1 overcomes the risk, and it is measured in terms of patient
2 performance and with the best measurements available.
3 That means we need to do the baseline, and do it
4 with an acoustic aid that is of the best technology
5 available, and fit it with the best known audiological
6 techniques, so that we can obtain what is their ultimate
7 performance with existing options. We need to compare that
8 baseline with the implant, again, utilizing the same
9 techniques. If we don't, we will skew the results one way
10 or the other.
11 And the outcome measurements have to be wide in
12 their range and in the systems that they use. They have to
13 be able to capture the nuances of this deficit, and they
14 have to be well validated and accepted by the community.
15 In summary, if this industry is going to succeed
16 in providing benefit to the substantial number of patients
17 that are very eager and sometimes desperate to obtain help,
18 we need to look at the measurement of benefit very, very
19 carefully, or else we will leave scores of unhappy patients,
20 numbers of practitioners that will be very skeptical. We
21 will leave the residual industry participants burdened with
22 those effects, and they in turn will dissatisfy their many
23 interests which are pushing them forward.
24 Thank you for your consideration.
25 DR. PATOW: Thank you.

1 Are there questions from the panel? Dr. Shelton?

2 DR. SHELTON: Clough Shelton. You had mentioned

3 the desirability to not make the patient's post-operative

4 hearing worse by 10 or 12 dB. How did you pick that number?

5 MR. BEDOYA: It is slightly above the test, retest

6 accuracy. If the question gets a little bit more technical,

7 I will defer to Dr. Soli.

8 DR. PATOW: Dr. Kileny?

9 DR. KILENY: Paul Kileny. You advocate baseline

10 to be best aided condition with standard hearing aids. Do

11 you have any thoughts of length of best aided trial you

12 would recommend? After all, not everybody improves

13 immediately in the clinic.

14 MR. BEDOYA: Absolutely. I believe that after the

15 acoustic aid is fitted appropriately, they need at least one

16 month if not more to stabilize, to acclimatize to the new

17 aid, and that is if it is an existing hearing aid user. If

18 not, it may be longer.

19 DR. KILENY: And a follow-up question: Do you

20 have any thoughts in terms of how to determine device

21 integrity and longevity? How long should we expect these

22 devices to function properly, and how should that be

23 determined?

24 MR. BEDOYA: That is a very good question. It is

25 a very difficult question to answer, as well. We should

1 target the usable expectancy in life of these patients as
2 the best range for function. However, that will only come
3 after vast experience is gained in actual usage, although we
4 can all make calculations and predict life expectancies of
5 the various components. It is component dependant, it is
6 design dependant, and even technique, surgical technique
7 dependent.
8 DR. PATOW: Dr. Middleton?
9 DR. MIDDLETON: You mentioned the improved sound
10 quality should not be the only factor that is taken into
11 consideration for market approval. Can you reiterate what
12 other variables you think should be considered and elaborate
13 on why that is?
14 MR. BEDOYA: First I will address the issue of
15 sound quality. I believe it is very difficult to make a
16 conclusive measurement of these subjective measures. There
17 are some tests that provide indications, but until we can
18 say this patient will benefit by the sound quality and be
19 able to target that patient, understanding their pre-implant
20 conditions, I say that I think that would be inappropriate.
21 This is going to be, I think, an overall result of what we
22 do. However, I think there are objective measures that we
23 can use to claim some performance or some benefit that we
24 can provide, and those are speech recognition under the
25 various conditions and the increased range of functional use

1 of a signal.

2 DR. MIDDLETON: Just a final question: How did

3 you establish the two-year stability time line for a

4 threshold?

5 MR. BEDOYA: On recommendation of our medical

6 panel. That is a fairly standard time to establish

7 stability, two years plus.

8 DR. PATOW: Dr. Uhthoff?

9 DR. UHTHOFF: Dr. Uhthoff, Health Canada. In the

10 surgical risk presentation you stated, "However many of

11 these devices are inserted peripherally to the inner ear and

12 serious complications are unlikely." Can you comment on

13 that, please?

14 MR. BEDOYA: Yes. In comparing it to stapes and

15 cochlear implant surgeries where you are very proximal to

16 the vestibular system, you penetrate the inner ear, there

17 you can say that the dangers are concentrated in that area.

18 If you approach this as anatomically superior, you get away

19 from all those sensitive areas and are not likely to have

20 the more serious complications. There are surgical

21 complications. There are complications of any surgery, but

22 I wouldn't consider them as serious.

23 DR. UHTHOFF: But aren't you in the middle ear?

24 MR. BEDOYA: Yes.

25 DR. UHTHOFF: So why isn't that similar to other

1 middle ear operations? I mean--

2 MR. BEDOYA: Again, I should maybe let a physician

3 comment on that, but this is--by not being directly on top

4 of the cochlea, the vestibular system, you have a lot more

5 room for error working in the superior section of the--for

6 example, as in our case, of the inferior malleular joint.

7 DR. PATOW: We have time for one more question.

8 DR. DUFFELL: Dr. Duffell, the industry rep. The

9 previous two manufacturers mentioned the use of the doppler

10 laser and the temporal bone. You didn't comment on that.

11 What are your views?

12 MR. BEDOYA: I think those are very good tools in

13 quantifying the performance of these devices when in the

14 pre-clinical stages. I think there are other means, as

15 well, but there needs to be a comprehensive battery of

16 experiments that defines the performance of these devices

17 before they go into the clinic. So I support them, and I

18 believe that they are correct in saying that we need

19 accurate assessment of the capabilities of these devices.

20 DR. DUFFELL: And you are comfortable with those

21 two performance indicators as being something that the

22 industry would be asked to produce as part of their

23 applications?

24 MR. BEDOYA: I think that they are, as has been

25 stated in the previous presentations, they require great

1 levels of sophistication. Results can be very or data could
2 be very variable, and a lot of care should go into how those
3 measurements are taken.
4 DR. PATOW: Thank you, Mr. Bedoya. I hate to
5 interrupt our questioning, but we need to move on.
6 Our next speaker is Ms. Pam Matthews from SoundTec
7 in Oklahoma City, Oklahoma.
8 MS. MATTHEWS: Good morning. Thank you for the
9 opportunity, on behalf of SoundTec, thank you for the
10 opportunity to be here this morning. My name is Pam
11 Matthews, and I am the primary audiologist for SoundTec,
12 Inc.
13 As a clinical and research audiologist for the
14 last 10 years, I have had the privilege to fit several
15 thousand hearing aids, and I have been involved with
16 research with both hearing aids and middle ear implantable
17 devices. Some of my research projects have included a
18 digital master hearing aid, evaluating electromagnetic
19 interference between digital cell phones and hearing aids.
20 I worked with Dr. Hough on the Hough-Xomed middle ear
21 implantable in the early 1990s, and now with SoundTec.
22 We are pleased to be presenting our views and very
23 specific recommendations to you today. We hope that you
24 will find our views to be helpful as you formulate the
25 industry guidelines for the future.

1 During the presentation today I will be covering
2 the following items: the pre-clinical standard, the
3 inclusion criteria, the control for baseline comparison,
4 safety issues, efficacy outcomes, statistical
5 considerations, and then I will conclude with a summary of
6 our recommendations.
7 Because of the lack of an appropriate animal
8 model, we strongly recommend testing the implant device in
9 fresh human temporal bones using laser doppler
10 interferometry as the pre-clinical standard. This provides
11 the closest representative model to the human ear for
12 evaluating safety and efficacy.
13 Our surgical approach for our device is a
14 transcanal stapedectomy-like approach, and the tiny size of
15 the device on the ossicular chain cannot be accurately
16 modeled on any animal species, either anatomically or
17 physiologically. Laser doppler interferometry can be used
18 with all the middle ear technologies, and the generic use of
19 laser doppler provides meaningful indicators for predicting
20 safety and efficacy.
21 We propose the following threshold range as
22 suitable for implant candidacy. As you can see, the maximum
23 hearing loss range in the speech frequencies is in the
24 moderate to severe range of about 50 to 85 dB HL, while the
25 hearing may be normal for 1000 Hz and below.

1 To derive benefit from a hearing aid or a middle
2 ear implantable, the subject must have some speech
3 discrimination capability. Therefore, we recommend a score
4 of 60 percent or greater for the NU-6 50 item word list when
5 presented at 40 dB above their SRT.
6 The presence of feedback, occlusion, and/or
7 dissatisfaction with a hearing aid must be substantiated.
8 Therefore, we do not believe in implanting mild hearing
9 losses nor profound hearing losses. Mildly hearing impaired
10 can be fit well with hearing aids with negligible feedback
11 and occlusion problems. The profoundly hearing impaired
12 have reduced speech perception capability.
13 We believe the best control condition is the
14 subject as his own control. Reasons include: The subject
15 cannot be blinded, and the outcomes are largely subjective,
16 and they are relative to the baseline condition. The
17 baseline condition for comparison that we recommend is an
18 optimally fit hearing aid.
19 We wanted to fit a wide range of technologies and
20 not be limited to just one type of technology, so we propose
21 the following as a definition of an optimally fit hearing
22 aid for the purpose of a carefully controlled study: The
23 hearing aid must meet the prescriptive target, NAL-R, within
24 an acceptable range. It must provide benefit, as evidenced
25 by the Abbreviated Profile of Hearing Aid Benefit, and it

1 must pass a hearing aid checklist.

2 Our criteria, the tolerance range for NAL-R is

3 plus or minus 5 dB for 500 through 2000 Hz, and plus or

4 minus 12 dB for 3000 and 4000 Hz. This is similar to what

5 respected researchers were able to obtain for hearing losses

6 similar to our proposed target population. We believe this

7 is a stringent yet attainable goal to be sure that the aid

8 was well fit as a baseline comparison.

9 Additionally, the hearing aid must provide at

10 least 10 points of average improvement for the three

11 subscales of Ease of Communication, Reverberant Noise, and

12 Background Noise. According to the author, this ensures

13 significance between the unaided and aided condition.

14 Additionally, the hearing aid checklist provides evidence

15 that the hearing aid is clean, that it is functioning

16 properly, and that it has been optimized for the patient.

17 The driving force has to be that the benefits well

18 outweigh any risk. The surgical risks include those

19 associated with any surgical procedure and the potential to

20 cause a severe to total loss of hearing. The more invasive

21 the surgical procedure, the greater the risk of harm from

22 the length of surgery, damage to important middle ear

23 structures such as the facial nerve, and increased chance of

24 infection.

25 We recommend the surgical risk of a potential

1 total loss of hearing not to exceed that of a stapedectomy.
2 Other risks include device failure and loading. Some
3 residual hearing loss resulting from loading is expected,
4 according to the laws of physics, and it has been well
5 documented in articles published by Goode and also in our
6 own bench tests using laser doppler interferometry.
7 Our view is that an average of 9 dB loss is not
8 harmful to the subject, nor is it clinically significant in
9 light of the presence of loading and test-retest
10 variability. Obviously, less loading is preferred. Each
11 implant company should strive to minimize the amount of
12 loading while making sure the performance of the device
13 overshadows any effect loading may have.
14 Implantable hearing devices are currently fit to
15 only one ear. This requires that binaural hearing aid
16 wearers forego the use of the implant in the non-implant
17 ear, at least for a brief period of time. Otherwise, an
18 acoustic hearing aid can be worn in that ear. Our view is
19 that once the technology has been proven, implanting both
20 ears is reasonable provided evidence of monaural implant
21 benefit and safety has been demonstrated and maintained for
22 at least a one-year period.
23 Efficacy outcomes must verify the benefits of the
24 device. Improved audibility is substantiated with the
25 Articulation Index, or as it is now called, the Speech

1 Intelligibility Index, functional gain measures, speech
2 recognition in quiet and in noise.
3 We propose that the amount of hearing loss that
4 must be made up to accommodate for the effect of loading is
5 one-half of the change in residual hearing. This half gain
6 value is to be used when calculating the functional gain
7 outcomes. Providing half gain for a hearing loss is
8 consistent to current hearing aid fitting practices.
9 We recommend the use of the APHAB for
10 demonstrating aided benefit, and again, we recommend a 10
11 point average of improvement or more for those three
12 subscales, Ease of Communication, Background Noise, and
13 Reverberant Backgrounds, over and above the optimally fit
14 hearing aid baseline condition.
15 There are other surveys that address the other
16 benefits of the device, such as sound quality, reduction of
17 feedback, and reduction of occlusion. Additionally, sample
18 size justifications are required for all primary outcomes.
19 The FDA has well defined parameters for protocol
20 development, including statistical considerations. We
21 believe the power of the study and the sensitivity to the
22 change of primary outcomes dictate the sample size. In our
23 model we use 100 subjects, we study them for a 6-month
24 period, and we are going to follow them post-market approval
25 to track the safety for at least one year. Therefore, we

1 recommend this as a reasonable approach.

2 In summary, we propose the following

3 recommendations. The pre-clinical standard we recommend is

4 the use of fresh temporal bones and laser doppler

5 interferometry. For inclusion, we recommend moderate to

6 severe sensorineural hearing loss as defined, and they may

7 have normal hearing for 1000 Hz and below. We recommend a

8 speech score of 60 percent or greater and the presence of

9 feedback, occlusion or dissatisfaction, substantiated.

10 The control condition is the subject as his own

11 control, and the comparison is an optimally fit hearing aid

12 with plus or minus 5 dB for 500 through 2000 Hz and plus or

13 minus 12 dB for 3000 and 4000 Hz for the NAL-R. Also, aided

14 benefit must be substantiated.

15 Safety issues include that the risk must be

16 outweighed by the benefit, and the risk of a severe or total

17 loss of hearing should not exceed that of a stapedectomy

18 procedure.

19 Efficacy. Audibility and benefit must be

20 demonstrated, and we recommend 10 point average of

21 improvement or more for the APHAB for the three subscales

22 over the hearing aid.

