1 Patient. Steep K is one.

2 DR. MAGUIRE: I am sorry, one other one -- I don't
3 know if this is an issue anymore but flexion of the base of
4 the keratome. I don't think this is a problem with the
5 steel-based instruments but I think there is some
6 scuttlebutt that there is some flexion with plastic and
7 people are getting into trouble. I don't know if that needs
8 to be an issue now or not.

9 DR. MCCULLEY: Well, I think it does because we
10 are looking to the future as well. How can that be stated in
11 the positive? Absence of flexion of the base, I guess? Base
12 plate stability? Good. Base plate stability/rigidity -- not
13 necessarily the appropriate word here but it gives the
14 intent.

15 Other operator issues here? I mean, the operator
16 clearly has to recognize the circumstances, as we said
17 above, and make adjustments. So, in terms of operator,
18 recognizing the situation and adjusting --

19 DR. MAGUIRE: One blade operator issue is
20 measurement of intraocular pressure. That should be one. I
21 will stop there unless you want an explanation.

22 DR. MCCULLEY: And that should go under one and
23 two, that the operator must ensure appropriate obtaining of
24 suction -- appropriate IOP.

25 DR. MAGUIRE: It is not measurement of; it is

1 confirmation of -- this isn't the right way to put it but
2 confirmation of adequate IOP.
3 DR. MCCULLEY: It is adequate suction. That is
4 what it is.
5 DR. REINSTEIN: And monitoring.
6 DR. MCCULLEY: Yes.
7 DR. REINSTEIN: Because you can check it and you
8 have to continuously monitor it.
9 DR. MCCULLEY: Okay, so confirmation of adequate
10 IOP and its maintenance. Dr. Higginbotham?
11 DR. HIGGINBOTHAM: I am going to try this again. I
12 still think that, for instance, a patient characteristic is
13 important as it relates to IOP, particularly if they have
14 had previous surgery such as filtration surgery. I would
15 think that would influence --
16 DR. MCCULLEY: That is a contraindication of the
17 surgery.
18 DR. HIGGINBOTHAM: But in the marketplace --
19 DR. MCCULLEY: It is not done. I mean, if a
20 patient has had previous filtering surgery -- previous
21 intraocular surgery in general is an absolute
22 contraindication for the procedure, except penetrative
23 keratoplasty. Glaucoma filtering operation would be an
24 absolute contraindication --
25 DR. HIGGINBOTHAM: Okay, because I know it has

1 been discussed.

2 DR. MCCULLEY: Not Lasik.

3 DR. HIGGINBOTHAM: Okay, I just thought I would

4 ask.

5 DR. MCCULLEY: Good, good.

6 DR. MACRAE: This will get into the whole patient

7 issue, if the anatomy is appropriate for surgery, whether

8 they have had retinal detachment surgery or filter surgery,

9 or they had some type of anatomical nuance -- that all falls

10 under that category.

11 DR. MCCULLEY: Anything else under operator? What

12 else, other than steep K under patient?

13 DR. REINSTEIN: Under operator, the operator needs

14 to know the patient's case before he chooses the right ring.

15 The operator needs to verify with the applanation lens

16 before passing the keratome.

17 DR. MCCULLEY: Mitigating circumstances. I mean,

18 those are solutions to it.

19 DR. REINSTEIN: They are possible causes of poor

20 precision. It is incorrect selection of rings, of

21 applanation --

22 DR. MCCULLEY: So, we can put under operator

23 incorrect selection of patient or microkeratome

24 characteristics.

25 MR. MASTEL: How about tremor?

1 DR. MCCULLEY: How about what?

2 MR. MASTEL: Tremor.

3 DR. MCCULLEY: None of us has that!

4 DR. MCCULLEY: So, under operator it really is

5 appropriate patient and keratome selection.

6 DR. REINSTEIN: I am not sure if this would fit

7 here but sterility of the device during --

8 DR. MCCULLEY: It doesn't fit under this.

9 DR. REINSTEIN: It doesn't? Okay.

10 DR. MCCULLEY: That is going to come under

11 infection and debris.

12 DR. REINSTEIN: Okay.

13 DR. MACRAE: This is very basic but the operator

14 really needs to assess the instrument before doing the pass.

15 In other words, look at the blade and make sure that the

16 blade is moving --

17 DR. MCCULLEY: Right, okay.

18 DR. MACRAE: -- there are certain elemental pieces

19 to --

20 DR. MCCULLEY: Right. Mr. Bartell?

21 MR. BARTELL: If you are going to be looking at

22 manual and automated I think you should put translation

23 speed under operator potentially as coming up with

24 inaccurate cuts because of the speed of the transition.

25 DR. MCCULLEY: Okay, yes, and we are looking at

1 automated and manual.

2 DR. PULIDO: It lists keratomes as being AC

3 powered or battery powered devices --

4 DR. MCCULLEY: Or automated. Yes, they are manual.

5 Maybe when we come to the document we need to make sure that

6 that guideline document addresses manual as well as

7 automated. Is your question are we addressing only automated

8 and not manual?

9 DR. PULIDO: Correct.

10 DR. ROSENTHAL: [comment off microphone].

11 DR. MCCULLEY: My impression from what we have

12 been directed is that we should be addressing automated as

13 well as manual microkeratomes in this.

14 DR. BEERS: That is correct. Battery and AC relate

15 to, for instance, blade oscillation where you still have

16 power even for a manual.

17 DR. MCCULLEY: Then we can get into synchronous,

18 and all that, but any other patient characteristics under

19 this category? This is our toughest and probably, as Scott

20 said, most important area. Any other patient

21 characteristics, other than steep K that we are going to

22 leave in there? Yes, Mr. Mastel?

23 MR. MASTEL: Would you include small eyes and

24 large eyes like diameters here, or not?

25 DR. MCCULLEY: Patient corneal diameter. Good

1 point. Well, that is probably overall and all patient
2 selection, operator. Let's just leave that under the broad
3 category of appropriate patient selection by the operator.
4 DR. REINSTEIN: The only thing that the patient
5 does to control the depth of the incision is to not sit
6 still or to squeeze his lids or not be relaxed, altering the
7 intraocular pressure during the procedure, to move so that
8 the passage of the keratome isn't smooth. So, it really has
9 to do with cooperation.
10 DR. MCCULLEY: Okay, can we put patient control
11 and cooperation to cover it all? Doyle?
12 DR. STULTING: I was going to say I think the issue
13 here is really a general one. It is the anatomy of the
14 patient. As Dan pointed out earlier, it is how much stuff is
15 sticking up through the hole when the blade comes by, and
16 that has to do with the Ks. It has to do with the way the
17 limbus is attached to the sclera. It has to do with the
18 diameter of the cornea. It also has to do with the looseness
19 of the conjunctiva, which is what the keratome attaches to.
20 So there is really a huge number of factors. People talk
21 about Ks, but that is just one of a number of factors, and I
22 think what you ought to do is put here anatomy and move
23 forward. When you move to cures, Dan mentioned a good one
24 and that is the applanator because it takes care of all of
25 them.

