1 it can survive. So I am going to defer to my retina
2 colleague on that issue. But from an optic nerve standpoint,
3 it is going to depend on individual characteristics.
4 DR. ROSENTHAL: I mean, I don't care what level
5 you decide to put it at but you don't want it to go beyond
6 that level. You want to have some fail-safe mechanism.
7 DR. MCCULLEY: But I don't think we know what it
8 is. We know that we are occluding the central retinal artery
9 and then it becomes the time, and the time typically in
10 clinical practice is that we absolutely do not want to go
11 beyond three minutes.
12 DR. ROSENTHAL: So do you want to make sure that
13 at two and a half minutes you press the button and the thing
14 releases --
15 DR. MCCULLEY: That you start bailing out, that is
16 right.
17 DR. HIGGINBOTHAM: What has been the longest time
18 reported with this procedure? Does anyone know? I mean,
19 typically in learning curves?
20 DR. MCCULLEY: I don't know, but I do know that
21 there is an article publication of suggested nerve fiber
22 layer loss with --
23 DR. MACRAE: With 60-80 seconds.
24 DR. MCCULLEY: Well, for that one it was 40
25 seconds. For that paper it was timed at 40 seconds, and it

1 was stated that with the device used to measure the nerve
2 fiber layer thickness there was loss of nerve fiber layer
3 thickness with a 40-minute elevation of intraocular pressure
4 with the device in question.
5 DR. PULIDO: The only experimental data available
6 is the Hayray data in young monkeys, and there you could go
7 for 90 minutes of total occlusion of the central retinal
8 artery and still get function returning. Now, again, those
9 were monkeys and it was difficult to determine macular
10 function in those cases but those eyes by ERG were perfectly
11 fine at 90 minutes. The normal person isn't, you know, a
12 young monkey but I don't know of any other experimental data
13 in that regard.
14 DR. MCCULLEY: What we would say here then is I
15 don't think we have an absolute number, Ralph. I think we
16 have a low number that if we are below that, about 65 mHg or
17 above that we need. I can tell you that with pneumatometry,
18 with the various devices we use, we typically get between 80
19 and 85 mHg as the intraocular pressure. I can tell you that
20 we have a bail out time of 3 minutes, and if we are at 2 and
21 it doesn't look like we are going to make it cleanly by the
22 3 we abort. But I don't know how much data there is on that,
23 but it is something to be concerned about and there are
24 these other issues about nerve fiber layer loss, whether
25 that proves to be true or not. So I think you guys need to

1 watch for those things and the devices need to have the
2 ability to be used effectively to accomplish what needs to
3 be accomplished in a reasonable period of time.
4 DR. HIGGINBOTHAM: Can I just make one final
5 comment?
6 DR. MCCULLEY: Yes, please.
7 DR. HIGGINBOTHAM: Since this may be my only
8 opportunity --
9 [Laughter]
10 -- since Dr. Rosenthal asked for a number, I mean,
11 certainly 80 mHg would be as best as I could give you
12 considering that we do see patients with angle closure with
13 that level, and it has been done clinically already with
14 this procedure, and I would say no more than 2.5 to 3
15 minutes because that seems to be the outside boundary of
16 what has already been done. So 80 and 2.5 to 3 minutes.
17 DR. MCCULLEY: That is what we are doing but we
18 have had people present at the panel in the past where they
19 have stated that the pressure is being elevated to 100 or
20 more. But you have all of that information. Mr. Mastel?
21 MR. MASTEL: I would first ask a question what is
22 causing the raise in intraocular pressure, to begin with. We
23 have to understand the physics involved. The second issue is
24 would you like to have definitive research that we have done
25 to know what the numbers actually are?

1 DR. MCCULLEY: I am sure the agency would love to
2 have you present that to them at your opportunity but I
3 don't think we can stop and do that now, but if you have
4 additional data to bring forward, by all means. If you could
5 summarize it in a sentence, we would love to hear the
6 summary.
7 MR. MASTEL: The pressure is raised by decreasing
8 the scleral curvature. The scleral curvature is an issue
9 which is addressed with multiple rings. The second thing is
10 you are reaching 200 mHg and more on a routine basis.
11 DR. REINSTEIN: For instance, eye rubbing produces
12 intraocular pressure rises to 300, 400 mHg and blinking
13 actually produces intraocular pressure elevations in the
14 100s mHg as well.
15 DR. MACRAE: There is a paper by Steve Trochell,
16 whom some of you may know, who basically measured
17 intraocular pressure with blinking and squeezing, and
18 intraocular pressure goes up to 80 with a hard squeeze. The
19 one thing that I want to comment on in terms of Dr.
20 McCulley's comment about pressure going up to 80 with a
21 pneumatometer, we routinely measure with a pneumatometer and
22 it does go up to 80. There is variance between the
23 pneumatometers that we have. One will go to 80 just right
24 away and the other one doesn't go to 80. So the
25 pneumatometers, I don't think, were designed to go up to

1 this level, first all, and I agree, I have seen a number of
2 studies, and talked to Dr. Ruiz a number of times about
3 this, and the pressures are going up much higher than
4 probably 80 and we are not able to measure that.
5 DR. MCCULLEY: I don't want to cut off discussion
6 so, Dr. Pulido?
7 DR. PULIDO: I would like to know -- it seems to
8 me once you got above systolic pressure it doesn't matter
9 whether it is 100 or 200 but Bullock has had several cases
10 of eye explosions with patients who had gotten intraocular
11 injections and the eyes exploded. Now, these are highly
12 myopic eyes with staphylomas. What kind of intraocular
13 pressure would be able to cause an ocular blowout?
14 DR. MCCULLEY: We don't know. So far as I know,
15 there has not yet been a report of that occurring but the
16 fear, if it went sufficiently high, is that presumably it
17 could happen. I think we have made this point. I really
18 would like to move forward.
19 DR. REINSTEIN: Let me just say that that data is
20 available because explosion studies were done for RK and PRK
21 eyes, and the number is somewhere in the region of 1500 mHg
22 for explosion.
23 On the point of intraocular pressure --
24 DR. MCCULLEY: That is your absolute number, Dr.
25 Rosenthal.

1 [Laughter]

2 Let's please get back to the document.

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

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

13 [No response]

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

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

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

1 ring. Patient is cooperation, non-movement. Any other thing
2 -- well, there is another, the anatomy. So conjunctival
3 scleral anatomy and curvature. Anything else?
4 [No response]
5 The next issue is interface debris -- metal
6 shavings. We have dealt somewhat with that with lamellar
7 keratitis for Meibomian secretions. Interface degree is
8 really mostly the blade, is it not? It is appropriate
9 maintenance of the microkeratome. But is it not blade QC?
10 DR. REINSTEIN: There are reported cases of oil
11 from the keratome in the interface.
12 DR. MACRAE: We have had a case of literally rust
13 dropping from a microkeratome into the field. I thought I
14 had a hemorrhage or something --
15 DR. MCCULLEY: You probably did when it happened.
16 [Laughter]
17 DR. MACRAE: Just a small one. So we have had
18 that, and I have heard of other cases where the device
19 actually lets oil or other parts of the microkeratome into
20 the field.
21 DR. MCCULLEY: So seal of motor and appropriate
22 maintenance of microkeratome. Is it fair to put QC of blade?
23 Will that cover it? QC of blade and blade reuse.
24 DR. MACRAE: For the record, this is actually an
25 area where I think we could really do some good today in

