alcohol or spraying something with a disinfectant, it will usually decrease rapidly the effect of the electric media, thus decreasing its efficiency. It's overwhelmed with capsule particles. Something you can just take home and try for yourself is your Swiffer. Your Swiffer is an electrostatic charge. Just kind of ruffle it up like you're supposed to, and you can see how it picks up, sprinkle a little bit of flour, and you can see it on a dark surface how beautifully it picks it up until you spray a little of disinfectant on it or a sanitizer, and it will rapidly lose that ability to pick up even nearly as well.

The electrostatic charge degrades further, decreasing the efficiency of many disposable

respirators. The orange line is an off-the-shelf respirator, and you can see it's starting to decrease. It starts up at 99 percent almost, and it comes down within three hours to 92 percent, improves a little bit with those droplets that were talked about, have been formed, it's trapping some, and then you have a sudden drop in efficiency as you get the critical size of the droplets that are now being inhaled. And at six hours, it is down to 84 percent.

Those hours seem a long time, and, as we're saying, you don't wear these things very long. But if you have SARS, if you have an avian flu, if you have anything that is working out with poultry or some farm, respirators are our first responders in search and rescue operations or military when you're waiting to put on your full gear or activity, it may be much longer than the short time.

Active protection with the antimicrobial technology that I'm addressing, but I would like to make it general for others as well, could be placed in many places. Our particular antimicrobial is in the center between two different filtrate medias. Triosyn

is thermally fused into a specialized polymeric resin of polystyrene-4-methyltrimethylammonium tri-iodide. The electrochemical bond maintains the tri-iodide integrity and sets up a demand release criteria, rather than just leaching off into the area. I2 is then released from the -- so you can see the tri-iodides at the top, three purple little circles representing the tri-iodide, the ugly-looking virus coming towards it. You then have a release of an I2 to the organism, and it works on the proteins on the surface. It is attracted to the organisms. It does not have to come into contact. It oxidizes it rapidly.

And here, just an example of the oxidation. This is a virus, but it could be a fungus or a protozoa or a bacteria and, basically, punches holes in it. You also have the effect on the RNA, the DNA, as far as a steric hindrance, as well, in capability of reproducing, but you've already killed the thing anyway.

CHAIRMAN JARVIS: Dr. Truscott, two more minutes.

DR. TRUSCOTT: Two more minutes. All right. Here comes the fast speaking. Triosyn resin addresses both passing error and microbial dump, so that you have the fiber, you have the triosyn all throughout it on a particular fiber captured organisms on the fiber. As you can see, they will come near contact or not all the way close right next to. This time when the droplet forms, it collects then not the live organisms but the non-viable ones.

So migration and dump is an issue, whether it be in a respirator or be it in a HEPA filter unit, counters the degradative effects as well. You can see that same effect here that the triosyn respirator has continued to function at the same 99.999 percent level in this particular study over the length of time that the commercial one was failing. Here's also a study by the Air Force, and you can see it at 99 percent with the failure of another respirator, commercial-standard respirators, with just the first two generations.

Here it is with SARS. You can see tested by the Health Canada government agency, 3,000, 30,000,

150,000, a total of two hours at 183,000 virions of corona virus with no detectable viruses. Influenza, a penetration with a 95 respirator and a standard respirator. You can see that it continues to stay below detectable levels at a challenge of a million virions. And here, again, looking at the performances up there in yellow, I mean not performance but challenge level reaching about 10,000 and the average is about 5,000 in the error. And over the 24-hour period, the failure or the penetration, I'm sorry, relevant to the orange and the red are standard respirators where the iodinated would be at the bottom at the blue.

Okay. What is the difference? So you've got a few organisms. Here's 99.999 percent. Let's look at 95 percent filtration comparison. If you have an exposure of 100,000 organisms in an area caring for a patient who is sneezing and coughing and very, very ill, the shedding may not be 100,000. But if it is, there would be one through with the antimicrobial treatment, where 10,000 would have gotten through with the standard ones, I'm sorry, 5,000 that we saw in the

previous studies.

Just the various virions. We won't go through them. Viruses, rather, and illnesses they cause. But the infectious dose is what we're focusing on here at 1 to 10, 10 to 100, 1 to 1,000, 1 to 740, depending upon the strains. The very, very low infectious dose rates.

These are just some of the microorganisms that have been tested against the surface and the airborne antimicrobial, the triosyn. You see a lot of organisms that would be appropriate. Some don't seem so but were requested at the time. And here are more for other triosyn products. Quite a plethora.

Toxicological results we believe are extremely important, and we have done those as far as inhalation, as far as contact sensitivities. So I believe that coming more and more to age will be a mechanical physical capture, an electric charge capture, as well as an antimicrobial act of protection capture.

We believe that antimicrobial characteristics should be broad-spectrum activity,

especially addressing envelope viruses, but also bacteria and fungi. Rapid activity are able to interact with microorganisms in the air stream passing at 85 liters per minute is a tall order and a very important one. Bactericidal, not static, as migration and dump phenomenon may place static microorganisms back into favorable human environment and enable reactivation.

Biocompatible at the extended use exposure levels, and then microbial with long-term use history and expectations would be preferable. Not known to instigate antibiotic resistance. Minimal development of resistance to antimicrobial self. Stable and expected manufacturing shipping storage, environmental use conditions. Effective for the entire duration of the use of the PPE, negligible efficiency degradation with time, and acceptable ease of breathing. Antimicrobial not a constant leach-out but instead delivered as needed. Just the comparison so you know that top, this is just a fungi, bacteria, and viruses in the three cornucopias you have there.

The big circle is what you test surgical

masks with. This bottom one just below that is the NIOSH N95 .3 micron. The avian flu virus is about 1.2 microns.

CHAIRMAN JARVIS: Can we wrap up? Any questions?

DR. TRUSCOTT: Okay. We believe it should be tested in that area. And you did ask about the testing. Let me just say this real fast. The appropriate preconditioning is important. .05 to .1 microns entered particle challenge, plus we believe that a virus aerosol challenge with the same controls and parameters very tightly held so that competitors can all compare with each other is extremely important also to show the effect of the antimicrobial. High humidity reflect exhalation 85 liters per minute and 3.4 hours. This is just a chart of the various organisms and bacteria that are small enough to have gotten through a HEPA filter.

Desired claims. You have them in front of you. I won't go through all of them, but there are many claims that we would like to be able to make, such as antiviral, antibacterial, antifungal, stating

that it can hold its percentage rate, and that just some recommendations on, perhaps, how they can be rated in comparison ways.

We'd like to say that it's a bactericidal. Identify with part of the device, and which part is antimicrobial, as stated earlier. Is it on the outside? Is it on the inside? Use terms like devitalize, neutralize, destroy, kill, deactivate, and rupture, which actually are not allowed for EPA. And I won't go on to the rest.

We believe that stopping penetration includes an excellent fit. We need to be teaching the whole thing, exceptional pathogen penetration prevention but also proper removal technique, hand-washing, surface disinfection, and focused attention to appropriate infection-control practices. This should be the responsibility of the manufacturer to make sure that the whole important information is given.

These are the various products that triosyn is already into. And I thank you very much.

CHAIRMAN JARVIS: Thank you. Are there

any questions?

DR. DAVID: You mentioned the biocompatibility.

DR. TRUSCOTT: Yes, I did.

DR. DAVID: Can you tell us what type of biocompatibility data you have identified?

DR. TRUSCOTT: Yes, certainly. We've done oral and mucosal type activity, eye irritation, in vitro cell culture assays, mutagenicity assays, hemolysis assays, skin irritation, mutagenicity, if I didn't already say that.

DR. DAVID: Any long term studies?

DR. TRUSCOTT: Long-term study, the longest we have really guinea pig sensitization and affect on mice when we were doing filtration exercises, but they're not very long term. So not extensive. However, the particular iodine, the I2, is already used for asthma treatment and various respiratory conditions, so we believe we can hold on that. It already has an FDA approval on wound dressings. So it's had a lot of testing that way. Yes?

DR. SPINDELL: Have you actually performed or do you have evidence of a clinical study in the intended use where it actually does decrease infections?

DR. TRUSCOTT: No, we have not done a clinical study at this point in time. It's all been in vitro or surface areas.

DR. SPINDELL: Thank you.

DR. TRUSCOTT: Yes?

DR. ARDUINO: What about people who we know have iodine sensitivities or allergies to shellfish and things like that?

DR. TRUSCOTT: Most of that, as you'll see in Quadier's document that's on the web site, actually addresses that as a misnomer as far as being the myocin with the shellfish, as far as being contrast media with the osmolar D type issues. But what we are doing, because I think it's still a controversy in some cases, is to go ahead and identify those individual physicians who can do the testing with our product to make sure that even people who strongly seems that they are allergic iodine will be fine with

it. At this point, we've not had any complaints or issues.

