it can survive. So I am going to defer to my retina colleague on that issue. But from an optic nerve standpoint, it is going to depend on individual characteristics.

DR. ROSENTHAL: I mean, I don't care what level you decide to put it at but you don't want it to go beyond that level. You want to have some fail-safe mechanism.

DR. MCCULLEY: But I don't think we know what it is. We know that we are occluding the central retinal artery and then it becomes the time, and the time typically in clinical practice is that we absolutely do not want to go beyond three minutes.

DR. ROSENTHAL: So do you want to make sure that at two and a half minutes you press the button and the thing releases --

DR. MCCULLEY: That you start bailing out, that is right.

DR. HIGGINBOTHAM: What has been the longest time reported with this procedure? Does anyone know? I mean, typically in learning curves?

DR. MCCULLEY: I don't know, but I do know that there is an article publication of suggested nerve fiber layer loss with --

DR. MACRAE: With 60-80 seconds.

DR. MCCULLEY: Well, for that one it was 40 seconds. For that paper it was timed at 40 seconds, and it

was stated that with the device used to measure the nerve fiber layer thickness there was loss of nerve fiber layer thickness with a 40-minute elevation of intraocular pressure with the device in question.

DR. PULIDO: The only experimental data available is the Hayray data in young monkeys, and there you could go for 90 minutes of total occlusion of the central retinal artery and still get function returning. Now, again, those were monkeys and it was difficult to determine macular function in those cases but those eyes by ERG were perfectly fine at 90 minutes. The normal person isn't, you know, a young monkey but I don't know of any other experimental data in that regard.

DR. MCCULLEY: What we would say here then is I don't think we have an absolute number, Ralph. I think we have a low number that if we are below that, about 65 mHg or above that we need. I can tell you that with pneumatometry, with the various devices we use, we typically get between 80 and 85 mHg as the intraocular pressure. I can tell you that we have a bail out time of 3 minutes, and if we are at 2 and it doesn't look like we are going to make it cleanly by the 3 we abort. But I don't know how much data there is on that, but it is something to be concerned about and there are these other issues about nerve fiber layer loss, whether that proves to be true or not. So I think you guys need to

watch for those things and the devices need to have the ability to be used effectively to accomplish what needs to be accomplished in a reasonable period of time.

DR. HIGGINBOTHAM: Can I just make one final comment?

DR. MCCULLEY: Yes, please.

DR. HIGGINBOTHAM: Since this may be my only opportunity --

[Laughter]

-- since Dr. Rosenthal asked for a number, I mean, certainly 80 mHg would be as best as I could give you considering that we do see patients with angle closure with that level, and it has been done clinically already with this procedure, and I would say no more than 2.5 to 3 minutes because that seems to be the outside boundary of what has already been done. So 80 and 2.5 to 3 minutes.

DR. MCCULLEY: That is what we are doing but we have had people present at the panel in the past where they have stated that the pressure is being elevated to 100 or more. But you have all of that information. Mr. Mastel?

MR. MASTEL: I would first ask a question what is causing the raise in intraocular pressure, to begin with. We have to understand the physics involved. The second issue is would you like to have definitive research that we have done to know what the numbers actually are?

DR. MCCULLEY: I am sure the agency would love to have you present that to them at your opportunity but I don't think we can stop and do that now, but if you have additional data to bring forward, by all means. If you could summarize it in a sentence, we would love to hear the summary.

MR. MASTEL: The pressure is raised by decreasing the scleral curvature. The scleral curvature is an issue which is addressed with multiple rings. The second thing is you are reaching 200 mHg and more on a routine basis.

DR. REINSTEIN: For instance, eye rubbing produces intraocular pressure rises to 300, 400 mHg and blinking actually produces intraocular pressure elevations in the 100s mHg as well.

DR. MACRAE: There is a paper by Steve Trochell, whom some of you may know, who basically measured intraocular pressure with blinking and squeezing, and intraocular pressure goes up to 80 with a hard squeeze. The one thing that I want to comment on in terms of Dr. McCulley's comment about pressure going up to 80 with a pneumatometer, we routinely measure with a pneumatometer and it does go up to 80. There is variance between the pneumatometers that we have. One will go to 80 just right away and the other one doesn't go to 80. So the pneumatometers, I don't think, were designed to go up to

this level, first all, and I agree, I have seen a number of studies, and talked to Dr. Ruiz a number of times about this, and the pressures are going up much higher than probably 80 and we are not able to measure that.

DR. MCCULLEY: I don't want to cut off discussion so, Dr. Pulido?

DR. PULIDO: I would like to know -- it seems to me once you got above systolic pressure it doesn't matter whether it is 100 or 200 but Bullock has had several cases of eye explosions with patients who had gotten intraocular injections and the eyes exploded. Now, these are highly myopic eyes with staphylomas. What kind of intraocular pressure would be able to cause an ocular blowout?

DR. MCCULLEY: We don't know. So far as I know, there has not yet been a report of that occurring but the fear, if it went sufficiently high, is that presumably it could happen. I think we have made this point. I really would like to move forward.

DR. REINSTEIN: Let me just say that that data is available because explosion studies were done for RK and PRK eyes, and the number is somewhere in the region of 1500 mHg for explosion.

On the point of intraocular pressure --

DR. MCCULLEY: That is your absolute number, Dr. Rosenthal.

[Laughter]

Let's please get back to the document.

DR. REINSTEIN: On this whole discussion about the pressure inside the eye with regards to keratome use, let's not forget that it folds back onto the precision of the depth, etc., etc. So it is not just an ischemic issue; it is an issue of accuracy of performance.

DR. MCCULLEY: Please. We have done this already in the other area. Right now I don't want to keep revisiting things we have already discussed. I want to move forward. So, is there anything else related to problems with increase in intraocular pressure?

[No response]

The other issue is decentration, which is not so much a pressure issue but the association of the suction ring to the globe. I don't know that that is a device issue. It may be.

DR. REINSTEIN: It can be. It is the experience that if the suction rise is slow it can produce a stimulation to the patient producing a bell effect. So the eye can be displaced during the increase of pressure and cause the immobilization to occur in the wrong position.

DR. MCCULLEY: Good point. So device issue there would be a slow acquisition of effective suction -- slow suction. Operator is appropriate centration of the suction

ring. Patient is cooperation, non-movement. Any other thing -- well, there is another, the anatomy. So conjunctival scleral anatomy and curvature. Anything else?

[No response]

The next issue is interface debris -- metal shavings. We have dealt somewhat with that with lamellar keratitis for Meibomian secretions. Interface degree is really mostly the blade, is it not? It is appropriate maintenance of the microkeratome. But is it not blade QC?

DR. REINSTEIN: There are reported cases of oil from the keratome in the interface.