1 DR. MCCULLEY: So, patient anatomy which includes
2 cornea, conjunctiva, sclera. It is important to consider all
3 of those that we don't necessarily have good measures for.
4 We find it out when we are putting the suction ring on.
5 Anything else under patient? If not, the next is
6 quality of bed and perimeter, chatter lines, scoring, steps.
7 Device. Clearly, an issue there relates to the appropriate
8 and fine manufacture of the instrument but a specific is
9 blade angle and oscillation speed.
10 MR. MASTEL: Blade characteristics again.
11 DR. MCCULLEY: Blade characteristics. What we
12 might be able to say with that is kind of see all of the
13 characteristics listed above where applicable rather than
14 restating many of the same things again. Dan gave us a nice,
15 long list of tolerances and characteristics that are going
16 to enter in here. The blade angle, oscillation speed --
17 DR. STULTING: Translation speed.
18 DR. MCCULLEY: Translation speed -- let's see, we
19 had translation speed above. I would say just see all of the
20 above characteristics that we listed for number two. Any
21 specific operator issues here with perimeter, chatter lines,
22 and so forth? Certainly chatter lines with automated versus
23 manual. Anything else?
24 DR. REINSTEIN: Under operator, translation
25 control in manual keratomes.

1 DR. MCCULLEY: Thanks for watching that, Dan.

2 DR. YAROSS: Also blade reuse, again, would come

3 in here.

4 DR. MCCULLEY: Good point.

5 DR. MAGUIRE: And also translation control in

6 automated because you can certainly have wear and some

7 maintenance issues come up.

8 DR. REINSTEIN: And there are some keratomes where

9 you can actually tell the keratome how fast to go across.

10 There are software modifications.

11 DR. MCCULLEY: Any other patient characteristics

12 here? Any other surgical characteristics? Mr. Mastel?

13 MR. MASTEL: Wouldn't surgical skill and

14 experience be a factor?

15 DR. MCCULLEY: We are not going to make that kind

16 of judgment but we are going to say -- I think we have taken

17 care of that with translational characteristics.

18 DR. YAROSS: But to Dr. Reinstein's point,

19 appropriate selection of speed for blade advancement. So,

20 that is really an operator issue, appropriate selection

21 among the parameters of the instrument.

22 DR. REINSTEIN: I think that would be more a

23 manufacturer dilemma because the interplay between

24 oscillation speed and translation speed is what produces the

25 chatter.

1 DR. YAROSS: Okay, I thought we were speaking to
2 the selection amongst those that have variable choices.
3 DR. MCCULLEY: Well, but when there is variable
4 you are going to have to match. I guess looking to the
5 future, if we have the ability to adjust, other than with
6 our manual translation speed, matching translational speed
7 to oscillation rate. Mr. Bartell?
8 MR. BARTELL: Possible causes under operator is
9 not really getting setting up properly. I think as far as
10 scoring, hitting the speculum, which is really an
11 observation that should be made prior to initiating any
12 pass, is going to give you an irregular cut.
13 DR. MCCULLEY: So, operator would be avoidance of
14 damage to microkeratome --
15 MR. BARTELL: And drapes and any other thing
16 [comment off microphone].
17 DR. MCCULLEY: Can you put that in a few words
18 that would cover the whole thing?
19 DR. MACRAE: I think a clear runway -- clearance,
20 adequate clearance.
21 MR. MASTEL: How about inspection and maintenance?
22 DR. MCCULLEY: Who said that? Please say your name
23 before you start.
24 MR. MASTEL: I am sorry, Doug Mastel. Inspection
25 and maintenance.

1 DR. MACRAE: I agree, but when I think of
2 inspection and maintenance I think of looking at the
3 microkeratome under the microscope before I actually do my
4 pass. I think clearance, for a clinician, captures that.
5 DR. MCCULLEY: Yes, well, they are both issues. As
6 you said, we have to have a clear runway but we have to make
7 sure the plane we are putting on the runway has been
8 inspected and gone through a check list. I think that is
9 what he was saying.
10 DR. MACRAE: I understand.
11 DR. MCCULLEY: Patient issues? Yes?
12 MS. HOANG: Did you want to add something in this
13 column as to verifying the clearance?
14 DR. MCCULLEY: I am sorry, I had asked you to wait
15 and we keep changing. Yes, put verification of -- let's just
16 put in quotes clear runway and that the microkeratome has
17 been appropriately inspected and its function verified.
18 DR. MACRAE: And adequate clearance?
19 DR. MCCULLEY: Well, that is what I meant by your
20 clear runway. Mr. Bartell?
21 MR. BARTELL: Yes, patients with small eyes are
22 particularly liable to cause the problems. I think that is
23 something you should reference.
24 DR. MCCULLEY: Well, you know, there are tight
25 lids, deep-set orbits, prominent brows. Let's just leave

1 that under appropriate anatomy and patient selection anatomy
2 issues. Those are important anatomy issues.
3 DR. REINSTEIN: What really needs to go into that
4 column is patient cooperation.
5 DR. MCCULLEY: Let's put ditto, that we have
6 patient control and cooperation and patient anatomy. We did
7 that before under item two above. We can bring that down.
8 Any other patient issues?
9 [No response]
10 We are going to have to make a decision here. We
11 are scheduled for lunch at 12:30. We can go till 1:00, I
12 have been told. So, we will go till 1:00 and if we can
13 complete this, we will. What I do not want us to is to fall
14 into the trap of rushing through this stuff because I think
15 that as we do this each column will get -- after we do this
16 column, the next column should be easy as long as we don't
17 embellish on our points.
18 The next item is epithelial ingrowth. Device
19 related. I mean, I think the bevel is an issue. Did we have
20 a nice, succinct summarizing term? I guess that came under
21 bevel. It needs to be a clean cut that doesn't muck up the
22 epithelium. So, absence of, you know -- kindness to
23 epithelium on the part of the device. That relates to blade
24 quality.
25 DR. MACRAE: This is a very complex area and for

1 us to try to describe all the components that give us a
2 clean cut -- we all know what it is but it is a long
3 discussion. So maybe we can just call it a good, clean cut
4 and leave it at that.
5 DR. MCCULLEY: Clean cut and appropriate bevel.
6 DR. MACRAE: A lot of that is design related with
7 all the different components.
8 DR. REINSTEIN: Probably the most important
9 predictor of epithelial ingrowth is the presence of an
10 epithelial defect after creating a flap. So, it is centered
11 on that. So, stated in the negative, we would say lack of
12 epithelial defect.
13 DR. MCCULLEY: So if we left it at clean cut,
14 appropriate bevel or avoidance -- anyway, in the positive,
15 clean cut, appropriate bevel, no epithelial defect that was
16 contributed to by the microkeratome. Mr. Bartell?
17 MR. BARTELL: What bevel are you talking about?
18 The bevel on the blade edge or the bevel --
19 DR. MCCULLEY: We are talking about the entry
20 wound --
21 MR. BARTELL: The gutter.
22 DR. MCCULLEY: Well, you know, it depends on how
23 you use the term. I think really what we are talking about
24 is do we have a zero angle of cut into the cornea or do we
25 have an angle cut into the cornea that does, indeed, create

1 a gutter as opposed to just a slice that floats. And, that
2 is good. I think most of us up here knew what we were
3 talking about, but it you guys don't and everyone doesn't,
4 then we are not being effective. So, thank you for bringing
5 that up.
6 Anything else on microkeratomes? Operator?
7 Appropriate flap alignment, you know, covers, to me, the
8 majority of it.
9 DR. REINSTEIN: Preoperative diagnosis of anterior
10 corneal disorders like basement-membrane disease.
11 DR. MACRAE: In terms of epithelial ingrowth, I
12 think the operator can have a huge impact on the epithelium.
13 We have learned a lot over the last two or three years in
14 terms of having good hydration throughout the procedure,
15 keeping the epithelium moist, things like celluvisc and
16 keeping the microkeratome well lubricated at the time of
17 pass, and those things are quite critical and if you make a
18 nice, clean pass generally without tilting the microkeratome
19 you will get a good result. So, this is a very operator
20 dependent issue usually.
21 DR. MCCULLEY: Okay, let me try and summarize what
22 I think I have heard everyone say. The operator must keep
23 the epithelium well lubricated and not traumatize it; that
24 there needs to be appropriate flap alignment and seating;
25 and that epithelial defects, when present, must be