DR. EDMISTON: Does that specific technology have any application to other masks besides N95 masks?

DR. TRUSCOTT: Yes, it should be very, it should help the efficiency of regular masks, as well. And it's also used in canisters now with the military, or, sorry, task testing for antivirals in canisters. And it's being sold now in Canada as a medical device. It's also sold in Australia, Germany, Italy, and England, and HEPA filtration, as well.

CHAIRMAN JARVIS: Are there any other questions?

DR. TRUSCOTT: Thank you.

CHAIRMAN JARVIS: Thank you very much. Our next speaker is Dr. Stephen Rothenburger from ETHICON. Dr. Rothenburger?

DR. ROTHENBURGER: All right. I wanted to thank the panel for allowing me to speak today. I'm going to take a step back a little bit. I'm Steve Rothenburger. I'm a microbiologist. I'm responsible

for the Product Microbiology Department at ETHICON. ETHICON is a Johnson & Johnson affiliate company, and our primary products are surgical devices. So we are in the implant business, not so much in the gowning and barrier business. But I think a lot of what I have to say today will be very relevant to all the areas that we discussed, particularly the topics discussed by Ms. Rios and Dr. Murphey, because it's really all the same. In a microbiological sense, I think we're talking about environmental control for pretty much all these things.

The assay that I'm going to discuss today is an assay that we developed to evaluate in vivo activity of an antimicrobial suture that we currently market. And the reason, obviously, to do this is because it gets us a little bit closer to the clinical situation and also helps us to validate our in vitro data, which we have an abundant quantity. I think we probably are the poster children for the zone of inhibition testing that was mentioned earlier. We do an awful lot of that. But that being said, we do need to move ahead and get as close to the clinic as we can

in our product development.

So this is my problem statement. I use this in most of my presentations because I think this adequately illustrates what we're trying to deal with. This is Staphylococcus on a suture in vitro, and I think the picture speaks a lot more than I can say to what the problem is. The objective of the assay development that we did was to make an assay that we could use to look at the antibacterial sutures in vivo, as I've already said, and it does support new product development for these kinds of products.

The background of the study. This study evaluated the ability of coated polyglactin 910 suture, which is, essentially viral, as most surgeons will know it, coated with triclosan to inhibit the colonization of bacteria on the suture after direct in vivo challenge with Staphylococcus aureus in a guinea pig model. I'll mention here that we tried a number of models here. This was not a trivial exercise where we just shoved it in and got a great result the first time. For example, we found that guinea pigs work a lot better with Staphylococcus, mice work a lot better

with E. coli. You have to really be careful in the model development because the variability, as you'll see later, can be significant.

This study is published in a public domain in the Surgical Infections Journal, and the references here for use. I have a couple of copies if people are interested in looking at them, but I can't photocopy because that would be against the copyright laws.

The methods. Fairly straightforward method. We had a control suture and one test suture that were implanted subcutaneously in dorsal lateral regions of guinea pigs using a catheter. That catheter is very important here because this allows us to keep very good control of where we put the device, for one thing. But more importantly, it allows us to control where the inoculum goes. One of the big issues that you'll see in the literature as you look up these kinds of models is people have all kinds of ways of inoculating things, and we found it to be very important in terms of the ability to control the experiments to put the inoculum as close to and in as intimate contact with the device as we could at the

time of implantation.

After 48 hours, the sutures were explanted, and the enumeration assay was performed to get quantitative data, as was mentioned earlier. A lot of the data around these types of products when they're first introduced for clearance from the FDA is in vitro, which, in general, tends to be qualitative. We have the ability to do some quantitative data there, as well. But the purpose here was to get quantitative measurements.

The result was that there was a significant difference in the number of bacteria recovered between the study groups at 48 hours post implantation. This was really the purpose of the study. You'll see that there aren't that many animals in the study, and the reason for that is that the statistical driver behind this was to be able to say that we can tell these things apart and that the test article, in this case the treated suture, was significantly different than the non-treated material in the direction that we were hoping to go.

The coated suture provided about a 30-fold

or a 96.7 percent reduction in the number of bacteria. Now, I'll mention that this study is about five years old now and that more recent studies, in fact one published this month in the same journal, we were able to get a three-and-a-half log reduction against Staph. aureus in a plus suture and also a two-log reduction in E. coli. So we are able to improve our technology by the use of this type of method to evaluate its efficacy.

This is a little bit of an eye chart. The main thing I wanted to point out is that the difference between the control and the test is significant and that the variability in the terms of standard deviation also plays a role in the kind of conclusion we can draw. Animal studies tend to have a lot of variability in them, and that's why we chose an endpoint here that was effectively very simple. It was to tell them apart. Is this one different than that one? Is it significantly different, and is it different in the direction that indicates that the performance is what we would expect?

So, in conclusion, the assay demonstrates

a difference in the activity between the treated suture, which was really the baseline data. And the assay also demonstrates that the coated suture inhibited bacterial colonization after direct in vivo challenge with a model.

So I don't know how I am on time. That was pretty quick, I think. But if there are any questions regarding that, I'll be happy to address them.

CHAIRMAN JARVIS: Are there any questions?

MS. KRZYWDA: Could you just give us your opinion on how you would translate this testing to the devices, the gloves and the masks?

DR. ROTHENBURGER: I guess I don't know how you would do it exactly, but I would think that the closer you can get to a model that simulates what's really happening in the clinic the better. And, obviously, guinea pigs are not exactly clinical. Most of our doctors don't work on guinea pigs unless they're coming in to practice their technique. But you could envision actually a, I suppose you could gown an animal or you could put a mask on it and use

that as a surrogate, perhaps. I don't really know. I'm not an animal expert. But the idea really is get the devices in vivo, if possible, because in vitro testing can be very convincing, but it can also be not exactly relevant all the time.

DR. DAVID: And those tests, those studies are all short term, right?

DR. ROTHENBURGER: These are short, and the reason they're short, actually, we talked to our surgeon customers, and we asked them specifically what is the time that you're interested in having activity demonstrated? And, of course, the answers were quite broad, and some people said, "Oh, as soon as I close it, that's fine." Some people said, "Gosh, I'd like to see it three weeks later." But the consensus, the general opinion was, you know, after a day or two, after the wounds had a chance to heal over a little bit and the fiber has all clotted up and everything else, that's what we're interested in because they don't expect any further penetration of bacteria into that wound after the closure has had time to seal up a little bit. So that's really the reason we did it

that way.

DR. DAVID: What is the shelf life for --

DR. ROTHENBURGER: For this? I believe it was launched with a two-year shelf life. The goal for most sutures is to have a five year, but that will be based on stability studies that are ongoing.

DR. EDMISTON: Hi, Dr. Rothenburger. I have a question relative to some of the toxicity issues, and I know you're not a toxicologist, but I know one of the issues and the concerns from a number of surgical practitioners is you take a suture that's loaded with an antiseptic impregnated material of some type and you put it into the wound bed, what impact does that have on the inflammatory and maturational processes associated with wound healing. So I think maybe what you can do is sort of enlighten us what has your experience been with your particular device in terms of looking at the animal studies and correlating that with the post-marketing studies in terms of any toxicity?

DR. ROTHENBURGER: Okay. The toxicity question does come up a lot, and I have a whole bucket

of slides in my bag there. If I had another hour, I would go through them. But the bottom line is this: when we designed the suture and did our initial testing, we are also, of course, required to do biocompatibility and toxicity testing, and we were able to clearly demonstrate through histology and pathology studies that there is absolutely no difference in the biocompatibility of these devices between a treated and an untreated device. So from a cellular level, if you are a histologist looking at these materials under a microscope in tissue, you would not be able to tell a difference. In fact, that was a primary voice of customer from our surgeon partners that they better not be able to tell the difference between this one and that one, or they would have a problem.

From a more general standpoint, in terms of toxicity, we know both from literature studies and other company studies of this material, as well as our own studies, that the suture itself, the impregnated suture, is non-carcinogen, not genotoxic, non-allergenic. The allergy question seems to come up

every time. There is no evidence at all, in fact, that triclosan causes any allergy issue. But in the case of our suture, the way the toxicologists like to say it is if you're allergic to Vicryl itself then you might have an issue with this. But that's an extraordinarily rare occurrence. Does that get to your . . . yes?

DR. GORDON: Did you do outcomes? I see that you did colonization studies, but did you actually do and see if there's a significant difference in how many of them got clinical infections?

