

UNITED STATES OF AMERICA
DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

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EAR, NOSE AND THROAT DEVICES PANEL

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OPEN SESSION

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Friday,

August 16, 2002

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The meeting was called to order at 12:37 p.m., in the Walker Room of the Gaithersburg Holiday Inn, 2 Montgomery Village Avenue, Gaithersburg, Maryland, Dr. A. Julianna Gulya, Chair, presiding.

PRESENT:

DR. A. JULIANNA GULYA, Chairperson

DR. HOWARD FRANCIS, Voting Member

DR. HERMAN A. JENKINS, Voting Member

DR. PAUL R. KILENY, Voting Member

DR. LINDA J. HOOD, Voting Member

DR. SIGFRID D. SOLI, Voting Member

DR. DEBARA L. TUCCI,, Voting Member

DR. BRENT A. BLUMENSTEIN, Consultant

DR. ROBERTO A. CUEVA, Consultant

DR. BRENDA L. LONSBURY-MARTIN, Consultant

DR. DONALD K. EDDINGTON, Consultant

DR. JOSEPH W. HALL, Consultant

DR. BRIAN E. WALDEN, Consultant

DR. CATALINA E. GARCIA, Consumer Representative

MR. MICHAEL CROMPTON, Industry Representative

FDA PARTICIPANTS:

SARA M. THORNTON, Panel Executive Secretary
DAVID M. WHIPPLE, Deputy Director,
Division of O&ENT Devices
DR. ERIC A. MANN, Chief, Ear, Nose, and
Throat Devices Branch
DR. TERI M. CYGNAROWICZ, Audiologist,
ENT Devices Branch
DR. JAMES KANE, Audiologist, Hearing Scientist ENT
Devices Branch
KAREN H. BAKER, Expert Nurse Consultant,
EN&T Devices Branch

MEMBERS OF THE PUBLIC PARTICIPATING:

DR. CHRISTOPHER TURNER
MS. DEBORAH ARTHUR

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P-R-O-C-E-E-D-I-N-G-S

(12:37 p.m.)

CHAIRPERSON GULYA: I would like to call this meeting of the Food and Drug Administration Center for Devices and Radiological Help, Ear, Nose, and Throat Devices Panel, into session. It is good to see a number of you who are interested in today's meeting regarding the draft guidance document for implantable middle ear hearing devices.

And as we have a full agenda, I will now turn to Ms. Sally Thornton, our executive secretary, for her introductory remarks. Sally, are you ready?

MS. THORNTON: Yes. Good morning, and welcome to the open public meeting of the Ear, Nose, and Throat Devices Panel. Before we proceed with today's agenda, I have a few short announcements to make. I would like to remind everyone here to sign in on the attendance sheets out in the registration area just outside the room here. All handouts for today's meetings are also available on that table. Messages for the panel members and FDA participants, information or special needs, should be directed through Ms. Jennifer Weber, or Bernadette Courtney McCray, who are available out there in the registration area.

Phone calls can be sent to (301) 948-8900. That is the number here at the hotel, and they should ask for the FDA panel. In consideration of the panel, the public, and the

1 agency, we ask that those of you with cell phones and pagers
2 read the pink signs on the door, and either turn them off, or
3 put them on vibration mode while you are in this room. We
4 certainly would appreciate it.

5 Lastly, I would like to ask all participants in
6 the meeting -- the FDA participants, as well as the panel -- to
7 please speak directly into the microphone -- I have been told
8 that the optimum distance is four inches or less -- directly
9 into the microphone, and not to the side, because then they
10 can't hear you and get your comments. So in the interest of
11 clear and accurate transcriptions, we would appreciate your
12 efforts on that.

13 At this time, I would like to announce the
14 confirmation of the new Ear, Nose, and Throat Devices Panel
15 Chair, Dr. Julianna Gulya, who is to my left. We also have
16 four new voting members who have been confirmed since the last
17 meeting in July of 2000. Those are Drs. Linda Hood, who is to
18 my right, Dr. Herman Jenkins, who is also to my right; Dr.
19 Sigfrid Soli, to my left, and Dr. Debara Tucci. And in
20 addition, we have with us today for the first time our new
21 consumer representative, Dr. Catalina Garcia, and our new
22 industry representative, Mr. Michael Crompton. Welcome to you.

23 Dr. Hood is a professor at the Kresge Hearing
24 Research Laboratory of the South, in the Department of
25 Otorhinolaryngology, at Louisiana State University Health

1 Sciences Center, in New Orleans.

2 Dr. Jenkins is the Chairman of the Department of
3 Otolaryngology at the University of Colorado Health Sciences
4 Center in Denver.

5 Dr. Soli is vice-president and head of the
6 Department of Human Communications Sciences and Devices at the
7 House Ear Institute in Los Angeles, California.

8 Dr. Tucci is an associate professor of surgery in
9 the Division of Otolaryngology, head of neck surgery at Duke
10 University Medical Center in Durham, North Carolina.

11 Dr. Garcia is a private practicing
12 anesthesiologist with the Dallas Anesthesiology Group of Dallas,
13 Texas.

14 And Mr. Crompton is the Vice President for
15 Regulatory and Clinical Affairs and Quality Assurance for
16 Odyssey Technologies of Los Gatos, California.

17 Our remaining voting members, who continue to
18 serve us faithfully, are Dr. Howard Francis, who is an Assistant
19 Professor with the Division of Neurotology and Skull Base
20 Surgery, in the Department of Otolaryngology, Head and Neck
21 Surgery, at the Johns Hopkins University School of Medicine, in
22 Baltimore, to my right. And also to my right is Dr. Paul
23 Kileny, who is a Professor of Otorhinolaryngology and Director
24 of the Division of Audiology and Electrophysiology at the
25 University of Michigan School of Medicine in Ann Arbor.

1 I would also like to extend a special welcome and
2 introduce to the public, the panel, and the FDA staff, six panel
3 consultants who are new and with us today for the first time.