1 appropriately managed -- appropriate management of
2 epithelial defects. Doyle?
3 DR. STULTING: We have data for two things, one is
4 epithelial defects which you already mentioned, the second
5 is the removal of fluid from beneath the flap when it is
6 replaced, and that is part of alignment so I think you can
7 generalize that to say flap replacement technique. That
8 includes alignment, removal of fluid, etc.
9 DR. MCCULLEY: Yes, the words I used were
10 alignment and seating.
11 DR. STULTING: But it is specifically removal of
12 fluid.
13 DR. MCCULLEY: That comes under seating, to me,
14 but okay. If that would not cover it in the minds of people,
15 then we need to put flap alignment, removal of interface
16 fluid --
17 DR. STULTING: And put removal in quotes. It is
18 indirectly done.
19 DR. MCCULLEY: -- and seating. Then the management
20 of epithelial defects, when present, is, as has been pointed
21 out, key in keeping the epithelium healthy. Anything else
22 under operator?
23 DR. REINSTEIN: Detection -- immediate
24 postoperative detection of epithelial plaques.
25 DR. MCCULLEY: That is postop. I agree with you in

1 the management and so forth of it that the sooner the
2 better.
3 DR. MACRAE: I agree. Generally you can inspect
4 the flap bed and see -- if you have an epithelial defect you
5 can see usually that there is a piece of epithelium, or
6 whatever --
7 DR. MCCULLEY: Right. So, in that context, yes.
8 Immediate inspection at the conclusion of the procedure to
9 be certain that there are not obvious epithelial tags tucked
10 or plugs seeded.
11 DR. STULTING: It would be my opinion that the
12 usual causes, the most frequent causes of epithelial defect
13 do not include dragging epithelium underneath the flap by
14 the microkeratome or its blade. If there is agreement of
15 that, it might be worthwhile to say that specifically
16 because that is something that has been discussed, and
17 certainly the agency might be interested.
18 DR. MCCULLEY: I don't know whether that is
19 appropriate or not. It would be opinion. Of course, all of
20 this is opinion. I would agree with you that it is not. The
21 biggest problems are when they communicate to the periphery
22 either because there is a defect there or because a tag has
23 been tucked under. Mr. Mastel?
24 MR. MASTEL: I think seeding is not what you want
25 in that context.

1 DR. MCCULLEY: What word do I want?

2 MR. MASTEL: Seating.

3 DR. MCCULLEY: Oh, seating, yes. I did make it

4 sound like seeding. It is my Texanese!

5 DR. MACRAE: While we are changing that, I just

6 want to sort of editorialize because I know that this helps

7 the agency, the epithelial ingrowth, in my experience, is

8 mostly operator driven. So, at least in my clinical

9 experience and in talking with other clinicians, most of

10 these are caused by somehow epithelium getting in the

11 interface, and usually it is related to some epithelium

12 literally being dragged into the interface or some other

13 reason. I haven't heard it as being a common problem as a

14 result of a microkeratome.

15 DR. MCCULLEY: Well, if the microkeratome gets a

16 bad bevel, it does. If the microkeratome leads to epithelial

17 defects at the border, it does. I think if the blades are

18 reused, it potentially does. So I think it does.

19 DR. REINSTEIN: And what is fascinating and has

20 been shown by a good statistical prospective study is that

21 even a central epithelial defect, which is nowhere near the

22 wound, is a risk factor for epithelial ingrowth.

23 DR. MCCULLEY: Okay. Patient characteristics -- as

24 has already been stated, clearly, avoidance of patients with

25 anterior membrane dystrophy.

1 DR. MAGUIRE: Previous corneal surgery.

2 DR. MCCULLEY: Anything else under patient?

3 MR. BARTELL: Rubbing of eyes.

4 DR. MCCULLEY: Yes, slippage or displacement of
5 the flap and rubbing. How should we put that? Rubbing leads
6 to -- let's just say flap dislocation under patient. It is
7 not always just rubbing. There are many times when it is
8 also dry-eye patients that have a tendency to displace, more
9 so. We will put it under flap dislocation issues. Dr.
10 Higginbotham?

11 DR. HIGGINBOTHAM: You said dry eyes. What about
12 systemic diseases -- diabetes, rheumatoid arthritis? Are
13 they contraindicated too?

14 DR. MCCULLEY: I don't know that those would
15 contribute to epithelial ingrowth.

16 DR. HIGGINBOTHAM: But you mentioned epithelial
17 defects. It falls into patient selection and anatomy but it
18 goes beyond.

19 DR. MCCULLEY: Well, systemic diseases that would
20 cause dry eyes --

21 DR. HIGGINBOTHAM: Plus menopausal women, all
22 those things.

23 DR. MCCULLEY: I don't know about postmenopausal
24 women. Mr. Mastel?

25 MR. MASTEL: Does it have anything to do with,

1 like, the contact lens bandage, patching or not patching?
2 DR. MCCULLEY: We put under operator appropriate
3 management of epithelial defects. That is where the bandaged
4 one would fall. So we have that covered.
5 DR. ROSENTHAL: What about previous surgery?
6 DR. MCCULLEY: If a patient had RK before and
7 there are epithelial plugs, keratoplasty, and so forth, yes,
8 that increase the risk for it happening.
9 Let's go on to flap dislocation, slippage, poor
10 alignment can result in wrinkles, microfolds, cracks,
11 irregular astigmatism. Device issues here? These really are
12 mostly operator and patient related.
13 DR. MACRAE: This area is a little bit of a
14 mystery to me. I want to be educated from other people. But
15 I do notice a difference between using the ACS in terms of
16 my rate of flap wrinkles and microstriae and things like
17 that compared to when I use a hand set.
18 DR. MCCULLEY: Which one being more?
19 DR. MACRAE: In the hand set I see microstriae
20 very, very infrequently and the flaps are much more stable.
21 So, I think there is an issue where one microkeratome may be
22 creating a different incidence of these types of events than
23 another microkeratome. It may be related to using a thicker
24 microkeratome plate.
25 DR. ROSENTHAL: Dr. McCulley, I would rather you

1 not discuss specific instruments. You can discuss issues
2 relating to them without naming them but this is not a place
3 where we are comparing and contrasting various types of
4 equipment.
5 DR. MCCULLEY: Thank you, point taken by everyone.
6 Can we put under device, in quotes, creation of a stable
7 flap? Then there would be characteristics -- is a thinner or
8 a thicker flap more or less stable; more apt to have
9 wrinkles? The amount of tissue that we have removed, I don't
10 know that that relates to the flap -- the characteristics of
11 the ablation bed as it relates to the flap. I am not sure
12 how we get at this, other than the nebulous confusing that,
13 you know, we need stable flaps, whether the hinge location,
14 flap thickness, diameter, how they relate -- I don't know
15 that we know the answer to it but we would like to have it.
16 DR. REINSTEIN: I agree. The flap bevel relates to
17 how stable the manhole cover is in the manhole, and the flap
18 thickness relates to the surgeon's ability to control it.
19 Thinner flaps are much more difficult to control than
20 thicker ones but they are more desirable for the patient's
21 long-term safety.
22 DR. MCCULLEY: If we summarize that, it could be
23 creation of a stable flap that relates to bevel, thickness,
24 diameter and relationship to ablation bed.
25 DR. STULTING: And hinge placement.