DR. ROTHENBURGER: That's a beautiful question. Not in this particular study. We have done studies to try to attempt that. Now, there's two reasons why we didn't do it for this study. One is that we do not claim that in our label, so we did not submit any data to the effect of infection control as a label claim. And that speaks to the information that we heard earlier. That's a different level of claim that we did not attempt with this device.

The second reason that I think we've had a

difficult time with that kind of study, and we do do gross anatomy and also histology of all these samples, as well, although I didn't mention that, is that we're effectively working in these studies on healthy animals, and they do not get infected easily at all. So to actually cause an infection in animals like this, we've had to, for example when we tried different kinds of materials, the inoculum and the challenge has to be so significant that it's difficult to tell whether something like the suture is going to have an effect. So I think that, to your point, it would be great to have an infected animal model, and we continue to strive for that because I think that's what the clinicians would prefer and would appreciate more if we could get it, but it has been difficult to develop.

DR. LURIE: Well, we, in fact, know that different suture materials do have different infection rates, and that's been extensively studied. Is there any human clinical data that suggests that this makes any clinical difference?

DR. ROTHENBURGER: Yes. I couldn't have

said that six months ago, but I think I can say that now. ETHICON themselves do not have any clinical studies that they have sponsored. However, there are at least three independent investigator studies ongoing at the moment. One has been partially published at probably a three-quarter weight point at this point. It was published last October in the Neurological Congress in Chicago. This was a study regarding using a ventricular shunt for hydrocephalus patients. And in this particular procedure, apparently the infection rate is quite high. It's about 10 percent, and that's kind of an ideal mode to test this kind of device. The outcome of an infection is obviously pretty catastrophic if they have to take the shunt in and out of somebody's brain.

So the investigator has a study ongoing with that. And at the halfway point of their study, they examined their data and found such a significant effect, I think it's on the order of 18 percent reduction in infection, that they stopped their control arm, and now all the patients are receiving this device.

So there are at least two other studies, larger studies in progress that I'm aware of, although I don't have information about them because they have not been published, and we don't have access to their specific data. Yes, sir?

DR. LURIE: Can I follow that up? Most of these studies are done on elective surgery patients getting hernia repair or other things. So in the five years that this product has been available, there haven't been any collected human studies that show any clinical improvement that are published, beside the neurosurgical one?

DR. ROTHENBURGER: I'm not aware of any that have been published. I'm aware of the ones that are in progress, which are significantly larger than that small neuro study. But, no, not as far as I'm aware.

DR. EDMISTON: Let me ask you a question relative to the resistance issue because people keep bringing this question up. Do you feel the onus is on the vendor to demonstrate when they present their data modeling systems which look at potential of resistance

with these impregnated devices? Is that a consideration we should have as part of the Panel's discussion?

DR. ROTHENBURGER: I think that the sensitivity to resistance is important, and what we should be responsible for is some evaluation of the probability of engendering that problem. I don't know whether or not a model is always going to be possible, depending on what the device is and what its use is. But in our case, for example, what we did at the launch of this device was to go to the literature and also go to the other expert users of these materials and say what is out there, what have you seen, and please give us your frank opinion about the risk of this potential issue.

We keep a very close eye on that question, as you might imagine. And most recently, the published studies are indicating that, for this type of use in particular in clinical situation where you've got already a lot of risk involved, the risk of additional resistance is pretty much nil. And the two studies that are most recent on that are the Aiello,

Levy, Larsen study with handwash, as well as Dr. Rutala and Weber study from North Carolina where they evaluate the impact of all these types of disinfectant antiseptic materials in the clinic.

So that's, to me, the kind of evaluation that would be required, at a minimum, to satisfy that. If there is a more specific risk identified or a higher-level risk identified, then probably more work would have to be done. Yes, sir?

DR. LIN: Well, to help the Panel, let me ask a question in regards to your presentation. You have mentioned the concentration of triclosan that they used the suture, and my next question is my understanding is that triclosan has to become a solution in order to help exhibit some antibacterial activity. How you control this concentration in order to ensure activity?

DR. ROTHENBURGER: Let's see. In terms of concentration, the current, this is out of my head. I have a slide, but not in this presentation. I believe the current concentration is about 400 parts per million in the coating of the Vicryl suture. In some

of the other varieties of polymer-based sutures, the concentration is higher. For example, in Monocryl, it's about 2,000 parts per million. So those levels are well above MIC levels for triclosan and for the susceptible organism.

In terms of control, these sutures actually degrade in vivo, so there is not a specific mechanism that we try to control the release with because these sutures degrade anyway. In fact, that probably is the mechanism that controls it the most. The sutures themselves hydrolyze and are falling apart, and, as they do, this material is released. We do know that for a coated suture, like Vicryl, the release profile is different than for a non-coated suture, like Monocryl for example, and that has to do entirely with the physical properties of the sutures themselves.

The test method, I'm really trying to get to the test method here. I'm happy to address all these other questions, too, but I think the important thing I was trying to get across is we have an abundance of in vitro data, tremendous volumes of in

vitro data. And this type of test, from a pre-clinical model standpoint, is pretty much what people do with suture. They put them into in vivo environments; they don't usually take them out and look at them. But I think, for our purposes, this has been a valuable tool for evaluating whether or not, you know, the device really has an impact on microbial colonization.

DR. EDMISTON: I guess the real question I have relative to the animal model is is there a value for an in vivo model in which you implant a component of the device, whether it's the filter component or the mask or a portion, a component of the gown into an animal model to demonstrate the ability of that release mechanism to eliminate a defined inoculum within that animal model? That's a real question that's important because these devices are different from a vascular graft, for instance. So I think your presentation sort of leads me to think that there may be a role for potential animal models in looking at a defined reduction inoculum.

CHAIRMAN JARVIS: Are there any other

questions? If not, thank you very much. I think, at this point, we'll take a break for lunch. It's 11:30. Why don't we plan to reconvene at 12:30?

(Whereupon, the foregoing matter went off the record at 11:32 a.m. and went back on the record at 12:37 p.m.)

CHAIRMAN JARVIS: Okay. Why don't we get started. Our next industry presentation is from Derek Warneke at MicroActive Corporation. Derek? Just as a reminder, if you'd just state your affiliation and financial interests and so forth before you present.

MR. WARNEKE: Will do. Thank you. I would like to thank the Panel and FDA for bringing us all together, and I do appreciate the opportunity to address this group. As a way of introducing myself, I certainly do have an industry affiliation and a vested interested in the progress of this group. For MicroActive, I'm the general manager. My background is predominantly in new product and technology commercialization.

MicroActive is an antimicrobial business. We develop and manufacture delivery systems for

antimicrobials. Our technology is all based on chlorine dioxide, and what we bring to the market is the ability to get chlorine dioxide gas to the point of need and deliver it in prescribed doses. MicroActive is a whole subsidiary of BarrierSafe Solutions International. BSSI is a leading provider of disposable hand protection, so we certainly have a focus on the glove side of this group's work. You may also be familiar with other companies that BarrierSafe owns, MicroFlex and Food Handler.

Really my objective today, in addition to the opportunity to present input and feedback on the direction of these articles, is really to establish a working relationship. I'd love to get a pulse on where the Committee sits in either resistance to antimicrobials in these applications or support of antimicrobials here. We certainly believe firmly that working together between industry and the regulatory agencies is the model for the greatest success.

The goal that I understand the Committee is really facing is what are we doing or how can we improve barriers to transmission. This would be

reducing transmission both to and from human pathogens. And I think these have been fairly clearly articulated: add a level of protection to the practitioner, as well as the patient.

What the industry really needs and why we're looking to this group is really define set of standards upon which we can work. How do we best evaluate the systems that we're using and best understand the needs of the end applications. Ultimately, developing fact-based or test-based protocols would be the greatest motivation.

And to start with, and this has been touched on, as well, really the current definition of antimicrobial, any agent that kills or suppresses the growth of microorganisms, is probably inadequate for personal protective equipment. Short duration, disposable life span, likely that a more refined focus, focusing on a biocidal effect, an agent that simply kills microorganisms. My other recommendations that there would be room here for defining potentially rapidly or within the time frame expected.

Some of the considerations. Again, speed,

certainly for a glove application. Resident time or time from patient to patient would be critical. Can an antimicrobial simply work fast enough to be meaningful? At 24-hour or even several-hour, efficacy would be relatively useless.

Second would be the spectrum of kill. This has been brought up. What specific pathogens are we working to attack in a static versus a cidal effect? Again, certainly in a glove application, and probably across the board, it's going to be important to have an actual biocidal effect.