DR. MACRAE: We have had a case of literally rust dropping from a microkeratome into the field. I thought I had a hemorrhage or something --

DR. MCCULLEY: You probably did when it happened.

[Laughter]

DR. MACRAE: Just a small one. So we have had that, and I have heard of other cases where the device actually lets oil or other parts of the microkeratome into the field.

DR. MCCULLEY: So seal of motor and appropriate maintenance of microkeratome. Is it fair to put QC of blade? Will that cover it? QC of blade and blade reuse.

DR. MACRAE: For the record, this is actually an area where I think we could really do some good today in

that, you know, we have heard some presentations about the variability of blades, and there is a lot of information that is being gathered now but one of the things I think the agency can help us with, particularly in this part of the industry, is just getting good blade quality control. Doug Mastel alluded to this, and I think this is an important issue and I would encourage the agency to establish clear guidelines for quality control for blades because in the field, in the real world, practitioners are using all different types of blades and I suspect -- you know, if my wife has Lasik surgery I want to have the smoothest interface that I can possibly have and I don't want to have an irregular blade quality. I think that those little irregularities in the interface to cause some glare and some nighttime vision problems.

DR. MCCULLEY: All of these come under device. What about operator? That is going to be maintenance of an isolated sterile field.

DR. YAROSS: And also blade reuse.

DR. MCCULLEY: Good point. Well, and it would be the microkeratome maintenance and blade reuse. For patient, some patients spew out more Meibomian secretions than others. Some people have scalier skin. But that really should be dealt with by the operator. So I think we will leave that on the operator. Anything else on interface

debris?

MR. MASTEL: How about gloves? How about whether people wear gloves or not gloves?

DR. MCCULLEY: Okay, so avoidance of introduction of particulate matter under operator. Anything else?

[No response]

Epithelial defects under device it is really maintenance of device. Avoid nicking it or having deposits on the device that dry, crust, stick.

DR. YAROSS: Well, for the device it would be the maintainability and then the maintenance itself is the operator.

DR. MCCULLEY: Good point.

DR. REINSTEIN: There is anecdotal evidence that blade characteristics can produce epithelial defects. So quality control.

DR. MCCULLEY: Same kind of thing for high quality blades, and potentially another cause would be reuse of blades as they dull, debris dries on between eyes. Anything else under device?

MR. MASTEL: Dr. McCulley, surface finish of the foot blade. We have scan electron microscopy of that that I would be happy to forward.

DR. MCCULLEY: Say that again, I am sorry.

MR. MASTEL: Surface finish of the metal foot

blade on top of the epithelium. It is a complex. It is the foot blade and the blade I think.

DR. MCCULLEY: Did Marcia's statement get that? What was your statement?

DR. YAROSS: Which one?

DR. MCCULLEY: The last one about --

DR. YAROSS: Maintainability versus maintenance.

DR. MCCULLEY: So yours would be manufacture of the foot plate --

DR. YAROSS: Surface quality of foot blade.

DR. MCCULLEY: Okay, so surface quality of foot blade as it can be maintained and so forth. I am sorry, I can't see your name tag.

MR. MASTELLONE: Charles Mastellone. Improper gap between the blade and the blade is a cause of epithelial defects. Excess of folding of the flap within the keratome as it passes would probably cause defects too.

DR. MCCULLEY: Would that be a device issue?

MR. MASTELLONE: Yes, if the keratome was designed where there wasn't proper area for the flap to be stored as the pass is made it would fold up on itself, and you could cause a defect.

DR. MCCULLEY: Okay, so under device it would be blade-plate association?

MR. MASTELLONE: Yes, and the gap between the

blade and the plate --

DR. MCCULLEY: That is what I meant, blade-plate association.

MR. MASTELLONE: And the other one that causes defects is if the keratome is too low in relationship to the suction ring you get an abrasion by the plate just physically shearing off the epithelium.

DR. MCCULLEY: Put that in two or three words for us.

MR. MASTELLONE: Plate hitting shearing off the epithelium.

DR. MCCULLEY: So design where plate trauma is excessive. Operator? Appropriate loving care of the ocular surface pre- and intraop.

MR. MASTEL: A question on the operator. What are the doctors doing to control the gap?

DR. MCCULLEY: Controlling what gap?

MR. MASTEL: The blade depth.

DR. MCCULLEY: Oh, blade depth? What are we doing to control the blade depth?

MR. MASTEL: Yes.

DR. MCCULLEY: If I am, I don't know how I am doing it. I am not sure I understand. Do we have anything to control that?

MR. MASTEL: I think we should.

DR. MCCULLEY: But we don't now, do we? So, put this into device design issues --

MR. MASTEL: Come up with a methodology for calibrating the depth of the blade.

DR. MCCULLEY: And that is irrespective of blade-plate association, just blade depth.

DR. YAROSS: Isn't that a mitigator for the issues of the precision of the cut dimensions to begin with? I think we come back to that under mitigators.

DR. MCCULLEY: Okay, so you hold that thought for mitigating events when we come back to this. Anything else under operator? It is appropriate surgical technique to maintain health of the epithelium with the preop and intraoperative maneuvers. Mr. Bartell?

MR. BARTELL: One of the things I might mention with the manual units that sometimes it does tend to cause epithelial abrasions, particularly close to the hinge. They make a very nice move slowly forward but once they hit the stop they think, oh, and they go backwards very quickly and they don't give that flap time enough to get back through that gap between the plate and the blade.

DR. MCCULLEY: So in manual operation pause between reverse translation.

MR. BARTELL: The reverse translation should be about the same speed as the forward translation, and that

usually will give the flap time enough to escape the area.

DR. MCCULLEY: So with manual operation consistent forward and reverse translational speed. Anything else on operator?

[No response]

Patient? There it is mainly avoidance of anterior membrane dystrophies. Avoidance of anterior membrane dystrophies and previous contact lens wearers --

DR. HIGGINBOTHAM: Or diabetics and glaucoma patients.

DR. MCCULLEY: Patients with underlying ocular or systemic disease, making the epithelium more vulnerable, and previous contact lens wear. Anything else on epithelial defects?

[No response]

Lid lacerations, I think we put that under something else, didn't we? Did we not effectively deal with that otherwise? No? We discussed it under infection but, yes, we fuzzed it under it.

DR. MAGUIRE: It is covered under keeping device from contacting non-sterile surfaces.

DR. MCCULLEY: Right. So we don't need to have this as a separate item at this point. I need an active "no" not a fatigues "no." No? Okay. So we have dealt with lid lacerations. Have we dealt with bleeding? I think we have.

Did that not come under corneal diameter -- under patient characteristics.

DR. MAGUIRE: And it also came under suction.