1 DR. MCCULLEY: And hinge placement, yes. Now,
2 under operator, it is going to be appropriate behavior to
3 create what we have already said for the microkeratome. It
4 is taking into consideration the characteristics that we are
5 going to ask the microkeratome to do to create a stable
6 flap. So from hinge placement, to thickness, to diameter to
7 seating in the bed.
8 Are you going to make me say it again? You have
9 all the issues that we had for characteristics of a stable
10 flap that relate to the microkeratome. So it basically is
11 surgeon behavior to complement what we have asked the
12 microkeratome to do -- in eloquent words.
13 DR. SUGAR: And amount of ablation or depth of
14 tissue removed.
15 DR. MCCULLEY: I tried to cover that by the
16 relationship to the ablation bed. Did that not get up there?
17 I had creation of a stable flap, bevel, thickness, diameter,
18 hinge placement in relationship to the ablation bed, and
19 then surgeon behavior to help to accomplish that. Patient
20 characteristics are going to be similar to those that we had
21 for epithelial ingrowth really.
22 DR. REINSTEIN: Under surgeon for flap
23 dislocation, it appears that amount of hydration by the
24 surgeon can affect the stability. So the amount of
25 irrigation --

1 DR. MCCULLEY: So, maintenance of appropriate flap
2 and bed hydration.
3 DR. REINSTEIN: Or ensuring that there is a proper
4 stick from flap to bed.
5 DR. MCCULLEY: Confirmation of flap adhesion.
6 Infection?
7 DR. STULTING: One other comment, we think tear
8 deficiency, keratoconjunctivitis sicca is probably the best
9 predictor of flap dislocation because the flaps dry out and
10 get sticky. So that is a patient, surgeon, postoperative
11 management issue that probably overrides most of the
12 microkeratome issues.
13 DR. MCCULLEY: We had that under concerns with
14 epithelial ingrowth and I wanted everything under epithelial
15 ingrowth to be brought down to this area as well, which
16 included the dry eyes.
17 DR. STULTING: I think it is different. For
18 epithelial ingrowth the problem is that the epithelium gets
19 knocked off. The flap becomes edematous and epithelium grows
20 under it. For flap dislocation the problem is that the
21 surface dries out even if the epithelium is there, and the
22 flap becomes sticky and gets moved.
23 DR. MCCULLEY: I am not bringing down the
24 explanation of the way it does it; I am bringing down the
25 association of dry eyes under both. But I understand what

1 you are saying -- different mechanisms.

2 DR. REINSTEIN: The patient's behavior after the

3 procedure affects wrinkles --

4 DR. MCCULLEY: Right.

5 DR. REINSTEIN: -- because if the patient does not

6 consciously blink frequently, if the patient does not insert

7 drops, it will dry the flap and cause --

8 DR. MCCULLEY: And they need not to rub. Mr.

9 Mastel?

10 MR. MASTEL: Dr. McCulley, I would like to go back

11 to what Dr. MacRae had brought up on the Ponsitilla --

12 DR. MCCULLEY: I am sorry, did you hear what Dr.

13 Rosenthal said after Dr. MacRae did that and got his wrist

14 slapped? We are not comparing machines. We are not comparing

15 microkeratomes.

16 MR. MASTEL: Well, I am talking about blade

17 physics. I don't care whatever --

18 DR. MCCULLEY: What I would ask is don't mention

19 names --

20 MR. MASTEL: Okay, I apologize. A straight across

21 microkeratome with a nasal hinge cuts when the chatter

22 window goes straight lines, whereas the vertical devices cut

23 in a mechanism that spans 90 degrees so you have a fan-

24 tailing of the chop. It could be a factor in the wrinkles. I

25 don't know; it is a theory.

1 DR. MCCULLEY: Okay. What are the two terms that
2 best give a broad category? Track-and rail versus pivotal
3 design. That is under flap slippage design, and that should
4 probably also be under quality of bed questions and
5 considerations.
6 DR. YAROSS: Then postop compliance.
7 DR. MCCULLEY: Okay, that is a good way to put it.
8 So patient compliance with instructions.
9 Infection -- device. I mean, the obvious,
10 appropriate sterility and maintenance thereof. Anything else
11 under device relative to infection? The other point that was
12 made before that, quite honestly, I never thought about -- I
13 learn a lot every time I come to these meetings, but one was
14 the possible association with infection in lid lacerations.
15 So if that is agreed upon, the machine that tends to have a
16 higher rate of lid lacerations theoretically might have a
17 higher rate of infection. So, sterility assurance and
18 maintenance, avoidance of lid lacerations relative to
19 device. Then there are obvious things. I mean, if you have
20 breaks in the epithelium and flap slippage then
21 theoretically that would also increase risk for infection.
22 Yes, Doyle?
23 DR. STULTING: First of all, the infection rates
24 are so low that we really don't have any solid data but I
25 think the record should reflect that, to me, it is the lid

1 lacerations is not the problem. The question is whether the
2 microkeratome base and blade touch the lid, or whether it is
3 designed in such a way that they touch surfaces that are
4 likely not to be sterile so that they then bring whatever is
5 on them into the bed. So, I think that is what the record
6 show. Our concern is not simply the fact that we get lid
7 lacerations.
8 DR. MCCULLEY: Yes, good point. Lid laceration
9 would be an effect of what the problem is. Good point. So,
10 assurance of non-contact of blade and keratome coming into
11 contact with the cornea and not coming into contact with any
12 other tissue.
13 Operator? I mean, the obvious maintenance of
14 sterile technique. We could argue, and there are no data and
15 never will be, appropriate use of prophylactic antibiotics.
16 DR. MACRAE: Previous corneal surgery and
17 immunocompromise.
18 DR. MCCULLEY: So appropriate patient selection;
19 beware of previous corneal surgery; beware of systemic
20 diseases that would affect; beware of patient hygiene and
21 presence or absence or concurrent local disease like
22 blepharitis.
23 Patient would relate to what we have said with the
24 operator needing to avoid.
25 DR. HIGGINBOTHAM: Appropriate use of medications.

1 Patients shouldn't touch the tip of the bottle to the lid.
2 DR. MCCULLEY: Patient compliance again.
3 DR. HIGGINBOTHAM: It goes beyond compliance.
4 DR. MCCULLEY: Okay, all right.
5 DR. HIGGINBOTHAM: Thank you.
6 DR. MCCULLEY: You win that one!
7 MR. BARTELL: How sterilizable are the devices?
8 Some of these devices don't really need to be sterilized.
9 DR. MCCULLEY: Well, we put in the very first
10 thing under device appropriate creation and maintenance of
11 sterility. Would that not cover it? If you can't do it, then
12 you flunk on that one. Dr. Pulido?
13 DR. PULIDO: Have you talked about bilateral use?
14 DR. MCCULLEY: We have not and we have left that
15 where I would hope we would still leave it. It is not an FDA
16 issue, and a practice of medicine issue. We have talked
17 about reuse of blades though, which, you know, implies
18 bilaterality.
19 DR. PULIDO: That is cause for an infection. I
20 mean, if one has one eye with a problem --
21 DR. MCCULLEY: I understand your point and I
22 understand not wanting to get into it, but I also understand
23 that we have gotten into it. So, I am going to leave it,
24 because of reuse of blades, that we have commented on it. I
25 will leave it to Dr. Rosenthal to get us out of it.