1 that, you know, we have heard some presentations about the
2 variability of blades, and there is a lot of information
3 that is being gathered now but one of the things I think the
4 agency can help us with, particularly in this part of the
5 industry, is just getting good blade quality control. Doug
6 Mastel alluded to this, and I think this is an important
7 issue and I would encourage the agency to establish clear
8 guidelines for quality control for blades because in the
9 field, in the real world, practitioners are using all
10 different types of blades and I suspect -- you know, if my
11 wife has Lasik surgery I want to have the smoothest
12 interface that I can possibly have and I don't want to have
13 an irregular blade quality. I think that those little
14 irregularities in the interface to cause some glare and some
15 nighttime vision problems.
16 DR. MCCULLEY: All of these come under device.
17 What about operator? That is going to be maintenance of an
18 isolated sterile field.
19 DR. YAROSS: And also blade reuse.
20 DR. MCCULLEY: Good point. Well, and it would be
21 the microkeratome maintenance and blade reuse. For patient,
22 some patients spew out more Meibomian secretions than
23 others. Some people have scalier skin. But that really
24 should be dealt with by the operator. So I think we will
25 leave that on the operator. Anything else on interface

1 debris?

2 MR. MASTEL: How about gloves? How about whether

3 people wear gloves or not gloves?

4 DR. MCCULLEY: Okay, so avoidance of introduction

5 of particulate matter under operator. Anything else?

6 [No response]

7 Epithelial defects under device it is really

8 maintenance of device. Avoid nicking it or having deposits

9 on the device that dry, crust, stick.

10 DR. YAROSS: Well, for the device it would be the

11 maintainability and then the maintenance itself is the

12 operator.

13 DR. MCCULLEY: Good point.

14 DR. REINSTEIN: There is anecdotal evidence that

15 blade characteristics can produce epithelial defects. So

16 quality control.

17 DR. MCCULLEY: Same kind of thing for high quality

18 blades, and potentially another cause would be reuse of

19 blades as they dull, debris dries on between eyes. Anything

20 else under device?

21 MR. MASTEL: Dr. McCulley, surface finish of the

22 foot blade. We have scan electron microscopy of that that I

23 would be happy to forward.

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

25 MR. MASTEL: Surface finish of the metal foot

1 blade on top of the epithelium. It is a complex. It is the
2 foot blade and the blade I think.
3 DR. MCCULLEY: Did Marcia's statement get that?
4 What was your statement?
5 DR. YAROSS: Which one?
6 DR. MCCULLEY: The last one about --
7 DR. YAROSS: Maintainability versus maintenance.
8 DR. MCCULLEY: So yours would be manufacture of
9 the foot plate --
10 DR. YAROSS: Surface quality of foot blade.
11 DR. MCCULLEY: Okay, so surface quality of foot
12 blade as it can be maintained and so forth. I am sorry, I
13 can't see your name tag.
14 MR. MASTELLONE: Charles Mastellone. Improper gap
15 between the blade and the blade is a cause of epithelial
16 defects. Excess of folding of the flap within the keratome
17 as it passes would probably cause defects too.
18 DR. MCCULLEY: Would that be a device issue?
19 MR. MASTELLONE: Yes, if the keratome was designed
20 where there wasn't proper area for the flap to be stored as
21 the pass is made it would fold up on itself, and you could
22 cause a defect.
23 DR. MCCULLEY: Okay, so under device it would be
24 blade-plate association?
25 MR. MASTELLONE: Yes, and the gap between the

1 blade and the plate --

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

3 association.

4 MR. MASTELLONE: And the other one that causes

5 defects is if the keratome is too low in relationship to the

6 suction ring you get an abrasion by the plate just

7 physically shearing off the epithelium.

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

9 us.

10 MR. MASTELLONE: Plate hitting shearing off the

11 epithelium.

12 DR. MCCULLEY: So design where plate trauma is

13 excessive. Operator? Appropriate loving care of the ocular

14 surface pre- and intraop.

15 MR. MASTEL: A question on the operator. What are

16 the doctors doing to control the gap?

17 DR. MCCULLEY: Controlling what gap?

18 MR. MASTEL: The blade depth.

19 DR. MCCULLEY: Oh, blade depth? What are we doing

20 to control the blade depth?

21 MR. MASTEL: Yes.

22 DR. MCCULLEY: If I am, I don't know how I am

23 doing it. I am not sure I understand. Do we have anything to

24 control that?

25 MR. MASTEL: I think we should.

1 DR. MCCULLEY: But we don't now, do we? So, put
2 this into device design issues --
3 MR. MASTEL: Come up with a methodology for
4 calibrating the depth of the blade.
5 DR. MCCULLEY: And that is irrespective of blade-
6 plate association, just blade depth.
7 DR. YAROSS: Isn't that a mitigator for the issues
8 of the precision of the cut dimensions to begin with? I
9 think we come back to that under mitigators.
10 DR. MCCULLEY: Okay, so you hold that thought for
11 mitigating events when we come back to this. Anything else
12 under operator? It is appropriate surgical technique to
13 maintain health of the epithelium with the preop and
14 intraoperative maneuvers. Mr. Bartell?
15 MR. BARTELL: One of the things I might mention
16 with the manual units that sometimes it does tend to cause
17 epithelial abrasions, particularly close to the hinge. They
18 make a very nice move slowly forward but once they hit the
19 stop they think, oh, and they go backwards very quickly and
20 they don't give that flap time enough to get back through
21 that gap between the plate and the blade.
22 DR. MCCULLEY: So in manual operation pause
23 between reverse translation.
24 MR. BARTELL: The reverse translation should be
25 about the same speed as the forward translation, and that

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

2 DR. MCCULLEY: So with manual operation consistent

3 forward and reverse translational speed. Anything else on

4 operator?

5 [No response]

6 Patient? There it is mainly avoidance of anterior

7 membrane dystrophies. Avoidance of anterior membrane

8 dystrophies and previous contact lens wearers --

9 DR. HIGGINBOTHAM: Or diabetics and glaucoma

10 patients.

11 DR. MCCULLEY: Patients with underlying ocular or

12 systemic disease, making the epithelium more vulnerable, and

13 previous contact lens wear. Anything else on epithelial

14 defects?

15 [No response]

16 Lid lacerations, I think we put that under

17 something else, didn't we? Did we not effectively deal with

18 that otherwise? No? We discussed it under infection but,

19 yes, we fuzzed it under it.

20 DR. MAGUIRE: It is covered under keeping device

21 from contacting non-sterile surfaces.

22 DR. MCCULLEY: Right. So we don't need to have

23 this as a separate item at this point. I need an active "no"

24 not a fatigues "no." No? Okay. So we have dealt with lid

25 lacerations. Have we dealt with bleeding? I think we have.