DR. PULIDO: I disagree.

DR. MCCULLEY: It is pannus. We are talking about superficial vessels in the cornea. When we make the cut, we cut across the vessels and we have surface bleeding. It is not a big deal as long as you know what you are doing.

DR. PULIDO: Conceivably it could have occurred --

DR. MCCULLEY: Into the mike, Jose.

DR. PULIDO: Conceivably it could have occurred if you started your cut too far towards the limbus.

DR. MCCULLEY: That would be the decentration that we have dealt with, yes. I need opinion -- you guys out there too. I really can't keep up with everything; I need help. Have we dealt effectively with bleeding or does that need to be yet another issue here? Mr. Mastel?

MR. MASTEL: Just having been developing a microkeratome for four years, hyperopic eyes are normally small and hyperopic ablations are like big flaps. So it seems to me where we are going to get into trouble is big flaps on small eyes.

DR. MCCULLEY: True. I agree with what you said; I still need help. Have we dealt effectively with bleeding?

DR. HIGGINBOTHAM: I would suggest that you leave

it as a category and just go ahead an put under patient, patient characteristics and that would include everything, just to eliminate the fact that it is not the device, etc.

DR. MCCULLEY: You are right. Well, the issue with device would be ability to adjust flap size to avoid vessels.

DR. YAROSS: That is mitigation.

DR. HIGGINBOTHAM: Yes, that is a mitigation.

DR. MCCULLEY: It is a mitigation. Keep that thought; that is your job. Operator -- many of these things actually that we have here we could move to mitigation. The operator, it is going to be decentration or inappropriate selection of flap size. You could put that in mitigation. We actually probably could take everything under causes out and put it under mitigation, just about.

Then patient, it is going to be small corneas --

DR. PULIDO: Jose Pulido, retina surgeon extraordinaire! What about things like antiplatelet factors, coumadin?

DR. MCCULLEY: Well, that is subconjunctival hemorrhages that we do see. So we have bleeding. The bleeding we have been talking about has been corneal and that would be under patient characteristics. We have not talked about subconjunctival hemorrhages because they are a nuisance to date and not a major problem, and relate to the

suction ring.

Now, we have gone down this and I think we have filled in everything as best we can. I honestly hope that when we get to mitigating factors we have, in effect, really dealt with a lot of them but we need to go through that process. I am not sure -- I need to ask you guys at the table whether you can print out the second half for us while you are scribing or whether you need a short break to give us the printout.

DR. ROSENTHAL: We have to break.

DR. MCCULLEY: Okay, we have to break.

DR. ROSENTHAL: We have to give it to both you and the public so we need to break.

DR. MCCULLEY: How long will it take you? I would remind everyone that it is 3:15. So how long will it take you to printout for us the second half?

MR. HOANG: Just the second page while you are going through the first page?

DR. MCCULLEY: We are going to take a break so you can print the second half out and then we will go back and start at the top, so you can scribe while we are doing the mitigations. So how long do you need to printout the second half?

MS. HOANG: About ten minutes.

DR. MCCULLEY: All right, a ten-minute break.

[Brief recess]

Session III: Steps to Mitigate Problems

DR. MCCULLEY: We have two more tasks ahead of us and it is 3:40, and we are going to start losing people. So I ask, please, succinct, to the point, no editorialization, no repetition, and everyone try to watch that when we do make a point that it effectively gets translated to the screen.

We have to go through mitigation and then we have to go through and rank order, the panel will rank order. We will go through mitigation with everyone. We will go through rank order with just the panel.

So let's go back to the top, imprecise diameter or flap hinge, e.g., free cap, short flap. We have listed the causes. In situations where we have really covered the cause that would lead to the mitigation, I can't keep up with doing it. If somebody would kind of flip-flop it around to, you know, okay, we have covered that and move it over there? So, let's help with that, and we will invite audience participation in that as well.

So, imprecise diameter of flap hinge -- how to mitigate that.

DR. YAROSS: I think primary mitigators here are good manufacturing practices, that they have to do with the day-to-day realization of the specifications and the

tolerances.

DR. MCCULLEY: That would come under device. But would it be reasonable to say that for device mitigation GMP would cover it?

DR. YAROSS: Well, QSR also with good design practices, quality systems regulation now calls for design controls for the more sophisticated of these devices. Anything that includes computer software is under design controls, which then does call for doing this type of a risk analysis, identifying the hazards, identifying the causes and the mitigators. So that, in effect, addresses a great many of these items that are at the device level.

DR. MCCULLEY: Mr. Sacharoff, you are leaning on the edge of your chair. Did you want to say something?

MR. SACHAROFF: I don't want to say anything on that very strong point but I would say that combined device and patient, if I can do that, patients aren't under QSR. Their eyes are unique to them; they are based upon their own nature itself. The ability of one microkeratome and another to be able to inform you as to the applanation size can lead to better control, given that you can't force the eye to have an identical shape, one to the next.

DR. MCCULLEY: Okay. Thank you. So, under device GMP and what was --

DR. YAROSS: QSR.

DR. MCCULLEY: QSR. What else needs to be added under device mitigation to those two? Anything?

DR. REINSTEIN: Something that is not present with all of the current keratomes is a device for determining what the flap diameter will be before passing the keratome, i.e., the applanation lens. It has disappeared from one or two keratomes.

DR. MCCULLEY: So applanation lens use. Anything else? Dr. Stulting?

DR. STULTING: Performance specifications -- although we can't specify patient anatomy we can get performance specifications so we know how the device will perform on a variety of anatomies. Then, lastly, device design so that there is a way to make a device perform in different anatomies in different situations.

DR. MCCULLEY: Doyle, under your device design, is there some -- how can that be -- you know, your device design, etc., are there two or three words that can be used with design flexibility? What would be the appropriate descriptors?

DR. STULTING: Well, let's talk about some concrete examples. You put --

DR. MCCULLEY: I know what you are getting at. I am trying to get words to cover it.

DR. STULTING: Oh. We are talking about diameter

of a flap and you need to know how the device will perform based on the patient's measurements, and you have to have a way to adjust to the patient's measurement or exclude that patient --

DR. MCCULLEY: Design customization ability.

DR. MAGUIRE: Design customized to anatomy.

DR. STULTING: There you go.

DR. PULIDO: How about topographic flexibility?

DR. MCCULLEY: We got it. Anything else under device mitigating this issue?

[No response]

So, we have GMP, QSR, applanation lens use and performance specifications, design customization to patient anatomy.

DR. MAGUIRE: Reliability of intraocular pressure.

DR. ROSENTHAL: Mr. Chairman, are you recommending clinical data? Do you think clinical data is necessary?