4 Dr. Roberto Cueva, to my left, is the co-director
5 and founder of the Skull Base Surgery Service at the Southern
6 California Permanente Medical Group, and an Associate Clinical
7 Professor and Co-Director of the UC San Diego Fellowship Program
8 in Otology, Neurotology, and Skull Base Surgery.

9 Dr. Donald Eddington to my left is the principal
10 research scientist at the Research Laboratory of Electronics at
11 the Massachusetts Institute of Technology, and Director of the
12 Cochlear Implant Laboratory at the Massachusetts Eye and Ear
13 Infirmary in Boston, Massachusetts.

14 Dr. Joseph Hall, to my right, is a Professor
15 and Chief of Audiology in the Department of Otolaryngology, Head
16 and Neck Surgery, at the University of North Carolina, in Chapel
17 Hill.

18 Dr. Brenda Lonsbury-Martin, to my right, is a
19 Professor of Otolaryngology at the University of Colorado Health
20 Sciences Center in Denver, and Vice Chair for Research in the
21 Department of Otolaryngology.

22 Dr. Brian Walden is the Director of Research in
23 the Army Audiology and Speech Center at Walter Reed Army Medical
24 Center in Washington, D.C.

25 And Dr. Brent Blumenstein is a biostatistician

1 and clinical trialist who is being shared from the FDA's General
2 Hospital and Plastic Surgery Devices Panel. We are grateful to
3 him for his willingness to do double-duty today. Welcome to you
4 all.

5 I would like to now read the conflict of interest
6 statement for this open public session, August 16th, 2002. The
7 following announcement addresses conflict of interest issues
8 associated with this meeting, and is made a part of the record
9 to preclude even the appearance of an impropriety.

10 To determine if any conflict existed, the agency
11 reviewed its submitted agenda and all financial interests
12 reported by the committee participants. The conflict of
13 interest statutes prohibits special government employees from
14 participating in matters that could affect their or their
15 employer's financial interests. However, the agency has
16 determined that participation of certain members and
17 consultants, the need for whose services outweigh the potential
18 conflict of interest involved, is in the best interests of the
19 government.

20 Therefore, a waiver has been granted for Dr.
21 Sigfrid Soli for his financial interests in a firm at issue that
22 could potentially be affected by the panel's recommendations.

23 The waiver allows this individual to participate
24 fully in today's deliberations. Copies of this waiver may be
25 obtained from the agency's Freedom of Information Office, Room

1 12A15 of the Parklawn Building.

2 We would like to note for the record that the
3 agency took into consideration other matters regarding Dr. Soli.

4 This panel has reported interests in firms at issue, but in
5 matters that are not related to today's agenda. In the event
6 that the discussions involve any other products or firms not
7 already on the agenda, for which an FDA participant has a
8 financial interest, the participant should excuse him or herself
9 from such involvement, and the exclusion will be noted for the
10 record.

11 With respect to all other participants, we ask in
12 the interest of fairness that all persons making statements or
13 presentations disclose any current or previous financial
14 involvement with any firm whose products they may wish to
15 comment upon. Thank you, Dr. Gulya.

16 CHAIRPERSON GULYA: Thank you, Sally. Now we
17 turn to the open public hearing session, and an opportunity for
18 members of the public who have an interest in addressing the
19 panel on today's topic or related matters.

20 As Sally alluded to, each presenter is asked to
21 state clearly for the record their name, affiliation, interest
22 in the topic at hand, any consulting arrangements or financial
23 interests with medical device firms, and if travel expenses have
24 been paid, by whom.

25 We have 30 minutes for this session, and from the

1 handout here, it appears that we have one speaker, Dr.
2 Christopher Turner, from the University of Iowa, scheduled. Dr.
3 Turner.

4 DR. TURNER: I have a couple of overheads.

5 (Discussion off the record.)

6 DR. TURNER: My name is Chris Turner, and I am a
7 Professor at the University of Iowa, and I also work as a
8 consultant on a per day basis for St. Croix Medical Corporation,
9 which produces an implantable device. They are a company from
10 my hometown of Minneapolis, mostly consisting of people that
11 work in pacemakers and things like that.

12 (Discussion off the record.)

13 DR. TURNER: And they mostly consist of pacemaker
14 kind of people. So they have asked me to come up on a per day
15 basis to help them think about ways to evaluate these devices as
16 an audiologist. And this is the second time this year that I
17 have worked for them on a per day basis, and they paid for my
18 airfare and hotel to say in wonderful D.C. last night.

19 I have been trying to think about how to evaluate
20 these devices, and I have a lot of experience in hearing aids
21 and some experience in Cochlear implants, and this has been a
22 lot of fun for me, because there are some issues that are very
23 different than what I am used to. And maybe the panel is
24 already familiar with these, but I thought that I would just
25 bring them up, because there are some things that I think we

1 might need to take into consideration. Can we start the
2 overheads there?

3 What I wanted to talk about here, and the thing
4 that makes this device different, I guess, in my mind is that it
5 is a totally implantable device, and that is one of the things
6 that I find so interesting. The eardrum is used as the
7 microphone, and then the ossicula are driven, and so the whole
8 device is underneath the skin, and has a long life, 7 or 8 year,
9 battery. So the fact that the input of the system is at the
10 eardrum all of a sudden makes things quite a bit different I
11 think acoustically, and we want to try --it has been an issue
12 for us to try to -- on how to evaluate that.

13 And the second thing is that it is totally
14 implantable. If I can have the next overhead there. That shows
15 what it looks like underneath or when it is actually in
16 somebody. So there is nothing hanging outside the head, and
17 that is real different than what I am used to I guess with
18 implants and hearing aids. Can I have the next slide, please?
19 That is the only real external thing that the patient carries
20 around, and it is like a volume control program. Otherwise,
21 everything is inside the head.

22 So this leads to a couple of things that I guess
23 I would like to just ask the committee to consider, and maybe
24 they are already thinking about these things, but when they
25 draft the guidelines for evaluation, there is some new issues

1 and maybe opportunities here that I just want to make sure that
2 we are all kind of aware of. Can I have the next one, please.