1 DR. ROSENTHAL: Well, just before lunch, because
2 it is one o'clock, Dr. McCulley, I thought I would inform
3 the panel that the agency is addressing the issue of reuse
4 of blades in single use instruments. It is doing it across
5 the board in all the divisions, and it will be addressing
6 this issue in our Division. That is all I can tell you right
7 now. It is going to be a risk based approach, and I think I
8 can say honestly we consider this a reasonably high risk. We
9 will bring it to the attention of the committee in
10 considering this issue. It is a major issue for the agency.
11 DR. MCCULLEY: Is that okay? It is a good point,
12 Jose. Any other points on infection, because we need to
13 break for lunch that was prepared for us? So, what we will
14 do is break for lunch. If, in the interim, you can provide
15 us hard copy for everything down to that point so you don't
16 have to do it for everything; you only have to do it for the
17 second half of it at the next break. Let's take 45 minutes
18 for lunch. I have a couple of minutes after 1:00. Let's try
19 and get back here and start up again at roughly 1:45. If
20 there is a majority of people here, that is what we will do.
21 So, if you are not here we will start without you.
22 [Whereupon, at 1:05 p.m., the proceedings were
23 recessed, to be resumed at 1:450 p.m.]

1 AFTERNOON PROCEEDINGS

2 DR. MCCULLEY: Everyone should have a hard copy
3 printout of the items that we have discussed so far. Put
4 that aside for now, and we are going to pick up where we
5 left off with interrupted movement, partial flap.

6 Let me also tell you that our agenda has been
7 changed for us and the current plan is that what we will do
8 is complete through causes and then go through the whole
9 document again relative to mitigating events, and we will
10 not do the scope of the proposed keratome guidance today. My
11 impression is that the meat that we are providing to the FDA
12 today they will use to create a draft -- a revised guidance
13 document that we will then be asked to discuss at a later
14 date.

15 We will maintain open discussion through causes
16 and mitigating events, and then it will be just panel who
17 will rank order. That does not include the public
18 participation. Through mitigating circumstances, we ask
19 still the public to actively participate.

20 MS. THORNTON: Just a point of order, Shirley
21 McGarvey, you are taking Judy Gordon's place? Is that
22 correct?

23 MS. MCGARVEY: That is correct.

24 MS. THORNTON: Could you give your name to the
25 transcriber?

1 MS. MCGARVEY: My name is Shirley McGarvey. I am
2 an regulatory consultant to Autonomous Technologies.
3 MS. THORNTON: Thank you.
4 DR. MCCULLEY: Same rules as before, before you
5 start to speak please state your name, and if you have not
6 yet spoken and it is your first time to enter into the
7 discussion, state your affiliation and conflicts.
8 Let's begin with interrupted movement, partial
9 flap. Device issues? I mean, we have the same things that we
10 had before -- clear runway. I guess that is operator issue
11 though, isn't it? Device? Anyone like to make a comment,
12 statement on that? I mean, it clearly has to function
13 reproducibly and go through its motions, and not jam, not
14 stop, not be easily stopped with minor instructions.
15 Anything beyond that? Scott?
16 DR. MACRAE: One question that I have, and this is
17 more a question to the agency and to the microkeratome
18 manufacturers, is how much of a tolerance there is for a
19 partial occlusion? Let's say you have a particle that gets
20 into the gears and slows it down, how much tolerance is
21 there for something like that? Or, if the system has more
22 friction on one of the units -- and I speak generically
23 here, but on one of the units there is a system which reads
24 out the amount of resistance in amps so that you know that
25 the system is running smoothly, which is actually very

1 helpful, and we talk about the ideal situation but after a
2 while these microkeratomes do run down and they probably do
3 need maintenance. What kind of sort of a maintenance
4 schedule do we keep with a microkeratome, and what is the
5 tolerance in terms of when do we send these microkeratomes
6 in for maintenance? It is kind of like driving a car, you
7 know, when do you go and get a checkup? It would be helpful
8 for the clinicians to have some kind of guidance from the
9 manufacturers as to when is it inappropriate to be running
10 your --
11 DR. MCCULLEY: That probably relates to a lot of
12 the functions -- translational speed, as well as
13 interruption of translation and oscillation of blade, and so
14 forth. So, we probably want to put that as a broad issue,
15 not just related to this one.
16 It seems to me, as a non-engineer, we are talking
17 about drive force and how sensitive to interruption the
18 drive is.
19 DR. MACRAE: Maybe to try and simplify this, we
20 need a mechanism to determine whether the keratome is going
21 to perform adequately in terms of the pass. Then, we also
22 need some guidance from the manufacturers in terms of how to
23 evaluate them.
24 DR. MCCULLEY: I guess the issue is what degree of
25 interference would result in a stoppage, and do we have any

1 way of assessing or testing that, and I don't think we do.

2 DR. MACRAE: We don't. You know, right now the

3 manufacturers -- it really depends upon your discussion with

4 the manufacturers. We have microkeratomes running kind of

5 slow; the amps are moving higher and higher; and we have a

6 harder and harder time to get it to keep our amps down so

7 that there isn't much resistance. Then the manufacturer

8 says, well, send it in but we don't have much good guidance

9 in terms of that. And, as the industry becomes more

10 sophisticated -- it is almost like driving a car -- we want

11 to have some type of guidance so that when a microkeratome

12 is likely to fail it gets into maintenance before it does

13 fail.

14 DR. MCCULLEY: I understand what you are saying,

15 some guidance that if the amperage required to drive reaches

16 a point that is a warning signal that the microkeratome

17 needs its 30,000 mile check.

18 DR. MAGUIRE: I think what Scott is saying is that

19 wear in a keratome can be keratome specific, and requires a

20 specific proactive schedule maintenance. Instead of the

21 keratome companies being reactive to a surgeon-identified

22 problem, we need proactive scheduled maintenance specific

23 for the wear of that keratome.

24 DR. MCCULLEY: Is that going to be number of cases

25 or is it going to be performance characteristics of the

1 keratome that can be quantified?

2 DR. MAGUIRE: Well, when it is unclear what the

3 wear of a keratome is, and when it is also unclear -- these

4 are things we know: it is unclear how wear varies between

5 keratomes by a specific company and between different

6 companies' keratomes. It is also unclear how wear is

7 affected by the expertise of the operator. So, when you are

8 faced with lack of information you need to generate it

9 proactively.

10 DR. MCCULLEY: And what I am saying is what do we

11 want as our indicators that this is a time to have the

12 microkeratome looked at by the manufacturer, sent in for a

13 check?

14 DR. REINSTEIN: Perhaps as headings for that box

15 we could divide the causes of interrupted movement to do

16 with the device as to do with the motor drive or to do with

17 the mechanics of the keratome. Because the motor drive needs

18 to have sufficient torque to make the passage in different

19 situations, and it has to have perhaps a feedback mechanism

20 to increase the torque in situations where the torque may

21 not be constant on a particular eye. There may be other

22 issues inside the machine. Then at the level of the keratome

23 on the eye, things that Scott mentioned -- debris in the

24 track, lids in the way, speculum in the way -- events that

25 can occur at the level of the eye that can make the passage

1 incomplete.

2 DR. MCCULLEY: Well, we have this -- device,

3 operator, patient.