The potential negative side effects I think have been covered very well today. And, certainly, a false sense of security. This issue faces every advancement in medical devices, so it is one to be grappled with. It certainly wouldn't preclude, you know, advances in personal protective equipment.

User safety I'll touch on briefly momentarily. And working with antimicrobials where at least we can have a reasonable assurance that we're not promoting the development of resistant strains.

So you certainly don't want to trade off one problem for a long-term greater problem.

In a nutshell, what the users really need and need to have confidently is biocompatibility through extended use. I can tell you that the food industry is facing this exact same issue right now as antimicrobials become more prolific in food safety and food handling. So now we're looking at antimicrobials in chronic use applications, not simply one-time use applications. A wonderful 50-year-old quote or nearly 50-year-old quote that, in essence, is still relevant today.

All right. I will wrap up with a few of the key points. I would venture to say that we all agree upon the need. There are technologies that can bring benefits to these applications. It has been proven and recognized in multiple applications, which have already been more eloquently discussed today in some of the prior presentations. Personal protective equipment certainly helps us address one of the most widely mobile and variable components within the healthcare setting. Great transport mechanisms. So

there's potential greater benefit here in really gaining an effect and aiding in that transmission. A recommendation would be to develop a multi-tiered system where specific levels of efficacy are tied to specific label claims, much the approach the FDA has used in the past.

I think the question was posed earlier in one of the presentations will antimicrobials prevent cross-contamination or transmission? Of course, the answer is no. Can they be a valuable contributor? You know, obviously, we believe the answer is yes. So one added level of protection.

We talked about safety. If I had a point that I really would love to leave the group with is that the technologies are available today that can deliver the types of benefits and efficacy that we're discussing and do it without creating new harmful side effects. We feel fairly confident about that. And what we would like to see or what I would certainly like to see going forward is a collaborative approach so that we can work together to bring these to the market.

CHAIRMAN JARVIS: Very good. Thank you. Are there any questions? If not, thank you very much.

MR. WARNEKE: Okay. Thank you.

CHAIRMAN JARVIS: And our last industry presentation will be Konstantin Goranov from NOVEKO International.

DR. GORANOV: Konstantin Goranov, NOVEKO International. Thank you to the FDA and the Advisory Panel for this opportunity to present a product that the company developed in the past two months and reflect some of the issues that support medical devices.

Certainly, we've had quite expansive coverage on the topic, and we had several speakers present the key issues. One key point. Yes, we have to collaborate in order to develop the right products for the applications. It seems like there is quite a vast majority of potential applications of the antimicrobials, and one key point is we find what would be the major advantage of the antimicrobial. And that's what we actually lack as developers. We like to provide the best device to the healthcare

providers and healthcare professionals, and still it's difficult to guide the development process. Why? It's lack of information actually, lack of good feedback. And we have to agree there are not clear directions and guidance on the criteria, what we assume to be an effective antimicrobial device, antimicrobial agent, how to apply it, the concentration, the safety factors. And that has to be addressed early on, before we start the development process.

That's why I would like to present three key points here. First of all, bring the awareness of the product NOVEKO International developed in the air filtration, and we certainly believe the prototype will find an application in safety masks, face masks. Secondly, to define what will be the key criteria to value the safety masks and personal protective equipment. And, third, to define how we will be able to collaborate.

In terms of the safety masks, our face masks, we do have a technology that proved to be very effective in the prototyping stage in all the panels

we tested, the compositions, the selections of antimicrobial agents. And through selections, we find very exciting performance in both from antimicrobial resistance and from performance characteristics, spread ability, protection against fluids. And in terms of our desire to bring the product to the market, we definitely would like to reflect this device from FDA and thank Dr. Murphey for her guidance to design the right methodology.

At that stage, we believe we have a product that has a very safe antimicrobial agent. It has been used in practice for quite some time. There are no reported serious safety concerns. Some antimicrobial agents have been used in different devices, not particular PPEs, but that have been used in the practice. Secondly, the performance characteristics as a safety mask, we agreed here that the mask, first of all, it's a device that brings mechanical filtration. We do have contamination in the air, and also contaminations are kept on the mask. Well, among them, we have microbial culture, and the case to define what will be the best, the most

effective way to protect the wearer from further contaminations, develop enough negative effects on health. And then after use, as we all agree it's a short-term use of those devices, what will be the effect on the environment and, once it's disposed of, whether it creates another level of contamination.

Well, we believe with the current technology with the current prototype we have those issues addressed. The durability has been tested and provide certainly performance after exposure to temperatures and time. At that stage, we'd like to hear from the Advisory Panel clear direction what will be the most critical criteria to address, what will be missing from a standard evaluation we currently have with a regular surgical mask. We definitely have something in addition to the materials we normally use in surgical masks, so what will be the most important part to test and provide evidence it works and it's safe?

On criteria issues, we definitely have a different material, different device. It's not the standard mask we have, so it has additional features.

And sometimes the antimicrobial additives help us to design a better product. We don't have to depend on a tight filtration anymore because we do have something to work in addition to the mechanical filtration. And that's why we need to come up with a better criteria, not to judge the antimicrobials by the same standards that we have. It's better than that.

And the industry has quite a few approaches to apply those antimicrobials in a variety of forms, and the delivery mechanisms are quite vast. We have several different tools that technology developed. That's what I bring to the Panel. The technology is advanced enough when we create a better product. We need the guidance what value to provide to the healthcare professionals, to the wearers, we want to protect.

In terms of finding the right protocols, as a scientist, I know it's very difficult to come up with the right methodology and especially something so new. Well, we have Dr. Karl Perkes from Nelson Labs, and I have to thank you, Dr. Perkes, about his

involvement with defining the right methodology. And I hope Dr. Perkes will be able to speak his mind after my presentation.

In terms of our collaboration, we certainly sit in close collaborations with the Advisory Panel, with FDA, and even with our partners in the industry. As collaborative growth, we'll be able to develop the right products much faster than trying to be separate for each own silo. Thank you.

CHAIRMAN JARVIS: Thank you. Are there any questions? If not, thank you very much. Oh, oops.

DR. LURIE: Sorry. A quick question. Is the technology that you're posing exclusively for safety masks or for other barrier protection systems?

DR. GORANOV: Well, this technology was developed originally as air filtration, antimicrobial air filters. And then in particular for the surgical masks and the respirators was enough to accommodate the safety concerns and some of the specifics of the safety masks. Yes, it's especially designed to handle the safety and performance.

CHAIRMAN JARVIS: All right. Thank you very much.

DR. GORANOV: Thank you.

CHAIRMAN JARVIS: Next, we'll ask the Panel do you have any questions for any of the other presenters from industry before we move on? Okay. If not, we'll now proceed with the second open public hearing portion of the meeting. And I believe we have two individuals who would like to present. First is Bob Weber from 3M Corporation. Mr. Weber?

MR. WEBER: Thank you for letting me present. I'm Bob Weber. I'm the Regulatory Affairs Manager at 3M in the Occupational Safety and Health Division. And we are the division that makes personal protective equipment, and one of the devices that we make are filtering face piece respirators.

The first thing I'd like to say is that we have been involved in this discussion for well over a year, if not two years, and there's a lot of misleading information that's being given out by different organizations, different individuals, on particle size. There's this misinformation that NIOSH

does not test at the most penetrating particle size. Albeit, some of the information that you saw earlier today about the ranges that it shifts, and it actually shifts not only based on the flow rate, if I increase the flow rate that shift to the most penetrating particle size will also shift, it will also shift based on this size and the filter media. NIOSH tests, and the individual was correct when she said it, at .3 microns, but the mask's median diameter is .3 microns. If you look at the actual aerodynamic diameter of sodium chloride, it's 0.75 microns. If you look at the, when you look in different tables about the size of viruses, the size they're actually referring to is more closer to an aerodynamic diameter than the mask median diameter.

So as you deliberate, please consider that there is a lot of different ways to discuss and to look at particle sizes, and they're not interchangeable. So that's number one.

Number two is that, and I've heard this said but I've never seen the data, that electrostatic filter media will degenerate with water. In fact, if

you look at Europe, Europe, for their filtering face piece respirators, they actually have a very difficult challenge that involves humidity and water and that you must meet it. So, again, I'm somewhat skeptical and I'd like to see the data because we have data that contradicts that.

The other area that I'd like to discuss is protection, and I don't know if all of you are aware of this, but I'm in full agreement that putting an antimicrobial sort of agent on a respiratory protective device or a mask might help in cross-contamination. And maybe you can decontaminate the device as you're actually wearing it.