3 So this is the first totally implantable device
4 that I guess that I have been -- that I am familiar with, and we
5 just wanted to make sure that the guidelines are going to take
6 whatever new principles that this has into consideration. And
7 what we are thinking is that a device like this offers benefits
8 or has the potential to offer benefits that go beyond just
9 typical laboratory measures. So we don't really know what the
10 right method of testing this is yet. Sort of a more quality of
11 life kind of benefits. I liken it almost to glasses, contact
12 lenses, and Lasik surgery, and each one has a different level of
13 quality of life benefits that goes with it, too.

14 So when I was asked how to evaluate it, of course
15 I immediately started thinking, well, the speech recognition,
16 and the ways that I evaluate implants. But maybe that we need
17 to think about some other things, and I have been studying it a
18 little bit. Can I have the next one?

19 So maybe the aspect of utility for totally
20 implantable devices might be a little bit different, or a little
21 broader than for the traditional devices that we have seen out
22 there, and we think that maybe patient satisfaction or how well,
23 or how and where they use this are important.

24 Another thing that comes up from the industry all
25 the time is that 80 percent, or some 70 to 80 percent of people

1 with significant hearing loss refuse to wear a hearing aid,
2 because they don't want to have something hanging outside their
3 head.

4 And this device, you know, may not fall into that category.
5 There may be some people that don't or wouldn't mind having an
6 invisible device. In that case, you know, I see that the
7 guidelines have in there unaided condition as one of the
8 controls to measure against. And that might actually be a
9 valuable condition, because that might be the only other
10 alternative that people would consider. You know, they might
11 say that I want nothing on my head, and so I want to compare to
12 unaided. I don't care if this really compares to a hearing aid
13 or not. So that is something that you might want to consider.
14 The next one, please. And here is what we have sort of come up
15 with as a list at one of our times when we sat down on how to
16 measure the utility of these devices.

17 Of course, there is the traditional ones like
18 bandwidth and gain, and those of you who know my research in
19 hearing aids know that I don't necessarily believe that more
20 bandwidth and more gain is always a good thing. We have shown
21 that when you get a severe hearing loss in the high frequencies
22 that sometimes an additional gain up there doesn't really help
23 you. So I don't think that these devices should be evaluated
24 strictly in terms of band width and gain. At some point, it is
25 diminishing return.

1 Speech recognition, of course, is the traditional
2 method, and I don't think anybody would find any fault with
3 that. But we were thinking of some other ones along the line,
4 and quality of life measures are probably going to be important
5 when you have a device that falls into a whole new category like
6 this.

7 A lack of occluded sensation and the eardrum is
8 used as the microphone, and when I put the last one down there,
9 the ability to hear in different environments, such as in the
10 shower or swimming, and athletics where they are sweating, and
11 pillow talk in bed, all these kinds of places.

12 So you might find that two devices, one
13 implantable and one not implantable, might give exactly the same
14 speech recognition score in a laboratory setting, but the
15 totally implantable device can give that same benefit of speech
16 recognition in a lot of other situations that the patient
17 wouldn't be able to wear the other device. So I think that
18 maybe we might want to take that into consideration. I mean,
19 people don't wear a hearing aid or implants when they are
20 swimming, and so this is something else that might need to be
21 taken into consideration. Next, please.

22 These are some things that we think could
23 potentially be benefits of totally implantable devices that may
24 be the measurements that we are looking at that you might want
25 to take into consideration if there are measures that could

1 incorporate this. No microphone wind noise, no ear canal
2 irritation, and there are probably going to be some advantages
3 in having the ear drum as a microphone, because you can use the
4 whole pinna in the ear canal then in a way that it is naturally.

5 So maybe there is going to be some test in terms of
6 localization in the vertical plane, and localization tests that
7 may really be around, and that might be something that we want
8 to take a look at, and it might be a real advantage in a device
9 like this. No daily maintenance. This thing has -- their
10 device has a 7 or 8 year battery. So that is not going to show
11 up in a speech recognition test, but it certainly would be an
12 advantage, I think, for people who want to wear them.

13 And usability, you might want to even look at how
14 many hours a day they wear this thing, and how many hours a day
15 they use it. That is sort of an objective measure sometimes of
16 how much utility something provides. And something like this,
17 they might use it almost all the time.

18 CHAIRPERSON GULYA: This is your two minute
19 warning.

20 DR. TURNER: Okay. The next one. We are almost
21 done. The only other thing we thought about in the draft that
22 we thought we might at least ask about is that it wasn't quite
23 certain when they did want to compare it to a hearing aid, we
24 used the words "state of the art hearing aid." We were sort of
25 thinking that if the patient has their own hearing aid that it

1 meets the NAL or some program standards that are out there, it
2 is probably a good enough comparison.

3 There is a bunch of research out of the
4 University of Iowa from Ruth Bentler's lab that shows that a
5 well-fit analog aid provides the same benefit as digital aid.
6 So really as long as the comparison can meet the canal targets
7 or something like that, it is probably going to be an
8 appropriate control, rather than having to buy a brand new
9 digital aid as a comparison, which can really do the same job.
10 Next.

11 So, in summary, I just wanted to point out and
12 familiarize the committee with some of the potential differences
13 that would come with a totally implantable device and some of
14 the questions that I have been finding, and applying a lot of
15 thought as to how to evaluate something like this, because it is
16 a whole new thing. So we might want to take into consideration
17 the ability to understand speech in basically any environment
18 the subject or the patient wants to, in swimming, shower, in
19 bed, and all those things. And I don't know whether that would
20 be audiological measures, which is one way, but there is also
21 questionnaires. I know that there are a lot of questionnaires
22 out there that asks those sort of things, like self-image and
23 stuff.
24 So it might lead to something that the committee wants to
25 consider, and that is all that I really wanted to say.

1 CHAIRPERSON GULYA: Thank you very much, Dr.
2 Turner. I guess I will let the panel have an opportunity to ask
3 Dr. Turner -- Dr. Turner, don't leave so quickly. I will see if
4 any of the panel members have any questions for you. Why don't
5 we start towards Dr. Walden, and then maybe work our way around.
6 Paul. Dr. Kileny.