4 DR. REINSTEIN: Right, so in terms of the device

5 we need to have perhaps feedback mechanisms that will enable

6 the keratome to overcome resistance.

7 DR. YAROSS: Dr. McCulley, I think if we wanted to

8 characterize the types of events we are talking about, they

9 could be characterized as excessive wear, inadequate

10 maintenance, inadequate torque, and then these issues as to

11 how you would monitor those, those again get into

12 mitigators. Potential mitigators could include things we

13 discussed such as maintenance schedules --

14 DR. MCCULLEY: Good point. So we will come to that

15 in a moment. Would you state then what the device issues are

16 that relate to interrupted movement, partial flaps?

17 DR. YAROSS: So, the ones we discussed are

18 excessive wear, inadequate maintenance and inadequate

19 control of torque.

20 DR. MCCULLEY: Anyone have anything to add to

21 that? No?

22 On operator we have the clear runway issue. Is

23 there anything else on the operator side? What about

24 patient? Patient cooperation I know is important because if

25 the patient becomes uncooperative in the process then one

1 can end up with a jamming in the system.

2 DR. SACHAROFF: If I could just add a comment on

3 the operator? Alex Sacharoff, Summit Technology. The

4 cleaning of the microkeratome is quite critical to its

5 optimal performance. So, I am concerned that this issue get

6 raised and awareness be put to the panel that the surgeon

7 and his staff plays a vital role in maintaining optimal

8 performance of the microkeratome by maintaining it, and

9 failure to do that can lead to problems.

10 DR. MCCULLEY: Okay. So, under operator would be

11 appropriate maintenance --

12 DR. SACHAROFF: By the user.

13 DR. MCCULLEY: Appropriate maintenance and

14 verification of function, regular verification of function.

15 DR. REINSTEIN: Under device we have mentioned

16 electrical failure, lights out in the middle of a keratome

17 passage. So, backup power systems. Under that, of course,

18 backup IOP.

19 DR. MCCULLEY: Maintenance of suction, backup

20 maintenance of power for the head, and then I guess -- it

21 would come under irregular flap. I guess we have that

22 somewhere further down, don't we? Yes. Disassociation of the

23 two if one fails.

24 Anything under patient other than patient

25 cooperation?

1 DR. MAGUIRE: Eyelid anatomy.

2 DR. MCCULLEY: Good point, patient anatomy.

3 DR. YAROSS: Actually, I think that was a good
4 point, that the adequate maintenance may be moved over to
5 the operator column.

6 DR. MCCULLEY: I think that is where we wanted it.
7 That is where we had it -- oh, she put it in the wrong
8 place? Everyone try to watch because she has a lot she is
9 trying to do. So try to watch to make certain that what we
10 are requesting is interpreted correctly.

11 DR. MAGUIRE: I think maintenance is a cooperative
12 effort between the manufacturer and the user. Someone who is
13 naive in the use and is just going through trying needs to
14 know how to do it, but they also need to get feedback.
15 Sometimes that is not easy to observe with the naked eye.
16 You need feedback. I think that is part of the scheduled
17 maintenance loop.

18 DR. MCCULLEY: Good point, and it also probably
19 should be a part of the initial introduction of the
20 instrument to the site, education of the operators. We can
21 put it under device, that there is appropriate education on
22 the part of the manufacturer to the users relative to
23 appropriate care and maintenance, and that the operator
24 follow those effectively.

25 Next topic is lamellar keratitis, either focal or

1 diffuse. Let's see, who came today to tell us what is
2 causing it?
3 [Laughter]
4 Okay, device. There are thoughts that interaction
5 of salts with motor head and oils, and the like, are a
6 culprit. So, I am not sure how we put that. That would be
7 relative to the device being developed in such a way that it
8 does not leak and that it is not susceptible to
9 contamination by salts or organisms, and that the
10 maintenance be accomplishable without compromising that
11 principle. That gets back probably to the issue that was
12 brought up before, the question of blades not being
13 contaminated in any way. Are there other things under device
14 on lamellar keratitis? Scott?
15 DR. MACRAE: Just a comment in terms of this
16 issue. As I watch the literature, initially I think there
17 was a wave of speculation that this was actually device
18 related. As I have seen papers come through the journals,
19 more and more it seems that interface keratitis can't be
20 characterized as always device related. As a matter of fact,
21 most of the time it is not related to the microkeratome,
22 from what we can determine or from what I see in the
23 literature. So, I just want to give that to the agency, that
24 interface keratitis, I believe, is not caused by the device.
25 In fact, we have had cases where we simply lifted the flap,

1 retreated a patient without using a microkeratome, and we
2 have had interface keratitis.
3 DR. MCCULLEY: But is it fair to say that from
4 what we know right now that we would have to view this as
5 not a single cause; that it is a heterogeneous etiological
6 problem, and possibly pathways, that the device may have an
7 operator role, and so on and so forth? And that is what we
8 are going to try to do, put the ones that go under each one.
9 But are you proposing that we take device out of potential
10 causes?
11 DR. MACRAE: No, I am just saying that as guidance
12 to the in-house people --
13 DR. MCCULLEY: It is not only a device related
14 issue.
15 DR. MACRAE: -- that it is certainly an important
16 concern, but the literature that I see -- and Dan is shaking
17 his head also -- indicates that the primary cause is
18 probably not the device in most cases.
19 DR. MCCULLEY: Okay. Point taken. Anything else
20 related to device in lamellar keratitis?
21 DR. REINSTEIN: I would add that the device may be
22 involved as a bystander because it appears that the
23 literature is leaning towards a theory of endotoxin and it
24 is a sterilization issue. That would explain why instruments
25 could contain endotoxin that were used under the flap under

1 the same sterilizing conditions. So, the keratome would be
2 involved in the sterilization issue if this is the true
3 story, but nobody has hard evidence for this yet in the
4 literature so it would be hard for us to recommend something
5 because --
6 DR. MCCULLEY: Well, no, we can recommend
7 something here and we can do it not too specifically but we
8 can say that it would be a device-operator interaction; that
9 if the device is not appropriately maintained it can be
10 contaminated with a stimulating substance, and that we need
11 to ensure that the device is appropriately maintained.
12 Again, would that be an issue here -- maintenance of a
13 device, not contaminating it with other substances; not
14 having our sterilization solutions or apparatuses become
15 contaminated where they possibly can kill the bacteria but
16 leave bacterial products around that could be introduced or
17 carried by the device into the interface. So, avoidance of
18 device contamination with living or dead organisms or other
19 stimulating substances.
20 DR. MAGUIRE: Is it appropriate for the panel to
21 put in a suggestion that when a cluster of cases occur that
22 we look more specifically at a device? Do we have any role
23 in that? Because certainly there are clusters that have been
24 reported, and with clusters you may be more suspicious.
25 DR. MCCULLEY: Ralph, you didn't hear that. If

1 there is a cluster of lamellar keratitis would it be
2 appropriate to charge the FDA with doing a CDC type of
3 analysis to try to determine the causative event in the
4 cluster?
5 DR. MACRAE: That is not what we are here for.
6 DR. MCCULLEY: I don't think it is. It would be
7 nice to saddle them with it.
8 DR. MACRAE: As long as we are on this, I just
9 want to say for the record that I think this would be an
10 ideal area where the Centers for Disease Control would get
11 involved because there are a lot of these cases being
12 observed now and most of us that are out in the field that
13 are seeing them are perplexed, and there doesn't seem to be
14 a lot of systematic evaluation in the way that CDC
15 approaches things, and that is exactly what is needed right
16 now with this problem. I think with that type of systematic
17 evaluation -- this certainly reminds of the acanthamoeba
18 keratitis problem where we had peripheral facts but we
19 didn't really have the bigger picture. I think CDC could be
20 extremely helpful, and I would just like to say for the
21 record that this would be an ideal situation --
22 DR. MCCULLEY: The reality of the acanthamoeba
23 situation was that CDC had it reported but it was the
24 individuals that figured out the problem more than the
25 agency. That is probably what it will take here unless the

1 ASCRS -- but we are getting afield. Dr. Rosenthal?

2 DR. ROSENTHAL: I might just add that if there is

3 a major issue related to something like this Larry Kessler's

4 group that does postmarket, does have an epidemiological

5 group that helps design and carry out studies that might be

6 of interest. That is a potential use of their facilities

7 but, of course, they have all the devices to deal with and

8 they have to have priorities. It depends on what the

9 priorities are.