23 For the statistics, the power of the study and the

24 sensitivity to change of the primary outcomes dictate the

25 sample size, and we propose a minimum of 100 subjects for

1 six-month study and at least one year post-market approval
2 surveillance.
3 Again, we thank you for the opportunity to share
4 our views and recommendations with you today. We would be
5 happy to discuss any of the items in greater detail.
6 MR. SAUBERMAN: Ms. Matthews, do we have copies of
7 these slides?
8 MS. MATTHEWS: I gave a copy of the slides, and I
9 am going to leave these notes with them as well.
10 MR. SAUBERMAN: Okay. We will need one copy for
11 our transcriber and one for our summary recorder.
12 MS. MATTHEWS: I only brought one copy, but I
13 can--
14 MR. SAUBERMAN: We can make another copy.
15 MS. MATTHEWS: Okay.
16 DR. PATOW: Are there questions from the panel?
17 Yes, Dr. Sininger?
18 DR. SININGER: Yvonne Sininger. You mentioned
19 half gain as a target for audibility--
20 MS. MATTHEWS: Yes.
21 DR. SININGER: --and yet previously you were
22 talking about comparison to conventional hearing aid use.
23 How do you compare that? If with a conventional hearing aid
24 let's say you can achieve greater than half gain audibility,
25 should that be taken into consideration?

1 MS. MATTHEWS: We are talking about two different
2 issues here, and this is a really tough question. You are
3 talking about the amount of accommodation for the effect of
4 loading, or are you talking about the gain that the device
5 is going to provide?
6 DR. SININGER: No, I am talking about audibility
7 with the device in regular use.
8 MS. MATTHEWS: We are limiting our pre-baseline
9 condition to the NAL-R gain. There is research out there
10 that shows a lot patients prefer less gain than that, even,
11 and limit the feedback, restrict the amount of gain that you
12 can give with hearing aids. With the electromagnetic
13 signal, we believe that they will be able to use more gain
14 if they find it desirable, so we don't have a limit or a
15 target that we are using for the device.
16 DR. SININGER: I am just saying there is two ways
17 to compare the gain. One would be half gain and the other
18 might be audibility provided by a standard, a conventional
19 hearing aid.
20 MS. MATTHEWS: We are looking at audibility, at
21 functional gain measures as well as speech measures, both
22 pre and post, yes.
23 DR. SININGER: Right.
24 DR. PATOW: Any other questions? Dr. Shelton?
25 DR. SHELTON: Clough Shelton. A question about

1 your recommendations for a speech discrimination score
2 better than 60 percent.
3 MS. MATTHEWS: Yes.
4 DR. SHELTON: If you had a patient that had poor
5 speech discrimination in both ears, say 40 percent, you
6 would exclude them? And why would that be?
7 MS. MATTHEWS: Well, we are trying to have a
8 carefully controlled study, and while I believe someone with
9 a 40 percent speech understanding could receive excellent
10 benefit with the device, we are trying to limit the amount
11 of central effects that the patient may have and keep it
12 more of a peripheral study of what the device is doing. So
13 for the sake of the study, we are limiting it so we have
14 more reliability, we don't have as much ceiling effects with
15 the speech discrimination.
16 DR. SHELTON: A follow-up question, then. Because
17 if you limit--if the device has greater fidelity, you might
18 see improvement in your speech discrimination scores, yet if
19 you only include patients with good scores, you wouldn't
20 appreciate that effect.
21 MS. MATTHEWS: I agree with you, and that is a
22 good point. Personally, I feel like 60 percent is not that
23 great, but when you get up around 80, 90 percent, then that
24 is a lot stronger speech score. So I really think other
25 people will get benefit. This is merely for the study

1 control situation.

2 DR. CAMPBELL: Dr. Campbell. Is that the same

3 reason that you are excluding those persons who have normal

4 hearing, as I understand it, at 250, the lower frequencies?

5 MS. MATTHEWS: They were allowed to have normal

6 hearing at 1000 Hz and below to be in the study.

7 DR. CAMPBELL: Allowed to?

8 MS. MATTHEWS: Yes.

9 DR. PATOW: Other questions?

10 Thank you very much for your comments.

11 MS. MATTHEWS: Thank you.

12 DR. PATOW: Our next speaker is Dr. Hans

13 Leysieffer and Dr. John McElveen from Implex America in

14 Washington, D.C.

15 DR. LEYSIEFFER: Good morning. Thank you very

16 much for this kind opportunity to tell you in 10 minutes

17 about a story that we began around 10 years back, and we are

18 talking about from the Implex side--Implex is a company

19 located in Munich, Germany--about the story of a totally

20 implantable hearing device that we began around 10 years

21 back. I will give you in the first around eight minutes an

22 overview about the system, and then Dr. John McElveen will

23 give you in around two or three minutes again some details

24 concerning clinical or surgical aspects.

25 The whole clinical research during the design

1 phase was done in collaboration with Professor Zenner at the
2 ENT Clinic, University Clinic in Tubingen, Germany. We call
3 the device TICA. That shall stand for the expression
4 Totally Implantable Hearing System. And the whole system
5 has four main components. We have a microphone, we have a
6 main module, a transducer, and external accessories.
7 The system, as you see here, is completely
8 implantable. The sound is picked up via a microphone that
9 is subcutaneously implanted in the posterior wall of the
10 auditory canal, and it will be covered completely by the
11 closed auditory skin.
12 The signal is processed in a main module, as we
13 call it, that is located like a cochlear implant in an
14 artificial bone bed drilled in the planum mastoideum,
15 compared to a cochlear implant, and the amplified and
16 preprocessed signal from this device is leading to the
17 transducer that is situated in the mastoid cavity and
18 directly couples with the mechanical vibrations to the, in
19 this case to the incus of the ossicular chain.
20 What you see in the first, then, is the microphone
21 here. The microphone, as I mentioned, positioned through a
22 drilling in the posterior wall of the auditory canal, and it
23 is held in place by a completely silastic encapsulation, and
24 we are using a small collar here that keeps the device in
25 place so it can't move forward or backward, and without use

1 of any glue or bone cement.

2 The main module of the system contains, as I
3 mentioned before, signal processing electronics as well as
4 the implantable battery, and this battery is a rechargeable
5 one. You see here the main module and the size comparison
6 of a normal adult ear. Here you see the microphone and the
7 transducer.

8 The main module looks like a cochlear implant. It
9 is a mixed housing of titanium in this section here and
10 biocompatible aluminum oxide ceramics, because we need this
11 electromagnetic window for bringing in the recharging
12 inductive energy to the device. But you also can see here
13 that we are using the device in specially designed
14 interconnector system for both the microphone and the
15 transducer, so that the main module can easily be exchanged,
16 for example, after the lifetime of the accumulator cell
17 internally has reached its end.

18 The signal processing electronics contain a broad
19 frequency, ranging between around 100 Hz and 10 kHz. In
20 this first generation we are using a three-channel automated
21 gain control with digitally programmable filter and gain
22 setting for each channel. We also have a digitally
23 programmed fast peak clipping unit due to the very fast
24 impulse response of our transducer, and the device contains
25 four individually adjustable programs for different hearing

1 situations, so the individual patient can be adjusted in
2 four different programs.
3 The implanted battery you see in the next slide.
4 This is an hermetically sealed accumulator cell that is
5 contained within the main module housing. You see the
6 electronics, the receiving coil here for energy received for
7 recharging this cell, as well as for the data communication
8 for the remote control for the patient, as well as for the
9 audiological fitting after implantation.
10 For size comparison I have put here the first
11 generation of the Advanced Bionics cochlear implant, so that
12 you can see that we have reached in the first generation the
13 size of the main module comparable to the first generation
14 of cochlear implants.
15 The implanted battery is a rechargeable cell in a
16 completely hermetically sealed casing. The recharging and
17 discharging of this cell is internally controlled by a
18 microcontroller and monitored during discharging, so to say
19 during normal daily operation. With a fully charged system,
20 the system allows continuous operation of around 60 hours,
21 so if you are using the device for let me say 16 hours per
22 day, with one charging you can operate the implant around
23 three days.
24 The estimated lifetime of this accumulator cell is
25 around three to five years. Then the main module can be

1 exchanged in a simple procedure under local anesthesia,
2 because the system can be disconnected from both the
3 microphone and transducer.
4 The transducer itself can be seen here. As I
5 mentioned, it is positioned in the mastoid cavity. It is of
6 basically piezoelectric design in the TICA, and it is
7 hermetically sealed. This is something would really be for
8 biostability. It is very important for especially the
9 transducer. And the vibrational output signal is directly
10 coupled through the natural aditus ad antrum to the middle
11 ear, and in this case here vibrating the body of the incus.
12 You can see the--excuse me. As I mentioned, the
13 piezoelectric system is a disk bonded to a titanium membrane
14 inside the transducer. This gives us the chance to
15 hermetically seal this transducer system. The vibration
16 transferred to the incus via a coupling rod made of pure
17 titanium, medical grade, and the transducer itself is fixed
18 to the skull and adjusted with a specially designed
19 micromanipulator.
20 You can see on this slide here, this is the
21 transducer, this the micromanipulator and fixing system.
22 This is screwed to the skull using a standard osteocentisis
23 technique with four screws. And this is the ball socket
24 joint that gives you the four freedoms of--four degrees of
25 freedom for freely adjusting the probe tip in the mastoid

1 cavity to the target point in the middle ear. Then you fix
2 it with these two screws, and then you have a linear drive
3 mechanism to very precisely position the depth of the probe
4 tip inside the middle ear for contacting the ossicular
5 chain.
6 External accessories of the system, we have a
7 programming station. This is meant for audiologically
8 fitting, like a conventional hearing aid, the patient after
9 implantation. The patient receives a remote control unit
10 and also a portable charger unit, and this charging unit is
11 as well established with a charging station for recharging
12 this portable charger.
13 You can see here the situation of audiologically
14 fitting a patient. The patient is wearing a headset. You
15 will see this in the following slide from the charging unit
16 once again. So the data are transmitted to the implant like
17 in a pacemaker programming situation, transcutaneously, via
18 an inductive link, and the audiologist sees on PC based
19 audiological fitting software as usual.
20 This is the remote control. You can select
21 between these four operating programs or individually fitted
22 programs for the patient. You can select the loudness via
23 these two knobs in 3 dB steps, and you can also switch off
24 the system completely. This is the bottom, beyond the
25 thumb. This remote control works around 15 centimeters in

1 distance to your head, and it is also working from the other
2 side, so it can be operated very easily.
3 Here you see the charging system. As I mentioned,
4 the patient wears only for charging a light headset with an
5 inductive coil. What we believe is very important for all
6 these devices, this system doesn't work with permanent
7 magnets, so we are not using any ferromagnetic materials
8 inside the implant, so we believe, this is not proven to
9 date, but we believe very strongly that the TICA device is
10 fully MRI compatible.
11 Here you see the charging unit. It has a size
12 comparable to a cigarette box with a cable to the headset,
13 and this is the recharging base station.
14 And here I want to stop with the system
15 presentation. I want to let John McElveen to give you some
16 details about the clinical and surgical aspects.
17 MR. SAUBERMAN: Before Dr. McElveen starts, for
18 the panel discussion this afternoon, it would be of great
19 benefit to us if we could have copies of your slides.
20 DR. LEYSIEFFER: We will provide you with those.
21 We can leave this here for you? Okay, no problem.
22 MR. SAUBERMAN: Well, we might like to have
23 something in hard copy. If you have something, we can copy
24 it over the lunch hour.
25 DR. LEYSIEFFER: Do you think this is possible?

1 We are looking after this, yes.

2 MR. SAUBERMAN: Okay.

3 DR. LEYSIEFFER: Thank you very much.

4 DR. McELVEEN: Thank you, Hans. I have been asked
5 to discuss really the surgical issues with respect to the
6 TICA device. How do we get the device into the ear in a
7 safe and effective manner?

8 Basically, as far as the incision, it is similar
9 to what you would see with a cochlear implant. You can
10 either use the incision in this fashion or a C-type
11 incision.

12 With this device you do not really have to do any
13 facial recess dissection. Basically, you can do a simple
14 mastoidectomy and gain exposure of the head on the incus;
15 so, again, really no dissection in the area of the facial
16 recess where you run the risk of potential injury to the
17 facial nerve or the chorda tympani.

18 Once the head of the incus is exposed, we are
19 using an erbium IAG laser to basically make about a five-
20 tenths of a millimeter indentation into the head of the
21 incus. And the reason we are doing this is, this is that
22 coupling rod that Dr. Leysieffer alluded to earlier, that
23 will be engaged into the head of the incus.

24 Once that indentation is created, this
25 micromanipulator allows us, by rotating this, allows to

1 advance in a very precise manner the indentation or
2 attachment of the transducer to the indented incus, and you
3 can see it now being advanced. The microphone is then
4 positioned in the auditory canal by drilling a small hole
5 here and then pulling this collar through, and then the
6 suture is removed, allowing this to expand. The skin is
7 intact over the microphone.
8 The main module is then implanted in a similar
9 fashion, by creating a bony bed as we do with cochlear
10 implantations. All of this has been secured to the squamous
11 portion of the temporal bone with this fixation device that
12 Dr. Leysieffer alluded to earlier.
13 The potential benefits obviously are improved
14 hearing, and by directly coupling into the ossicular chain,
15 we may eliminate some of the problems you have with the
16 distortion you get from the tympanic membrane. As an
17 alternative to conventional aids, it may allow these
18 individuals to resume sporting activities without concerns
19 with a hearing aid, and may obviously be psychologically
20 beneficial.
21 In summary, then, Implex has developed a totally
22 implantable hearing system that may very well indeed be MRI
23 compatible. The clinical trials are ongoing in Germany. I
24 think they have implanted 20 patients, and Dr. Leysieffer
25 will be able to answer questions regarding this. They are

1 expecting to get the CE mark within the next few weeks.

2 The device may definitely improve the quality of

3 life for these individuals. As you have seen from these

4 sides, the surgical approach or procedure is not technically

5 difficult for the otologic surgeon.

6 Thank you very much.

7 DR. PATOW: Thank you.

8 Are there questions from the panel? Dr. Campbell?

9 DR. CAMPBELL: Yes. Dr. Campbell. As far as the

10 microphone, are there any problems with erosion? You only

11 have skin of the ear canal, and if there are problems--

12 DR. McELVEEN: To my knowledge--and the question

13 is, is there any problem with erosion with that microphone

14 adjacent to the skin--using the technique with the silastic

15 collar, that is very flush. It is not like it is protruding

16 into the external canal, and to my understanding and to my

17 knowledge, there has not been a problem.

18 I also asked that same question to the

19 manufacturers, and as it turns out, if there were ever a

20 problem or if we wanted to add increased security, you could

21 place a small piece of fascia over this. The microphone is

22 extremely sensitive and really does not alter that. But as

23 it turns out, from the initial 20 patients, that has not

24 been a problem to date.