7 DR. KILENY: Thank you, Dr. Gulya. Dr. Turner,
8 you mentioned quality of life as an indicator of efficacy. Do
9 you have any specific quality of life assessment tools in mind
10 that could be applied for this particular device, or this class
11 of devices rather?

12 DR. TURNER: You know, the general quality of
13 life stuff is not my field, and so I don't know that. I am sure
14 that there is some general ones that are used for devices, and
15 so that I could not tell you about.

16 I mentioned the Robin Cox ones and I know the
17 AFAB and she has a new one called the SADL, SADL or something,
18 that gets at -- oh, what do they call it -- patient self-image
19 and quality of life. I think with a little modification of the
20 wording in those, they might be appropriate, because some of the
21 questions say, you know, how do you feel with the hearing aid
22 on, and you couldn't really say that with an implantable device.
23 Those might be appropriate to use, and that's all that I have
24 found so far, but there is probably more out there. I am sure
25 there is people that know that stuff even better than I do.

1 CHAIRPERSON GULYA: Anybody else with a question?

2 Brenda.

3 DR. LONSBURY-MARTIN: Dr. Turner, with this
4 device that uses the eardrum as the microphone as you stated, is
5 it still possible to do middle ear testing, or is there a load
6 on the drum, or --

7 DR. TURNER: You know, every day I learn
8 something new about this, and I asked that same question
9 yesterday when I was -- you know, I said what happens when you
10 do a tympanigram on somebody like this, and they showed me what
11 it looked like, and it looked like of normal. I don't know why,
12 but --

13 DR. LONSBURY-MARTIN: So it isn't a drag on the
14 drum?

15 DR. TURNER: It looked kind of normal, I guess.
16 I am not sure what all that means, because there is hardware
17 back there that basically is broken, and maybe there is a sensor
18 to pick up the vibrations and a sensor to drive it. I am not
19 sure why it looked normal. I would imagine that if there was
20 fluid behind the drum that it probably would give us like
21 tympanigram skill, but I am guessing. I have no comparable
22 data.

23 CHAIRPERSON GULYA: Dr. Tucci.

24 DR. TUCCI: Yes. Dr. Turner, since this is
25 totally implantable, I was just wondering how the power issues

1 were addressed. I remember that orange rule.

2 DR. TURNER: I am an audiological consultant,
3 right? So I don't really make the product. The engineers just
4 told me that the battery lasts 6 or 7 years, and that is about
5 all the more that I can say. I don't really know. Oh, here is
6 an answer.

7 MS. MANN: My name is Jennifer Mann, with St.
8 Croix Medical. I would like to point out that the battery is
9 only 4 to 5 years, depending on usage.

10 DR. TURNER: Oh, sorry.

11 CHAIRPERSON GULYA: Dr. Soli.

12 DR. SOLI: Yes. One of the measures that you
13 have proposed to characterize the division was its gain, and I
14 am curious as to how you would suggest we might measure that,
15 because it is a fully implanted device, and how would you
16 propose to measure its gain?

17 DR. TURNER: Again, I got no right answers on
18 this one. But you obviously don't have the luxury that you do
19 in a traditional hearing made by sticking a probe on the other
20 side. The company before I came along, and they have continued
21 it this last couple of weeks I see, is to measure functional
22 gain. You know, aided and unaided audiograms. We know that
23 there is problems with functional gain, and we don't use it in
24 hearing aids anymore.

25 DR. SOLI: How can you measure functional gain if

1 the ossicular chain is disarticulated?

2 DR. TURNER: Functional gain is aided versus
3 unaided threshold.

4 DR. SOLI: How can you measure unaided?

5 DR. TURNER: Pre. Pre. The odd thing, too, is
6 that when you measure aided thresholds with this, you can
7 measure them under headphones. You don't need sound field any
8 more. That was strange, huh?

9 MR. CROMPTON: Dr. Turner, you mentioned state of
10 the art --

11 CHAIRPERSON GULYA: Can you identify yourself,
12 please.

13 MR. CROMPTON: Oh, I'm sorry, Mike Crompton,
14 Industry Rep. You mentioned the challenge compared to a state-
15 of-the-art hearing aid, and I was wondering -- and this is one
16 thing that I had some input on. As a baseline measure, you
17 measured NAL target, and then some sort of reference or
18 certification by
19 the audiologist on the subject or patient that the hearing aid
20 was in fact optimally fit. In your experience would that serve
21 as a valid baseline?

22 DR. TURNER: I think it is about the best that
23 people can do these days. I mean, the NAL, the most recent
24 version of NAL is what people tend to say as being the best job.
25 I mean, people don't know what exactly the right formula is,

1 but NAL seems to have the most validation studies done of any
2 formula, and so I am going to guess that that is about the best
3 one. I am sure that the committee agrees or disagrees, but NAL
4 seems to be the only people that have done any validation on
5 that stuff.

6 DR. BLUMENSTEIN: Brent Blumenstein. What you
7 are suggesting here is to up-weight a quality of life, or
8 measures along those lines in the consideration of the overall
9 performance of the device, in addition to the performance of the
10 device.

11 Suppose the device comes in to have a slightly
12 less performance than is considered to be standard, but has a
13 higher quality of life measure. How would you weight those?

14 DR. TURNER: I don't know, but that is a real
15 good issue, and I think it is a good point I personally take a
16 little less correction in my glasses for distances so that I can
17 read the print close, and so things like that, people make
18 compromises all the time. I don't know, but that is an
19 interesting issue though. Some patients may say that it is
20 implantable or nothing. I don't know what the right answer is,
21 but what I am saying is that I think it should be taken into
22 consideration.

23 CHAIRPERSON GULYA: Joe Hall. Dr. Hall, identify
24 yourself for the transcriber.

25 DR. HALL: Joe Hall. Do we know the implications

1 of using the eardrum as the microphone for the frequency
2 response of the eardrum?