1 Did that not come under corneal diameter -- under patient
2 characteristics.
3 DR. MAGUIRE: And it also came under suction.
4 DR. PULIDO: I disagree.
5 DR. MCCULLEY: It is pannus. We are talking about
6 superficial vessels in the cornea. When we make the cut, we
7 cut across the vessels and we have surface bleeding. It is
8 not a big deal as long as you know what you are doing.
9 DR. PULIDO: Conceivably it could have occurred --
10 DR. MCCULLEY: Into the mike, Jose.
11 DR. PULIDO: Conceivably it could have occurred if
12 you started your cut too far towards the limbus.
13 DR. MCCULLEY: That would be the decentration that
14 we have dealt with, yes. I need opinion -- you guys out
15 there too. I really can't keep up with everything; I need
16 help. Have we dealt effectively with bleeding or does that
17 need to be yet another issue here? Mr. Mastel?
18 MR. MASTEL: Just having been developing a
19 microkeratome for four years, hyperopic eyes are normally
20 small and hyperopic ablations are like big flaps. So it
21 seems to me where we are going to get into trouble is big
22 flaps on small eyes.
23 DR. MCCULLEY: True. I agree with what you said; I
24 still need help. Have we dealt effectively with bleeding?
25 DR. HIGGINBOTHAM: I would suggest that you leave

1 it as a category and just go ahead an put under patient,
2 patient characteristics and that would include everything,
3 just to eliminate the fact that it is not the device, etc.
4 DR. MCCULLEY: You are right. Well, the issue with
5 device would be ability to adjust flap size to avoid
6 vessels.
7 DR. YAROSS: That is mitigation.
8 DR. HIGGINBOTHAM: Yes, that is a mitigation.
9 DR. MCCULLEY: It is a mitigation. Keep that
10 thought; that is your job. Operator -- many of these things
11 actually that we have here we could move to mitigation. The
12 operator, it is going to be decentration or inappropriate
13 selection of flap size. You could put that in mitigation. We
14 actually probably could take everything under causes out and
15 put it under mitigation, just about.
16 Then patient, it is going to be small corneas --
17 DR. PULIDO: Jose Pulido, retina surgeon
18 extraordinaire! What about things like antiplatelet factors,
19 coumadin?
20 DR. MCCULLEY: Well, that is subconjunctival
21 hemorrhages that we do see. So we have bleeding. The
22 bleeding we have been talking about has been corneal and
23 that would be under patient characteristics. We have not
24 talked about subconjunctival hemorrhages because they are a
25 nuisance to date and not a major problem, and relate to the

1 suction ring.

2 Now, we have gone down this and I think we have

3 filled in everything as best we can. I honestly hope that

4 when we get to mitigating factors we have, in effect, really

5 dealt with a lot of them but we need to go through that

6 process. I am not sure -- I need to ask you guys at the

7 table whether you can print out the second half for us while

8 you are scribing or whether you need a short break to give

9 us the printout.

10 DR. ROSENTHAL: We have to break.

11 DR. MCCULLEY: Okay, we have to break.

12 DR. ROSENTHAL: We have to give it to both you and

13 the public so we need to break.

14 DR. MCCULLEY: How long will it take you? I would

15 remind everyone that it is 3:15. So how long will it take

16 you to printout for us the second half?

17 MR. HOANG: Just the second page while you are

18 going through the first page?

19 DR. MCCULLEY: We are going to take a break so you

20 can print the second half out and then we will go back and

21 start at the top, so you can scribe while we are doing the

22 mitigations. So how long do you need to printout the second

23 half?

24 MS. HOANG: About ten minutes.

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

1 [Brief recess]

2 **Session III: Steps to Mitigate Problems**

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

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

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

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

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

1 tolerances.

2 DR. MCCULLEY: That would come under device. But

3 would it be reasonable to say that for device mitigation GMP

4 would cover it?

5 DR. YAROSS: Well, QSR also with good design

6 practices, quality systems regulation now calls for design

7 controls for the more sophisticated of these devices.

8 Anything that includes computer software is under design

9 controls, which then does call for doing this type of a risk

10 analysis, identifying the hazards, identifying the causes

11 and the mitigators. So that, in effect, addresses a great

12 many of these items that are at the device level.

13 DR. MCCULLEY: Mr. Sacharoff, you are leaning on

14 the edge of your chair. Did you want to say something?

15 MR. SACHAROFF: I don't want to say anything on

16 that very strong point but I would say that combined device

17 and patient, if I can do that, patients aren't under QSR.

18 Their eyes are unique to them; they are based upon their own

19 nature itself. The ability of one microkeratome and another

20 to be able to inform you as to the applanation size can lead

21 to better control, given that you can't force the eye to

22 have an identical shape, one to the next.

23 DR. MCCULLEY: Okay. Thank you. So, under device

24 GMP and what was --

25 DR. YAROSS: QSR.

1 DR. MCCULLEY: QSR. What else needs to be added
2 under device mitigation to those two? Anything?
3 DR. REINSTEIN: Something that is not present with
4 all of the current keratomes is a device for determining
5 what the flap diameter will be before passing the keratome,
6 i.e., the applanation lens. It has disappeared from one or
7 two keratomes.
8 DR. MCCULLEY: So applanation lens use. Anything
9 else? Dr. Stulting?
10 DR. STULTING: Performance specifications --
11 although we can't specify patient anatomy we can get
12 performance specifications so we know how the device will
13 perform on a variety of anatomies. Then, lastly, device
14 design so that there is a way to make a device perform in
15 different anatomies in different situations.
16 DR. MCCULLEY: Doyle, under your device design, is
17 there some -- how can that be -- you know, your device
18 design, etc., are there two or three words that can be used
19 with design flexibility? What would be the appropriate
20 descriptors?
21 DR. STULTING: Well, let's talk about some
22 concrete examples. You put --
23 DR. MCCULLEY: I know what you are getting at. I
24 am trying to get words to cover it.
25 DR. STULTING: Oh. We are talking about diameter

1 of a flap and you need to know how the device will perform
2 based on the patient's measurements, and you have to have a
3 way to adjust to the patient's measurement or exclude that
4 patient --
5 DR. MCCULLEY: Design customization ability.
6 DR. MAGUIRE: Design customized to anatomy.
7 DR. STULTING: There you go.
8 DR. PULIDO: How about topographic flexibility?
9 DR. MCCULLEY: We got it. Anything else under
10 device mitigating this issue?
11 [No response]
12 So, we have GMP, QSR, applanation lens use and
13 performance specifications, design customization to patient
14 anatomy.
15 DR. MAGUIRE: Reliability of intraocular pressure.
16 DR. ROSENTHAL: Mr. Chairman, are you recommending
17 clinical data? Do you think clinical data is necessary?
18 DR. MCCULLEY: Well, I guess if the design
19 customization is accomplished there would have to be
20 clinical data to support it.
21 DR. YAROSS: I think if you can specify what you
22 are looking for, what the range of anatomy is, it should be
23 possible to identify in the laboratory if a certain device
24 can accommodate those dimensions. So, I think we need to be
25 careful in terms of this aspect here. First, what are the

1 characteristics of the device that we need, and then can you
2 determine those characteristics.
3 DR. MCCULLEY: And a surrogate potentially to the
4 human situation could be devised. Mr. Sacharoff?
5 MR. SACHAROFF: In a nutshell, I think you either
6 can control or you adapt. The device would have to do one or
7 the other. If it can't control, then it has to adapt and has
8 to be adaptable. It doesn't mean you have to collect
9 clinical data; it just means you have to have clinical
10 adaptability for any given circumstance you may encounter.
11 DR. MCCULLEY: But you would have to have some
12 mechanism of demonstrating that, indeed, you accomplish what
13 you theoretically wanted to accomplish, and that could be
14 done potentially with a surrogate. Shirley?
15 MS. MCGARVEY: In all of the operator-related
16 situations, certainly training by the manufacturer is one of
17 the mitigating factors that can be implemented. And, some of
18 this has been done by keratome manufacturers with respect to
19 their willingness to ship blades to people who are not
20 certified in their course. So, if they restrict access in
21 this way -- it has not been well received in the
22 marketplace, but certainly manufacturers have tried to have
23 an impact and tried to mitigate in this way, any lack of
24 training, lack of understanding of their product line. So,
25 as we look at mitigations, the degree to which a