25 DR. CAMPBELL: The other question I have is, what

1 is the stability of the incus attachment, since it is not a
2 clip method? Can that, can the size of the hole get deeper?
3 Can it erode through? Is it going to stay there?
4 DR. McELVEEN: One of the reasons we use the
5 erbium IAG laser as opposed to other laser as opposed to
6 other laser technology is, the erbium IAG does not really
7 burn bone. If you look at histology from laser-treated
8 tissue, if you look at the other lasers, you get actually an
9 additional loss of bone. With the erbium IAG, basically you
10 are letting the water vapor sort of pop or explode and
11 remove the bone in that fashion. That gives you a very
12 precise hole, and if you look at the histology over time, it
13 stays the same size.
14 In this situation it makes an opening of
15 approximately five-tenths of a millimeter or six-tenths of a
16 millimeter. The coupling rod is conical in shape, has a
17 roughened surface, so it actually engages into that area,
18 and it is five-tenths of a millimeter, so it is a very snug
19 fit. In addition, being titanium, you would anticipate some
20 osseointegration.
21 DR. CAMPBELL: My last question is, any problems
22 with and what is the ease of detachment? You said you could
23 do it with local anesthesia. Is there a problem in
24 detachment, that special tools are needed, or is there a
25 risk of detaching or pulling out the device when you--

1 DR. McELVEEN: Are you referring to changing the
2 battery system?
3 DR. CAMPBELL: Yes, when you go in to change the
4 battery.
5 DR. McELVEEN: Dr. Leysieffer?
6 DR. LEYSIEFFER: During this German clinical trial
7 that John just mentioned, we had to explant one device, so
8 we have the experience in the moment after three months
9 operated. It was a procedure of about 30 minutes, and you
10 just make an incision behind the ear and you can easily pull
11 it out, and opening and reclosing this interconnective
12 section was possible without any difficulties.
13 DR. CAMPBELL: That is not what I am asking.
14 DR. LEYSIEFFER: No? Excuse me.
15 DR. McELVEEN: The nice thing about this device is
16 that you do not have to do anything to the microphone or the
17 part that is engaged to the incus when you are changing it.
18 If you are changing a battery or updating the device,
19 basically that is limited to that main module section that
20 Hans alluded to earlier.
21 Basically, that is done by simply replacing the
22 entire main module; freeing the main module from its site,
23 loosening the pressure connector to release the transducer
24 and microphone leads, reconnecting those leads to the new
25 main module. And they have a special system for putting

1 those back in so that everything is sealed, and again, you
2 do not have to manipulate any of the connections to the
3 ossicles or the microphone.
4 DR. PATOW: A short question.
5 DR. SININGER: Yvonne Sininger. How critical is
6 the angle of that coupling rod to the incus, in terms of if
7 you had different surgical approaches, let's say, or slight
8 differences between surgeons? The angle of that driver
9 seems to be critical in terms of how much gain might be
10 achieved.
11 DR. McELVEEN: I think that is a good question.
12 Obviously, by changing that angle you very well may alter
13 the energy and so forth that you can impact onto the incus.
14 In these temporal bones that have been done, you have
15 adequate access to the incus. I think it is an important
16 point that you want to be as perpendicular to that as
17 possible.
18 DR. PATOW: Dr. Khan.
19 DR. KHAN: Anjum Khan. I have two questions.
20 One, you said that it would be MRI compatible. I knew that
21 titanium was, but is aluminum MRI compatible?
22 DR. McELVEEN: Excuse me? Is the--
23 DR. KHAN: A portion of this thing is aluminum,
24 isn't it?
25 DR. McELVEEN: Ceramic.

1 DR. KHAN: Only ceramic? There is no--

2 DR. McELVEEN: No problem.

3 DR. KHAN: Is ceramic okay with MRI?

4 DR. McELVEEN: Right.

5 DR. KHAN: Okay. The second question is that, I
6 know this is a little far-fetched, we had concerns with
7 osseointegrated implants with radiation, and is there any
8 concern with these implantable parts here and the screws,
9 with people who might have had radiation to the area?

10 DR. McELVEEN: That is something--you mean as far
11 as having prior radiation and so forth to the skull? I
12 think anytime you implant a device in someone who has had
13 radiation, you have to keep in mind you are going to have
14 decreased vascularization of the bone. How much of a
15 problem, I can't really answer that for you. I think
16 obviously that would be a concern with anyone having
17 previous radiation with any implanted device.

18 DR. PATOW: Dr. Kileny?

19 DR. KILENY: Thank you. Just a quick question.
20 How is the base charging unit powered? Is it AC powered?
21 Or it is DC?

22 DR. LEYSIEFFER: This is a battery powered device,
23 and if the charging unit is placed in the charge base
24 station, it is automatically closed so you can't charge the
25 system. So the only possibility that you can take it with

1 you is to put it out, and then it is not AC coupled. It is
2 completely free of any organic problem. This is proven due
3 to EN 46001. It is already proven in Germany.
4 DR. PATOW: Thank you very much. Oh, we have one
5 more question.
6 DR. WOODSON: Yes. Having had experience in a few
7 patients now, it would be interesting to us to hear what you
8 might have encountered along the lines of what we heard from
9 the patient concerns. Have patients had any problems with
10 interference from microwaves? Can they use the telephone?
11 And then one other thing. This remote control
12 looked nice as a way of controlling things, but I know in
13 our house we frequently lose the remote to our TV, and I
14 wonder if that is a concern for the patients.
15 MR. SAUBERMAN: Can you identify yourself for the
16 transcriber?
17 DR. WOODSON: Yes. This is Dr. Woodson.
18 MR. SAUBERMAN: Thank you.
19 DR. LEYSIEFFER: Okay. Those are many questions.
20 I think I wanted to mention this during my talk. This is
21 something that we already heard in the morning.
22 Making normal telephone calls, not with cellular
23 phones but with normal telephones, is not a problem. Every
24 patient in our German group can telephone without any
25 problem. As far as mobile phones are concerned, our

1 patients can use the mobile phone on the contralateral ear
2 without any disturbations.
3 And losing the remote control is a problem, so we
4 have to build up a good service, that is clear. But if you
5 are losing it and if you don't have a spare one, and the
6 system is operating on a sound level that is switched on via
7 the remote control, and after a certain time the accumulator
8 charge is going down, and then the system automatically
9 switches off. It monitors the discharge. So in this case
10 you have to wait for two or three days, and then it is
11 switching off, and then in these two days I hope you get a
12 new remote control.
13 DR. PATOW: Thank you.
14 DR. LEYSIEFFER: Okay.
15 DR. PATOW: Our next presenters are Mr. Michael
16 Crompton, Mr. Bob Katz, and Ms. Deborah Arthur from
17 Symphonix Devices in San Jose, California.
18 MR. CROMPTON: Good morning. I am Mike Crompton,
19 Vice President of Regulatory Affairs and Quality Assurance
20 at Symphonix, and we do thank the FDA for arranging this
21 meeting today. The turnout has been great, and we are very
22 excited to be here today.
23 We are going to focus really on the proposed
24 guidance document that this panel will be reviewing in the
25 future, and we want to talk about three aspects of that:

1 Regulatory considerations; Bob Katz, our Vice President of
2 Research and Development, will talk about technical
3 considerations; and then Deborah Arthur, our Vice President
4 of Clinical Affairs, will talk about clinical
5 considerations.
6 By way of introduction, a little bit about
7 Symphonix. We were founded in 1994 as a hearing management
8 company, and our goal is to develop a family of products
9 that improve communication ability and quality of life for
10 the hearing impaired. We operate ISO certified facilities
11 in California and in Switzerland, and I asked that we pass
12 around a demo of our device.
13 This device is now commercially available in
14 Europe and in certain South American companies. We have an
15 approved IDE here in the United States, and we are subject
16 to the modular PMA process. I am going to talk a little bit
17 about that today. We have an accepted investigational
18 testing application approved by Health Canada, and we are
19 working with FDA and Health Canada on this pilot Partnership
20 Review Program.
21 From a regulatory perspective, the importance of
22 this guidance document can't be understated. Harmonized
23 regulatory requirements, they really do advance the
24 introduction of new medical technology and benefit public
25 health. As sponsors, I think all of us in the room, we

1 accept the different regulatory and legal requirements, but
2 it is very challenging to accept different scientific and
3 clinical outcomes for clinical studies or engineering
4 standards that could be imposed by regulators.
5 So our experience in the partnership review, which
6 is an open dialogue really between regulators and the
7 regulated, we are able to get the concerns on the table. We
8 are able to understand the different regulatory processes.
9 We can address up front the different scientific and
10 engineering requirements, and it makes the process go a lot
11 quicker. But appropriate guidance will support this
12 harmonization goal, because the FDA and Health Canada are
13 viewed as leaders, and if we have appropriate guidance we
14 can use that worldwide.
15 In the United States this will be a Class III
16 medical device, subject to IDE pre-market approval for
17 marketing authorization, or a Product Development Protocol
18 will be required. In Canada it has already been determined
19 it will be a Class III medical device. They have an
20 Investigational Testing Application which is similar to the
21 IDE process, and they have a Device License Application
22 which is somewhat similar to the Pre-Market Approval
23 application.
24 In Europe we are regulated as Active Implantable
25 Medical Devices. That is the highest category of risk

1 determination. We have to conform with EN 540 requirements,
2 which are like IDE requirements, and we file what they call
3 a design dossier or technical file for marketing
4 authorization. That is the CE mark that you have heard
5 about before.
6 We have proposed an identification and
7 classification definition for these devices to the agency,
8 and we would like this to be considered by the panel. We
9 want the identification to be broad enough to encompass this
10 entire category of devices. We recognize, and you have
11 heard it already today, there are partially implantable
12 devices, there are totally implantable devices. The mode of
13 action is different but the way that we actually give energy
14 to the cochlea, that can vary, but the identification of
15 these devices should be broad enough to encompass all
16 technologies. And, again, the classification is Class III.
17 So in concluding my remarks, we would really from
18 a regulatory perspective ask the panel to use the available
19 tools that have already been reviewed and accepted by this
20 panel. One is design controls. IDE studies should conform
21 to design controls. That way, up front we have addressed
22 some of the key safety aspects related to these devices.
23 We would ask and urge the panel to recognize the
24 use of consensus standards in the guidance where
25 appropriate. Some of these are going to be evolving. We

1 have heard about laser doppler vibrometry this morning, but
2 there are a lot of standards for biocompatibility,
3 electromagnetic interference, and from a sponsor's
4 perspective, if we can use a consensus standard that
5 satisfies FDA, satisfies Health Canada, satisfies the
6 European notified bodies, it makes our life a lot easier and
7 it is a uniform playing field.
8 Finally, we would urge the panel to consider using
9 a previous guideline as a model. The details will be
10 different, but FDA and this panel developed an excellent
11 guideline for Pre-Market Approval applications for cochlear
12 implants, detailed enough to allow manufacturers to know
13 what they need to do to get an IDE approved and eventually a
14 marketing authorization approved, but not so restrictive
15 that it couldn't transfer between different device designs.
16 I would like to turn it over to Bob Katz now to
17 talk about the technical considerations.
18 MR. KATZ: I would like to reiterate Mike's thanks
19 for the opportunity to address you this morning. I would
20 like to start by reiterating that conformance to design
21 controls and consensus standards is an important aspect of
22 what we do from a technical and design perspective. We
23 think it is important that design controls be mandated for
24 IDE devices because we believe any device that is evaluated
25 in a patient should have the minimum necessary testing and

1 safety aspects considered before it leaves the laboratory.

2 Conformance to design controls also help ensure

3 achievement of design considerations if it is applied in the

4 appropriate manner, and we have learned that lesson after

5 many years of being in the implantable device field.

6 And then, lastly, even though this is a new

7 technology in many ways, it is also the extrapolation of

8 existing technologies that have been used for many years,

9 and there are some very well defined standards that have

10 been developed both domestically and internationally which

11 help ensure product safety, biocompatibility, consistency,

12 compatibility to other devices, medical and non-medical

13 devices, such as the EN 601 series of standards and so

14 forth, that we believe should be adhered to as part of the

15 development process.

16 As far as design considerations go, Dr. Richard

17 Goode in 1995 published a series of approximately a half a

18 dozen points on design considerations for implantable

19 hearing devices at the beginning of this new era of

20 implantable devices, looking at things that he felt were

21 appropriate on a consensus basis for what middle ear devices

22 should try and achieve. We believe that this is an

23 appropriate list from a design perspective, that should be

24 adhered to as best possible as new devices and modifications

25 to existing devices come along.

1 The provision of better cosmesis, no reduction in
2 original hearing, no limitation to patient activities, and
3 of course implant reliability and biocompatibility and
4 provision of better sound, are all important aspects from a
5 design perspective that need to be considered.
6 The Vibrant Soundbridge was developed in
7 conjunction with understanding these design considerations
8 and an attempt to meet these considerations in a uniform and
9 controlled fashion. The Vibrant Soundbridge consists
10 basically of an implantable portion, the most important part
11 of which is the floating mass transducer, which is an
12 electromagnetic transducer and it is connected to a receiver
13 portion under the skin of the mastoid, and then the device
14 is provided signal and power from an external device called
15 the audioprocessor which provides all of the signal
16 processing capability for this device.
17 We feel it is important, particularly in the
18 infancy of this type of development, that we are able to
19 provide easy and opportunistic updates in terms of signal
20 processing and other matters as we develop these devices, so
21 that as we learn new and different things over the years of
22 development, we can apply them to existing patients who have
23 been implanted with early devices, as well as at some point
24 incorporate them into more finalized devices in the future,
25 which is why we chose this semi-implantable approach.