3 DR. TURNER: Yes, the people there have looked at
4 that, particularly in the animal model, and then from --I think
5 Eric Duvall helped them do some analysis on what the human thing
6 would be. And from what I could tell, the eardrum itself rolls
7 off above 2K, and so you are going to lose a little bit of the
8 high frequency on that. But the other implications of it are
9 that you get to use the whole ear canal, and so you are going to
10 get the boost of the canal from 2 to 4. That would be my guess.

11 CHAIRPERSON GULYA: Any other questions from the
12 panel? Paul. Dr. Kileny.

13 DR. KILENY: Do you know what is the average
14 conductive hearing loss due to the cyclical change of articulation
15 in these patients in the unaided measurement?

16 DR. TURNER: I don't know, but I am guessing that
17 it is -- you know, it is a real factor. I think if you just
18 articulate the cyclical change in surgery, what do they get, 50 dB
19 or something probably, right? So I don't know what the data on
20 that is, and maybe somebody from the company knows, but I would
21 imagine that it would be in that range.

22 CHAIRPERSON GULYA: Okay I think we have
23 addressed all of the panel questions. Thank you very much, Dr.
24 Turner.

25 DR. TURNER: Thanks for letting me share

1 something that is really interesting to me. Thank you.

2 CHAIRPERSON GULYA: Thank you for making the
3 effort to be here. We appreciate it. Do we have any other
4 presenters at this time? Okay. Seeing none, I think we will
5 move on to our open committee discussion session, and we will
6 lead off with David Whipple, the Deputy Director of the Division
7 of Ophthalmic and Ear, Nose, and Throat Devices. David, would
8 you like to take it away?

9 MR. WHIPPLE: Yes. I am David Whipple, and good
10 afternoon, everybody. And welcome to the dog days of
11 Washington, D.C. We want to thank you for traveling here in
12 this hot humid weather to be with us and help us out.

13 This is the first opportunity that I have had to
14 address this panel specifically, and usually the gentleman
15 sitting in this chair is our division director, Dr. Ralph
16 Rosenthal. I am usually behind the scenes doing my thing, and
17 whispering in his ear after the panel meetings. Today, however,
18 he couldn't be with us, and he asked me to sit in for him, and I
19 was glad to do that. But he does send his regards to this panel,
20 and will be visiting you and seeing you at the next panel
21 meeting.

22 Before I turn this meeting over to our new ENT
23 branch chief, Dr. Eric Mann, who I will formally introduce in a
24 few moments, I have a couple of specific announcements that I
25 would like to make, personnel announcements.

1 The Director of our Office of Device Evaluation,
2 Dr. Bernie Statland, will be leaving the Food and Drug
3 Administration at the end of next week. Dr. Statland has
4 supported our division while he has been here, and we want to
5 thank him for his support and his generosity to our division
6 while he has been here. He will be leaving and he will be
7 taking up residency in Minnesota, where he is going to pursue
8 his law degree there. So we wish him well on that.

9 At this time, I would also like to announce his
10 replacement, and that is Dr. Dan Schultz. Dr. Schultz is
11 currently our Deputy Office Director for Clinical Policy, and he
12 has been promoted up to the Office Director, and he will take
13 that particular position as soon as Dr. Statland leaves next
14 week. I don't see him here and so I was going to go through a
15 long bio on him, but I will try the short version just for the
16 record.

17 Dr. Schultz received his medical degree from the
18 University of Pittsburgh in 1974. Upon graduating, he entered
19 the Public Health Service, serving in hospitals in the west and
20 southwestern United States, where he was involved in general
21 practice, a surgical residency, and a pediatric surgery
22 fellowship. He also served as the chief of surgery at the Sante
23 Fe Indian Hospital in New Mexico. Dr. Schultz came to the FDA
24 in 1994 as a medical officer in the general surgery devices
25 branch in the Office of Device Evaluation. He was promoted to

1 the chief medical officer in the Division of Reproductive,
2 Abdominal, and ENT Radiology Devices Division, and eventually
3 became Director of that division in the year 2000. Some of you
4 may remember Dan, or have worked with Dan, when he was the
5 division director when ENT was under that division. And as I
6 said, Dan is currently serving as the deputy director for
7 clinical and review policy, and device evaluation, and we
8 congratulate him on his new appointment.

9 Now, last, but not least, I would like to
10 introduce to you our new Chief of the ENT Branch, Dr. Eric Mann.

11 Eric has been with us since November of 2001, and it is truly
12 has been a baptism of fire for that man since he has been here.

13 Eric received his MD and his Ph.D. degree in Immunology from
14 the Medical College of Pennsylvania 1988. He did his residency
15 in Otolaryngology, Head and Neck Surgery, at the University of
16 Connecticut Health Center in 1993. Eric served on active duty
17 in the United States Army at Walter Reed Army Medical Center
18 until 1997, where he later joined the Public Health Service and
19 served as a Medical Officer in the Division of Anti-Infective
20 Drug Products with the FDA until 1999. He then accepted a
21 position as Senior Staff Otolaryngologist in the Otolaryngology
22 and Speech Section at NIH, where he worked until November of
23 2001, when we made him an offer that he couldn't refuse. We
24 stole him from NIH, and we made him our chief of the ENT branch.
25 He is probably having second thoughts about accepting that

1 position at this time, but we are certainly grateful that he
2 accepted it, and certainly proud to have him as our new chief.
3 So, Eric, you've got the floor.

4 DR. MANN: Thank you, Dave. Well, good
5 afternoon, everyone. Since the panel last convened about two
6 years ago, in July of 2000, we have had a number of notable PMA
7 and PMA supplement approvals, and I would like to go over those
8 over the next few minutes and briefly mention some of these
9 devices, and their approved indications for use before we go
10 ahead and move on to the panel discussion of the draft industry
11 guidance document.

12 I have already introduced the members of the Ear,
13 Nose, and Throat Devices Branch to the panel during the closed
14 session this morning, but for members of the audience, aside
15 from myself, the branch consists of Ms. Karen Baker, who is our
16 expert nurse consultant. We have two audiologists scientific
17 reviewers, Ms. Teri Cygnarowicz, and Dr. James Kane. Dr. Sid
18 Jaffee is an otolaryngologist, and provides medical reviews for
19 the branch. And we have Dr. Vasant Malshet, who is a
20 toxicologist, and does toxicology reviews for the breach. We
21 are also privileged to have Ms. Maritze Ortega for outstanding
22 administrative support as our branch secretary. Next slide,
23 please.