DR. MCCULLEY: Well, I guess if the design customization is accomplished there would have to be clinical data to support it.

DR. YAROSS: I think if you can specify what you are looking for, what the range of anatomy is, it should be possible to identify in the laboratory if a certain device can accommodate those dimensions. So, I think we need to be careful in terms of this aspect here. First, what are the

characteristics of the device that we need, and then can you determine those characteristics.

DR. MCCULLEY: And a surrogate potentially to the human situation could be devised. Mr. Sacharoff?

MR. SACHAROFF: In a nutshell, I think you either can control or you adapt. The device would have to do one or the other. If it can't control, then it has to adapt and has to be adaptable. It doesn't mean you have to collect clinical data; it just means you have to have clinical adaptability for any given circumstance you may encounter.

DR. MCCULLEY: But you would have to have some mechanism of demonstrating that, indeed, you accomplish what you theoretically wanted to accomplish, and that could be done potentially with a surrogate. Shirley?

MS. MCGARVEY: In all of the operator-related situations, certainly training by the manufacturer is one of the mitigating factors that can be implemented. And, some of this has been done by keratome manufacturers with respect to their willingness to ship blades to people who are not certified in their course. So, if they restrict access in this way -- it has not been well received in the marketplace, but certainly manufacturers have tried to have an impact and tried to mitigate in this way, any lack of training, lack of understanding of their product line. So, as we look at mitigations, the degree to which a

manufacturer should be able to restrict access should be considered.

With respect to the question on whether or not clinical data is needed, that is another issue of where does the liability for taking information to the labeling lie. There is no information in any microkeratome on complications or adverse reactions associated with this product. The laser manufacturers are the ones who have to take the hit in their labeling with respect to the problems associated with this product, and it just seems to me that that is fundamentally wrong.

DR. MCCULLEY: Okay. Related to your first point, I would propose working assurance of adequate manufacturer training.

Relative to operator, that would relate to the operator. The last point covers not only the design but also the operator.

The flat Ks, mitigating relates to ability to adjust the microkeratome with its suction ring to accommodate to the individual patient cornea. Any other mitigating factors on the first point?

[No response]

The second point is poor precision and reproducibility, mean (desired versus achieved), standard deviation, range, maximal thick, thin, donut, free, AC

perforation, ectasia. We have a number of causes. Some of them relate to the things above -- assurance of maintenance of adequate suction and the ability -- well, let's do device first. So, maintenance of adequate suction. We can put probably everything related in one. So, see above, and add to it. What do we want to add to it?

DR. REINSTEIN: It is known that no matter how well the tolerances of the instruments are met for each specific keratome, the inter-keratome variation will exist. I would like to see -- and this is really a serious point for the record -- perhaps a suggestion that keratomes be sold with a unique descriptor certificate of the performance of that keratome because of the variation between them.

DR. MCCULLEY: Somewhere in the discussions I heard the term or phrase used before that sounded really good but I didn't hear it in what you just said, and I don't remember what it was. Can you come up with it? To put into a short phrase, it was --

DR. MACRAE: Fingerprinting --

DR. MCCULLEY: Yes, but there was a term used today.

DR. REINSTEIN: Certificate?

DR. MCCULLEY: No, it wasn't certificate. No, no, no.

DR. YAROSS: Inter, intra.

DR. MCCULLEY: It wasn't inter, intra. It was something that related to that, that each instrument would have provided with it its performance standards.

DR. REINSTEIN: Correct, and those performance standards would be described by the mean standard deviation and range using the elements that come with that keratome. In the case of keratomes that have several rings, they would have to be tabulated so that you could look up -- as a user you could look up a way of predictably performing a keratectomy.

DR. MCCULLEY: Just so we are clear and that we are understanding one another, that is each microkeratome that is delivered is delivered with its performance standards.

DR. REINSTEIN: Unless it can be demonstrated that they are all very close to each other. I mean, it is a point of long-term safety that is very important.

DR. YAROSS: Dr. McCulley, from a practical standpoint, to get the type of statistics you are talking about on each device we would essentially be selling used devices in the sense that to get the mean, standard deviation with every possible -- for some of the complex machines, with the different combinations, you are talking about potentially tens to hundreds of measurements per device when really the endpoint is predictability. And I

think that it is potentially more doable for manufacturers to set appropriate specifications and then have their quality system ensure the day-to-day realization of those specifications than to -- and I would think that that would be more useful to the clinician than to say, okay, we are going to accept that there is wide variability and we will just tell you what yours is.

DR. MCCULLEY: Marcia, can you give us a guideline for that? Can you state how you think this ought to be worded?

DR. YAROSS: Appropriate specifications and effective quality systems.

DR. REINSTEIN: I see your point, and I agree that what I suggested is ominous. However, we are not dealing with an event that is going to be sporadic. We are dealing with an event, called Lasik, which is going to run into the millions of eyes. Therefore, the small complication rates which are being experienced, for example, now when only hundreds of thousands of eyes are being done, will multiply. I agree with what you are saying and I think that the compromise is probably going to be reached in terms of the labeling of the performance of the keratome so that the keratome will be sold with a promise that it will perform at least to the standard.

That is something which will involve a lot of

industry ratification of what they are producing because without that we have a situation, as we do now, where the keratome is being used as an access instrument to the stromal bed when, in fact, it was designed to produce a cap for surgery on the cap. It is a different situation that we are in now. Lasik is a different situation, and I don't know how we can get out of this because even Barraquer, who made these keratomes by hand, said each and every keratome must be tested in human eyes to know what it does, and he had tolerances which are way beyond what we heard this morning. I don't know the answer to this.

DR. MCCULLEY: The answer is somewhere between the ideal and the practical, and I am not sure how to state it. Ma'am?

MS. GOVINGUENE: Yes, I am Anne Govinguene. I wanted to add that it is difficult for a manufacturer to guarantee, for example, when it depends, as you said, on many parameters that could be the speed of translation and the patient characteristics. So, it is very difficult for us to say, you know, you are going to get this and this. It is easier to say this is the difference between this part of the head and this part of the head.

DR. MCCULLEY: I suspect we could keep going on for ever on this point and not arrive at anything definitive. If there is a point of information that can help

the FDA decide -- our role here is to advise, and this is going to be one of those situations, I am afraid, where we are going to need to give your our best input. You are then going to do the best you can with it and it will come back to us when you are doing your guidance document and we will have another shot at it. A lot of this relates to your engineers and your engineering. Scott?