1 From a device design perspective, we believe that
2 adhering to understanding what the surgical risks and trauma
3 potentials can be for an implanting device and in reaching
4 the middle ear, that devices should be designed to minimize
5 those risks from a surgical perspective. Therefore, we have
6 attempted to approach device design understanding the types
7 of surgical approaches that have been developed already for
8 the middle ear and have been well proven, in terms of
9 cochlear implantation as well as stapedectomy and
10 stapedotomy type procedures that do occur in the middle ear,
11 and we have attempted to follow those guidelines, which have
12 been well established now and have provided very good
13 success surgically for reaching the middle ear space.
14 So this portion just basically shows you the
15 minimum components necessary on the implant side of a device
16 in order to receive the signal from the external processor
17 and then provide that signal to the floating mass
18 transducer, our electromagnetic device designed to impart
19 the vibratory energy to the middle ear via attachment to the
20 long process of the incus. This device, as we believe all
21 devices should be from a performance design perspective, is
22 designed to be as small as possible physically so that it
23 can accommodate all middle ears that it approaches, can be
24 flexible enough to accommodate variances in anatomy that
25 will inevitably be seen from device to device--or patient to

1 patient, I should say--and have masses below the minimum
2 requirements to ensure that we don't get into loading
3 issues, as has been previously discussed.
4 We believe the design of any device should ensure
5 that its performance in terms of how it operates closely
6 mimics the natural frequency response of the middle ear, so
7 that we get the best and most natural, quote/unquote, sound
8 qualities by mimicking what the normal middle ear would do
9 from a mechanical perspective.
10 We believe that attachment to the middle ear
11 should be accommodated in such a way that it can be done
12 easily by the surgeon, that it does not require significant
13 advances into the middle ear space to achieve this
14 attachment; that the attachment should be capable of being
15 reversible, meaning removed without any harm to the
16 ossicular chain; that no alterations, modifications or any
17 necessary changes be made to the ossicular chain to attach
18 it. And yes, we believe firmly that attachments can be made
19 to normal, healthy ossicular chains as long as you respect
20 the vasculature and the blood supply which currently supply
21 the healthy bony structure.
22 This simply shows you the surgical approach for
23 the implantation of the Soundbridge, looking very familiar
24 to a cochlear implant on the left at the mastoid, and then
25 the attachment of the transducer in the middle ear space to

1 the right.

2 Material construction is a very important quality

3 of any implantable devices, and we believe that well

4 characterized material should be a fundamental of any design

5 that is implanted into the body.

6 The external audio processor or whatever signal

7 processor that is used should be capable of accommodating

8 the best and the latest in developments in signal processing

9 as they can be applied for sensorineural hearing loss, so

10 that patients can benefit from those advances as they come

11 along; and that we achieve the type of cosmesis that

12 patients are looking for, so that not only will the device

13 work but they will be willing to wear these devices for 16

14 hour or 18 hours a day, as we would anticipate.

15 And this simply shows you, the picture on the left

16 shows you an audio processor in place at about 10 o'clock on

17 the patient's pinna, and then by simply folding down the

18 hair, the improvement in cosmesis, of course the open ear

19 canal, and all of the other positive benefits that have been

20 described about implantable devices.

21 DR. PATOW: We are essentially out of time at this

22 point. What I would suggest, since there is some critical

23 information at the end of the presentation, is that we skip

24 from this point, if we would, to the slide "Clinical

25 Considerations for Guidance Document" and see your last six

1 slides--

2 MR. KATZ: Absolutely.

3 DR. PATOW: --because I think they are very

4 important to the deliberations today.

5 MS. ARTHUR: Thank you very much. I am Deborah

6 Arthur. I want to give you a quick overview of the device

7 status worldwide. We have implanted the Vibrant Soundbridge

8 in over 200 individuals in Europe and the United States and

9 some countries in South America. Presently we are

10 commercially available in over a dozen countries.

11 Of those 200 individuals who have been implanted

12 with the Soundbridge, some of them are part of the two

13 multi-center control clinical trials that the company has

14 engaged in to date. One of those was an EN 540 trial in

15 Europe which was completed in late 1997 and resulted in the

16 authorized to affix a CE Mark. The other is a United States

17 clinical trial, where we have enrollment completed, all test

18 subjects have completed all test intervals, and we are

19 presently in the data analysis and writing of the PMA stage.

20 DR. PATOW: Can you advance two more slides, then?

21 MS. ARTHUR: Certainly.

22 DR. PATOW: Thank you.

23 MS. ARTHUR: Under clinical considerations for the

24 guidance document, as our other predecessors have indicated,

25 we think that the pre-selection process in terms of

1 selecting those candidates who would best be served by
2 implantable middle ear hearing technology is critical. Part
3 of that criteria would of course be the Standard Audiologic
4 Battery, which is appropriate to these types of devices as
5 well as selecting acoustic hearing aid devices.
6 As part of that assessment battery, you are going
7 to look at behavioral tests, and the behavioral tests not
8 only need to be done on the implant ear but also need to
9 take into consideration the non-implant ear, and then how
10 the two ears function together. As a component of that
11 assessment battery, we also recommend the use of
12 uncomfortable as well as comfortable listening levels, and
13 also the use of loudness growth measures or loudness
14 perception measures.
15 As also has been mentioned by some of the other
16 manufacturers, we think it is critical to look at the
17 existing amplification system on the subject, whether it be
18 binaural or monaural amplification. In our particular
19 situation it was binaural amplification. We think it
20 provides incredible information regarding what the patient's
21 not only existing performance levels are, but certainly
22 expectations out of the device, and as we have come to find
23 out, that plays a significant role in the success of the
24 patient later on.
25 Objective measures of immittance audiometry go

1 without saying, and all of these tests need to be done
2 preoperatively as well as postoperatively, so that we can
3 monitor not only the performance of our device against that
4 of the hearing aid but, as significantly, the status of
5 residual hearing in the patient preoperatively to the
6 postoperative state.
7 The use of self-reporting or self-assessment
8 questionnaires also has proved to be a valuable tool. These
9 have been normed and standardized, are available, and as has
10 been mentioned by some of our other speakers this morning,
11 have proven to be quite insightful in determining the
12 patient's perception of how they are performing with
13 amplification systems, whether it be their hearing aid or
14 the implantable device.
15 And finally what I would like to say is that we
16 believe the implanting procedure as well as the device
17 should have no adverse effect on residual hearing.
18 Counseling, and assessing realistic expectations on the part
19 of the candidates, is critical to success. And we feel that
20 device placement should be revisable, which will allow the
21 patient to revert back to the use of a hearing aid, should
22 he need to or choose to for a variety of reasons.
23 Thank you very much.
24 DR. PATOW: Thank you.
25 MS. ARTHUR: And I apologize for trying to

1 interpret that, because I know I was speaking very rapidly.
2 Do you have any questions?
3 DR. PATOW: Are there questions from the panel?
4 Okay. Thank you very much. I am sorry we didn't
5 get to those middle slides, but I think it is important that
6 we give Dr. Maniglia time to present his material. And we
7 will bump into the lunch time a bit, but I think it is very
8 important we have everyone speak.
9 So our next presenter is Dr. Anthony Maniglia from
10 Case Western Reserve University in Cleveland, Ohio.
11 DR. MANIGLIA: Thank you very much, Dr. Patow,
12 members of the panel, guests, public. I am from Case
13 Western Reserve University, professor and chairman of the
14 department for the past 14 years, and my trip here is paid
15 by my department only.
16 For the past 14 years I have been doing research
17 in this field. We have published about 19 papers. We share
18 all of our work with the scientific community. We have
19 published in the Annals of Otology, American Journal of
20 Otology, Otolaryngologist of North America, and many others.
21 We have done bench experiments, acute and chronic animal
22 studies, fresh human temporal bone studies, and implanted
23 patients with our device.
24 Basically, our device contains in the internal
25 unit--it is semi-implantable--do I have the laser pointer

1 here? Semi-implantable. Here is an electromagnetic coil,
2 supporting shaft, connecting shaft, flexible. Cochlear
3 implant from the Cochlear Corporation. Antenna, with a
4 magnet antenna on the outside.
5 The external unit is a cochlear implant, a
6 transmitting antenna, and here we have a Simmons tri-tone
7 304 programmable, the best technology of Simmons, at least
8 until two years ago, but they keep coming and develop even
9 more, better technology. The receiver has been removed by a
10 transmitting system, sigma delta modulator, and the hearing
11 aid basically is very similar to the Simmons hearing aid.
12 So we want to compare Rolls Royce technology with our
13 implantable, with bilateral fitting.
14 Here is the device. The antenna has been coupled.
15 External unit, internal unit.
16 I like to show this very two-minute videotape. We
17 are implanting here in a patient. A mastoidectomy has been
18 done. A magnet is cemented to the body of the incus. This
19 is hermetically sealed, and then the internal unit, there is
20 a space here, give us half a millimeter to one millimeter.
21 It is a contactless system. We decided this device was
22 going to be minimally invasive, at least, with no contact to
23 the ossicular chain except to the magnet cemented.
24 Here is the device which is being implanted, and
25 with the antenna, and the unit as you can see works in a

1 similar fashion as many other semi-implantable devices.

2 I must say that we have had our success, our

3 failures, and our recommendation is that the semi-

4 implantable technology, at least to the state of our art, is

5 not a workable situation. We have patients with more than

6 two years after implantation. The device has proven to be

7 safe, function, but not effective enough to compare with

8 binaural fitting of the best hearing aid that there is. We

9 believe that the criteria has to be strict. We must really

10 compare with the best technology, and it has to be a

11 binaural comparison.

12 So my implantable has many advantages. Here are

13 just a few of them: better clarity, fidelity of sound, and

14 speech intelligibility. Noisy environment, we don't really

15 know if really it is much better, if you compare with the

16 best hearing aid in the market. It must be the best hearing

17 aid in the market because the device is very expensive.

18 Disadvantages: expensive invasive surgical

19 procedure; semi-implantable; inefficient transmission of

20 energy; loss of RF; ossicular chain dissipation of

21 mechanical energy; and currently can only have unilateral

22 implantation. Loss of canal resonance. Possible

23 complications: infection, extrusion, malfunction, erosion

24 of ossicles. Post-operative hearing losses.

25 Probably this semi-implantable device is going to

1 have an average of 25 dB average, and that probably is not
2 good enough to beat the best hearing aid in the market with
3 binaural fitting.
4 Cost, probably anywhere from $11,000 to $17,000.
5 Therefore, every patient must be fitted with the best
6 hearing aid, not with his own, or hers, hearing aid but what
7 is the best hearing aid in the market. Bilateral fitting
8 gives 5 dB more of gain and 10 percent better speech
9 discrimination, hard to beat.
10 The unit probably requires similar maintenance as
11 the hearing aid external unit. Future developments of the
12 technology are really on the side with the totally
13 implantable device. I would say that at best the semi-
14 implantable probably will be short-lived, four to five
15 years. Is it worth the effort? In my opinion, based on my
16 estimation by my work and my associates of 14 years, we
17 think it is better to emphasize the totally implantable
18 technology.
19 And this group of patients in this category,
20 severe, profound unacoustic patients, maybe about 2 million
21 people that are cochlear implant candidates, probably should
22 benefit the most by totally implantable cochlear implant.
23 The current cochlear implant technology, semi-
24 implantable, similar to what we just showed, but instead of
25 having a middle ear device, it goes into the cochlea, an

1 electrode in the cochlea, 20,000 patients have been
2 implanted successfully, most of them, worldwide. But the
3 implantable battery which is available in this country in
4 the research stage, as well as in Germany and in Japan, made
5 a big difference.
6 We have developed, and we already have a patent
7 which was issued about three weeks ago, a totally
8 implantable cochlear implant. Basically we use the eardrum
9 and the magnet as a diaphragm. Sound comes naturally,
10 activates the magnet, picked up by the coil and is
11 amplified, goes through a speech processor and into the
12 cochlea, with an antenna which is used for the programmable
13 on and off switch, volume control, and an implantable
14 battery.
15 So this is the totally implantable cochlear
16 implant. We feel that at this point in time probably it is
17 better to concentrate on the totally implantable cochlear
18 implant. Patients have nothing to use as far as hearing is
19 concerned. There are FDA guidelines for extended use.
20 Patients with a profound loss of discrimination score less
21 than 30 percent. They can benefit by probably this
22 technology. Then it will be totally implantable, excellent
23 for children. Children have problems with the external
24 units, falling, losing them in playing, et cetera.
25 If we concentrate on the totally implantable

1 cochlear implant, if this technology proves to be very good,
2 then we can go and remove the incus. Probably the only way
3 that the total implant will work is by removing the incus to
4 avoid all the problems. We have to imitate nature, and the
5 best way to imitate nature is to use the eardrum as a
6 microphone, take advantage of the pinna, of the ear canal
7 resonance, and then a type of a system with a driver right
8 on the head of the stapes, eliminate the incus. Then I
9 believe that we will have a successful device.
10 I am going to skip that. Maybe we can discuss
11 this in the future discussions in the afternoon. I am just
12 going to finish this videotape and show you the totally
13 implantable cochlear implant.
14 I agree that fresh human temporal bones are
15 excellent, can give you superb results. Laser doppler is
16 fine, but I believe that music with a wide dynamic range is
17 better to evaluate a device. This is our totally
18 implantable cochlear implant, a CD player playing Vivaldi
19 "La Primavera," whereby we introduce sound in the external
20 ear canal. Here we have a fresh human temporal bone with a
21 microphone in the ear canal, and the incus has been removed.
22 The magnet is implanted on the head of the malleus, same as
23 magnet that we used before. Our device was not a good
24 driver but is a very good microphone used in a reverse mode.
25 This is the music presented. As you can see, that

1 is the coil. By removing the coil, pulling away from the
2 magnet, you are going to see the music disappears, proving
3 that distance is very critical, like at one millimeter.
4 There is no more music. Now, as we go back to the magnet,
5 one millimeter away gives you the very good, clear, crystal
6 clear dynamic range sound of Vivaldi with his violin.
7 In summary, a semi-implantable device probably is
8 short-lived. The future research of this technology lies in
9 the totally implantable, and I believe that in the best
10 interests of the patient--most important is the patient, I
11 have been practicing medicine for 37 years, and I always
12 want to work in the best interests of my patients--I believe
13 that totally implantable technology probably, especially
14 with the cochlear implant, is going to give us the best
15 yield, and then if it works well we can do the totally
16 implantable for the patients with partial hearing loss.
17 In summary, I would like to thank the panel, and I
18 would like to entertain any possible question. Thank you
19 very much.
20 DR. PATOW: Thank you, Dr. Maniglia.
21 Any questions from the panel? Yes, Dr. Kileny.
22 DR. KILENY: Paul Kileny. Dr. Maniglia, do you
23 have any thoughts regarding some type of preclinical bench
24 testing, some sort of accelerated testing that would
25 actually evaluate and simulate device use over many years?