24 So moving on to the approvals, I will first cover
25 the implantable middle ear hearing devices. Next slide.

1 The month following our last panel meeting, the
2 Vibrant Soundbridge was approved in accordance with the panel's
3 recommendation for the intended use of providing a useful level
4 of sound perception to individuals via mechanical stimulation of
5 the ossicula. Next slide. It consists of an externally-worn
6 audio speech processor here which converts sound into an
7 electromagnetic signal, and it is transmitted across the skin to
8 an implanted internal receiver.

9 The signal then travels down a conductor link
10 attached to a floating mass transducer, and this is attached to
11 the long process of the incus, and it causes vibration of the
12 ossicular chain and stimulates the cochlea. Next slide, please.

13 This product is indicated for adults with
14 moderate to severe sensory neural hearing loss who desire an
15 alternative to acoustic hearing aids. It is recommended that
16 perspective patients have experience with appropriately fit
17 hearing aids prior to implantation.

18 The FDA has also since approved another
19 implantable middle ear hearing device, the Soundtec Direct Drive
20 System in September of last year, with again essentially the
21 same indications for use as the Vibrant Soundbridge. Next
22 slide, please.

23 The Direct Drive system is a bit different from
24 the Vibrant Soundbridge in that you have an externally worn
25 processor again, but this in-turn connects to an ear mold coil

1 assembly, which is located in the ear canal. This assembly
2 generates an alternating electromagnetic field, which drives a
3 small magnetic implant, which is attached at the ossicles at the
4 incudostapedial joint as shown here in the illustration.

5 That is the only implanted portion of this
6 device, is the magnet, which attaches to the ossicular chain and
7 drives the ossicular chain. Next slide, please.

8 Regarding Cochlear implant devices, since the
9 last panel meeting, we have also had a number of these approved.

10 The COMBI 40 Plus Implant System by MED-EL Corporation received
11 approval almost exactly one year ago from today.

12 It is similar to other approved Cochlear implants, and consists
13 of an externally worn speech processor, which converts sound to
14 an electrical signal, and delivers it to the implant electronics
15 package as is shown here, housed in a ceramic case. The signal
16 is then sent along the electrode to 12 channels along the
17 electrode array, which stimulate the cochlea to produce sound
18 sensation. Next slide, please.

19 The COMBI 40 Plus device, as indicated for
20 patients or for adults with bilateral severe to profound sensory
21 neural hearing loss, with limited benefit from amplification,
22 and limited benefit is defined as hearing in noise test scores
23 less than equal to 40 percent in the best aided condition. In
24 pediatric patients, it is approved for bilateral profound
25 sensory neural hearing loss, with lack of benefit from

1 amplification defined as lack of auditory skill development in
2 younger children, and is less than a 20 percent score on the
3 multi-syllabic lexical neighborhood test, or the lexical
4 neighborhood test.

5 As of last month, MED-EL also has received
6 approval for the COMBI 40 Plus S Electrode Array, which is also
7 known as the compressed array, and has also received approval
8 for the COMBI 40 Plus GB, also known as the split electrode
9 array. Next slide, please.

10 The approved indications for these new electrodes
11 are for individuals with severe to profound hearing loss, with
12 ossified and/or malformed cochleas, who obtain little benefit
13 from acoustic amplification in the best-aided condition. Of
14 note, Cochlear Corporation has also recently received approval
15 for a double electrode array, which is analogous to the MED-EL
16 split ray, and is indicated for patients who have cochlear
17 ossification preventing full insertion of a standard Nucleus 24
18 cochlear implant electrode array.

19 Now as an extension of their cochlear implant
20 technology, the Cochlear Corporation has also developed and
21 received approval from the FDA for the first auditory brain stem
22 implant device, and this was back in October of 2000. Its
23 intended use is to restore useful hearing via electrical
24 stimulation of the cochlear nucleus. A body worn speech
25 processor delivers the electrical signal to the implant

1 receiver/stimulator shown here, and it looks very similar to
2 that of the nucleus cochlear implant, and then the signal
3 travels along the electrode array here to terminate in a 21
4 electrode brainstem array. And as shown here in the diagram the
5 electrode lead traverses the temporal bone and terminates here,
6 and the brain stem over the cochlea nucleus. Next slide,
7 please.

8 This device is indicated for use in patients aged
9 12 and older with neurofibromatosis Type 2. It can be implanted
10 either during the first or second side tumor removal in
11 patients, or in patients with previously removed tumors
12 bilaterally.

13 Because patient results are typically less than
14 achieved with cochlear implant recipients, it is important that
15 the patient have realistic expectations preoperatively, and a
16 high level of motivation for rehabilitation.

17 Finally, I would like to conclude the branch
18 update by reading a brief statement on the recently publicized
19 issue meningitis in cochlear implant recipients, and I would
20 also refer you to the FDA website on this issue, which is at the
21 bottom of the slide, for further details on this. I would point
22 out that this website is administered by the Office of
23 Surveillance and Biometrics, and that is OSB if you were a
24 little confused about that terminology during the closed
25 session.

1 So I will now read the statement about meningitis
2 in cochlear implant recipients. The FDA has recently become
3 aware of a possible association between cochlear implants and
4 the occurrence of bacterial meningitis. We have received more
5 than 25 reports from the United States, and more than 20 reports
6 from abroad, of bacterial meningitis associated with cochlear
7 implantation.

8 Cases have occurred in children and adults,
9 ranging in age from 21 months to 82 years. The onset of
10 meningitis symptoms has ranged from less than 24 hours to
11 greater than 5 years from the time of implant. At least 12
12 known deaths have resulted from these cases, with three of these
13 deaths occurring in the United States. Although most cases have
14 been caused by staphylococcus pneumoniae, also known as
15 pneumococcus, other organisms, including Hemophilus influenza,
16 enterococcus, escherichia E. coli, and streptococcus viridans
17 have also been cultured.