DR. MACRAE: I am not a quality expert but I think that the manufacturers could take, let's say, five systems and test them and see what the variability between the systems is using, as Doug Mastel suggested, a silicone type system --

MR. MASTEL: A standard --

DR. MACRAE: A standard system or you could use a standard pig eye that had a certain curvature, and do enough of those tests to show that the microkeratomes would perform within a relative range, and periodically test that, by the manufacturer, in their system. I agree, I think it is absolutely critical that, you know, I get the same type of microkeratome in Portland, Oregon as Dr. McCulley gets in Dallas, Texas and that it has almost the same characteristics. And, I think that the industry can do that. It is not going to be quite as precise as we want it to be but, with time, I suspect it will get even better than we anticipate.

DR. MCCULLEY: I think our concerns and sentiments have been stated. Are you satisfied with us leaving it like this, that you develop what you are going to do with the guideline that takes into reasonable balance between the ideal and the practical? Do you need any further input from us on this point?

DR. ROSENTHAL: I think we understand the goldest of all gold standards and what is a practical solution. I think the sense is there has to be some way of ensuring that there is some standardization and that one can feel that when it is used some sort of predictability and reproducibility, both intra and inter, is there. This happens in all types of devices. This isn't the first device that has come along in which one requires certain standards.

DR. MCCULLEY: I think from where we have come with this, essentially we would say "see above" that relates to device, operator, patient. Is there reasonable agreement on that point, and we will let Dan put another two cents worth in. Dan, two cents worth.

DR. REINSTEIN: Two cents. One penny I would like to spend on the labeling issue, which is that at the moment different companies are labeling the keratome depth differently. There is a keratome which is labeled --

DR. MCCULLEY: Dan, please, make your point but we don't really have time for --

DR. REINSTEIN: Okay. Well, the point is that some companies are saying the 160 keratome cuts 160 when, in fact, it cuts a lot less with a standard deviation. That means that few eyes will go over 160.

DR. MCCULLEY: Okay.

DR. REINSTEIN: Whereas some companies say it is 160 and that is the mean, therefore, 50 percent will be thicker than 160.

DR. MCCULLEY: Okay.

DR. REINSTEIN: So we have to --

DR. MCCULLEY: That is your labeling point. That is one penny. Is the second penny spent there too? Mr. Mastel?

MR. MASTEL: My grandfather was a carpenter for many years and he had a phrase which was "I but it three times and it was still too short." I think that we need to measure the gap.

DR. MCCULLEY: Okay. Dr. Maguire?

DR. MAGUIRE: One point before we leave this has to do with corneal perforation. I strongly believe that one mitigator is that the design should be made so that even with misuse you cannot perforate an eye.

DR. MCCULLEY: We request idiot perfect.

DR. MAGUIRE: That is an extremely serious, potentially blinding complication.

DR. MCCULLEY: Okay. The next point is quality of bed and perimeter, chatter lines, scoring, steps, jagged perimeter, entry wound, edge, tearing and entry angle. Are there specifics that we would need to add to the principles that were previously stated for number one and two? Dr. Pulido?

DR. PULIDO: Dr. McCulley, regarding the "idiot proofing," I don't think that we should make it such that it is not possible because with biology there is never 100 percent and we can't just put it onto the company's shoulders to try and make a machine that doesn't allow something like that to happen.

DR. MCCULLEY: Yes, the reality of the situation is that what led to it was that we had a plate we had to put in or could put in that could be put at various depth plates, and I think what Leo is saying is that we need set heads that we don't have to assemble. Yes, the idiot will find a way around it. So. But the majority will not.

Quality of bed, perimeter, chatter -- that seems again to come under the same kinds of heading as the first two, and the mitigating events or circumstances related to the device, patient and surgeon would be the same. Doyle?

DR. STULTING: I would like to add one issue here. This is clearly a blade quality issue, or at least part of it is a blade quality issue and I think we should go back to

the things that were raised earlier about substitute blades or generic blades or blades added to the system. It would be my opinion that if we are going to ask a manufacturer to generate a device the device includes the blade, and if a substitute blade is used that you have to have performance data for the blade in that device before it is marketed as a substitute, with the guarantee to users that it is going to work. I think that is very important.

DR. MCCULLEY: Sounds reasonable to me. Does that fit with reality with the FDA?

DR. ROSENTHAL: Yes, it does.

DR. MCCULLEY: Doyle, can you put that in a few words for us?

DR. STULTING: I would just say the blade is to be considered part of the device.

DR. MCCULLEY: But that doesn't then effectively address the generic blades.

DR. ROSENTHAL: I would think that the generic blades have to meet the specifications of the device blades.

DR. MCCULLEY: Okay.

DR. MACRAE: The performance standards.

DR. ROSENTHAL: The original manufacturer specifications.

DR. MAGUIRE: And you are going to figure out how to do that based on what you discussed in the first row up

here. Right? I mean number two, poor precision, reproducibility and standard deviation.

DR. MCCULLEY: Dr. Pulido?

DR. PULIDO: So theoretically you could have a generic blade that, if it met certain characteristics on a microkeratome machine, could then be used interchangeably with the company's blades. Is that what you are saying?

DR. MCCULLEY: Yes. I think that is what is being said, but it would have to demonstrate the standard.

Epithelial ingrowth. The way we worded these actually was clean cut, appropriate bevel, no epithelial defects, that is the mitigating. We have often, in these causative issues, stated the mitigating as well. I think we will leave it to you guys to work out which column you move them into and out of. Are there any other thoughts related to this in the mitigation of epithelial defects that are not already stated in the causes or implied very directly in the causes? Dr. Pulido?

DR. PULIDO: Dr. McCulley, I still have a problem with the generic situation because they could meet the same tolerances; there could be the same lab tolerances, but when it comes out, then in practice there could be a difference in the quality of the bed, etc., and you wouldn't have known that until after the fact.

DR. MCCULLEY: Can I ask you to bring that back up

again when we are between topics rather than in the middle?

DR. PULIDO: Yes, sir.

DR. MCCULLEY: Epithelial defects. Anything else to be added here? Doyle, you started to say something. Was it dealt with?

DR. STULTING: I was going to say smooth surfaces, etc., etc., but I was also going to bring up another issue, and that is that on many of these topics, like epithelial defects, I don't see how you can learn the performance of the device unless it is done on a living human because I know of no adequate model that would tell you whether or not you would knock the epithelium off. It has to do with too many things. If that is the case, then what we are moving toward is that there needs to be some human data somewhere. I don't want to see approval of the devices slowed down but, at the same time, when I am looking at a microkeratome I would like the manufacturer to give me the data in the labeling showing the performance of the device in a human.

DR. MCCULLEY: That is a sticky wicket. How do we deal with that? Mr. Mastel?

MR. MASTEL: We have done 80 eyes, and they could all be done histologically because Dr. Bizzard did them on corneal transplant patients and then went on to do the graft. That is how we have approached the clinical setting, and we would have ruined some corneas had we not done that.