1 Since some of these middle ear implantable devices have
2 mechanically moving parts, and there is going to be a
3 certain amount of wear and tear, and you have been working
4 on this for 14 years, do you have any thoughts on this?
5 DR. MANIGLIA: We have worked in animals. Our
6 model was the cat, and we kept the implants for about two or
7 three years, and it worked well. But I think it is very,
8 very difficult to work with animals. The Rhesus monkey, Dr.
9 Fredrickson has worked with the Rhesus monkey for quite some
10 time, but it is very hard.
11 The electronics implanted can last for 100 years,
12 I hear. Titanium can last forever. The problem is the
13 coupling. That is why my device was designed to be
14 contactless. We just cement it with a matabond cement to
15 hold the magnet to the incus, and it has proven to be good.
16 We have done animal experimentation on that. We have
17 published several papers on that. And one of our patients
18 has been wearing more than two years that magnet, but it is
19 working well. So the biologic effect of holding that magnet
20 on the incus is very good. We don't even use laser, just
21 etch it with a chemical, and then the matabond, it is used
22 for dentistry, for crowns, a tremendous amount of work in
23 the mouth, it works well.
24 I think anything that is going to be attached to
25 the ossicular chain eventually is going to be eroded,

1 especially if you get close to the incudo-stapedial joint,
2 because the blood supply is very tenuous, as we saw in that
3 very good slide. The wear and tear, specially the relative
4 motion of a device, is going to wear and tear. So we have
5 to watch those things for many--for several years to come,
6 to be sure that is working well.
7 And the danger is that it erodes, then the stapes
8 can erode, and also the footplate and the inner ear can
9 erode, and you have a dead ear.
10 DR. KILENY: Thank you.
11 DR. PATOW: Any other questions from the panel?
12 Thank you, Dr. Maniglia.
13 DR. MANIGLIA: Thank you very much.
14 DR. PATOW: We will break now for lunch, and
15 resume the open committee discussion at 1:30.
16 [Whereupon, at 12:40 p.m., a luncheon recess was
17 taken.]

1 A F T E R N O O N S E S S I O N

2 [1:35 p.m.]

3 MR. SAUBERMAN: If people would take their seats,
4 we can get started. We have a fairly long afternoon, and I
5 want to use all the time available for the panel's
6 discussion.

7 Over the lunch hour I did hand out to all of the
8 panel members copies of all of the slides, the identical
9 slide presentations that were made this morning, so you
10 should have all of that material in front of you at that
11 time.

12 Let me return to our Chair, now.

13 DR. PATOW: Thank you. At this time we would like
14 to continue the open committee discussion with the questions
15 for the panel discussion and narrative, and these will be
16 presented by Sid Jaffee, Dr. Sid Jaffee, and Teri
17 Cygnarowicz of the FDA.

18 MR. SAUBERMAN: And the purpose of these
19 narratives is to add value to the questions that FDA
20 compiled, and was the backbone for the discussion, for this
21 meeting.

22 DR. JAFFEE: Dr. Patow, panel members and guests,
23 first let me say to be asked to speak after lunchtime is a
24 challenge unto itself, and to be asked to speak after lunch
25 on Friday is even a greater challenge, but I will do my

1 best.

2 This morning we all heard about this wonderful new

3 category of hearing devices. These talks were presented by

4 some very distinguished and renowned individuals. Because

5 surgery for hearing loss is moving ahead so rapidly, I

6 thought it might be appropriate to step back in time and

7 briefly review its evolution.

8 The 1950s, '60s and '70s was really a

9 breakthrough, breakthrough decades. The advent of these

10 early surgeries all followed the development of the

11 operating microscope. This brought new enthusiasm to our

12 specialty, and many doctors, like myself and many others in

13 this room, trained to become otolaryngologists.

14 These were the decades of middle ear and tympanic

15 membrane surgery for conductive hearing loss. The surgeons

16 who helped develop these concepts and surgeries should be

17 recognized. There were Drs. Willstein and Zollner from

18 Germany on the tympanoplasty and the typing of

19 tympanoplasties. Dr. Sam Rosen in New York on stapes

20 mobilization. Dr. John Shea in Memphis, the stapedectomy.

21 And Billy Armstrong with the tympanotomy tubes from

22 Charlotte, North Carolina. The objective of these surgeries

23 was to correct structural pathology causing hearing loss.

24 The 1980s and '90s, and actually before, became

25 the decades of inner ear surgery for sensorineural hearing

1 loss. Dr. Bill House certainly was the conceptual genius
2 about this and performed the first operations. The
3 objective here was to stimulate hearing that was not
4 possible with conventional hearing aids.
5 For many of these years I was a voting or
6 consulting member of the panel, and many of those meetings
7 were devoted to the cochlear implant. I might say that
8 currently the FDA is still very busy reviewing new cochlear
9 implant submissions.
10 And now we come to the millennium, the 2000's, at
11 least hopefully just the first decade, and now we are
12 talking about again returning to basically middle ear
13 surgery, this time primarily for inner ear hearing loss. We
14 have the semi-implantable hearing devices and the totally
15 implantable hearing devices. The objective is to improve
16 the fidelity of hearing currently obtained by conventional,
17 state-of-the-art hearing aids.
18 As physicians we strive for good results, but
19 safety must be of paramount importance. Let me list some
20 important factors that should be taken into account when
21 discussing this new class of devices.
22 We have the morbidity of the surgical procedure;
23 the potential conductive hearing loss secondary to the
24 procedure itself; the potential loss of nerve function
25 secondary to the proximity of stimuli to the inner ear; the

1 potential need for surgical revisions; the necessity for
2 battery replacements in some of these devices; the question
3 of physical activity limitations; and certainly the
4 important subject of MRI compatibility.
5 At this time I would like to direct your attention
6 to the following issues pertaining to safety that we at the
7 FDA consider important. This outline has previously been
8 sent to the panel members. Many of these issues have
9 certainly already been mentioned by myself and previous
10 speakers today, and this is what was sent out:
11 What are the significant issues of safety and
12 effectiveness for purposes of development of a guidance
13 document for implantable middle ear amplification devices?
14 Various modifications are made to the ossicular
15 chain, ranging from placing a device on an ossicle, to
16 separation of the incudo-stapedial joint, to removing all or
17 part of an ossicle. Concerning the issues of performing
18 these types of surgeries in normal middle ears:
19 How much benefit justifies performing surgery on a
20 normal middle ear?
21 Should the risks that are found in stapes surgery
22 for otosclerosis be equated to implantable middle ear device
23 surgery which is performed on a normal middle ear?
24 Are there any concerns for further impairment of
25 the auditory system over time?

1 What pre-clinical data would be most beneficial in
2 predicting safety and effectiveness of these devices in
3 humans?
4 And, fifth, what concerns do you have that
5 patients may not be able to have MRI examinations after
6 implantation?
7 There were several issues mentioned earlier that
8 did not appear on the questions that were just read, and I
9 would like to repeat those. They were the potential need
10 for surgical revisions, the necessity for battery
11 replacement in the totally implantable devices, and any
12 possible limitations of physical activity. We would like
13 the panel members to include them in their discussions.
14 I would now take this time to introduce Teri
15 Cygnarowicz, clinical audiologist in the ENT Branch. She
16 will address the efficacy of these devices.
17 MS. CYGNAROWICZ: Thank you, Dr. Jaffee.
18 Mr. Chairman, distinguished panel, I would like to
19 present to you the following efficacy issues which generally
20 pertain to the risk versus benefit of these devices. The
21 value of these questions may be enhanced with some
22 additional comment.
23 As you know, audiology plays a major role in
24 evaluating both the safety and effectiveness of these
25 devices. As with many hearing aid studies, determining the

1 optimal control condition is fundamental to judging the
2 validity of the study. This has been an issue of great
3 discussion here at FDA.
4 As you address this issue, you may want to
5 consider the many optional control choices. One control may
6 include the patient's unaided condition. Another control
7 may be the patient's own hearing aids, and yet another
8 control may include state-of-the-art conventional hearing
9 aid technology, such as digital signal processing circuitry
10 and/or directional microphone technology, for example.
11 Binaural amplification should also be a factor in
12 determining the optimal control.
13 What, in your judgment, is an optimal control
14 condition for assessing the performance of these devices?
15 Keep in mind that when effectiveness data is
16 obtained and analyzed from these studies, statements,
17 conclusions and claims regarding the effectiveness of the
18 specific device will be made in comparison to this optimal
19 control condition.
20 During your discussion, please also take into
21 consideration the risk versus benefit of the control device
22 compared to risk versus benefit of these middle ear
23 implantable hearing devices.
24 Secondly, the question of what constitutes a
25 significant change in residual hearing has also been

1 discussed in detail here at FDA. For purposes of this
2 issue, we understand that residual hearing is defined as
3 hearing that remains following the surgery, following the
4 appropriate post-operative recovery and healing.
5 Ideally, implantation of these devices should have
6 no effect upon residual hearing. To make this
7 determination, accurate documentation and careful
8 description of these changes is critical.
9 Generally, residual hearing is measured by testing
10 for both air and bone conduction thresholds. Changes in
11 speech perception test results may also be considered.
12 What, in your judgment, do you consider to be
13 clinically significant changes in residual hearing?
14 In your discussion of this question, we would like
15 you to directly address the specific audiological test
16 measures for determining and describing residual hearing
17 changes, with specific attention to the effects of dB step
18 size. Please discuss to what extent test-retest reliability
19 should be taken into consideration. Discuss whether or not
20 changes in hearing across frequency ranges taken as an
21 average, versus changes at specific individual frequencies,
22 should be included.
23 Next, should the device be restricted to patients
24 who demonstrate certain types or degrees of hearing loss?
25 Here we would like you to discuss considerations

1 of the device sensorineural versus conductive versus mixed
2 hearing losses. Comment on whether or not the device should
3 be limited to a specific degree or range of hearing loss,
4 including a discussion of the appropriateness of these
5 devices for mild hearing loss.
6 Given that one proposed benefit of these devices
7 is to improve the fidelity of sound, are there any criteria
8 that can be used to help determine patient candidacy? How
9 can this benefit be measured?
10 We know from more recent hearing aid research that
11 in most cases binaural amplification is preferred and
12 results in a better communication improvement.
13 Considering this, what are your concerns for
14 patients going from binaural hearing aids to monaural
15 implants? Under what conditions would you recommend
16 binaural implantation?
17 And, finally, as an audiologist I am familiar with
18 hearing loss changes over time, including that of patients
19 who wear hearing aids. We do not yet have evidence of what
20 hearing changes may occur over time in patients with these
21 implants.
22 How should these devices accommodate for future
23 hearing changes?
24 In your discussion, please address the features of
25 programmability you recommend to address potential changes

1 in residual hearing.

2 In summary, these questions here today are not the

3 only issues and concerns regarding this device technology.

4 Therefore, you need not limit your discussion to only these

5 questions. As you have been introduced to this technology

6 this morning, and introduced to vast details and issues

7 concerning these devices, topics for discussion here today

8 and in the future are limitless.

9 Thank you.

10 DR. PATOW: At this time I would like to turn the

11 microphone over to Dr. Clough Shelton, who will be the

12 discussant or lead the discussion for questions of safety.

13 DR. SHELTON: Thank you very much, Carl.

14 We are to go back to the first set of questions

15 that Dr. Jaffee proposed. I don't know if there is a way to

16 get them on the screen.

17 Thank you. The first question was, how much

18 benefit justifies performing surgery on a normal middle ear?

19 I would like to open that question up for discussion with

20 the panelists. Does anyone have a comment on that?

21 This morning we heard Dr. Glasscock's comments on

22 the ethics of operating on normal ear anatomy. As

23 otologists, many times we will operate on a normal structure

24 to accomplish some type of therapy.

25 My own thought on this is, this is very analogous

1 to laser surgery for vision correction for the eye, where
2 again there is an eye that sees, it is correctable with
3 glasses to 20/20, yet we are going to do surgery on it to
4 make it better. There is risk that is involved in that
5 procedure, as well. Are the risks that we are talking about
6 for an implantable hearing aid analogous to this kind of
7 risk for eye surgery?
8 DR. DUFFELL: I will make a comment. Bill
9 Duffell. I mean, I think part of the risk has to be
10 justified against the reversibility of the procedure. Some
11 of these procedures sounded to me as though they are more
12 easily reversible than others, as far as whatever lingering
13 morbidity there may be associated with the initial one.
14 If they were completely reversible, then the
15 potential benefits that you derive from the procedure do not
16 need to be as high as they would need to be for one in which
17 the reversibility of it is in question, or is likely to
18 leave some additional impairment in hearing.
19 DR. SHELTON: Gayle?
20 DR. WOODSON: I guess one of the questions here is
21 how much we can do in terms of telling some patient-doctor
22 pair how much risk they should accept for a certain benefit.
23 The patient advocate that was here talking today,
24 was talking about the fact that some patients may prefer
25 having an implantable hearing aid even if it is not better

1 than the external one, because of the cosmesis and the
2 benefits of not having to deal with an external hearing aid.
3 On the other hand, Dr. Glasscock said that probably
4 ethically we shouldn't do the surgery unless the results
5 were better than the best air conduction aids.
6 So I think that is a fundamental question to think
7 about. I mean, do we just have to adequately inform all the
8 involved people of the risk levels, or do we make a decision
9 on what we think risk should be?
10 DR. KHAN: The risks would also involve the
11 operating surgeon putting this device in and their
12 capabilities, and I think some sort of a quality control as
13 to people doing this. When they do stapes surgery, you
14 know, it is people who do it repeatedly who close the
15 smaller gap, as opposed to people who go for the bigger gaps
16 to close that.
17 DR. SHELTON: So would you say that a training
18 course would be a very important prerequisite for this type
19 of surgery?
20 DR. KHAN: I think the people who are going to
21 approach this will have to be technically very good and be
22 able to control those risks.
23 DR. SHELTON: Dr. Campbell?
24 DR. CAMPBELL: I want to speak on the training.
25 This came up with the cochlear implants. Whether the