However, if you're looking at a filtering face piece respirator, and you want to put an antimicrobial agent on there to reduce exposure to the wearer, I doubt whether or not that's going to do any benefit whatsoever. And this is the reason why. NIOSH test filtration, and you say it's 95-percent efficient at this penetrating particle size. And they're very good, by the way. But the other aspect that people forget about is the face piece leakage.

Half-mask respirators, as defined now by OSHA, have an assigned protection factor of ten. That means that you are permitted to have a ten-percent face piece space seal leakage. So if you go out and you put an antimicrobial agent in the filter media, okay, granted, you might make it a little bit more efficient, but that half-mask respirator still has an assigned protection factor of ten.

So the thing that you must consider, and I really applaud the FDA because they actually address that, is what are you going to state about this agent being put on that device? You know, stating that it will reduce the wearer's exposure, I don't believe you can say that because half-mask respirators have this protection factor of ten. So consider that.

And that's about all I want to say, so thank you very much. And I do have one, not a comment but a question. I have got a couple of documents that summarize a lot of what I said, and I'm wondering if I could leave those with you for your deliberation, if that would be okay?

LT. COLBURN: Yes, if you could hand those

maybe to Ann Marie, I'll try to pick them up.

MR. WEBER: Okay, all right. Thank you.

CHAIRMAN JARVIS: All right. Thank you very much. Are there any questions?

DR. DAVID: I have a question relating to your challenge of the tests. What do you mean by the various particular diameter changes? Are you suggesting a different test, or are you just trying to define?

MR. WEBER: No, no, what I was trying to say is that when people talk about NIOSH and the test that they do for filtering face piece respirators and for filters, they tested at a particle size, and it's called a mass medium aerodynamic diameter. It looks at the mass of the sodium chloride, also, and it's .3 microns. If you convert that to the aerodynamic diameter, the size, the median size, it's .075. So it's much smaller than .3. The chart that you saw this morning started, in my opinion, because I didn't see how it was actually the X axis was presented, it's confusing because they talk about .3 microns out of one side, and the other side they start talking about

just the aerodynamic diameter.

So, again, as you deliberate, you need to understand that there's just different ways you can interpret and present the size of particles. Sometimes people use them interchangeably.

DR. EDMISTON: I'm going to guess, based on your presentation, that you're skeptical of the use of antimicrobials, especially in N95-type devices; is that correct?

MR. WEBER: No.

DR. EDMISTON: All right.

MR. WEBER: What I'm skeptical of is that they would benefit in reducing an individual's exposure to the agent inhaling it. Because you're allowed that respirator, you're allowed ten-percent leakage. So even if you make the filtration aspect more efficient, you still are allowed ten-percent leakage and you'll still get it because you're not evaluating the fit of the device. If you were to treat filter media that you can put in other types of respiratory protective devices, like air-puring devices, power devices that have higher levels of

protection, then I think you might be onto something.

DR. EDMISTON: What are your thoughts about other types of masks, like the traditional surgical mask which doesn't fit very tight at all compared to some of these other devices?

MR. WEBER: The other thing I'd like to add is I think, what I said before, too, if you're looking at reducing exposure to the particles, I'm skeptical. But if you're looking at a way to actually reduce cross contamination and somehow and in some way break that barrier of transmission, then I'm in complete agreement. So I'm okay with it, but, again, the claim of what it actually does has to be extremely defined, and it's very --

DR. EDMISTON: So if a claim came out for a device such as that indicating decreasing the dissemination of nasopharyngeal flora from the wearer into the nosocomial environment, that could be a reasonable claim if they could prove based on their technology; would that be correct?

MR. WEBER: So going the other way?

DR. EDMISTON: Going the other way. Like

you're using a surgical mask, you're looking into a surgical wound, and we know traditional surgical masks has a phenomenon called venting. You've got a biomedical device in that wound bed. If there was a technology impregnated on the surface of that mask that could reduce the burden of these potentially pathogenic organisms from shedding into that wound, that would be a valuable device, wouldn't it?

MR. WEBER: I think I'd have to look at the data and understand it, but, yes, I think that could be a benefit. Again, though, there's leakage around the outside. But there might be some reduction, yes. The other thing is understanding the velocity that you're talking about. As you're talking and if you're coughing and you're sneezing, if you're not the patient, if you're the healthcare provider, that's a very high velocity so --

DR. EDMISTON: Is there a standard methodology available to measure that kind of --

MR. WEBER: No, not that I'm aware of.

CHAIRMAN JARVIS: Have you done any studies -- one of the issues in terms of preventing

cross-transmission, I'm assuming that, theoretically, it's release of organisms from the external surface of the mask. Do you have any data from any studies you may have done looking at either virus particles or bacteria or even microbacteria as to whether, once they have contact with a mask and pulled into the fibers, are attaching, the likelihood that they would ever be released?

MR. WEBER: No, but I wish we did.

CHAIRMAN JARVIS: Can you identify yourself?

MR. RENGASAMY: I'm Samy from NIOSH Pittsburgh.

CHAIRMAN JARVIS: Okay.

MR. RENGASAMY: The reaerosolization of particles that have been captured with a mask is very negligible. Once the particles are captured by the filter, the number of particles that are coming out of the filter by sneezing and coughing, even at a high velocity, is very negligible. There are studies already that have been done on this kind of thing.

CHAIRMAN JARVIS: So your opinion is that

that's not something we should even think about as being a theoretical possibility in causing infections?

MR. RENGASAMY: These are not definite answers. I'm not saying there shouldn't be any study.

CHAIRMAN JARVIS: Okay.

MR. RENGASAMY: It depends on the situation and what kind of organism. In some cases, people say one organism is good enough to cause infection. In that situation, we have to be worried. But for other organisms, we cannot just take it very seriously.

CHAIRMAN JARVIS: Because, at least my understanding, if you're really believing that cross-transmission, again, I'm talking specifically to respirators and masks, that they're going to be transmitting pathogens, I would assume you're not taking it off and rubbing it on the patient. You're talking about release of those pathogens or the healthcare worker touching them and then touching a patient as being a primary host.

MR. WEBER: And I think that's where I see a potential real benefit is that cross contamination

of taking it off and then, you know, maybe not washing your hands well enough or even if you're looking at the general population ever getting their hands on anything like this, where that could help. Anything to help. Maybe not all the time, but at least something to break that mode of transmission. It's better than nothing. So just one extra step in the whole process of trying to, like I said before, break that transmission.

CHAIRMAN JARVIS: Let me ask maybe the gentleman from NIOSH. Have you done any studies looking at, particularly at bacterial and fungal pathogens and maybe even viruses, attaching to the external surface of the mask and then having contact with it and the likelihood the organisms are released?

MR. RENGASAMY: I didn't do any studies, but there are one or two studies where they have loaded filters with the particles, and then they dropped the filter at a distance, and looked at whether there any organisms come out of the filter. Even then, there's no significant number of particles coming out the filter. But these studies could be

done under different conditions. Just by looking at one study, if it doesn't show any problem, we cannot assume that it is the real truth. There should be many studies to confirm this, and then maybe we can take it as a reality.

CHAIRMAN JARVIS: Okay, thank you. Are there any other questions? Oh, here we go.

DR. EDMISTON: One more question. In looking at the efficiency of these masks, there's a lot of data out there on particle size and particle dissemination and capture of these masks. Where does biological data come in here, especially with now we're talking about an antimicrobial impregnated device? Obviously, particulate, the usual particulate data will not be sufficient to evaluate these devices. Where does the biological component come in here?

MR. WEBER: There have been a number of studies looking at how filters work against biological agents. And all of the literature states that a biological agent is a solid, and it will behave like a solid. And, actually, it's in some of the documents that I'll give to you actually cites a lot of that

information of where you can find those studies that have looked at the efficiency of filters with capturing biological agents, if that's what your question is.

DR. EDMISTON: But with an antimicrobial substrate then, you're talking about the ability to statically prevent growth or cidal to kill the organism on contact. That's not picked up on these traditional particulate studies because --

MR. WEBER: That's correct.

DR. EDMISTON: -- they're inanimate studies. So what I'm saying is that do you have any recommendations, 3M is a big operation, do you guys have any recommendations in terms of looking at some of these biological entities in terms of measuring efficiency --

MR. WEBER: How it can increase the efficiency --

DR. EDMISTON: Right.

MR. WEBER: All I can say right now is that we've got some research underway that we're studying and we're looking at it, and it won't be done

for a while, but we're looking at it because we're trying to take some technologies that we have, and we're trying to better understand. We've partnered with some universities to do some research in the area. So at this time, I can't tell you what we have because it's still --

DR. EDMISTON: What you're saying as a leader in the field is that, at this point, there will be no standard methodology that this panel could come up with to validate the efficacy of some of these devices?