10 DR. MCCULLEY: All right, we have gone from a "no"

11 to a "yes" and "maybe."

12 Okay, operator issues related to lamellar

13 keratitis -- any others? Patient issues?

14 DR. YAROSS: Back to operator issues, I think

15 someone mentioned the importance of cleaning the equipment

16 and maintenance. So, I think that needs to be under

17 operator.

18 DR. MCCULLEY: Oh, that was not put in. Thank you

19 for putting that up. It was intended to be put in there.

20 Everybody please try to watch because, again, they have a

21 tough job there and I can do more than one thing but I can't

22 do unlimited numbers and I can't watch that too to be sure

23 that it gets put in. So, all of you, please watch that.

24 DR. SUGAR: Lid isolation and suction to take away

25 secretions may pay a role.

1 DR. MCCULLEY: So, operator maintenance of an
2 isolated field, isolated sterile field. Patient issues, any
3 thoughts of patient issues being involved where it is the
4 patient's fault?
5 DR. MACRAE: This is actually a combination of
6 operator and patient, we have observed a few cases of
7 interface keratitis in patients that have atopic disease,
8 and we think that there is a relationship between the
9 atopism and their inflammatory reaction.
10 DR. MCCULLEY: Why don't we put under patient, you
11 know, the concern about there being individual patient or
12 type of patient contributory factors, e.g., atopic?
13 DR. MACRAE: And this gets back to the issue of,
14 you know, we need a good, large case-controlled type series
15 that could evaluate who is at high risk for this and how it
16 occurs.
17 DR. MCCULLEY: Other comments about lamellar
18 keratitis? Doyle, you don't have anything to add to that?
19 You have a lot of experience.
20 DR. STULTING: I think everything I would add has
21 already been said.
22 DR. MCCULLEY: Thank you.
23 DR. STULTING: I agree that most of the cases are
24 probably not caused by the microkeratome, based on our data.
25 DR. MCCULLEY: The next item is jagged perimeter,

1 entry wound, edge, tearing and entry angle. Device is
2 critical here. This gets back to our bevel issue. I guess
3 for a device it would be insurance of an appropriate bevel,
4 a non-traumatic appropriate bevel.
5 DR. SUGAR: Didn't we really cover this under
6 number three, quality of bed and perimeter?
7 DR. REINSTEIN: Well, it went up from there
8 actually. The entire box under device could just be copied
9 and pasted in there.
10 DR. MCCULLEY: All right, do we need to leave this
11 as a separate line, or did we not already cover this under
12 other things? That is not a rhetorical question; that is a
13 real one. Looking back up at the other things, is there
14 anything that we would put here or need to put here that we
15 have not otherwise covered? Scott? Dan? Leo? Anybody?
16 DR. MAGUIRE: I think it is redundant.
17 DR. MCCULLEY: Okay, let's X that box.
18 DR. ROSENTHAL: May I just suggest we put it under
19 poor precision and reproducibility as another line under the
20 second?
21 DR. MCCULLEY: It goes under bed and perimeter,
22 quality of bed and perimeter.
23 DR. ROSENTHAL: Okay, quality of bed and
24 perimeter.
25 DR. MCCULLEY: We have covered it there.

1 Reproducibility of cut -- we have covered that. Now we come
2 to suction, consistency of, loss of, maintenance or,
3 ischemia of, decentration of flap. Device.
4 DR. YAROSS: This is one where I think it goes
5 under the possible causes, and we have already picked it up
6 in several other places. There have been several places
7 where we have said you can get decentration, etc., by poor
8 suction control.
9 DR. MCCULLEY: Okay, well, let's go through them
10 one at a time. Consistency, we have stated that needs to be.
11 We don't want a loss. The only thing we have not covered
12 with loss, and we may get that -- where is our irregular
13 flap? I guess we had that under precision. We did not
14 address, did we, in that the issue with loss of suction,
15 that we need a fail-safe in the machine, that if suction is
16 lost the machine stops cutting.
17 DR. YAROSS: That is the mitigators.
18 DR. MCCULLEY: Good point. Maintenance of? Okay.
19 Ischemic globe -- that probably hasn't been covered.
20 DR. MACRAE: I would make one comment. I think
21 most people around this table would agree that maintenance
22 of intraocular pressure is one of the most important
23 components of this, and that is evidenced by the fact that
24 it shows up again and again in our other subcategories. So
25 for the record, it is extremely important. I think all the

1 keratome operators also believe that at least in some cases
2 when a machine registers good suction the manufacturer
3 assumes that that suction has been translated to increased
4 intraocular pressure, and we all recognize that there are
5 times when there is a disconnect between the pressure
6 chamber and its connection to the intraocular pressure. That
7 disconnect very frequently leads to trouble.
8 DR. REINSTEIN: There is that, and there is also
9 the fact that scleral rigidity determines the coupling
10 between vacuum pressure in the system and the intraocular
11 rise in pressure.
12 DR. MAGUIRE: So that is one component. Another
13 thing for the record that I think is extremely important is
14 accurate measurement of intraocular pressure by the
15 operator. I think some of the methods that we use to do that
16 are difficult for the operator to use, especially someone
17 who is relatively new to some of the applanation devices,
18 and I think -- I don't know how everybody feels, but there
19 should be some discussion about having some kind of a
20 quantitative measurement of intraocular pressure by the
21 operator.
22 DR. MCCULLEY: Let me get us on track here if I
23 can, or try to. Do we need to add anything anywhere? You
24 brought up some issues. I want to be certain we don't need
25 to add back up somewhere else, and if we do, where they

1 should go. Consistency -- we talked about establishment and
2 maintenance of. Mitigating factor -- some of the issues you
3 brought up, to ensure that we have it with, for instance, a
4 pneumatometer or a quantitative device would come under
5 mitigation to avoid the problem.
6 DR. REINSTEIN: Perhaps it should actually be part
7 of the way of doing this, rather than --
8 DR. MCCULLEY: Well, we don't have a way of doing
9 columns so we have a cause problem --
10 DR. REINSTEIN: But under device -- what we are
11 talking about is producing adequate intraocular pressure
12 elevation and a stable intraocular pressure.
13 DR. MCCULLEY: Right.
14 DR. REINSTEIN: So we need a way of measuring that
15 we have adequate pressure.
16 DR. MCCULLEY: Right.
17 DR. REINSTEIN: At the moment the systems that are
18 used are basically using what is called an applanation
19 tonometer which, as Leo suggested, is not easy to use, is
20 quite dependent on how wet the surface is, and it is only a
21 threshold measurement. It only tells you that the pressure
22 is above a certain level.
23 DR. MCCULLEY: But, wait, wait. That is one of the
24 ways. There are other ways to do it. We have our columns of
25 causes and then we have mitigating factors that we are going