DR. SUGAR: But the measurements you would get would not be comparable to those done on a normal cornea if you are doing it on a keratoconus cornea or edematous cornea. I don't know regulatorily, for a 510(k) do you get an IDE first? So, if you have an IDE you can ask for data on X number.

DR. ROSENTHAL: If clinical data is required by the agency, then it has to be done under an IDE. Some 510(k)s do require clinical data.

DR. SUGAR: So then it would be appropriate for there to be a pre-approval acquisition of data on a limited number of patients establishing that you can set up a pneumogram for this system that shows that it is either comparable or, if it is a new system -- not a new blade, that you have reproducibility. And, that can only, I think, be acquired on a living eye.

DR. ROSENTHAL: That is why I brought up the issue of clinical data before. It is just being addressed again. If this panel feels that clinical data is required, that is the recommendation they might make. Of course, the guidance document would reflect lots of considerations including that advice, but not necessarily only that advice.

DR. MCCULLEY: I think we are off of epithelial defects right now. But --

DR. SUGAR: It is more global.

DR. MCCULLEY: I agree. This was brought up before. I don't know that we dealt with it effectively. What is the sense of the group, and keep in mind that the audience is still invited to participate? What is the opinion as to whether clinical data on microkeratomes that are coming to the FDA, whether or not there should be the requirement for clinical data? Yes or no? Marcia?

DR. YAROSS: I think both the clinical and the regulatory issue is what is the indication for the device because under the situation that we have with these devices, if the indication is the same as the predicate devices, then the regulatory burden, as well as the clinical burden or the scientific burden, is to show that the product is equivalent to the predicate device. None of the devices out there yet has labeling regarding the Lasik procedure and that is where we keep getting kind of tied up in knots here. If someone comes in for a new microkeratome for the current indications, then I think the type of data need to be equivalent to what they have been before. If someone wants to come in for a new indication, then I think one discusses what is necessary to show that indication.

DR. MCCULLEY: We are getting into some significant regulatory issues here that are going to get increasingly muddy. So, I would like for you to direct us to move on.

DR. ROSENTHAL: Yes, please move on. They are complicated. They are issues that have to be discussed at the highest level of the organization, and I think it is inappropriate for us to have any further discussion.

DR. MCCULLEY: Keep in mind we got into that based on your question of whether there should be clinical data.

[Laughter]

Epithelial ingrowth. That is where we were before. Is there anything that needs to be added to the information that is on this page? Mitigating events, any that cannot be extracted from what we have said under causes?

DR. YAROSS: Dr. McCulley, just in terms of the patient issues, patient education because we have some issues here on patient compliance that we have not yet addressed.

DR. MCCULLEY: Okay, point well taken. I would have said that it is understood that we have to educate the patient on compliance but okay.

Flap dislocation, slippage, misalignment, wrinkles, microfolds, cracks, irregular astigmatism. Again, I think we have covered everything there. That would include the machine, patient, patient education and so forth.

Infection --

DR. ROSENTHAL: I think operator education as well. I heard that from the back of the room and, I mean,

just underlying all of this is operator education.

DR. MCCULLEY: Yes, right, and I think that that needs to be -- I mean, we kind of half covered that with adequate manufacturer training of operator and I don't know where the burden is going to fit on that, but a good point. That needs to be a recurring sentiment throughout.

Infection. We have lid laceration under infection. I don't think we want lid laceration parenthetically under infection there. That related to other anatomical issues, and clean runway, but it did come up as a possible infection issue but let's take it out from there.

Mitigating circumstances -- I think we have kind of stated them indirectly. Dr. Pulido?

DR. PULIDO: Not using the blade bilaterally.

DR. MCCULLEY: The issue there was not reusing the blade. That gets into --

DR. PULIDO: That is mitigation.

DR. MCCULLEY: That not everybody will agree with, unfortunately. You and I might.

DR. SUGAR: We discussed really that that is a practice of medicine issue. We can't, I think, add to this.

DR. PULIDO: I disagree because, for instance, when I do a vitrectomy I can't reuse my microvette in a second patient, not even a second eye.

DR. MCCULLEY: This is a tough philosophical issue

that gets into the practice of medicine, similar to some of the other things that we talked about. I think we could keep going around on it forever, and it relates as well to some FDA policy. I think for today's purposes we need to maybe leave it alone, maybe where it is, for the moment.

DR. SUGAR: And another issue, that the device should be constructed in such a way that it can be adequately cleaned and disinfected.

DR. MCCULLEY: Okay. Interrupted movement, partial flaps. I think we have implied the mitigating circumstances under our enumeration of causes.

Lamellar keratitis.

DR. STULTING: Are we assuming that you would take things from the device column and translate them to mitigated when they are obvious?

DR. MCCULLEY: That is my assumption.

DR. STULTING: Okay. So it says device not stopped because of minor obstructions -- that would mean that it would be sufficiently powered to overcome a minor obstruction. Right? Okay.

DR. MCCULLEY: Interrupted movement, partial flap. That is what we just did, isn't it? Lamellar keratitis. Is there anything that needs to be added to our list of causes that would need to come into the mitigation column?

DR. MAGUIRE: Is this a place to insert the

possible use of Dr. Kessler's group for --

DR. MCCULLEY: For postmarket surveillance.

DR. MAGUIRE: For postmarket surveillance for clusters of complications.

DR. MCCULLEY: I don't know that it would need to go in this table but I think that avenue being available to us and our awareness of it, and the FDA's awareness of it, needs to be stated but it probably doesn't need to go into this document.

DR. REINSTEIN: In the three causes it doesn't mention sterilization procedure, and the latest evidence, as we mentioned earlier, for probably cases of lamellar keratitis is to do with biotoxins and endotoxins. There is one study that is unpublished that I know of that showed that a specific sterilization protocol reduced the incidence.

DR. MCCULLEY: Those thoughts were introduced before under cause, and we tried to get it, which was equipment maintenance, operator maintenance and isolation of sterile field. I mean, when they look at the transcript and they look at the words here, that is there.

DR. REINSTEIN: Right. Perhaps what Dr. Sugar suggested, which was to make sure that the device is easily sterilizable and access to the inside of it is such.

DR. MCCULLEY: Okay, add that. It is not just the

device, it is what the device is being sterilized in. That gets back to education relative to appropriate maintenance of the device.

Next is suction, consistency of, loss of maintenance of. That has been discussed otherwise.

Ocular ischemia. I think we have talked about mitigating events, elevated intraocular pressure and the duration of it, and the machine being efficient so that time is not stretched. Anything else under ischemia?

[No response]

Decentration of flap. Any other mitigating factors that are not stated or implied?