MR. WEBER: In fact, the first phase of our research that we're doing is to look at some test methods. First, generating the aerosol, and the measuring the aerosol, so that we can then start doing some comparison because there is not a standard test method.

DR. EDMISTON: Thank you.

CHAIRMAN JARVIS: All right. If there are no other questions, thank you very much. Our second presentation is by George Laventure from the Air Force Research Laboratory.

MR. LAVENTURE: Thank you. I'm going to follow up more from an engineering perspective what Brian Heinbuck, also from the AFRL, presented this morning. I think that's interrelated to some of the work we're doing under the Chem Biodefense program.

But what I'd like to share with you, I'm a retired civil engineering officer that wore the protective garb, the full ensemble. And what we're relating down there is also to the Surgeon Generals. So the medical part of what our surgeon general people wear in the field is very applicable to this antimicrobial. In fact, some of the protective device enhancements have been marketed to the Surgeon General. We then have come back to the Air Force Lab to ask can we validate the information that's been presented, and we've done that to a degree.

But what I'd like to share with you, the challenge that I think this group faces really is separating perception from scientific fact. The last speaker really addresses protection factor, and that's a very key issue of what you get and what's the incremental improvement that you get from an

antimicrobial device.

So I'm going to tick through some things, just food for thought. We all know that the perception is that they're protected, but really what is the stuff that gets through? How good is this protective barrier? And that's some of the questions that we're trying to answer for our Surgeon General people in terms of what's the significance of these enhanced findings applications that we're looking at.

So FDA did a good job of talking about qualifying and quantifying what gets through and how you measure it. So I broke my idea down to two different ones. One is the practical questions or the so what test. And then the second one has to do with the technical questions that result that I believe this panel is going to have to address.

So one of the first things that we were asked is what is the benefit cost ratio of enhanced protection? The surgeon generals of both the Air Force and the Navy are always looking for improvements. But right now we currently have no D requirement for this enhanced protection. And they've

1 come back to us and said, you know, is what we have
2 good enough? There are a lot of body of people that
3 believe what we have in terms of particle capture and
4 efficiency protection is good enough.
5 I heard today the question raised about
6 false sense of security. Two aspects of that. The
7 first is one already exists. People believe that what
8 we have out there, the 95 on up, provides adequate
9 protection. The new bio challenge and, specifically,
10 viruses, there's been very little research. There's
11 been certainly a body of evidence, and I'm going to
12 share a couple of other things, but we know particles
13 get through. The question is, in those particles, how
14 many of those are viable, and how does that relate to
15 infectious dose?
16 There has been presentation about
17 mechanical efficiency. That's well known. There's
18 theoretical physics that talks about, for a HEPA
19 material, you're going to get 99.97 percent
20 protection. You're going to get viruses through.
21 What we don't have is a viral reduction efficiency
22 standard, and this is some of what we're trying to

work on at the Air Force Weapons Lab. So in the particle, how many of those viruses or virions are viable that will cause the infectious dose? And Brian, if I get into chemistry, I'm coming from an engineering perspective. He can talk to that.

So we're talking about really neutralization and killing. What we saw in the lab is roughly a one to two-log reduction depending upon challenge level. What does that mean? How good is that? Obviously, it's based on the challenge, the virus challenge of whatever that you're challenging this filter and what you get out at the end.

So the second part that was asked under a false sense of security talked about the risk of people not using PPE properly. Well, one of the things that you'll see in just a minute that we're faced with is not only addressing the scientific question but addressing operational questions, such as fit, leakage, those types of things. So if this body is going to focus on the scientific question of, given a challenge, will the protective barrier allow what to get through, that's one part. But if you're going to

try to answer the question that the last gentleman put up, when it comes out with a ten percent, we're getting told that that's far more of a bigger contribution to the protection thing than you worrying about getting two more logs of protection. We can't answer that. We're dealing with the science.

Another thing to consider is additional cost. The end item is going to be probably a couple dollars more per item. I think it was in the billions of how many of these things are out there. So, of course, the military is concerned about the end amount of cost.

The second thing that has not been addressed is the testing cost. Not only do we not have the standards, manufacturing is going to have to gear up to testing and, more importantly, the regulatory agency is going to have to gear up to testing. This is not a trivial matter.

Another part: significance and vulnerability. So how much gets inhaled into the lungs, and what is the infectious dose that we are trying to protect against? We cannot even get closure

from our medical community in terms of what they would like. We're in the process of trying to translate that to what level of protection we need to provide.

So what is the most important issue that we're trying to address? Is it penetration? Is it leakage? Contribution? Fit? Cost? Standardized testing? Cross contamination? Just a quick and dirty. So that's the practical questions that I see that we're trying to wrestle with, and I believe this Committee is wrestling with some of those, also.

But now get onto the technical questions, trying to interpret scientific data and what we really know. So what about understanding this reaction chemistry based on a given challenge? Whether it's a biothreat, as in terms of a weapon or a viral threat, these reactive components are going to have interaction with what it's presented against. We don't know all of what that really means in terms of does the protection we provide by adding additional things make the situation worse or better? We don't' have the answers to all those things.

Already's been mentioned is livid and

inadequate test or performance standards. We have a fairly good handle, I believe, around particle efficiency testing. There's NIOSH and a bunch of other ones out there. There are no viable reduction efficiency tests that we know of, and we're in the process of trying to make some up as we go along. If they exist in industry or regulatory bodies, the military will adapt them. If they don't exist, then we basically start, as Brian has talked about, working on developing some.

Off gassing. And I'll just use the term. FDA put this out. In the terms of iodine, which we've looked at from a military standpoint, we looked at this threshold limit value. Is this good enough? You know, is there a cumulative dose rate over time? Some of those questions are just, there's not a body of scientific data out there to evaluate them.

So how to handle the different types of enhanced PPE improvements. You've heard today from several people, whether it's iodine, copper, electrics, and then silver ion, and there's a host of other ones out there, so you're talking antimicrobial

here. What all falls into that pot of enhanced protection, so the test methodology you're developing has to address these things at some point in time as a new manufacturer brings you those products.

Test methods. There's a heck of a lot more that we don't know. The challenge level we found to be very significant. We get two-log reduction at ten to the eighth challenge level. If we go below that, we're looking at much smaller challenge levels. The incremental improvement is much further reduced.

Flow rates. We talked a lot about just a typical respirator, 85 liters per minute. But for military applications, especially in the field and under a lot of patients coming in, say on a natural disaster or something like that, those flow rates could get up to 300 liters per minute. Big difference in flow rate, as other people talked about.

Shelf life, another issue. Very limited data, especially on these new devices, in terms of shelf life. Particle size. This is a real challenge in terms of what that translates to, whether the most penetrating particle sizes we've already talked about

is between 0.01 to 1. That really depends on a lot of factors in terms of what that means.

What hasn't been talked about is detectors, detection limits, and measuring, and what it means to be below detection limits. Right now, that whole science is very limited and often very time consuming. There are improvements being made, but you really need to understand that process, too.

So those are the two things from the standpoint of practical questions and technical questions. And the last thing I just would like to make the group aware of, we just recently convened a subject matter expert panel to look at virus penetration through HEPA material, and that group met last week. It's composed of DoD laboratories: Army, Navy, Air Force; limited input from the CDC and NIOSH; some industry, Research Institute, Battelle; some university participation. This was a quick and dirty, low-cost six-month effort to try to answer the question to the military standpoint what's the significance of what gets through the HEPA membrane and how does that translate to vulnerability.

Currently, no EPA or FDA persons on the panel, and we certainly would like someone to be on the panel because I think those same questions is very relevant to what I believe you're addressing.

So with that in mind -- oh, by the way. We were told don't just worry about the science penetration question, but you tell us about this leakage fit issue that the Surgeon General says that, in their mind, is the most significant question that they would like answered. That concludes my comments.

CHAIRMAN JARVIS: Thank you very much. Are there any questions?

DR. EDMISTON: I have a technical question. You mentioned that you work within a world where there's a two-log reduction with the ten to the eight inoculum; is that correct?

MR. LAVENTURE: Yes.

DR. EDMISTON: How did you determine that? How did you come up with a log reduction of 2 rather than a log reduction of 2.5 or 3 or 3.5? I'm curious about that because you use a similar log reduction for topical antiseptics on a dry surface. So I'm curious

how your industry has derived that two log reduction because that may actually be applicable to what we do --

MR. LAVENTURE: Well, I think it's very applicable. I'll let Brian talk because he actually tested I think it was three commercial respirators on our BAT System, our biological testing, and I'll let him talk to you about that.