18 Most of the patients have been children,
19 predominantly under the age of five, but some adults with
20 cochlear implants have also developed meningitis.
21 The cause of meningitis in cochlear implant recipients has not
22 been established.

23 A small percentage of deaf patients may have
24 congenital abnormalities of the cochlea or inner ear which
25 predispose them to meningitis even prior to implantation.

1 Patients who become deaf as a result of meningitis are also at
2 increased risk of subsequent episodes of meningitis compared to
3 the general population.

4 Other predisposing factors may include young age,
5 less than five years, otitis media, immunodeficiency, or
6 surgical technique. The cochlear implant, because it is a
7 foreign body, may act as a nidus for infection when patients
8 have bacterial illnesses.

9 Design of the electrode has also been considered
10 as a predisposing factor. The Advanced Bionics Clarion device
11 differs from other currently marketed cochlear implants, because
12 it uses an additional piece called the positioner, which is
13 introduced next to the electrode into the cochlea to facilitate
14 transmission of sound information to the auditory nerve.

15 Advanced bionics has agreed to discontinue use of
16 the positioner in these countries and will be marketing one of
17 their cochlear implant systems containing the hypoelectrus
18 electrode without positioner. The company has also initiated a
19 voluntary recall of the unimplanted Clarion device in the United
20 States, and has announced that it will be seeking FDA approval
21 for the hypoelectrus electrode without positioner.

22 The FDA believes that cochlear implant
23 candidates, as well as those already implanted, may benefit from
24 vaccinations against organisms that commonly cause bacterial
25 meningitis, particularly streptococcus pneumoninae, and

1 Hemophilus influenza. The immunizations status should be
2 ascertained for all candidates for cochlear implants prior to
3 surgery, as well as for those with an existing implant. We
4 would again refer you to the FDA website on the screen for
5 specific vaccination recommendations. In some of the reported
6 cases of meningitis in cochlear implant recipients, patients may
7 have had overt or subclinical signs of otitis media prior to
8 surgery, or before the meningitis developed. Physicians are
9 encouraged to consider appropriate prophylactic perioperative
10 antibiotic treatment, and to diagnose and treat otitis media
11 promptly in patients with cochlear implants.

12 We encourage you to report cases of meningitis in
13 cochlear implant. Next slide, please. You can report these
14 either directly to the manufacturer or you can report them to
15 MedWatch, the FDA's voluntary reporting program. You may submit
16 these reports to MedWatch in one of four ways. You can access
17 the website listed there, and you can call the phone number, or
18 fax number, or mail to the address shown on the slide.

19 A team of experts from various offices within
20 CDRH has been formed to assess this issue and we are working
21 closely with manufacturers and collaborating with our colleagues
22 at the CDC to gather complete information on all cases that have
23 occurred within the United States. Although the FDA is
24 carefully investigating these reported cases of meningitis, we
25 recognize that cochlear implantation has been a highly effective

1 procedure to restore hearing function in over 20,000 patients in
2 the United States, and approximately 60,000 patients worldwide.

3 We are currently working with the CDC to investigate ways to
4 better define any risk of meningitis associated with cochlear
5 implantation in this population, and to develop measures that
6 can be implemented to reduce any identified risks. This
7 concludes the branch update. Thank you.

8 CHAIRPERSON GULYA: Eric, would it be fair game
9 for any of the panelists to ask you any questions on anything
10 they need clarified? Any questions from the panel or anything
11 that needs clarification? Are we okay?

12 (No audible response.)

13 CHAIRPERSON GULYA: Okay. Thank you. And I
14 guess next we are going to have Teri Cygnarowicz give us the FDA
15 presentation.

16 DR. CYGNAROWICZ: Good afternoon, distinguished
17 panel. It is an honor to be here and to present to you the
18 draft guidance for the implantable middle ear hearing device or
19 IMEHD for discussion and review at today's open public hearing.

20
21 It is always a disadvantage to be after lunch,
22 because listening to anything is always -- it is just hard to
23 stay awake, and it is also difficult because I have been so
24 close to this project that I can't see the forest or the trees,
25 and of course I have gotten to the point that I think it is all

1 very boring. But I think that it is a very important area, and
2 it is an exciting device area that I have been involved in for
3 quite some time now, probably since the very beginning of it.
4 And I think that it is important for me to give you some
5 background as to what went into the development of this document
6 that is before you today.

7 The guidance has been based upon the following
8 conditions and events. These include the June 1999 ENT Device
9 Advisory Panel Meeting, current scientific knowledge, clinical
10 experience with IMEHDS, and very importantly, the knowledge that
11 we have gained and continue to gain along the way.

12 Much effort and input has taken place to develop
13 and write such a draft. Let me highlight some important aspects
14 of these efforts. Next.

15 You may be aware that in the June of 1999 panel
16 meeting -- and some of you may have participated, we discussed
17 issues regarding this new device technology. We asked the
18 advisory panel assembled at that time specific questions that we
19 had regarding the preclinical and clinical study of IMEHDS. We
20 also had been working with different firms who had started their
21 clinical trials. It was the answers and discussion at that time
22 which helped form the basis for this guidance, as well as
23 assisting companies develop their clinical studies. Next.

24 This slide highlights the areas of concern that
25 we brought before the panel in 1999. Simply put, we asked

1 questions regarding safety, i.e., how much benefit justifies
2 performing surgery on an oftentimes perfectly normal middle ear.

3 We also asked questions related to the broader issue of risk
4 versus benefit of these devices, and how best to evaluate the
5 effectiveness of the IMEHD. We specifically asked the panel
6 about the comparative control condition and measuring changes in
7 residual hearing. Next.

8 As with any area of medicine, but in particular
9 with medical devices, our current scientific knowledge is really
10 an ongoing constantly evolving, and changing, and hopefully
11 improving scientific knowledge. Even so, we continue to learn
12 from each other. Next.