DR. REINSTEIN: We discussed them but they are not stated, and multiple suction ports and an alarm that would go off after X number of minutes or seconds alerting the surgeon that the keratome has been on suction for that amount of time were two things that we discussed.

DR. MCCULLEY: Right. You had that job, and you had a job to remember something, Mr. Mastel, for a mitigating event. Have we covered it effectively? And Marcia had one to remember. You don't remember what you are supposed to remember?

MR. MASTEL: I am sorry, I am zoned out.

DR. MCCULLEY: Okay. Decentration of flap.

DR. REINSTEIN: That was to do with having an

adequate increased suction time, and not too slow.

DR. MCCULLEY: Adequate rate of accomplishment of suction.

MR. MASTEL: Excuse me, could we quantify that somehow?

DR. MCCULLEY: No, let's not. We have adequate and we will leave adequate for you and the engineers. Anything else? I did see a hand. Yes, Mr. Bartell?

MR. BARTELL: As relates to suction, something I think you should consider is -- you seem to be talking about the intraocular pressure that results when you get the suction ring on. I think you should also request from the manufacturer what is the IOP during the cut because as the plate applanates the eye, I think it may be reaching the 300 and 400 levels that Mr. Mastel mentioned, whereas, when you are measuring it just with a vacuum ring you are looking at 80-100, and there is ischemia and all these factors.

DR. MCCULLEY: That sounds very good but how are we going to accomplish that? I don't have room for my tonometer there when I have my keratome in there.

MR. BARTELL: I think that is a manufacturer's responsibility probably to give us some kind of an idea.

DR. MCCULLEY: Okay. Mr. Mastel?

MR. MASTEL: Dr. McCulley, the Germans corroborated evidence. We did a 0.25 mm accuracy transducer

that we placed in the whole globes and that is how we calibrated our tonometers. We put them on at 16 mm, very carefully controlling that they went to 180-200 before the microkeratome pass. That was only one microkeratome though. So I don't know what the others do.

DR. MCCULLEY: What eyes were these?

MR. MASTEL: Human globes.

DR. MCCULLEY: Live or cadaver?

MR. MASTEL: Cadaver. You have to put it into the chamber.

DR. MCCULLEY: So that comes down to a manufacturing request. Interface debris, metal shavings. Anything in mitigating factors that we have not stated or implied in causative events? I don't think so.

Epithelial defects. Ditto to what I just said.

Bleeding. Ditto. Ditto head movements.

That I think completes our task for this portion. I do want to give brief opportunity if anyone thinks there is a significant oversight that we have; not restating what has already been stated before. Dr. Stulting?

DR. STULTING: I don't know whether this is a restatement or not. I am speaking on behalf of what I consider to be my constituency of this meeting, and that is consumer ophthalmologists. Right now microkeratomes are manufactured and they are approved and they are sold, and

sort of after they are sold, in the back room in an informal discussion you figure out how thick a flap they make, how much variance they have, and what their complications are. That is not good. I think we need to put in place a system that will prevent that and give clinicians access to clinical information without doing it on their own in an informal way. And, I am not sure that this discussion has accomplished that. We have gone and enumerated some fairly obvious things that need to be taken into account when these things are manufactured, but I am not convinced that what we have done here today has led the FDA to a point where we can get that information efficiently, putting the fewest number of patients at risk and causing the fewest number of ophthalmologists to make errors with microkeratomes because of design problems.

DR. MCCULLEY: What I hear you saying relates back to the question that Dr. Rosenthal posed before, that we went astray on, but I hear you saying that you would call for a reasonable but not excessive amount of clinical data to be provided along with the request for FDA approval.

DR. STULTING: Frankly, yes. I think that is the prudent way to behave and it is in the best interests of ophthalmologists and patients.

DR. MCCULLEY: What I do not want to do now -- I think you have stated it well. I don't think it is necessary

for each of us to editorialize whether we agree or disagree, but I think it would be worthwhile for us to indicate whether we are in agreement with Dr. Stulting's statement.

[Panel members indicate agreement]

I think it is a unanimous yes, that we would like to see what he said.

Any other statements or comments where you feel strongly we have not adequately covered the issue?

Rank Ordering of Identified Problems

Seeing none, the panel will now do ranking. I am told that we want to ensure that the audience is aware that there will be an opportunity for open public comment, after we do the ranking, on issues that you feel the need to comment on, with time limitations being in place. So, no filibusters.

DR. ROSENTHAL: I would like you to rank them, not in actual order of priority but, very simply, as high, medium or low, if you would, please.

DR. MCCULLEY: All right.

DR. ROSENTHAL: Taking everything into consideration, high, medium, low.

DR. MCCULLEY: The open public hearing period is now closed. We will not rank order, we will indicate our severity scale as low, medium, high. But also there is severity and there is frequency, just to muddy the water,

that weighs into it. So, how would you like for us to deal with that?

DR. ROSENTHAL: Maybe you could do high, medium, low for seriousness and then high, medium, low for frequency, and we will put together some formula.

DR. MCCULLEY: Okay. We will do a seriousness score and a frequency score in that order.

DR. SUGAR: Can I ask Ralph why we are doing this?

DR. MCCULLEY: Don't ask; let's just do it!

DR. SUGAR: I would just ask you, Ralph, why we are doing this because I think it is pretty obvious from the discussion that has already taken place.

DR. ROSENTHAL: You are doing it because I would like to have some sense of what really is of crucial importance and what is just of academic interest because this panel can be very academic sometimes, and very erudite, but --

DR. MCCULLEY: We are always erudite!

DR. ROSENTHAL: -- but I want to be sure that it is of significant clinical importance.

MS. HOANG: Initially it was our plan, because we did not know how much time we would have to discuss the outline, which now we are not planning to discuss at all -- we were hoping that by ranking it you can, depending on the time allotment, discuss just the top five, or whatever, but

if you feel as though everything here is important and you would prefer not to rank it, then please let us know.

DR. MCCULLEY: Can I ask if we do this, Ralph, that we indicate whether we think this is important or not, important or minor?

DR. ROSENTHAL: Yes.

DR. PULIDO: Excuse me, a point of clarification to Dr. Rosenthal, when it comes to asking to asking for new clinical data for the keratomes would the ones that are already out there have been grandfathered in so we would not be asking for any clinical data for those. So we would be raising a new bar for the ones that have not been grandfathered in.

DR. ROSENTHAL: Dr Pulido, this is a very complex regulatory issue and I really cannot give you any answer to that now. It will have to be discussed at the highest levels of the organization.

DR. MCCULLEY: The only insight I would have for that may not be an appropriate insight, and I would just say remember Dr. Kessler's presentation this morning. That may not be apropos.

DR. PULIDO: In that case, when you asked for our opinions, I would say the bars should be the same for all the keratomes.