MR. HEINBUCK: Yes. So the test method is pretty straightforward. And where the questions come is there's a lot of different ways to do the tests, but, generally, you're just applying challenge upstream and downstream of a filtration device. You measure the challenge upstream and downstream, and then you can figure what your challenge was and what got through, and you can determine a log reduction from that calculation. There's some other things that go into it as far as quality assurance of the test rig that you also correct that number for, but, you know, it's a fairly straightforward --

DR. EDMISTON: Does the log reduction of two represent the maximal log reduction under your

test conditions or again --

MR. HEINBUCK: No, that's just what was measured.

DR. EDMISTON: That was measured.

MR. HEINBUCK: And what George is referring to is that two-log reduction was in reference to two logs reduction better than a normal fibrous filtered median. So, ideally, you'd do your quality assurance upstream and downstream, you should get very similar counts. I mean, there shouldn't be, I think the co-efficient or the variation that's allowable on the test methods that he wrote was, you know, you'd like it to be at least 90-plus percent the same upstream and downstream, if there was no device installed. But then you simply put in your fibrous filter material without antimicrobial, and you get an upstream/downstream count, and then you do the with the antimicrobial and you get your upstream/downstream count. It's simple math.

DR. EDMISTON: Let me ask you a question. So you've done this already with certain agents with and without antimicrobials; correct?

MR. HEINBUCK: Yes.

DR. EDMISTON: What do you see? I mean, this obviously is not proprietary. This is within the realm of disclosure. But what do you see when you add an antimicrobial in terms of log reductions in some of your experiments?

MR. HEINBUCK: We've seen up to two log reductions. We've not tested any flat, so in the devices we've seen up to two-log reductions. We've not tested any flat-sheet material. But we've not been able to --

DR. EDMISTON: That's two-log reduction above and beyond --

MR. HEINBUCK: Above and beyond. So if I said a HEPA filter we got so many through.

DR. LURIE: Is that bacteria and viruses?

MR. HEINBUCK: No, just viruses. Bacteria are very efficiently captured by filtration media, particularly HEPA. So if you understand that penetration curve with HEPA, you know, when you get to one micron in size, you're way to the right and you're efficiently captured.

CHAIRMAN JARVIS: But you had mentioned that that was somewhat, if not very, dependent upon flow rate.

MR. HEINBUCK: Well, yes.

CHAIRMAN JARVIS: And if you move the flow rate down to, you know, healthcare workers usually aren't carrying patients upstairs or doing jumping jacks. They're usually basically at rest. What happens there?

MR. HEINBUCK: There's more to that because there's two mechanisms for fibrous filter capture. There's impaction, and then there's diffusional capture, as we learned this morning. The diffusional capture mechanism are more affected by flow rate than the impaction is. So smaller particles at higher flow rates will have more penetration. Larger particles are largely unaffected.

CHAIRMAN JARVIS: So, generally, you'd expect then for a healthcare worker and the working situation that they're in that the filtration is going to have an even greater impact on reducing the biological growth?

MR. HEINBUCK: Well, again, then you come back to leak tests. There's a whole host of parameters. When we do our test, we're assuming a perfect environment. We're wanting to evaluate the performance of the media or the canister itself, so we're not evaluating leaks, you know, and penetration around the seals and things of that nature.

CHAIRMAN JARVIS: But if you were guessing at, given a healthcare worker's situation, given a viral load that's probably not going to be ten to the sixth, ten to the eighth, it's going to be much lower than that, is your guess that you probably get more colony-forming units or --

MR. HEINBUCK: Plaque-forming units?

CHAIRMAN JARVIS: -- plaque-forming units through leakage than you would ever get through the mask?

MR. HEINBUCK: I'm probably not the most qualified person to state that, but that would be my guess.

MR. LAVENTURE: The whole issue of fit, especially from the Surgeon General's standpoint, is

critical to them deciding what they want to field and whether they want to create a requirement for this enhanced protection. There are groups that do fit tests. When we do fit tests in military, it's primarily for our mop gear type, full face mask type setups. I don't believe our surgeon generals are doing any special fit test on their respirators.

Another interesting part, when we convened this panel for the first meeting last week, when we talked about the particles that got through, we asked if anybody really had detection techniques that could tell which were viable or not, other than plating them out. And no one at the meeting could say that they could tell. If you look at the scientific research papers, we see both extremes in terms of argument, whether one virion is in one particle or whether there's 50 or more in one particle when you're trying to figure out infectious dose. That's some of the questions we're going to try to answer, but we certainly don't have the answers to those now.

DR. GORDON: I know this is redundant, but this is a very important issue I guess. So I have the

ten-percent leak, and I've got a big ocean of organisms that are getting around. Then I've got my N95 that has a minority of them anyway, so when I decrease that by two logs, I pretty much have an imperceptible impact on a total exposure anyway. So the question is what's being done about the ten percent?

MR. LAVENTURE: I can tell you that, for respirators, the military is not doing anything that I know of in terms of getting better seals on that. Now, I think some industry is, and maybe some of the people that presented here today can talk about that. In our military full-face mask, yes, we're looking at all different kinds of things to get better seals than what we're currently getting. And the protection factor on them, I'm not sure what it is, and maybe somebody knows, but it's much less than ten.

MR. RENGASAMY: The protection filter, the ten percent that we are talking about, is for the best fitted respirators. If the respirator is not fitting well at all, then it's not anymore than ten percent that you expect. It will be a higher number. So a

lot of respirators, actually they have the respiratory program in workplaces. The workers are to be trained to wear them, they should be informed about the free testing procedures so that when they put on the respirator, they should have seal tests are done. There are ways to check how good the seal is, so they ought to be trained that these are some of the things going on. So if you just pick up any respirator, you cannot assume it is fitting well and it is going to give you protection.

DR. GORDON: So if I go into a room with a patient with TB and they're coughing, they have cavitary disease, and there's all kind of acid-fast floating around, and I go in wearing an N95 respirator, I have no typical N95 respirator, I have no reasonable expectation that that's going to provide me any great degree of protection?

MR. RENGASAMY: It will give you protection. It all depends on the size of the particles, the outer flow goes out and where the person is standing in front of you, things like that.

DR. GORDON: If I'm getting exposed to ten

percent through the side, then I can get rid of 100 percent through the front, and I'm still getting exposed to ten percent.

CHAIRMAN JARVIS: But I think certainly if you look at the MDR TB outbreaks where the implemented use of respirator, N95 type or dust mist, in the past, there was no skin test conversion. So even though we're talking about ten-percent leak, it's not that you've got ten to the sixth organisms coming around that ten to the sixth leak.

LT. COLBURN: I just want to make a motion that if you want to address the panel, you please grab the attention of the chair so that he can recognize you to make sure we're giving the gentleman who's presenting right now the time to do so.

CHAIRMAN JARVIS: Are there any further questions for Mr. Laventure?

DR. LURIE: You know, I think you're addressing the real question which I see is important is what's the clinical significance of this not for the military community but for the hospital-based community.

MR. LAVENTURE: We have a big military community, too, you know, when we're out there, too, that uses the same respirators quite frequently.

DR. LURIE: So my question then it sounds like, to me, who's not well educated in this, the defense industry is primarily focusing in these studies on getting rid of the viruses. And we in the hospital-based community are worried about the bacteria. And so it sounds to me like there would be a different standard then for the defense industry than one might recommend for the hospital-based community because we're trying to filter out different things. So my question is, if you were making these rules, how would these standards be different for the hospital-based or community-based community?

MR. LAVENTURE: Again, I want to go back before I get to your question. I think you have to separate the scientific facts of what antimicrobial material gives you relative to a challenge, assuming a perfect fit. You've got to evaluate that, I think, separately in terms to be fair to the manufacturer. When you talk about the operational constraints, which

may be the over-driving thing in this whole event, whether it's a hospital or a field application, what we do, we don't do it for the respirator, but what we do for the other one is obviously fit, whether you have the sizes. And by the way, small, medium, and large, and all this, and whether you have facial hair. I mean, there's a lot of things that come in to getting a tight fit. So even though ten percent is recognized on an N95, some may get two-percent fit. Some may get 15 or 20-percent fit. So we don't know enough about that. There are people who do that, and I don't know if anybody is here that addresses that. Maybe you could do that. But I think it's really a key issue for you in terms of this thing about false sense of security and awareness that we're trying to make the people aware that, you know, when you buy these things, yes, you get protection, but that's given a set of conditions.

So I can't really, as far as the test standard, I think we have to get some agreement on challenge level, what is a reasonable challenge. In the military, we're concerned about what can be

aerosolized as a weapon, whether that's by a terrorist or a nation threat. And your application, you know, what exists in the operating room, what could exist in an emergency response generation, in a city or something like that, whether it's a backpack sprayer or it's a crop-duster or whatever. How can that be aerosolized and what kind of concentration are they going to see if they're wearing these things.