1 to come back to in a moment. We discussed at length before
2 establishment of and maintenance of adequate suction
3 intraocular pressure. Do we need to embellish on that any
4 more, keeping in mind that we are going to comment on
5 mitigating factors and how to avoid the problems?
6 So let me start once again keeping that in mind,
7 and keep in mind what we have already discussed and said. Do
8 we need to add anything else to that? Consistency of I think
9 we have discussed. Loss of we have discussed. Maintenance of
10 we have discussed. So all of those relate to decrease in
11 effective suction and increase in intraocular pressure.
12 Ischemic globe, that is too much for too long. That we have
13 not covered.
14 DR. YAROSS: From a formal standpoint, I think
15 everything except ischemic globe has been addressed
16 elsewhere. The question is, is ischemic globe a separate
17 clinical issue that you need to then identify the causes of.
18 DR. MCCULLEY: Yes, it is, and an important one.
19 But before we narrow it to that, did we cover -- and you
20 guys help me, looking back up before -- did we have
21 decentration of flap because that is not too much or too
22 little; it is just unusual and relating to other anatomy? I
23 don't think we covered that.
24 DR. REINSTEIN: Therefore, in that box we should
25 have conjunctival occlusion as a device cause of loss of

1 suction.

2 DR. MCCULLEY: No. What I was trying to do -- I am
3 not doing this well because we are not all staying on the
4 same page. We have talked about decrease otherwise in other
5 sections. So, a cause for an inadequate pressure that we
6 have already discussed would be conjunctival occlusion.
7 Would we not address that in mitigating circumstances to
8 ensure that we do not have conjunctival occlusion that,
9 indeed, we do have true suction and true increase in
10 intraocular pressure?

11 What I am trying to get at is I think we have
12 dealt with the issues that relate to low or loss of suction
13 and high intraocular pressure. We have dealt with that. We
14 have dealt with those. We have two other issues under here.
15 One is too much for too long, resulting in an ischemic
16 globe. The other is some kind of weird anatomical situation
17 or poor surgeon placement of suction that results in
18 decentration of the flap.

19 DR. REINSTEIN: But nowhere above here does it say
20 conjunctival occlusion.

21 DR. MCCULLEY: No, because it is going to come
22 under mitigating events and we are not yet to mitigating
23 events.

24 DR. REINSTEIN: But, for example, having multiple
25 ports for suction would be a device element --

1 DR. MCCULLEY: And that would be under mitigating
2 events.
3 DR. REINSTEIN: All right.
4 DR. MCCULLEY: Unless someone has something
5 different, I think we have dealt with low, inadequate, loss
6 of suction in other areas. We will address them again with
7 mitigating circumstances. Yes?
8 MR. BARTELL: A factor that might come under
9 suction --
10 DR. MCCULLEY: Mr. Bartell?
11 MR. BARTELL: Yes, Mike Bartell -- as you evaluate
12 microkeratomes it would be build up time of suction and it
13 would be suction release as a factor also.
14 DR. MCCULLEY: And that would probably come under
15 too much or too long kind of circumstance. How would that
16 relate to a problem?
17 MR. BARTELL: Just not letting loose of the eye
18 when you are there in the OR. You know, it can be a problem.
19 The suction doesn't vent. You know, if you are talking about
20 the subject of suction, if your vacuum buildup time is
21 exceptionally long or the patient's eye moves, that leads to
22 your decentration. In evaluating a microkeratome one of the
23 things I would like to know or would like to see is what the
24 suction buildup time is and what the release time is.
25 DR. MCCULLEY: Good point. So, now we would go

1 back under possible causes where we discussed the issue of
2 inadequate suction and have -- well, we can still work that
3 in. Keep the thought. We can work it into mitigating issues
4 rather than redoing the other, and put that there needs to
5 be appropriate buildup and release time. So please hold the
6 thought. You have the responsibility for that.
7 DR. YAROSS: I think what may do it, if we want to
8 differentiate the clinical issue from the device issue, is
9 that the clinical issue could be undesired IOP and the
10 device issue is suction control.
11 DR. MCCULLEY: We are tying the two together
12 already. So under suction we are dealing, have dealt with or
13 will deal under mitigating circumstances the low suction.
14 Let's see, it would be excessive -- we may have to break
15 this into two; I am not sure how to put it into one. But it
16 would be suction resulting in too high an intraocular
17 pressure. The clinical event would be ischemic globe
18 phenomenon.
19 DR. PULIDO: Excuse me, a point of clarification,
20 so a clinical problem is ischemic globe, probable cause for
21 device --
22 DR. MCCULLEY: Good point, let's do it that way.
23 Thank you, Jose. Well put. So, under the clinical problem
24 put ischemic globe -- just put ischemia, ocular ischemia.
25 MR. MASTEL: Excuse me, Dr. McCulley, what is

1 excessive IOP?

2 DR. MCCULLEY: Too much for too long. It is very
3 individual. It is like defining glaucoma. Okay, so we have
4 ocular ischemia as the event. Cause -- and there is going to
5 be some individual variability that is going to contribute
6 to this so it is probably not a single number, and it is
7 going to take into account both the degree of increase and
8 the duration of the increase, and there is going to be some
9 individual variability. So, I can't tell you an exact, Mr.
10 Mastel, what that would be because there are variables.

11 But the things that would contribute to the event
12 would be a device that created excessive suction resulting
13 in increase in intraocular pressure. From a device
14 standpoint, it would be a device where the operator cannot
15 accomplish the event in a timely fashion because of design
16 that requires excessive time for the suction. Operator
17 standpoint would be -- I don't know how to put it in a non-
18 pejorative way, but inability to use the machine efficiently
19 and in a short period of time. Patient -- there is then
20 going to be the individual variability of susceptibility to
21 ischemia.

22 Let me make sure we have all three of these and
23 then we will go on and we can rip it completely apart if we
24 want. That is going to be individual susceptibility to
25 ischemic damage.

1 DR. ROSENTHAL: I need Dr. Higginbotham's advice,
2 but there is a pressure above which one should never go. I
3 know there is going to be individual variability based on
4 lots of factors but I think there should be something in
5 there that the thing doesn't just put on suction and
6 continue to put on suction. There has got to be a means by
7 which it stops at the level which you have chosen.
8 DR. MCCULLEY: Dr. Rosenthal, are you aware that
9 we occlude the central retinal artery not uncommonly in this
10 procedure? So, we are shutting off the blood supply to a
11 significant degree. Is there an absolute above --
12 DR. ROSENTHAL: I don't know; I am asking you.
13 DR. HIGGINBOTHAM: It doesn't sound like it is
14 really magnitude -- well, the magnitude is excessive but the
15 duration is really the issue here, and certainly my
16 colleague to my left could contribute to this answer but
17 certainly the shorter the better, but no more than, say, a
18 minute to a minute and a half. I mean, the magnitude is 60-
19 80.
20 DR. MCCULLEY: We have to be careful about that
21 because there is a device approved that requires elevation
22 of intraocular pressure that not uncommonly will exceed a
23 minute to a minute and a half of very high pressure.
24 DR. HIGGINBOTHAM: So now we are getting really
25 into the entire retina in terms of good circulation and what