DR. MCCULLEY: I do not want to read these. Number

one, the precision -- all we are going to do is say this is important or this is for consideration. We are not going to say unimportant but important.

Another precision item, number two, is important.

PANEL MEMBER: Very important.

DR. MCCULLEY: Number three, quality of bed, a precision item, is important.

Epithelial ingrowth is an issue that is important. Please, some of you, identify yourself.

DR. REINSTEIN: Important.

DR. MCCULLEY: Okay. If there is disagreement -- I know none of you is shy -- I want you to jump in. I am going to take silence as concurrence.

Flap dislocation, etc., is --

PANEL MEMBER: Important.

PANEL MEMBER: I would say that for the manufacturers this is a surgical issue.

DR. MCCULLEY: We are not making subcategorical judgments. Is this an important consideration or not? The consensus is important. Patients don't do too well if their flap is not in place.

Infection is an issue that is --

PANEL MEMBER: Important.

DR. MCCULLEY: Partial flaps is an issue --

DR. REINSTEIN: Well, it depends on whether it

affects patient outcome. And, we all only from doing Lasik that interrupted movement and partial flaps does not affect patient outcome in almost all cases.

DR. MCCULLEY: In general it is a less critical issue. Not minor, but it is less critical.

DR. REINSTEIN: And infections are so rare --

DR. MCCULLEY: But if they happen they are bad. So we have two things we are weighing simultaneously in our minds, frequency and severity and infection sure as heck comes down as important. The partial flap, of all of the things, this point would be -- we don't like them; it is not good but it is not the end of the world.

Lamellar keratitis is an issue that is --

PANEL MEMBER: Important.

DR. MCCULLEY: The suction creation, maintenance, etc., are all issues that are --

DR. HIGGINBOTHAM: Very important.

DR. MACRAE: Very important.

DR. MCCULLEY: Interface debris are issues that are --

DR. HIGGINBOTHAM: Less important.

PANEL MEMBER: Less important.

DR. MCCULLEY: Less important but somewhere possibly -- well, yes, less important in general but still important.

DR. ROSENTHAL: Excuse me, Dr. McCulley, you have important, very important, less important and for consideration. So you, in fact, have four categories now.

DR. MCCULLEY: We do.

DR. HIGGINBOTHAM: It is extremely important.

DR. MCCULLEY: Interface debris, not as. Epithelial defects --

PANEL MEMBER: Important.

DR. MCCULLEY: They can be very important but they are common and most of the time or no consequence. So that is a toughie.

DR. HIGGINBOTHAM: But it could lead to infection and affect your outcome.

DR. MCCULLEY: Point taken. Bleeding.

PANEL MEMBER: No.

DR. HIGGINBOTHAM: Less important.

DR. MCCULLEY: Less important. You are frowning. It is less important.

DR. ROSENTHAL: I thought maybe it would be for consideration.

DR. MCCULLEY: Oh, for consideration. Okay.

DR. ROSENTHAL: But I am not allowed to lead the panel so --

PANEL MEMBER: I said that.

DR. ROSENTHAL: Thank you.

MS. THORNTON: Dr. McCulley, you have less critical and less important. Are they the same?

DR. MCCULLEY: Can you guys figure out that? I think we have given you our sentiment and I really would like not to beat on this anymore. I think we have let you know our thoughts on it.

Are there any other comments that the panel would like to make? Marcia?

DR. YAROSS: Just one comment for the panel's consideration regarding the recommendation on clinical data. I think it is important to note that the microkeratome is a device that is not used in isolation and, therefore, it is not entirely clear how one would use the clinical data that came out of it because the device is typically used in a procedure that is followed by use of another device. So, I think that is something to think about.

Just as a comparison to think about, it might be worthwhile for the panel -- if they are not aware that phacoemulsification machines are probably something that is of comparable seriousness and severity in terms of the types of things that can go wrong, but it has been well established that you can specify what the properties of phaco machines would be and, therefore, measure in a laboratory setting or in animal setting whether or not the device does meet those specifications. So, I think it is

worthwhile, in development of a guidance, to look and see whether or not a similar type of situation exists.

DR. MCCULLEY: Thank you. Point taken. I would like for us not to debate it. I understand your point and your viewpoint. Does the FDA feel a need for further comment on the point that has been made and the industry perspective?

DR. ROSENTHAL: No, I don't think we need further discussion on that issue.

DR. MCCULLEY: Thank you. Now, we have an opportunity for public comment. This is the closing portion of this meeting. If there is further comment that a member of the public would like to make relating to the proceedings today or the issues at hand, please so indicate. Seeing none, Dr. Rosenthal?

DR. ROSENTHAL: I would like just to make a final comment. I would like to thank very much the individuals from the audience who I thought made some extraordinarily fine comments, and who complemented the panel in providing us with an outstanding overview of the issues on microkeratomes. I very much appreciate them coming and I very much appreciate their input, as I do the panel's.

DR. MCCULLEY: Thank you. Any other comments? Do you have any further administrative issues?

MS. THORNTON: I would just like to say that we

will make every effort to get this chart in its final form up on our web site. I am going to see if they can do that. I can't guarantee it but we will have it available to be faxed to you if you would like to have it as we, you know, finally put it together. And, I would like to add my thanks to Dr. Rosenthal's. I know you all have worked very hard today and I appreciate your perseverance and tenacity on these issues, and we all do. And, I would like to thank Quynh and Joe for, without them, this would not have been possible and they have done a lot of good preliminary work on it and i know your input has been very helpful to them.

DR. ROSENTHAL: I would like to second that because, I mean, I take them for granted. They have done an enormous amount of work and have become quite expert in this area and I really appreciate the work they have done that has allowed us to do the kind of work you have done.

DR. MCCULLEY: From my perspective, I think this has been a very productive day, with very valuable and tough input from any one of a number of people. So my thanks to everyone.

MS. THORNTON: Adding to that, this is a new format for us. We have not done this particular kind of thing before, and I would like to let me know what you think of this as a working session. We would like to, hopefully, use this in the future, and if we can get your input and

improve it I think we can do some other things like this, on some other topics. And, to thank Dr. McCulley. He has done a great job.

[Applause]

It has been tough.

DR. MCCULLEY: Thank you all. The meeting is adjourned.

[Whereupon, at 4:40 p.m. the proceedings were adjourned]

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CERTIFICATE

I, **ALICE TOIGO,** the Official Court Reporter for Miller Reporting Company, Inc., hereby certify that I recorded the foregoing proceedings; that the proceedings have been reduced to typewriting by me, or under my direction and that the foregoing transcript is a correct and accurate record of the proceedings to the best of my knowledge, ability and belief.

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