1 manufacturer should be able to restrict access should be
2 considered.
3 With respect to the question on whether or not
4 clinical data is needed, that is another issue of where does
5 the liability for taking information to the labeling lie.
6 There is no information in any microkeratome on
7 complications or adverse reactions associated with this
8 product. The laser manufacturers are the ones who have to
9 take the hit in their labeling with respect to the problems
10 associated with this product, and it just seems to me that
11 that is fundamentally wrong.
12 DR. MCCULLEY: Okay. Related to your first point,
13 I would propose working assurance of adequate manufacturer
14 training.
15 Relative to operator, that would relate to the
16 operator. The last point covers not only the design but also
17 the operator.
18 The flat Ks, mitigating relates to ability to
19 adjust the microkeratome with its suction ring to
20 accommodate to the individual patient cornea. Any other
21 mitigating factors on the first point?
22 [No response]
23 The second point is poor precision and
24 reproducibility, mean (desired versus achieved), standard
25 deviation, range, maximal thick, thin, donut, free, AC

1 perforation, ectasia. We have a number of causes. Some of
2 them relate to the things above -- assurance of maintenance
3 of adequate suction and the ability -- well, let's do device
4 first. So, maintenance of adequate suction. We can put
5 probably everything related in one. So, see above, and add
6 to it. What do we want to add to it?
7 DR. REINSTEIN: It is known that no matter how
8 well the tolerances of the instruments are met for each
9 specific keratome, the inter-keratome variation will exist.
10 I would like to see -- and this is really a serious point
11 for the record -- perhaps a suggestion that keratomes be
12 sold with a unique descriptor certificate of the performance
13 of that keratome because of the variation between them.
14 DR. MCCULLEY: Somewhere in the discussions I
15 heard the term or phrase used before that sounded really
16 good but I didn't hear it in what you just said, and I don't
17 remember what it was. Can you come up with it? To put into a
18 short phrase, it was --
19 DR. MACRAE: Fingerprinting --
20 DR. MCCULLEY: Yes, but there was a term used
21 today.
22 DR. REINSTEIN: Certificate?
23 DR. MCCULLEY: No, it wasn't certificate. No, no,
24 no.
25 DR. YAROSS: Inter, intra.

1 DR. MCCULLEY: It wasn't inter, intra. It was
2 something that related to that, that each instrument would
3 have provided with it its performance standards.
4 DR. REINSTEIN: Correct, and those performance
5 standards would be described by the mean standard deviation
6 and range using the elements that come with that keratome.
7 In the case of keratomes that have several rings, they would
8 have to be tabulated so that you could look up -- as a user
9 you could look up a way of predictably performing a
10 keratectomy.
11 DR. MCCULLEY: Just so we are clear and that we
12 are understanding one another, that is each microkeratome
13 that is delivered is delivered with its performance
14 standards.
15 DR. REINSTEIN: Unless it can be demonstrated that
16 they are all very close to each other. I mean, it is a point
17 of long-term safety that is very important.
18 DR. YAROSS: Dr. McCulley, from a practical
19 standpoint, to get the type of statistics you are talking
20 about on each device we would essentially be selling used
21 devices in the sense that to get the mean, standard
22 deviation with every possible -- for some of the complex
23 machines, with the different combinations, you are talking
24 about potentially tens to hundreds of measurements per
25 device when really the endpoint is predictability. And I

1 think that it is potentially more doable for manufacturers
2 to set appropriate specifications and then have their
3 quality system ensure the day-to-day realization of those
4 specifications than to -- and I would think that that would
5 be more useful to the clinician than to say, okay, we are
6 going to accept that there is wide variability and we will
7 just tell you what yours is.
8 DR. MCCULLEY: Marcia, can you give us a guideline
9 for that? Can you state how you think this ought to be
10 worded?
11 DR. YAROSS: Appropriate specifications and
12 effective quality systems.
13 DR. REINSTEIN: I see your point, and I agree that
14 what I suggested is ominous. However, we are not dealing
15 with an event that is going to be sporadic. We are dealing
16 with an event, called Lasik, which is going to run into the
17 millions of eyes. Therefore, the small complication rates
18 which are being experienced, for example, now when only
19 hundreds of thousands of eyes are being done, will multiply.
20 I agree with what you are saying and I think that the
21 compromise is probably going to be reached in terms of the
22 labeling of the performance of the keratome so that the
23 keratome will be sold with a promise that it will perform at
24 least to the standard.
25 That is something which will involve a lot of

1 industry ratification of what they are producing because
2 without that we have a situation, as we do now, where the
3 keratome is being used as an access instrument to the
4 stromal bed when, in fact, it was designed to produce a cap
5 for surgery on the cap. It is a different situation that we
6 are in now. Lasik is a different situation, and I don't know
7 how we can get out of this because even Barraquer, who made
8 these keratomes by hand, said each and every keratome must
9 be tested in human eyes to know what it does, and he had
10 tolerances which are way beyond what we heard this morning.
11 I don't know the answer to this.
12 DR. MCCULLEY: The answer is somewhere between the
13 ideal and the practical, and I am not sure how to state it.
14 Ma'am?
15 MS. GOVINGUENE: Yes, I am Anne Govinguene. I
16 wanted to add that it is difficult for a manufacturer to
17 guarantee, for example, when it depends, as you said, on
18 many parameters that could be the speed of translation and
19 the patient characteristics. So, it is very difficult for us
20 to say, you know, you are going to get this and this. It is
21 easier to say this is the difference between this part of
22 the head and this part of the head.
23 DR. MCCULLEY: I suspect we could keep going on
24 for ever on this point and not arrive at anything
25 definitive. If there is a point of information that can help

1 the FDA decide -- our role here is to advise, and this is
2 going to be one of those situations, I am afraid, where we
3 are going to need to give your our best input. You are then
4 going to do the best you can with it and it will come back
5 to us when you are doing your guidance document and we will
6 have another shot at it. A lot of this relates to your
7 engineers and your engineering. Scott?
8 DR. MACRAE: I am not a quality expert but I think
9 that the manufacturers could take, let's say, five systems
10 and test them and see what the variability between the
11 systems is using, as Doug Mastel suggested, a silicone type
12 system --
13 MR. MASTEL: A standard --
14 DR. MACRAE: A standard system or you could use a
15 standard pig eye that had a certain curvature, and do enough
16 of those tests to show that the microkeratomes would perform
17 within a relative range, and periodically test that, by the
18 manufacturer, in their system. I agree, I think it is
19 absolutely critical that, you know, I get the same type of
20 microkeratome in Portland, Oregon as Dr. McCulley gets in
21 Dallas, Texas and that it has almost the same
22 characteristics. And, I think that the industry can do that.
23 It is not going to be quite as precise as we want it to be
24 but, with time, I suspect it will get even better than we
25 anticipate.