MR. HEINBUCK: I'll just follow up on that a little bit because we're actually, when the Technical Support Working Group put out their call for proposals, that's one of the things that they wanted the proposers to delineate, create test methods that were specific more for a hospital environment and for, say, a bioterrorism environment and military environment.

And maybe I confused people earlier on the test methods because there was some questions about how we did this. The test methods of how to do bioaerosol penetrations are well worked out, I mean how to measure and how to count and all those things. It's just the actual details of the test and, you

know, what are the challenge levels, what are the protective factors, and how you actually go about doing the test, not doing the test but actually the parameters of the test is what needs to be decided. But to actually do the test it's not difficult to do.

CHAIRMAN JARVIS: Are there any further questions? If not --

MR. WEBER: Bob Weber with 3M again. I guess I'd just like to clarify this whole fit issue. As far as the ability to do that, I'm also a certified industrial hygienist, and I've worked in safety and health for a lot of years prior to even being a part of 3M. So when you look at a half-mask respirator, as defined by OSHA, and it's being used in the workplace, you have to pass a fit test. It's required in a hospital situation because you're an employer. And if you pass that fit test and every individual has to take it for that half-mask respirator and a full face and any type of tight-fitting device, it then says that your exposure will be reduced by ten percent. That's the way that you can look at it.

So if you pass the fit test with that

respirator that you're going to use in the workplace, that half-mask respirator, and there's training that goes along with it, it will reduce the exposure ten times. If you want to start moving up as far as reducing exposure, the next step is a full face negative pressure. There you reduce the exposure by 50 times if you're in the United States. If you go to another country, sometimes they say 100 times. So even this level of reduction is open for debate globally. You start going into powered-air type systems, you start then moving up to 1,000. So, again, it all has to do with half mask, full face, powered air, supplied air, and that's what reduces the exposure.

CHAIRMAN JARVIS: But isn't it true that, I believe there's at least one NIOSH study and maybe more than one that showed healthcare workers that were fit tested that when they finished their fit testing and had their evaluation of face leakage with the fit test and then they went on the floor and started doing their job, they found there was no correlation between what happened during fit testing and what happened

when they were actually doing their job.

MR. WEBER: There has been quite a few workplace studies in industry, in dirty industry let's say. And in that dirty industry were these workplace studies, and what you're doing is you're measuring the exposure inside and outside while they're actually working, so it's harder work then let's say on the floor in a hospital. What we've showed is that if you pass a fit test and you go out in the workplace that you can get a level of reduction that's greater than ten, and that's why we have assigned protection factor of ten for a half mask. It's because of these studies.

Now, can you get more? Yes, you probably can, and that's more device, you know, dependent. Again, but at least it's minimum for respirators.

CHAIRMAN JARVIS: See, I just wonder how applicable that is to healthcare because when I'm a healthcare worker going into the room, I'm not worried about getting mercury exposure or some other aerosol that's really toxic, whereas most people working in industry realize that they are really wearing a

respirator for a very good reason to protect themselves. And so much of healthcare workers tend to do what protects themselves, not as much protecting the patient, and most don't really, you know, I can tell you just from watching people go into TB patient rooms, they don't put on a respirator because they don't have a sense that they're at risk.

MR. WEBER: But, see, that's a function of your respirator program. That's a function of behavior. That's not a function of the device. So, you know, and when you start talking about behavior and respirator programs, I do agree that the mentality might be different versus industry versus healthcare, but the function of the device would be the same, no matter where you work.

CHAIRMAN JARVIS: Are there other questions? At this point, let me ask if there is anybody else in the audience that would like to say anything. If you'd come up and give us your affiliation and name, etcetera.

DR. PERKES: My name is Karl Perkes. I'm with Nelson Laboratories. Sorry I don't have a fancy

PowerPoint presentation. I just found out about this meeting last minute. We are an independent test lab that helps the medical device industry with obtaining their performance and safety data that will then be submitted to the FDA. Obviously, from our perspective, we're not really focused on weighing whether the benefits or importance of having the antimicrobial present on the product. We are more focused on the actual test methods and their development. We agree with what the FDA has said in their questions earlier this morning that many of the parameters need to be evaluated. For example, sterilization, aging.

So in addition to the normal testing, we would encourage those parameters be looked at, any type of variable that might impact the performance of the antimicrobial. Also, due to cost, we would encourage the Panel to discuss using standard methods that are already out there and possibly just modifying from those methods. Like what the gentleman from the Air Force Research Lab has said, aerosol generation is a standard approach. There are, however,

difficulties, minor difficulties, in tweaking some of the, say, concentrations and things like that.

So it is possible to do this work, but we definitely need established guidelines, requirements, on what you're looking for and to address those types of situations. If you look at, obviously we're looking at all PPEs, so gloves, gowns, in addition to just masks. You will find that with the gloves there really is no microbial testing at this point. There are toxicological, and so there would need to be something established there on how to go about looking at antimicrobial performance and safety, obviously, for gloves.

With gowns, there are standard methods for microorganism testing, and you could just modify off of one of those. And we believe the same thing with the face masks. Thank you.

CHAIRMAN JARVIS: Thank you. Any questions?

DR. EDMISTON: Well, you're the man. You're the guy they're going to go to if this Panel deems minimum requirements. Are you comfortable, in

your professional opinion, with the microbiological methods that are available in tweaking them a little bit? For instance, with the gown. I remember Ron Nichols many years ago who looked at MRSA penetration through surgical gowns, and I'm not sure if that was a standard test methodology, but it was something that was published in a peer-reviewed literature. Is that kind of testing relevant to what we're talking about here?

DR. PERKES: Yes, absolutely. ASTM has a standard test method for evaluation. Now, what would have to be altered is the organism that's selected. Currently, they're using a bacteriophage that may not be the best choice for the antimicrobial. So you may have to look at -- and it's used because it's a viral surrogate. You may have to look at the organism. You may have to look at the contact time, other issues such as that. But it would definitely be beneficial if there was an established method for everyone to follow that could be worked out.

DR. EDMISTON: Thank you.

CHAIRMAN JARVIS: Any other questions? If

not, thank you very much. Is there anybody else in the audience that has anything to say? No. All right. Well, at this point, I think I'll take the chairman's prerogative and drive on rather than take a break. Is everybody okay with that? In which case, we'll move on to the deliberations on the FDA questions. I wonder if, at this point, we could get the FDA to read or summarize the discussion questions and summarize exactly what we're looking at.

DR. MURPHEY: Thank you very much, ladies and gentlemen of the Panel. You've had a chance to hear all the speakers. You've had the questions at place, but now I'd like to read them for you, and, of course, the audience will also hear them, as well. FDA has reviewed for the Advisory Panel the current review process for PPE without antimicrobial agents, our current experience with evaluation of antimicrobial agents on devices, including selected aspects of performance testing, and the potential indications for use for PPE with antimicrobial agents as based on public information.

Now that the Panel has heard our

presentations and the comments from industry and public speakers, FDA asks the Advisory Panel to discuss and comment on the following questions. Dr. Jarvis, would you like me to go through them all now, or just one at a time?

CHAIRMAN JARVIS: I think just one at a time.

DR. MURPHEY: Okay.

LT. COLBURN: I'd also like to mention that the questions are listed in a handout and some notes on each side in your packages, so you can look at them yourself.

DR. MURPHEY: All right. Question number one for the Panel: various indications for use might be sought for PPE incorporating antimicrobial agents. Please discuss what types of indications may be appropriate for PPE with antimicrobial agents. Please describe the meaning of various indications and what types of performance testing should support such indications. What would a reduces contamination or a prevents/protects from microbial contamination indication mean for PPE with added antimicrobial

agents? How might performance for such an indication for use be evaluated? What might a reduces colonization indication mean for PPE which can become contaminated during use but are probably discarded after use? How should such an indication be supported?

CHAIRMAN JARVIS: Okay, panel members, it's open for discussion. Let me ask you, Dr. Murphey, one of the slides you showed was prevent contamination, prevent colonization, prevent infection.

DR. MURPHEY: That's right.

CHAIRMAN JARVIS: And my sense is that when you use the word "prevent," it's not a whole lot different here than reduce, and that prevent could be prevent one percent of what might have occurred otherwise all the way to 100 percent of what might have occurred otherwise.

DR. MURPHEY: That's correct. As we usually see these terms and claims, they're not described in terms of prevent entirely, reduce by a certain amount. So they're rather nonspecific in that