1 training should be optional, suggested, or required is a
2 question, too, and I think it should be optional. It should
3 not be required, but it should be there.
4 And of course I agree with everything so far, that
5 it depends on the adequacy of the training, because you are
6 near the facial nerve here, in very, very critical areas,
7 and absolutely. I don't know how you can regulate the
8 surgeon, though.
9 DR. ROSENTHAL: Excuse me. This is Ralph
10 Rosenthal. Excuse me, but what the agency does have the
11 option to do is require training, and it has the option to
12 require that training, you know, in a certain environment.
13 It does not dictate the training. That we allow, obviously,
14 the trainers to do.
15 But we can require that certain training be done,
16 and we have done so with exomer lasers. There is a certain
17 training requirement as part of the exomer lasers.
18 Sometimes they weren't so happy--well, I think everybody was
19 reasonably happy about the concept of training. There were
20 a lot of issues about it.
21 DR. CAMPBELL: You have the foreign countries, you
22 have different problems with training, as we understood it
23 before with cochlear implant, but the requirement as to
24 whether they have to be trained in this. For instance, if
25 you have just the facial recess and that area open, the

1 surgeon should be skilled in this area. He is going to get
2 into some problems. If you open up the posterior
3 tympanotomy, just exposing the body of the incus and
4 drilling the hole in the incus body is critical.
5 DR. ROSENTHAL: Well, we don't have--this is Ralph
6 Rosenthal--we don't have control over what goes on in
7 foreign countries, but we can put a training requirement in,
8 ultimately into a PMA. But I think that is a long way down
9 the line, and I would really rather be discussing some of
10 the other issues relating to risk.
11 I'm sorry, Dr. Sauberman.
12 MR. SAUBERMAN: If I can just second what Dr.
13 Rosenthal has said, in an earlier PMA discussion that came
14 before the ENT Panel on an autofluorescence device for a
15 pre-cancer determination, we have indicated in the labeling
16 that training is a requirement. So, yes, the FDA can
17 mandate that certain training be there.
18 DR. SININGER: Yvonne Sininger. It seems if we
19 are going to compare the risk and the benefits, one of the
20 things we need to do is maybe have a little better handle on
21 what the range and incidence of complications for this kind
22 of surgery are, because those of us who are not surgeons
23 don't have a good feeling for that. And clearly with
24 different devices, with different approaches, there is going
25 to be different risk, but I don't know what the incidence of

1 complications are in other surgeries that are similar.

2 DR. SHELTON: We are going to talk about risk in

3 the next question. We will address that further.

4 Dr. Middleton?

5 DR. MIDDLETON: I think my comments then might be

6 appropriate at the next, my comments would be more

7 appropriate at the next question.

8 DR. SHELTON: Carl?

9 DR. PATOW: Carl Patow. Is there a minimum

10 benefit that we would consider? For example, if the benefit

11 was no better than an air conduction hearing aid, then even

12 if the patient would accept the risk and the patient

13 considered this a cosmetic procedure, would we not consider

14 that that is inappropriate, to do an implant when the

15 benefit doesn't exceed that of an air conduction aid? Is

16 there a minimum threshold that we could consider?

17 DR. SHELTON: I think that is a very important

18 point, and you could take that one step further. Is it

19 equal to an air conduction aid that is a digital aid, or is

20 it just an analog air conduction aid. You know, it

21 certainly does come down to a question of patient choice, as

22 well, because they may want to have this done just because

23 of the cosmetics that are involved.

24 DR. MIDDLETON: That was my comment. If I am a

25 patient and my only reason for wanting it is purely

1 cosmetic, what amount of choice then is left to the patient?
2 Because I think there should be some consideration there.
3 It may not improve it over an air conduction aid for me, but
4 I prefer it because of cosmetic purposes. Clearly not
5 everybody is going to be able to afford it for that reason
6 alone, but I think that needs to be a consideration.
7 Is that something we should consider, patient
8 choice, if the patient chooses knowing that there probably
9 isn't any more significant benefit of this over air
10 conduction aids, should they be given that option of still
11 making that selection?
12 DR. KILENY: Paul Kileny. Well, we are talking
13 about the range here. We are not talking about black and
14 white, I think, good or bad in terms of outcome. There is a
15 range, and there is a possibility that a patient might
16 request this procedure even though there may be a
17 possibility that the results would be poorer than with a
18 standard state-of-the-art hearing aid. What about, what if?
19 That is a possibility.
20 DR. DUFFELL: My comment feeds right off of the
21 last one, and that is, I think that is the place for
22 labeling for the manufacturers. I think patient choice and
23 the right to choose is really important to most citizens in
24 the United States. They don't need other people making
25 those decisions for them.

1 I think what is important from a clinical
2 standpoint and from a manufacturer's standpoint is that
3 there be accurate and complete disclosure about the risk and
4 benefits, you know, perceived as well as measured, in the
5 labeling so that they can make that decision for themselves,
6 even if it is a range which could go all the way from zero,
7 no improvement, to whatever that improvement might be, as
8 well as some sort of probability factor based on clinical
9 trials as to what those improvement rates might be, you
10 know, given population of patients.
11 DR. ROSENTHAL: This is Ralph Rosenthal. There
12 also is the issue that, since you were comparing it to
13 exomer laser surgery, there we do bring people back to 20/20
14 and that is their expectation under most circumstances.
15 Whereas in this environment you are taking a damaged system
16 and just helping it, rather than bringing them back to
17 normal. I mean, if we could use normalcy as where they
18 should be, that is quite easy, I think. You can determine
19 what is normal quantitatively. But we can't do that, so--
20 DR. SININGER: It seems to me that there should
21 be, though, in terms of benefit, some minimum audibility
22 that this can restore, some minimum degree of speech
23 intelligibility in noise. Clearly we don't have good
24 answers about what is a benefit in amplification. I mean,
25 we don't have things that we consider completely adequate,

1 but we have some pretty good tests of that.

2 And we haven't discussed this much at all, but

3 there should be some basic level of audibility provided by

4 these devices before it can be offered as an option to

5 patients, and then you can take into consideration the

6 cosmetic value, the value of having an open ear canal. Some

7 of those other values are difficult to quantify, but ones

8 that we should not ignore. It could be very important to

9 patients, but only if the device is going to provide some

10 minimum amount of hearing for communication.

11 DR. SHELTON: Dr. Middleton?

12 DR. MIDDLETON: I thought your comment about

13 exceeding levels of audibility is important, because it

14 might be possible for you and I to have the same type or

15 amount of hearing loss, but functionally I may have more

16 difficulty than you in hearing and understanding speech. So

17 I think it needs to be more than just how well it improves

18 my ability to hear, that there need to be other factors as

19 well beyond audibility.

20 DR. SHELTON: Peter?

21 DR. UHTHOFF: Peter Uhthoff, Health Canada. My

22 preference is to talk about risks prior to benefits, and I

23 think you should have a detailed listing of the risks

24 involved prior to discussing benefits. I think you should

25 start with risks and then go to benefits, and not the other

1 way around.

2 DR. SHELTON: Paul?

3 DR. KILENY: Perhaps one other approach is to

4 compare the benefits to whatever baseline of whatever

5 control we are going to end up recommending, and to the fact

6 that the benefits would be equal or better than whatever the

7 control is going to be. I believe we have not that part

8 yet, but we need to have a control before we make some

9 recommendations regarding benefits.

10 DR. ROSENTHAL: This is Ralph Rosenthal. I do get

11 the sense that the panel feels that if there are benefits,

12 hearing benefits, it is worthwhile having surgery on a

13 normal middle ear.

14 DR. KHAN: Yes.

15 DR. CAMPBELL: Yes.

16 DR. ROSENTHAL: I mean, is that the correct sense?

17 DR. PATOW: Yes.

18 DR. SHELTON: Let's go on, and move on to the

19 second question about risks. The second question is, are

20 the risks encountered in stapes surgery equivalent to the

21 risks encountered in placing these devices into a normal

22 middle ear? Dr. Campbell, do you want to comment on that,

23 because you mentioned that earlier.

24 DR. CAMPBELL: Yes. In my opinion, I don't think

25 the risk is as serious as far as damaging, further damaging

1 the inner ear with these devices, than it is with--it is
2 more risky in stapes surgery that you could injure the inner
3 ear. I think it is less risky.
4 However, there are other risks involved. For
5 instance, if you take out the incus completely and implant a
6 device on the stapes, you have lost that conductive factor.
7 Second is the danger of the facial nerve, which is a big
8 risk. But comparing it with stapes surgery, I think it is
9 less risky compared with stapes surgery.
10 DR. SHELTON: Could you estimate what the risk
11 would be, given the--we have seen a whole gamut of different
12 surgical techniques today, different procedures, but could
13 you like give a ball park guess at what you think the risk
14 might be to further sensorineural hearing loss, to facial
15 nerve injury? We won't talk about additional conductive
16 loss because that varies so much with the procedure, but
17 would you think facial nerve injury would be equivalent to
18 that in cochlear implant surgery, perhaps?
19 DR. CAMPBELL: Yes, equivalent. Those procedures
20 that involve opening up the facial recess, very definitely.
21 DR. SHELTON: And would--
22 DR. CAMPBELL: And also you are going to, we are
23 going to open this up to a different group of doctors, too,
24 those who are just not doing cochlear implant surgery but
25 the general ear, nose and throat doctors who will be doing

1 this, and therefore their expertise in working close to the
2 facial nerve is therefore increased, the dangers.
3 DR. SHELTON: But the risk to the facial nerve in
4 implant surgery or mastoid surgery would be somewhere in the
5 order of from 1 to 100 to 1 to 1,000, wouldn't you think, in
6 that range?
7 DR. CAMPBELL: Well, I am not sure I understand
8 your question here.
9 DR. SHELTON: One in 100 cases, someplace between
10 1 in 100 cases and 1 in 1,000 cases, the published data on
11 facial nerve injury for mastoid surgery varies within that
12 range.
13 DR. CAMPBELL: Yes.
14 DR. SHELTON: And given the approaches that we are
15 talking about today, I would anticipate that the risk to the
16 facial nerve would fall within those same ranges.
17 DR. CAMPBELL: I would think so, too. And you
18 asked a question about the stapes surgery risk.
19 DR. SHELTON: Well, as far as the risk to further
20 sensorineural hearing loss with a procedure like this,
21 attaching a device to the ossicular chain, or
22 disarticulating the ossicular chain and causing further
23 nerve loss, where do you think that that--
24 DR. CAMPBELL: I think it would be minimal.
25 DR. SHELTON: Yes. Anybody?

1 DR. CAMPBELL: So far, everything that I have
2 heard so far, the risk is very minimal that you are going to
3 further damage the inner ear.
4 DR. SHELTON: You think less than 1 percent would
5 be--
6 DR. CAMPBELL: Yes. Very definitely, much less
7 than that. Stapes surgery is less than that.
8 DR. SHELTON: Any other comments about risk?
9 DR. ROSENTHAL: What you are saying, then--because
10 I am not an otolaryngologist, and I am sorry, so please
11 excuse my ignorance--is that if you operate and put one of
12 these devices in, that the hearing that you measure before
13 you put it in should be equal to the hearing you measure
14 after you put it in, I mean before you turn it on?
15 DR. CAMPBELL: Yes. That is surgical.
16 DR. SHELTON: The nerve conduction.
17 DR. ROSENTHAL: The nerve conduction.
18 DR. SHELTON: The cochlear hearing, yes.
19 DR. ROSENTHAL: Okay.
20 DR. SHELTON: Because, you know, those techniques
21 where the incus is removed, they will obviously have a
22 maximum conductive loss if you just measure the air
23 conduction hearing.
24 DR. CAMPBELL: And also those procedures where you
25 remove the incus and implant this on the stapes, the risk of

1 hurting the stapes is much greater.

2 DR. SHELTON: Paul?

3 DR. KILENY: Yes. I just have a question, really,

4 rather than an answer. Can you actually evaluate risk for

5 this class of procedures, given the diversity in these

6 implantable devices, as far as how they couple, whether they

7 require disarticulation of the ossicular chain, et cetera,

8 et cetera? It seems to me that there are some differences

9 here.

10 DR. PATOW: Carl Patow. This does back, I think,

11 to the issue that William brought up, of proper labeling,

12 since these devices are very different, that when it comes

13 down to assessing an individual device, the labeling is

14 going to be very critical and the risk will be different for

15 each device.

16 DR. SHELTON: Peter?

17 DR. UHTHOFF: Peter Uhthoff, Health Canada. Just

18 everything is the balance, benefit versus risk. And (b),

19 this question here, I am not sure it is really relevant to

20 compare it to stapes surgery. I think it has to stand by

21 itself, and I think there are five families of risks.

22 They are the type of contact this device makes

23 with the middle ear bones; the effects of that contact in

24 the long term; whether there is any disarticulation of the

25 bones. The fourth family is surgical, and that can be

1 further divided into the expertise and thus many potential
2 training requirements; the approach taken; and also the
3 complications of the surgery. And the last is the
4 indications, because certainly if there are minimal
5 indications or minimal gain, like cosmesis, then I think the
6 benefit has to be far greater.
7 So those are the five families of risks I look at,
8 and I don't know, comparing it--I mean, my viewpoint,
9 comparing it to the stapes surgery is not really that
10 relevant.
11 DR. SHELTON: Any other comments on this question?
12 DR. CAMPBELL: I agree, it shouldn't be compared
13 with stapes surgery. It is a middle ear surgical procedure.
14 DR. SHELTON: Do you think it is middle ear or
15 mastoid? Because--
16 DR. CAMPBELL: Well, it is both.
17 DR. SHELTON: It is both.
18 DR. CAMPBELL: But the danger is in the middle
19 ear.
20 DR. SHELTON: Let's move on, then, to the third
21 question. What concerns do you have that patients may not
22 be able to have MRI examinations after implantation?
23 MS. CYGNAROWICZ: This is Teri Cygnarowicz, FDA.
24 We had changed the order of these when we did up the slides
25 from what was sent to you, so I apologize. If you want, we

1 will go ahead and talk about this.

2 DR. SHELTON: That sounds good. Let's do this

3 question. Any of the panelists have any comments here?

4 Bill?

5 DR. DUFFELL: I know the Food and Drug

6 Administration has some standards for labeling that pertain

7 to MRI compatibility, and I would ask maybe the agency,

8 would those standards be sufficient to meet the needs of

9 this category of product? And if so, why not just use those

10 rather than, you know, kind of address the question

11 separately? Because they are already there, they have been

12 tried and proven, they are defined measurement criteria for

13 establishing, saying you are MRI safe, MRI compatible, so on

14 and so forth.