1 DR. MCCULLEY: I think our concerns and sentiments
2 have been stated. Are you satisfied with us leaving it like
3 this, that you develop what you are going to do with the
4 guideline that takes into reasonable balance between the
5 ideal and the practical? Do you need any further input from
6 us on this point?
7 DR. ROSENTHAL: I think we understand the goldest
8 of all gold standards and what is a practical solution. I
9 think the sense is there has to be some way of ensuring that
10 there is some standardization and that one can feel that
11 when it is used some sort of predictability and
12 reproducibility, both intra and inter, is there. This
13 happens in all types of devices. This isn't the first device
14 that has come along in which one requires certain standards.
15 DR. MCCULLEY: I think from where we have come
16 with this, essentially we would say "see above" that relates
17 to device, operator, patient. Is there reasonable agreement
18 on that point, and we will let Dan put another two cents
19 worth in. Dan, two cents worth.
20 DR. REINSTEIN: Two cents. One penny I would like
21 to spend on the labeling issue, which is that at the moment
22 different companies are labeling the keratome depth
23 differently. There is a keratome which is labeled --
24 DR. MCCULLEY: Dan, please, make your point but we
25 don't really have time for --

1 DR. REINSTEIN: Okay. Well, the point is that some
2 companies are saying the 160 keratome cuts 160 when, in
3 fact, it cuts a lot less with a standard deviation. That
4 means that few eyes will go over 160.
5 DR. MCCULLEY: Okay.
6 DR. REINSTEIN: Whereas some companies say it is
7 160 and that is the mean, therefore, 50 percent will be
8 thicker than 160.
9 DR. MCCULLEY: Okay.
10 DR. REINSTEIN: So we have to --
11 DR. MCCULLEY: That is your labeling point. That
12 is one penny. Is the second penny spent there too? Mr.
13 Mastel?
14 MR. MASTEL: My grandfather was a carpenter for
15 many years and he had a phrase which was "I but it three
16 times and it was still too short." I think that we need to
17 measure the gap.
18 DR. MCCULLEY: Okay. Dr. Maguire?
19 DR. MAGUIRE: One point before we leave this has
20 to do with corneal perforation. I strongly believe that one
21 mitigator is that the design should be made so that even
22 with misuse you cannot perforate an eye.
23 DR. MCCULLEY: We request idiot perfect.
24 DR. MAGUIRE: That is an extremely serious,
25 potentially blinding complication.

1 DR. MCCULLEY: Okay. The next point is quality of
2 bed and perimeter, chatter lines, scoring, steps, jagged
3 perimeter, entry wound, edge, tearing and entry angle. Are
4 there specifics that we would need to add to the principles
5 that were previously stated for number one and two? Dr.
6 Pulido?
7 DR. PULIDO: Dr. McCulley, regarding the "idiot
8 proofing," I don't think that we should make it such that it
9 is not possible because with biology there is never 100
10 percent and we can't just put it onto the company's
11 shoulders to try and make a machine that doesn't allow
12 something like that to happen.
13 DR. MCCULLEY: Yes, the reality of the situation
14 is that what led to it was that we had a plate we had to put
15 in or could put in that could be put at various depth
16 plates, and I think what Leo is saying is that we need set
17 heads that we don't have to assemble. Yes, the idiot will
18 find a way around it. So. But the majority will not.
19 Quality of bed, perimeter, chatter -- that seems
20 again to come under the same kinds of heading as the first
21 two, and the mitigating events or circumstances related to
22 the device, patient and surgeon would be the same. Doyle?
23 DR. STULTING: I would like to add one issue here.
24 This is clearly a blade quality issue, or at least part of
25 it is a blade quality issue and I think we should go back to

1 the things that were raised earlier about substitute blades
2 or generic blades or blades added to the system. It would be
3 my opinion that if we are going to ask a manufacturer to
4 generate a device the device includes the blade, and if a
5 substitute blade is used that you have to have performance
6 data for the blade in that device before it is marketed as a
7 substitute, with the guarantee to users that it is going to
8 work. I think that is very important.
9 DR. MCCULLEY: Sounds reasonable to me. Does that
10 fit with reality with the FDA?
11 DR. ROSENTHAL: Yes, it does.
12 DR. MCCULLEY: Doyle, can you put that in a few
13 words for us?
14 DR. STULTING: I would just say the blade is to be
15 considered part of the device.
16 DR. MCCULLEY: But that doesn't then effectively
17 address the generic blades.
18 DR. ROSENTHAL: I would think that the generic
19 blades have to meet the specifications of the device blades.
20 DR. MCCULLEY: Okay.
21 DR. MACRAE: The performance standards.
22 DR. ROSENTHAL: The original manufacturer
23 specifications.
24 DR. MAGUIRE: And you are going to figure out how
25 to do that based on what you discussed in the first row up

1 here. Right? I mean number two, poor precision,
2 reproducibility and standard deviation.
3 DR. MCCULLEY: Dr. Pulido?
4 DR. PULIDO: So theoretically you could have a
5 generic blade that, if it met certain characteristics on a
6 microkeratome machine, could then be used interchangeably
7 with the company's blades. Is that what you are saying?
8 DR. MCCULLEY: Yes. I think that is what is being
9 said, but it would have to demonstrate the standard.
10 Epithelial ingrowth. The way we worded these
11 actually was clean cut, appropriate bevel, no epithelial
12 defects, that is the mitigating. We have often, in these
13 causative issues, stated the mitigating as well. I think we
14 will leave it to you guys to work out which column you move
15 them into and out of. Are there any other thoughts related
16 to this in the mitigation of epithelial defects that are not
17 already stated in the causes or implied very directly in the
18 causes? Dr. Pulido?
19 DR. PULIDO: Dr. McCulley, I still have a problem
20 with the generic situation because they could meet the same
21 tolerances; there could be the same lab tolerances, but when
22 it comes out, then in practice there could be a difference
23 in the quality of the bed, etc., and you wouldn't have known
24 that until after the fact.
25 DR. MCCULLEY: Can I ask you to bring that back up

1 again when we are between topics rather than in the middle?
2 DR. PULIDO: Yes, sir.
3 DR. MCCULLEY: Epithelial defects. Anything else
4 to be added here? Doyle, you started to say something. Was
5 it dealt with?
6 DR. STULTING: I was going to say smooth surfaces,
7 etc., etc., but I was also going to bring up another issue,
8 and that is that on many of these topics, like epithelial
9 defects, I don't see how you can learn the performance of
10 the device unless it is done on a living human because I
11 know of no adequate model that would tell you whether or not
12 you would knock the epithelium off. It has to do with too
13 many things. If that is the case, then what we are moving
14 toward is that there needs to be some human data somewhere.
15 I don't want to see approval of the devices slowed down but,
16 at the same time, when I am looking at a microkeratome I
17 would like the manufacturer to give me the data in the
18 labeling showing the performance of the device in a human.
19 DR. MCCULLEY: That is a sticky wicket. How do we
20 deal with that? Mr. Mastel?
21 MR. MASTEL: We have done 80 eyes, and they could
22 all be done histologically because Dr. Bizzard did them on
23 corneal transplant patients and then went on to do the
24 graft. That is how we have approached the clinical setting,
25 and we would have ruined some corneas had we not done that.