15 DR. SHELTON: Gayle? Harry, have you got a

16 comment?

17 MR. SAUBERMAN: Yes. This is Harry Sauberman.

18 The agency has an internal, very focused MRI Working Group,

19 and we would be pleased to take any concerns you have

20 regarding MRI or any of the data that we see regarding the

21 materials that are embodied in these implants to the MRI

22 Working Group, and at any time we can call the group

23 together and get an assessment from them, which I would be

24 happy to do. But I would like to take this occasion to hear

25 your thoughts about how you feel about MRI exams?

1 DR. SHELTON: And if I understand this question,
2 what it meant is if these devices were not MRI compatible,
3 would that be a big obstacle for the patient? How big an
4 obstacle is that? Gayle, did you have a comment?
5 DR. WOODSON: Yes, Gayle Woodson. Yes, I think
6 that would be a big obstacle. I think it is one thing for a
7 patient to decide whether or not they want to have a
8 surgical risk, but a patient may not comprehend what it
9 means to not be able to have an MRI examination. And as
10 MRIs are becoming more and more used for more and more
11 things, we can't project into the future. So it would seem
12 that if it is possible to make an implant and have it be MRI
13 safe, if we can establish that that is possible, then that
14 maybe should be the standard.
15 DR. SHELTON: Dr. Jaffee, did you want to make any
16 comments on this issue? I know you had some thoughts on it
17 earlier.
18 DR. JAFFEE: Well, I have maintained that this is
19 probably the major issue about these devices, because as
20 Gayle just said, MRIs are a very--I shouldn't say it, but
21 almost an everyday request for exams for so many people for
22 so many things. And when and if we can get of some kind of
23 magnet type thing and get the MRIs going, this would just
24 clear the air an awful lot. But it is of great concern to
25 me personally.

1 DR. SHELTON: Peter?

2 DR. UHTHOFF: Peter Uhthoff, Health Canada. I am
3 actually of the completely opposite viewpoint. In Canada we
4 have a social health care system, and we don't have MRIs in
5 every corner grocery store.

6 And the quote or the figure I read in the States,
7 that is, one quarter of all Americans will have an MRI in
8 their lifetime, the question I have is, are those necessary
9 or not? Have these patients undergone what you learn in
10 first year medical school as a proper history and physical
11 prior to getting an MRI? And I would invite comment on
12 that. I believe they have not.

13 I think that a CT scan, computerized tomography,
14 is an adequate way of analyzing most things. An MRI is not
15 needed, and in the very small percentage of patients where
16 it is absolutely required, then explantation is an option.

17 The other thing, too, is as the population ages,
18 you usually don't use an MRI as much. It is usually in the
19 younger population where you use an MRI. So my belief is,
20 it is less and less of an option, and actually
21 electrocardery is more of an issue than an MRI.

22 DR. ROSENTHAL: This is Ralph Rosenthal. I would
23 really rather this panel not get into a discussion about the
24 frequency of MRI use in this country, in this system versus
25 another system. But I think the issue is, it is used a lot,

1 and is it concerning that somebody who is going to have one
2 of these implants will unlikely be able to have an MRI if it
3 is incompatible?
4 DR. SHELTON: I think the point, though, is
5 relevant in that how often is an MRI absolutely necessary?
6 Because we deal with the same issues in cochlear implants in
7 patients with pacemakers, where they can't have MRIs, yet we
8 get around that issue. And I am old enough to have trained
9 before we had MRIs, and we could evaluate a number of things
10 without them.
11 So I think we want to make a distinction between
12 how often MRIs are done versus how often they have to be
13 done, because the patients where they have to be done are
14 the ones where they would have trouble with the implant.
15 Yvonne?
16 DR. SININGER: It seems--Yvonne Sininger--it seems
17 like it might also be important to weigh out whether or not
18 there are alternatives for those patients who do have to
19 have an MRI. Is the magnet removable for a small period of
20 time? And weigh that against the day-to-day use of an
21 amplification device.
22 DR. SHELTON: Bill?
23 DR. UHTHOFF: I would throw it back to you, so to
24 speak. I mean, you just mentioned these other technologies
25 where it is an issue but yet you are working around it. I

1 would presume that there is adequate labeling that has been
2 put forth in those manuals and all that provide cautions to
3 the health care professionals about using MRI with people
4 implanted with them, and I am not sure why there would be
5 any difference with this particular technology, either. I
6 mean, whatever you see in a pacemaker labeling has told you
7 what it is you know.
8 DR. SHELTON: I would certainly agree with that,
9 but the magnitude of the problem that we are dealing with in
10 a pacemaker is somewhat different than in an elective
11 hearing amplification, and I am not sure that labeling
12 itself would overcome that, those differences.
13 Carl?
14 DR. PATOW: I think that is one issue that I would
15 agree that there is a difference between a life-threatening
16 situation that you are trying to treat with a pacemaker and
17 something that is quite different.
18 The other issue is especially in treatment of
19 trauma and unconscious patients and delirious patients,
20 where you are more apt to get a head MRI, and the patient
21 may simply not be able to communicate that this device has
22 been implanted.
23 DR. SHELTON: Do you have a comment, too?
24 DR. CAMPBELL: Yes. Dr. Campbell. I come from
25 the era of CAT scans and histories and physicals, too, where

1 we didn't have the MRIs and CT scans, so we can always go
2 back to basic principles. But the question just came up
3 about the unconscious patient, which is certainly a
4 consideration. Is it possible that we could recommend that
5 they be MRI compatible? Rather than insist, recommend.
6 DR. UHTHOFF: Could I ask also that we discuss
7 electrocardery? Because I think it is as much of an issue
8 as MRI is.
9 DR. SHELTON: Do you want to make a comment about
10 that?
11 DR. UHTHOFF: I mean, as I said a minute ago, I
12 feel that it is a greater issue, the fact that
13 electrocardery, I believe bipolar is acceptable in most
14 cases, monopolar is not, but I think that should be well
15 indicated on the product.
16 DR. SHELTON: Dr. Rosenthal, do you have another
17 comment?
18 DR. ROSENTHAL: My only comment is, I get the
19 feeling--again, Rosenthal--I get the feeling that you would
20 rather have it MRI compatible. What if it isn't MRI
21 compatible? Is it worth pursuing? I mean, it is a decision
22 we are going to have to make.
23 DR. SININGER: Again--Sininger--it is--
24 DR. ROSENTHAL: We may have to make.
25 DR. SININGER: --it is a risk-benefit issue. In a

1 child who needs a cochlear implant, there are not a lot of
2 good alternatives for that child, and the benefits are well
3 established. For a patient who is going to choose one of
4 these devices, they do have alternatives, and so there is
5 where you have to weigh those things out.
6 DR. ROSENTHAL: I know, but that is what we are
7 asking you to do.
8 DR. WOODSON: Gayle Woodson. So your question is,
9 if we thought it was impossible to do this and still be able
10 to do an MRI, is it still worth pursuing? I think yes, as
11 long as patients can be warned. Anybody else feel
12 differently?
13 DR. SHELTON: I think to make that decision
14 personally, I would like to be able to have a handle on what
15 is the chance that I would have to have an MRI, and I
16 couldn't have a CT scan to do the same thing. I don't have
17 a good handle on that, that chance or that possibility.
18 DR. ROSENTHAL: Well, I mean, it is probably
19 likely we could--they do it with pacemakers, don't they? If
20 somebody has a brain lesion with a pacemaker, they do a CT
21 scan. I mean, you know, I presume--I mean, I am not an
22 expert in MRI and CT either, but I presume you can get
23 around the MRI issue by other means of imaging, and so
24 therefore I think your answer would be, it is worth
25 pursuing.

1 DR. CAMPBELL: Dr. Campbell. This comes up with
2 the eighth nerve tumors, also. We do a CT scan versus an
3 MRI. So you can go back to the CT scanning if necessary.
4 DR. SHELTON: Yes, so we do have alternatives in a
5 lot of the different cases, I think.
6 So let's go on down to the next question, and I
7 have--okay, we will do that question. Are there any
8 concerns for further impairment of the auditory system over
9 time?
10 DR. WOODSON: Okay, I will chime in. Gayle
11 Woodson again. I think it is--yes, it is a big concern. We
12 don't know yet whether or not it would happen, but it is a
13 big concern that if repetitive vibration or manipulation of
14 the vibrator, under what circumstances--a number of
15 different circumstances, there is opportunity that you could
16 have further degradation of the sensorineural loss over
17 time. And we won't know that, maybe with animal studies but
18 ultimately not until, you know, humans have them implanted
19 for a time.
20 DR. ROSENTHAL: Rosenthal. It does bring up the
21 issue of the duration of the study, then, doesn't it?
22 DR. WOODSON: Yes, yes. But then the question is,
23 if you--it becomes relevant when you start thinking about
24 should we do it binaurally or monaurally, and it probably
25 would be better initially just to do it monaurally until you

1 could establish that yes, they were safe over time, before
2 you went to binaural implantation. I think that is where
3 the real concern comes in.
4 DR. SHELTON: I think we ought to separate this
5 question into sensorineural degradation versus conductive
6 degradation, because they are different issues. And with
7 the sensorineural degradation, I think the question there
8 is, is stimulating the ossicular chain mechanically any
9 different than stimulating it acoustically? You know, the
10 sound pressure level at the cochlea you are going to see is
11 any different regardless of the stimulus source? Does
12 anyone have any thoughts on that?
13 DR. SININGER: Yvonne Sininger. It seems there is
14 going to have to be maximum output levels. In other words,
15 there has to be some sort of cutoff on the amount of power
16 that can be applied, the same way there are with acoustic
17 hearing aids. And so I wouldn't immediately think that
18 there is any greater damage, acoustic trauma, from these
19 devices than there would be from a standard amplification
20 device.
21 DR. SHELTON: Carl?
22 DR. PATOW: It sounds like what you are saying,
23 though, as part of the guidance document we would recommend
24 there be a cutoff energy level to prevent damage from
25 excessive stimulation.

1 DR. SININGER: Right. How that would be
2 characterized isn't exactly clear, but--
3 DR. PATOW: I don't know.
4 DR. SININGER: --there would need to be something
5 similar to a compression type of circuit or some way of
6 limiting the maximum output, as there always is in acoustic
7 devices.
8 DR. WOODSON: Can I say--Gayle Woodson again--
9 isn't one of the reasons for using the implantable is that
10 you can't get a high enough, loud enough level with an
11 acoustic hearing aid because of the problems of feedback and
12 stuff? So inherently you are wanting it to be greater
13 stimulation than you would get with an acoustic. And we can
14 certainly look maybe at OSHA standards of just noise
15 tolerance in general. You know, how does the stimulation
16 that the ear gets from the middle ear implant compare to
17 what they would get working in a noisy factory?
18 DR. SININGER: Again, Yvonne Sininger. But the
19 amount of gain that is applied to a low level stimulus is
20 not the same as the amount of gain that becomes applied when
21 the stimulus level is higher. So it is the maximum, say,
22 displacement of the stapes that would be the important
23 factor, and you need to apply enough gain for low level
24 stimuli to make them audible, but not so much gain for
25 higher level stimuli that there can be damage. And I think

1 that is a circuitry issue and not related to this device any
2 more than it is to acoustic devices.
3 DR. SHELTON: I guess the other issue--we are
4 talking about adult patients here--is if we fit an adult
5 patient with this device, if it was too loud, loud enough to
6 damage the hearing, would they tolerate that setting, or
7 would they tell you that it is too loud and you need to turn
8 it off? Is there a safety factor from the patient itself
9 that can give us information? Dr. Soli, you nodded your
10 head. Do you want to make a comment?
11 DR. SOLI: Yes. In fitting air conduction hearing
12 aids, adults are very good at self-reporting when it is too
13 loud. So I think that is an additional safety factor, as
14 long as there are controls in the processor for the device
15 that allow you to adequately limit the output so that you
16 don't exceed that loudness tolerance level.
17 DR. SHELTON: Thank you. If there are no other
18 comments on this question, let's go on to last question on
19 the slide.
20 DR. ROSENTHAL: You didn't--Rosenthal--you
21 didn't--
22 MR. SAUBERMAN: You divided it in two.
23 DR. SHELTON: Oh, I'm sorry. Thank you very much.
24 DR. ROSENTHAL: You divided it in two, and you
25 took the neural.

1 DR. SHELTON: The other part is the part of the
2 conductive loss, and I think that this has to do with how
3 the device affects the ossicular chain; and as a subset of
4 that is for those devices that disarticulate the ossicular
5 chain, taking out the incus.
6 Do any panelists have any comments regarding long-
7 term effects to conductive hearing loss for these devices?
8 And I think this is beyond what we would see just from
9 loading the ossicular chain from the device placement
10 itself. Dr. Campbell?
11 DR. CAMPBELL: Dr. Campbell. I would like to know
12 if there was any--were there any studies by the
13 manufacturers of the clip-on devices that clipped onto the
14 incus, as to what happened over a period of time with those
15 patients? Did any erode through or not? Do we have any
16 prediction? Because those that clip onto the distal end of
17 the stapes, you are going to lose--it is a crimping of the
18 blood supply to the incus-stapes joint. And we have seen
19 that in stapes surgery, that does interfere, it will, over
20 time.
21 DR. SHELTON: Can we ask the Symphonix
22 representative to respond to that?
23 MS. ARTHUR: Deborah Arthur from Symphonix. Yes,
24 we have up to 33 months of patient usage time with our
25 device to date, and no incidence of any type of ossicular

1 vascular supply disruption, no evidence of any degradation
2 of the sensorineural component of hearing, nor an induced
3 conductive loss as a consequence.
4 DR. CAMPBELL: I have a question. This is Dr.
5 Campbell. I understand that in the techniques of putting
6 the clip on, it is not crimped tightly. One of the
7 recommendations is that it is put on loose so to allow for
8 that.
9 MS. ARTHUR: We have designed the attachment clip
10 so that--and we dissuade everybody within the company from
11 using the word "crimp" because of what the inference is. In
12 fact, what we have is an attachment clip that has been
13 preformed, so that when you use the specially designed
14 forming forceps over the attachment clip--and I believe Bob
15 Katz has some nice pictures of that if you want to see it--
16 then what happens is that the forming forcep goes around the
17 attachment clip, and the attachment clip is designed so it
18 can only clamp so far, without crimping and disrupting that
19 blood supply. And it is also quite easy to see visually
20 during the surgical procedure whether or not you have it
21 around there so tight that the disruption of the blood
22 supply is in fact in place, or if you have got it secure but
23 not disrupting that blood supply.
24 DR. CAMPBELL: And some surgeons want to use a
25 forceps rather than, yes, a crimping forceps rather than the

1 device.