1 DR. SUGAR: But the measurements you would get
2 would not be comparable to those done on a normal cornea if
3 you are doing it on a keratoconus cornea or edematous
4 cornea. I don't know regulatorily, for a 510(k) do you get
5 an IDE first? So, if you have an IDE you can ask for data on
6 X number.
7 DR. ROSENTHAL: If clinical data is required by
8 the agency, then it has to be done under an IDE. Some
9 510(k)s do require clinical data.
10 DR. SUGAR: So then it would be appropriate for
11 there to be a pre-approval acquisition of data on a limited
12 number of patients establishing that you can set up a
13 pneumogram for this system that shows that it is either
14 comparable or, if it is a new system -- not a new blade,
15 that you have reproducibility. And, that can only, I think,
16 be acquired on a living eye.
17 DR. ROSENTHAL: That is why I brought up the issue
18 of clinical data before. It is just being addressed again.
19 If this panel feels that clinical data is required, that is
20 the recommendation they might make. Of course, the guidance
21 document would reflect lots of considerations including that
22 advice, but not necessarily only that advice.
23 DR. MCCULLEY: I think we are off of epithelial
24 defects right now. But --
25 DR. SUGAR: It is more global.

1 DR. MCCULLEY: I agree. This was brought up
2 before. I don't know that we dealt with it effectively. What
3 is the sense of the group, and keep in mind that the
4 audience is still invited to participate? What is the
5 opinion as to whether clinical data on microkeratomes that
6 are coming to the FDA, whether or not there should be the
7 requirement for clinical data? Yes or no? Marcia?
8 DR. YAROSS: I think both the clinical and the
9 regulatory issue is what is the indication for the device
10 because under the situation that we have with these devices,
11 if the indication is the same as the predicate devices, then
12 the regulatory burden, as well as the clinical burden or the
13 scientific burden, is to show that the product is equivalent
14 to the predicate device. None of the devices out there yet
15 has labeling regarding the Lasik procedure and that is where
16 we keep getting kind of tied up in knots here. If someone
17 comes in for a new microkeratome for the current
18 indications, then I think the type of data need to be
19 equivalent to what they have been before. If someone wants
20 to come in for a new indication, then I think one discusses
21 what is necessary to show that indication.
22 DR. MCCULLEY: We are getting into some
23 significant regulatory issues here that are going to get
24 increasingly muddy. So, I would like for you to direct us to
25 move on.

1 DR. ROSENTHAL: Yes, please move on. They are
2 complicated. They are issues that have to be discussed at
3 the highest level of the organization, and I think it is
4 inappropriate for us to have any further discussion.
5 DR. MCCULLEY: Keep in mind we got into that based
6 on your question of whether there should be clinical data.
7 [Laughter]
8 Epithelial ingrowth. That is where we were before.
9 Is there anything that needs to be added to the information
10 that is on this page? Mitigating events, any that cannot be
11 extracted from what we have said under causes?
12 DR. YAROSS: Dr. McCulley, just in terms of the
13 patient issues, patient education because we have some
14 issues here on patient compliance that we have not yet
15 addressed.
16 DR. MCCULLEY: Okay, point well taken. I would
17 have said that it is understood that we have to educate the
18 patient on compliance but okay.
19 Flap dislocation, slippage, misalignment,
20 wrinkles, microfolds, cracks, irregular astigmatism. Again,
21 I think we have covered everything there. That would include
22 the machine, patient, patient education and so forth.
23 Infection --
24 DR. ROSENTHAL: I think operator education as
25 well. I heard that from the back of the room and, I mean,

1 just underlying all of this is operator education.

2 DR. MCCULLEY: Yes, right, and I think that that

3 needs to be -- I mean, we kind of half covered that with

4 adequate manufacturer training of operator and I don't know

5 where the burden is going to fit on that, but a good point.

6 That needs to be a recurring sentiment throughout.

7 Infection. We have lid laceration under infection.

8 I don't think we want lid laceration parenthetically under

9 infection there. That related to other anatomical issues,

10 and clean runway, but it did come up as a possible infection

11 issue but let's take it out from there.

12 Mitigating circumstances -- I think we have kind

13 of stated them indirectly. Dr. Pulido?

14 DR. PULIDO: Not using the blade bilaterally.

15 DR. MCCULLEY: The issue there was not reusing the

16 blade. That gets into --

17 DR. PULIDO: That is mitigation.

18 DR. MCCULLEY: That not everybody will agree with,

19 unfortunately. You and I might.

20 DR. SUGAR: We discussed really that that is a

21 practice of medicine issue. We can't, I think, add to this.

22 DR. PULIDO: I disagree because, for instance,

23 when I do a vitrectomy I can't reuse my microvette in a

24 second patient, not even a second eye.

25 DR. MCCULLEY: This is a tough philosophical issue

1 that gets into the practice of medicine, similar to some of
2 the other things that we talked about. I think we could keep
3 going around on it forever, and it relates as well to some
4 FDA policy. I think for today's purposes we need to maybe
5 leave it alone, maybe where it is, for the moment.
6 DR. SUGAR: And another issue, that the device
7 should be constructed in such a way that it can be
8 adequately cleaned and disinfected.
9 DR. MCCULLEY: Okay. Interrupted movement, partial
10 flaps. I think we have implied the mitigating circumstances
11 under our enumeration of causes.
12 Lamellar keratitis.
13 DR. STULTING: Are we assuming that you would take
14 things from the device column and translate them to
15 mitigated when they are obvious?
16 DR. MCCULLEY: That is my assumption.
17 DR. STULTING: Okay. So it says device not stopped
18 because of minor obstructions -- that would mean that it
19 would be sufficiently powered to overcome a minor
20 obstruction. Right? Okay.
21 DR. MCCULLEY: Interrupted movement, partial flap.
22 That is what we just did, isn't it? Lamellar keratitis. Is
23 there anything that needs to be added to our list of causes
24 that would need to come into the mitigation column?
25 DR. MAGUIRE: Is this a place to insert the

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

2 DR. MCCULLEY: For postmarket surveillance.

3 DR. MAGUIRE: For postmarket surveillance for

4 clusters of complications.

5 DR. MCCULLEY: I don't know that it would need to

6 go in this table but I think that avenue being available to

7 us and our awareness of it, and the FDA's awareness of it,

8 needs to be stated but it probably doesn't need to go into

9 this document.

10 DR. REINSTEIN: In the three causes it doesn't

11 mention sterilization procedure, and the latest evidence, as

12 we mentioned earlier, for probably cases of lamellar

13 keratitis is to do with biotoxins and endotoxins. There is

14 one study that is unpublished that I know of that showed

15 that a specific sterilization protocol reduced the

16 incidence.

17 DR. MCCULLEY: Those thoughts were introduced

18 before under cause, and we tried to get it, which was

19 equipment maintenance, operator maintenance and isolation of

20 sterile field. I mean, when they look at the transcript and

21 they look at the words here, that is there.

22 DR. REINSTEIN: Right. Perhaps what Dr. Sugar

23 suggested, which was to make sure that the device is easily

24 sterilizable and access to the inside of it is such.

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

1 device, it is what the device is being sterilized in. That
2 gets back to education relative to appropriate maintenance
3 of the device.
4 Next is suction, consistency of, loss of
5 maintenance of. That has been discussed otherwise.
6 Ocular ischemia. I think we have talked about
7 mitigating events, elevated intraocular pressure and the
8 duration of it, and the machine being efficient so that time
9 is not stretched. Anything else under ischemia?
10 [No response]
11 Decentration of flap. Any other mitigating factors
12 that are not stated or implied?
13 DR. REINSTEIN: We discussed them but they are not
14 stated, and multiple suction ports and an alarm that would
15 go off after X number of minutes or seconds alerting the
16 surgeon that the keratome has been on suction for that
17 amount of time were two things that we discussed.
18 DR. MCCULLEY: Right. You had that job, and you
19 had a job to remember something, Mr. Mastel, for a
20 mitigating event. Have we covered it effectively? And Marcia
21 had one to remember. You don't remember what you are
22 supposed to remember?
23 MR. MASTEL: I am sorry, I am zoned out.
24 DR. MCCULLEY: Okay. Decentration of flap.
25 DR. REINSTEIN: That was to do with having an

1 adequate increased suction time, and not too slow.