2 MS. ARTHUR: And the manufacturer does recommend

3 using the forming forceps.

4 DR. MIDDLETON: Just for my own understanding from

5 a consumer perspective, when we talk about long term

6 effects, it sounds like--I know there was one group that did

7 trials, I think in Japan and Germany, and from Deb Arthur's

8 comments they are out to like three years and not noting any

9 effect on the stapes. Is that--what is our baseline or time

10 line for long term effects?

11 I mean, how do--and should we--should they--should

12 we maybe provide some, ask the manufacturers to provide at

13 least what they know to date with their studies, and how far

14 out they extend, and then still have some type of disclaimer

15 that says beyond that we are not sure what the impact may

16 be? I know people might not be comfortable with it, but how

17 do we know what is long term?

18 DR. ROSENTHAL: Dr. Rosenthal. That is really one

19 of the issues that the agency grapples with all the time,

20 and I don't think we do know what is long term. I think

21 what we can ask you, though, and I will put you on the spot

22 if you don't mind, and that is, how long do you think an IDE

23 should be carried on? I mean, we can't carry it on

24 indefinitely to look for these things. I mean, you know, do

25 you think one year, two years, three years?

1 DR. MIDDLETON: Five years.

2 DR. ROSENTHAL: Five years?

3 DR. MIDDLETON: I mean, what is--

4 DR. DUFFELL: In making those types of remarks,
5 you need to think about the implications of what that means
6 to other people. I mean, that is a long time when you
7 consider the development cycle for one of these devices is
8 probably already on the order of three to eight years. With
9 a five-year follow-up you could be talking as much as a 15-
10 year lag time before something like this ever reached the
11 market. So, I mean, reasonableness--I mean, I think Dr.
12 Woodson mentioned, you know, it depends on whether you are
13 doing one year or both ears type things, again because I am
14 sure she is thinking risk, risk-benefit type things.

15 So I think initially a lot of implants usually
16 require at least some number of patients that have been
17 followed for about one year, and then you have like, I think
18 you were saying before something in the labeling about the
19 knowns and unknowns, about beyond that, and then that is
20 where this thing of conditions of approval, post-market
21 surveillance come into play, where the agency can require
22 the manufacturer to revisit these topics on an ongoing
23 basis, annualized, and then update that labeling accordingly
24 about those risks that occur two, three, five, ten years
25 out.

1 DR. MIDDLETON: From a consumer perspective we are
2 talking about then one to two years. I would feel better,
3 then, saying that after that time that there be some comment
4 made that ongoing follow-up isn't necessary, so that the
5 patient knows. That is just--if I were a consumer, you
6 know, knowing what I know, and you just said, "Well, we
7 looked at this for one year and nothing happened," I still
8 think that some kind of non--I don't know--threatening
9 comment or something needs to be made to the consumer, that
10 this is all we know based on this--
11 DR. ROSENTHAL: This is Rosenthal. There is no
12 question that will be made. The issue is, we need some
13 recommendations from you all about the length of time you
14 think a study should be carried on. I don't really want to
15 get into post-approval just now. I think to discuss that
16 now is premature, and we don't have any data. You know, I
17 can assure you, you will be put on the spot, or one of your
18 colleagues will, when these come to PMA.
19 But right now I think what we would like to know
20 is how long you think we should require the companies to do
21 a monaural implant, to follow a monaural implant, before
22 they can come in with their data for approval?
23 DR. SHELTON: Peter, do you have a comment?
24 DR. UHTHOFF: Yes. Peter Uhthoff, Health Canada.
25 I am not that concerned about long term effects. Maybe I am

1 a bit naive, but I feel the technology is going to advance
2 so much that if we have a problem 10 or 15 years down the
3 line, the technology will have caught up and allowed us to
4 correct it. I am more concerned about short term, actually,
5 and that is where my emphasis is. I mean, if I am concerned
6 about long term, I can't do anything about it because, quite
7 rightly, I cannot ask for a 10-year study, and so I just
8 hope that technology will catch up. Short term, two or
9 three years.
10 DR. SININGER: Yvonne Sininger. You have to weigh
11 not only how long but how many people are being followed. I
12 mean, following a couple of patients for three years is
13 inadequate. Following a larger group for two to three years
14 may be adequate, because you are not going to be able to
15 sample what kinds of problems you are going to have unless
16 you have a large enough sample. So it seems to me there has
17 got to be a combined approach to this.
18 DR. ROSENTHAL: Rosenthal. I think you--I can
19 tell you that in the device world two years is a long time.
20 You might think it is a short time, but with other devices
21 two years is considered very long and rather unacceptable.
22 And, you know, we also have a charge to have the least
23 burdensome requirement for companies, and I want to ensure
24 that we do that, but based on the best possible advice we
25 can obtain.

1 DR. SHELTON: Carl, did you have a comment?

2 DR. PATOW: I think some of the--Carl Patow--some
3 of the issues, for example, the crimping of the stapes,
4 those are long term issues and cannot be addressed in that
5 short period of time. But there are other issues, for
6 example, how the software works, how the chips are
7 performing, microphone performance, battery performance,
8 that I think could be answered in a year, 18 months, a
9 shorter range of time, and I think that is probably--I am
10 more worried about those things than I am about the stapes
11 itself over the long term.

12 DR. SHELTON: Yes, but if we go back to the
13 device-ossicle interface, that connection right there, how
14 long do you think you need to follow that? Because I think
15 I would agree with what you just said, that those are long
16 term issues. I think that if you have problems in that
17 area, if we use another analogy like middle ear ossicles, we
18 may not see problems early on but we may see them later on,
19 like at one or two years.

20 DR. CAMPBELL: Dr. Campbell. I would suggest a
21 year. In stapes surgery we proceed to the other ear, then
22 realize it a safe time, after six months. Some people do it
23 after three months. So there is nothing going wrong, even
24 the worst scenario, in stapedectomies.

25 DR. MIDDLETON: Can we compromise and say then 18

1 months, since it sounds like some of us are leaning towards
2 two years and some are leaning towards one year? Because I
3 would like to see it extended beyond a year.
4 DR. DUFFELL: Well, the other key component is how
5 many patients, again, too. And is it how many patients for
6 whatever period of time, or is it patient-years of data? I
7 mean, typically in the device and pharmaceutical industry,
8 sometimes we talk of things in patient-years of data, so you
9 calculate out.
10 DR. ROSENTHAL: I think this would--excuse me,
11 Rosenthal--I mean, I have a prejudice against that in a
12 device environment. I think you have to look at number of
13 patients over a certain period of time. You know, you can
14 recommend one to two years. We are going to have to make
15 the take, anyway, but if there is a feeling that one year is
16 good enough, good. If it is a feeling that 18 months is
17 better, good.
18 I mean, you know, I don't know what kind of
19 problems--the thing you have to say is, what kind of
20 problems are you going to get into between a year and 18
21 months. I mean, if you are worried about short term, three
22 to six months, well, then, okay, maybe a year just for
23 comfort level. But if you think, well, after a year bad
24 things are going to happen, then you extend it out. I need
25 your advice. We need your advice.

1 DR. KILENY: Kileny. Well, I don't know. It
2 seems to me maybe we are straying a little bit, but is the
3 coupling of these devices more traumatic to the ossicles
4 than the various ones that have been used for years? And if
5 the answer is it is more traumatic for whatever reason, then
6 obviously we need to pay attention to that. But if the
7 coupling is equally traumatic, we know a lot about how long
8 those last and what sort of problems are associated with
9 those in the long term.
10 DR. SININGER: This is Yvonne Sininger. Just for
11 what it is worth, this isn't related to risk but in terms of
12 benefit, we are going to know what the benefit of these
13 devices is very soon. You don't need a year to see the
14 benefit. And so from that standpoint, you know, we don't
15 need more than--certainly more than a year.
16 DR. SHELTON: Peter, do you?
17 DR. UHTHOFF: Yes. I would like to qualify my
18 statement. It all depends upon what the risks are. I mean,
19 if you are doing little involvement of the ossicles, two or
20 three years is not acceptable. You are right, one year is
21 adequate. But the more manipulation, the more potential,
22 the more comfortable I feel in extending the study. So I
23 think those who do more damage must have a greater burden of
24 proof to show safety.
25 DR. SHELTON: Do you want us to try to reach

1 consensus on this, or is that adequate?

2 DR. ROSENTHAL: I think you have done an excellent

3 job.

4 DR. SHELTON: So we will go on and move on, then,

5 to the last of the submitted questions: What pre-clinical

6 data would be most beneficial in predicting safety and

7 efficacy of these devices in humans?

8 And so we have discussed some of these issues

9 already. Are there any other issues that we haven't

10 discussed, that we should consider? Paul?

11 DR. KILENY: Well, I want to bring up an issue

12 that we have already touched upon, but I think it is an

13 important one, and that relates to the maintenance of the

14 integrity of the device itself over a long term, separate

15 from its coupling to the ossicular chain, separate from the

16 auditory system, just the device, especially if it is a

17 device that has some mechanical, moving parts where some

18 wear and tear can be expected.

19 And I am just wondering if there is some type of

20 accelerated benchtop testing that could be done to

21 substantiate that, yes, this device will be able to continue

22 vibrating and doing its thing for a considerable amount of

23 time, especially considering that we will be implanting

24 young adults, probably, not just older adults.

25 DR. SHELTON: So whether the moving parts would

1 wear out or not would be a concern that you would have. Any
2 other--
3 DR. PATOW: This is Carl Patow. In addition,
4 there are very fundamental issues of biocompatibility and
5 new materials, and that would need to be considered for any
6 implanted device, and it would be no different for these
7 devices.
8 DR. ROSENTHAL: Rosenthal. Just, I am curious,
9 what is your feeling about batteries?
10 DR. SHELTON: That is something that Dr. Jaffee
11 also brought up about the need for battery replacement but
12 also--when you say batteries, you have some biocompatibility
13 issues--
14 DR. ROSENTHAL: Well, no. Those are given.
15 DR. SHELTON: That is already taken care of with
16 pacemaker technology, I assume.
17 DR. ROSENTHAL: I imagine so.
18 DR. SHELTON: Okay, so just the idea of replacing
19 batteries?
20 DR. ROSENTHAL: Yes, the issue of a battery-
21 driven--I mean, I don't know. Do you have to go back in and
22 open up the surgical wound and replace the battery? How
23 long? If you do, then you have a potential other risk of
24 surgery, other chance of infection.
25 DR. SHELTON: Any comments?

1 DR. KILENY: Well, for a totally implantable
2 device, obviously current battery technology is such that it
3 doesn't last a lifetime. We heard three to five years, so
4 these patients over the life of the device or their life
5 span will probably have several surgical procedures to
6 replace the battery. For those that are partially implanted
7 and the battery is external, it is not an issue.
8 DR. SHELTON: Carl?
9 DR. PATOW: Carl Patow. Are there--I just don't
10 know--are there standards for implantable batteries? If
11 someone would conceive of a new battery type to put
12 specifically in this device, would that need to be
13 independently tested? I just don't know.
14 DR. ROSENTHAL: Yes, I am sure it would be
15 independently tested. We have asked the ENT Branch to go to
16 the Pacemaker Branch and talk to them about batteries. I am
17 just curious if you had any feeling about it.
18 DR. PATOW: It sound like we are making an
19 assumption that batteries are safe because they have been
20 out there, but in fact one could make an unsafe battery
21 and--
22 DR. ROSENTHAL: I mean, the agency must have a lot
23 of experience. In ophthalmics we have no experience with
24 batteries, other than for cautery, but we will certainly
25 consult parts of the agency, of the center, that deal with

1 batteries all the time. I am just curious about having to
2 re-operate several times.
3 DR. SHELTON: Let me state the question
4 differently, then. The panelists, would anyone have any
5 objections to a device that had to have the battery replaced
6 periodically like a pacemaker, similar type operation like a
7 pacemaker, the battery replaced like a pacemaker? Are there
8 any philosophical or ethical problems here? Assuming the
9 batteries were safe and everything else was safe.
10 DR. UHTHOFF: Peter Uhthoff. Assuming that the
11 disconnecting of the battery is easy. That is what I would
12 have as a basic requirement.
13 DR. CAMPBELL: That was my question also. When
14 they disconnect the battery, does it wiggle something in
15 there and dislodge the device? I don't think that was
16 clearly explained.
17 DR. WOODSON: Woodson. The other thing is, how
18 accessible is the battery. You know, in a pacemaker they
19 put it in a nice pocket where it is easy to get and it is
20 far away from the problem. So the question is not only
21 disconnect but surgical accessibility without getting into a
22 space where you might, say, be near the facial nerve again
23 or something like that.
24 DR. SHELTON: Okay. I have got a couple of other
25 points that Dr. Jaffee wanted me to cover. One is, what

1 about the issues involved with surgical revision, the need
2 for surgical revision? Any special considerations here, any
3 device design considerations? If the device needs to be
4 revised, should they be designed in a way to help that?
5 Anyone have any concerns with that?
6 DR. CAMPBELL: I do.
7 DR. SHELTON: Okay.
8 DR. CAMPBELL: Dr. Campbell. If the device fails
9 because of the compression of the incus, what alternative is
10 there to go back in? You have to place that device clip
11 somewhere or have another method, so the company perhaps
12 might have another alternative in case there is a failure of
13 the incus. That is my concern.
14 DR. SHELTON: Okay. Anybody else?
15 DR. WOODSON: Woodson again. So I guess device
16 failure is one thing, but another is device upgrade. Say
17 something comes out that works much better, or some
18 component can be improved on. There is no way to predict
19 that, but it is something to be considered.
20 DR. SHELTON: And then the last point was, what
21 about any limitations of physical activity implantation of
22 these devices might impose? Does anyone have any concerns
23 about that?
24 DR. PATOW: Can you give us some examples, or
25 perhaps scenarios? Is this scuba diving or--