2 DR. MCCULLEY: Adequate rate of accomplishment of

3 suction.

4 MR. MASTEL: Excuse me, could we quantify that

5 somehow?

6 DR. MCCULLEY: No, let's not. We have adequate and

7 we will leave adequate for you and the engineers. Anything

8 else? I did see a hand. Yes, Mr. Bartell?

9 MR. BARTELL: As relates to suction, something I

10 think you should consider is -- you seem to be talking about

11 the intraocular pressure that results when you get the

12 suction ring on. I think you should also request from the

13 manufacturer what is the IOP during the cut because as the

14 plate applanates the eye, I think it may be reaching the 300

15 and 400 levels that Mr. Mastel mentioned, whereas, when you

16 are measuring it just with a vacuum ring you are looking at

17 80-100, and there is ischemia and all these factors.

18 DR. MCCULLEY: That sounds very good but how are

19 we going to accomplish that? I don't have room for my

20 tonometer there when I have my keratome in there.

21 MR. BARTELL: I think that is a manufacturer's

22 responsibility probably to give us some kind of an idea.

23 DR. MCCULLEY: Okay. Mr. Mastel?

24 MR. MASTEL: Dr. McCulley, the Germans

25 corroborated evidence. We did a 0.25 mm accuracy transducer

1 that we placed in the whole globes and that is how we
2 calibrated our tonometers. We put them on at 16 mm, very
3 carefully controlling that they went to 180-200 before the
4 microkeratome pass. That was only one microkeratome though.
5 So I don't know what the others do.
6 DR. MCCULLEY: What eyes were these?
7 MR. MASTEL: Human globes.
8 DR. MCCULLEY: Live or cadaver?
9 MR. MASTEL: Cadaver. You have to put it into the
10 chamber.
11 DR. MCCULLEY: So that comes down to a
12 manufacturing request. Interface debris, metal shavings.
13 Anything in mitigating factors that we have not stated or
14 implied in causative events? I don't think so.
15 Epithelial defects. Ditto to what I just said.
16 Bleeding. Ditto. Ditto head movements.
17 That I think completes our task for this portion.
18 I do want to give brief opportunity if anyone thinks there
19 is a significant oversight that we have; not restating what
20 has already been stated before. Dr. Stulting?
21 DR. STULTING: I don't know whether this is a
22 restatement or not. I am speaking on behalf of what I
23 consider to be my constituency of this meeting, and that is
24 consumer ophthalmologists. Right now microkeratomes are
25 manufactured and they are approved and they are sold, and

1 sort of after they are sold, in the back room in an informal
2 discussion you figure out how thick a flap they make, how
3 much variance they have, and what their complications are.
4 That is not good. I think we need to put in place a system
5 that will prevent that and give clinicians access to
6 clinical information without doing it on their own in an
7 informal way. And, I am not sure that this discussion has
8 accomplished that. We have gone and enumerated some fairly
9 obvious things that need to be taken into account when these
10 things are manufactured, but I am not convinced that what we
11 have done here today has led the FDA to a point where we can
12 get that information efficiently, putting the fewest number
13 of patients at risk and causing the fewest number of
14 ophthalmologists to make errors with microkeratomes because
15 of design problems.
16 DR. MCCULLEY: What I hear you saying relates back
17 to the question that Dr. Rosenthal posed before, that we
18 went astray on, but I hear you saying that you would call
19 for a reasonable but not excessive amount of clinical data
20 to be provided along with the request for FDA approval.
21 DR. STULTING: Frankly, yes. I think that is the
22 prudent way to behave and it is in the best interests of
23 ophthalmologists and patients.
24 DR. MCCULLEY: What I do not want to do now -- I
25 think you have stated it well. I don't think it is necessary

1 for each of us to editorialize whether we agree or disagree,
2 but I think it would be worthwhile for us to indicate
3 whether we are in agreement with Dr. Stulting's statement.
4 [Panel members indicate agreement]
5 I think it is a unanimous yes, that we would like
6 to see what he said.
7 Any other statements or comments where you feel
8 strongly we have not adequately covered the issue?
9 **Rank Ordering of Identified Problems**
10 Seeing none, the panel will now do ranking. I am
11 told that we want to ensure that the audience is aware that
12 there will be an opportunity for open public comment, after
13 we do the ranking, on issues that you feel the need to
14 comment on, with time limitations being in place. So, no
15 filibusters.
16 DR. ROSENTHAL: I would like you to rank them, not
17 in actual order of priority but, very simply, as high,
18 medium or low, if you would, please.
19 DR. MCCULLEY: All right.
20 DR. ROSENTHAL: Taking everything into
21 consideration, high, medium, low.
22 DR. MCCULLEY: The open public hearing period is
23 now closed. We will not rank order, we will indicate our
24 severity scale as low, medium, high. But also there is
25 severity and there is frequency, just to muddy the water,

1 that weighs into it. So, how would you like for us to deal
2 with that?
3 DR. ROSENTHAL: Maybe you could do high, medium,
4 low for seriousness and then high, medium, low for
5 frequency, and we will put together some formula.
6 DR. MCCULLEY: Okay. We will do a seriousness
7 score and a frequency score in that order.
8 DR. SUGAR: Can I ask Ralph why we are doing this?
9 DR. MCCULLEY: Don't ask; let's just do it!
10 DR. SUGAR: I would just ask you, Ralph, why we
11 are doing this because I think it is pretty obvious from the
12 discussion that has already taken place.
13 DR. ROSENTHAL: You are doing it because I would
14 like to have some sense of what really is of crucial
15 importance and what is just of academic interest because
16 this panel can be very academic sometimes, and very erudite,
17 but --
18 DR. MCCULLEY: We are always erudite!
19 DR. ROSENTHAL: -- but I want to be sure that it
20 is of significant clinical importance.
21 MS. HOANG: Initially it was our plan, because we
22 did not know how much time we would have to discuss the
23 outline, which now we are not planning to discuss at all --
24 we were hoping that by ranking it you can, depending on the
25 time allotment, discuss just the top five, or whatever, but

1 if you feel as though everything here is important and you
2 would prefer not to rank it, then please let us know.
3 DR. MCCULLEY: Can I ask if we do this, Ralph,
4 that we indicate whether we think this is important or not,
5 important or minor?
6 DR. ROSENTHAL: Yes.
7 DR. PULIDO: Excuse me, a point of clarification
8 to Dr. Rosenthal, when it comes to asking to asking for new
9 clinical data for the keratomes would the ones that are
10 already out there have been grandfathered in so we would not
11 be asking for any clinical data for those. So we would be
12 raising a new bar for the ones that have not been
13 grandfathered in.
14 DR. ROSENTHAL: Dr Pulido, this is a very complex
15 regulatory issue and I really cannot give you any answer to
16 that now. It will have to be discussed at the highest levels
17 of the organization.
18 DR. MCCULLEY: The only insight I would have for
19 that may not be an appropriate insight, and I would just say
20 remember Dr. Kessler's presentation this morning. That may
21 not be apropos.
22 DR. PULIDO: In that case, when you asked for our
23 opinions, I would say the bars should be the same for all
24 the keratomes.
25 DR. MCCULLEY: I do not want to read these. Number

1 one, the precision -- all we are going to do is say this is
2 important or this is for consideration. We are not going to
3 say unimportant but important.
4 Another precision item, number two, is important.
5 PANEL MEMBER: Very important.
6 DR. MCCULLEY: Number three, quality of bed, a
7 precision item, is important.
8 Epithelial ingrowth is an issue that is important.
9 Please, some of you, identify yourself.
10 DR. REINSTEIN: Important.
11 DR. MCCULLEY: Okay. If there is disagreement -- I
12 know none of you is shy -- I want you to jump in. I am going
13 to take silence as concurrence.
14 Flap dislocation, etc., is --
15 PANEL MEMBER: Important.
16 PANEL MEMBER: I would say that for the
17 manufacturers this is a surgical issue.
18 DR. MCCULLEY: We are not making subcategorical
19 judgments. Is this an important consideration or not? The
20 consensus is important. Patients don't do too well if their
21 flap is not in place.
22 Infection is an issue that is --
23 PANEL MEMBER: Important.
24 DR. MCCULLEY: Partial flaps is an issue --
25 DR. REINSTEIN: Well, it depends on whether it

1 affects patient outcome. And, we all only from doing Lasik
2 that interrupted movement and partial flaps does not affect
3 patient outcome in almost all cases.
4 DR. MCCULLEY: In general it is a less critical
5 issue. Not minor, but it is less critical.
6 DR. REINSTEIN: And infections are so rare --
7 DR. MCCULLEY: But if they happen they are bad. So
8 we have two things we are weighing simultaneously in our
9 minds, frequency and severity and infection sure as heck
10 comes down as important. The partial flap, of all of the
11 things, this point would be -- we don't like them; it is not
12 good but it is not the end of the world.
13 Lamellar keratitis is an issue that is --
14 PANEL MEMBER: Important.
15 DR. MCCULLEY: The suction creation, maintenance,
16 etc., are all issues that are --
17 DR. HIGGINBOTHAM: Very important.
18 DR. MACRAE: Very important.
19 DR. MCCULLEY: Interface debris are issues that
20 are --
21 DR. HIGGINBOTHAM: Less important.
22 PANEL MEMBER: Less important.
23 DR. MCCULLEY: Less important but somewhere
24 possibly -- well, yes, less important in general but still
25 important.

1 DR. ROSENTHAL: Excuse me, Dr. McCulley, you have
2 important, very important, less important and for
3 consideration. So you, in fact, have four categories now.
4 DR. MCCULLEY: We do.
5 DR. HIGGINBOTHAM: It is extremely important.
6 DR. MCCULLEY: Interface debris, not as.
7 Epithelial defects --
8 PANEL MEMBER: Important.
9 DR. MCCULLEY: They can be very important but they
10 are common and most of the time or no consequence. So that
11 is a toughie.
12 DR. HIGGINBOTHAM: But it could lead to infection
13 and affect your outcome.
14 DR. MCCULLEY: Point taken. Bleeding.
15 PANEL MEMBER: No.
16 DR. HIGGINBOTHAM: Less important.
17 DR. MCCULLEY: Less important. You are frowning.
18 It is less important.
19 DR. ROSENTHAL: I thought maybe it would be for
20 consideration.
21 DR. MCCULLEY: Oh, for consideration. Okay.
22 DR. ROSENTHAL: But I am not allowed to lead the
23 panel so --
24 PANEL MEMBER: I said that.
25 DR. ROSENTHAL: Thank you.

1 MS. THORNTON: Dr. McCulley, you have less
2 critical and less important. Are they the same?
3 DR. MCCULLEY: Can you guys figure out that? I
4 think we have given you our sentiment and I really would
5 like not to beat on this anymore. I think we have let you
6 know our thoughts on it.
7 Are there any other comments that the panel would
8 like to make? Marcia?
9 DR. YAROSS: Just one comment for the panel's
10 consideration regarding the recommendation on clinical data.
11 I think it is important to note that the microkeratome is a
12 device that is not used in isolation and, therefore, it is
13 not entirely clear how one would use the clinical data that
14 came out of it because the device is typically used in a
15 procedure that is followed by use of another device. So, I
16 think that is something to think about.
17 Just as a comparison to think about, it might be
18 worthwhile for the panel -- if they are not aware that
19 phacoemulsification machines are probably something that is
20 of comparable seriousness and severity in terms of the types
21 of things that can go wrong, but it has been well
22 established that you can specify what the properties of
23 phaco machines would be and, therefore, measure in a
24 laboratory setting or in animal setting whether or not the
25 device does meet those specifications. So, I think it is

1 worthwhile, in development of a guidance, to look and see
2 whether or not a similar type of situation exists.
3 DR. MCCULLEY: Thank you. Point taken. I would
4 like for us not to debate it. I understand your point and
5 your viewpoint. Does the FDA feel a need for further comment
6 on the point that has been made and the industry
7 perspective?
8 DR. ROSENTHAL: No, I don't think we need further
9 discussion on that issue.
10 DR. MCCULLEY: Thank you. Now, we have an
11 opportunity for public comment. This is the closing portion
12 of this meeting. If there is further comment that a member
13 of the public would like to make relating to the proceedings
14 today or the issues at hand, please so indicate. Seeing
15 none, Dr. Rosenthal?
16 DR. ROSENTHAL: I would like just to make a final
17 comment. I would like to thank very much the individuals
18 from the audience who I thought made some extraordinarily
19 fine comments, and who complemented the panel in providing
20 us with an outstanding overview of the issues on
21 microkeratomes. I very much appreciate them coming and I
22 very much appreciate their input, as I do the panel's.
23 DR. MCCULLEY: Thank you. Any other comments? Do
24 you have any further administrative issues?
25 MS. THORNTON: I would just like to say that we

1 will make every effort to get this chart in its final form
2 up on our web site. I am going to see if they can do that. I
3 can't guarantee it but we will have it available to be faxed
4 to you if you would like to have it as we, you know, finally
5 put it together. And, I would like to add my thanks to Dr.
6 Rosenthal's. I know you all have worked very hard today and
7 I appreciate your perseverance and tenacity on these issues,
8 and we all do. And, I would like to thank Quynh and Joe for,
9 without them, this would not have been possible and they
10 have done a lot of good preliminary work on it and i know
11 your input has been very helpful to them.
12 DR. ROSENTHAL: I would like to second that
13 because, I mean, I take them for granted. They have done an
14 enormous amount of work and have become quite expert in this
15 area and I really appreciate the work they have done that
16 has allowed us to do the kind of work you have done.
17 DR. MCCULLEY: From my perspective, I think this
18 has been a very productive day, with very valuable and tough
19 input from any one of a number of people. So my thanks to
20 everyone.
21 MS. THORNTON: Adding to that, this is a new
22 format for us. We have not done this particular kind of
23 thing before, and I would like to let me know what you think
24 of this as a working session. We would like to, hopefully,
25 use this in the future, and if we can get your input and

1 improve it I think we can do some other things like this, on
2 some other topics. And, to thank Dr. McCulley. He has done a
3 great job.
4 [Applause]
5 It has been tough.
6 DR. MCCULLEY: Thank you all. The meeting is
7 adjourned.
8 [Whereupon, at 4:40 p.m. the proceedings were
9 adjourned]
10 - - -

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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