13 I must underscore a very important item, and that
14 is this guidance is just that, guidance. Often times technology
15 of IMHEDs differ from each other, and as the technology evolves
16 over time, some of the items contained in this document may be
17 impossible, or there may be a better way of answering a
18 particular question. I want to point out for those of you who
19 have actually taken the document itself, the guidance itself,
20 from the table outside, that the format on the pagination of
21 that document out there slightly differs from what was mailed to
22 the panel in your panel mail outs. So when you discuss it, each
23 of you may be talking about a particular page number, and it
24 might be more helpful to talk about it in a section.

25 Okay. At the inset, I would like you to refer to

1 the draft guidance, and turn to page 1, or there is actually a
2 boxed paragraph above the introduction, and I just want to point
3 out that specifically the last sentence states, "An alternative
4 approach may be used if such approach satisfies the requirements
5 of the applicable statutes and regulations." Next.

6 If you will notice, in the introduction on page
7 one further down, it does explain in paragraph 3 that deviations
8 from this guidance are allowed, but the FDA would like to see an
9 explanation and justification for such a deviation. Also, a
10 sponsor is encouraged to examine the least burdensome approach
11 website referenced on the following page. Just remember,
12 guidance is guidance, and at this point, this is a draft
13 guidance. Moving on. Next slide.

14 Today we have many clinicians in-house who have
15 come to the FDA with a variety of experience, and of course the
16 agency has you, our advisory panel, to supplement our knowledge
17 and expertise. Next. But also other disciplines, such as those
18 listed here, are typically involved in every submission for a
19 new product or significant change to a product. These same
20 disciplines, and the individuals behind them, had a lot to do
21 with developing this document, including commenting on several
22 drafts of the version that you will be discussing today. And
23 let's not forget the input that we received from this panel in
24 1999, but also that in July of 2000, when the first IMEHD PMA
25 was presented, discussed, and an approval was recommended to the

1 FDA for the symphonic Vibrant Soundbridge.

2 Also, last September, the FDA approved the second
3 IMEHD PMA for the Soundtec Direct System. Next. Which brings
4 me to today. The draft guidance document before you has been
5 publicly available for comment since June 12th, 2002.

6 The 90 day comment period ends on September 12th, at which time
7 we will take into consideration and address all written
8 comments, revisions to the document, if necessary, will then be
9 made, and the final guidance will be published shortly
10 thereafter.

11 Today, we ask next that you review and discuss
12 the guidance. You will notice via the table of contents that
13 there are seven sections and two appendices. The goal here was
14 to prevent areas that the FDA would want to see in a pre-market
15 notification, or pre-market approval application. Excuse me.
16 This information, unique to the IMEHD, includes device
17 description, manufacturing information, pre-clinical testing,
18 clinical trial details, including unique aspects of the clinical
19 protocol, and clinical results. The appendices provides areas
20 of importance regarding informed consent and labeling. You can
21 scroll down. Next. In developing this guidance and during the
22 review of proposed clinical trial protocols, and applications
23 for PMA approval, there have been repeated areas of concern that
24 continue to arise, both in the pre-clinical and clinical
25 studies.

1 Today we have asked you to address and discuss
2 three questions we have that will assist us in ensuring a
3 quality document. We sincerely appreciate your assistance.
4 Next.

5 The following slides will have each question
6 detailed. We have asked Dr. Paul Kileny, University of
7 Michigan; Dr. Sigfrid Soli, House Ear Institute; and Dr. Donald
8 Eddington, Massachusetts Institute of Technology, to lead the
9 discussion for questions 1, 2(a) and 3, respectively. Dr. Julia
10 Gulya, the panel Chair, will lead the discussion for the
11 remaining questions, 2(b) and (c).

12 So we start with this question. A device which
13 has patient contacting material must have specific
14 biocompatibility testing, such as cytotoxicity. Also,
15 historically, we have seen specific animal studies to examine
16 the load of the device on the ossicles, erosion of the ossicles,
17 or effect of stimulation on residual hearing, just to name a few
18 examples. As stated on page 6 of the document, testing at all
19 may depend upon the device design.

20 What I am going to do is I am going to go through
21 and I am going to read each question, starting with this one.
22 This must have been an earlier draft of these slides, because I
23 did change these to have a number on them. So, just work with
24 me here.

25 "What is the role of animal studies in the

1 development of an IMEHD? When should preclinical animal studies
2 be performed to support the safety and performance of an IMEHD?"

3 That is question number one.

4 Question Number 2. "What additional assessments,
5 if any, would you recommend be included in Section 5,
6 Investigational Device Exemptions, to evaluate the safety and
7 effectiveness of the IMHED?"

8 "(a) Currently, there are several hearing aid
9 fitting algorithms for conventional hearing aids, based on real
10 ear measurement techniques. These algorithms predict
11 appropriate gain as a function of frequency for various
12 patterns/magnitudes of hearing loss and hearing aid circuitry.
13 For example, linear versus compression."

14 "Should the IMEHD manufacturers be responsible
15 for developing similar fitting algorithms for their devices?"

16 "And if so should there be common units of
17 measurement among different manufacturers?"

18 Question Number 2(b): "What control conditions
19 should studies with an IMEHD include? Should it be state of the
20 art acoustic hearing aids? If so, how does one define state of
21 the art or optimally fit if they are to be utilized in the
22 controls? Should the condition include a comparison to the best
23 aided condition, including binaural amplification?"

24 Question Number 2(c): "Previous clinical studies
25 with two approved IMEHDs showed enhanced patient satisfaction

1 with these devices despite the fact that objective hearing
2 assessment results were similar to those using conventional
3 hearing aids. What additional assessments, if any, could be
4 used to demonstrate an enhancement in hearing performance to
5 account for a subjective improvement in patient satisfaction?"
6 Next.

7 And lastly, Item 3, "Conventional hearing aid
8 labeling includes performance characteristics based on
9 standardized measurement methodology, i.e., ANSI S3.22 1996."
10 Until we get another one out.

11 "Given the different types of implantable middle-
12 ear hearing devices, i.e., semi versus totally -implantable,
13 electromagnetic versus piezoelectric, what if any performance
14 characteristics can be shared among these different device
15 types? What performance characteristics would you want to
16 standardize and include in device labeling (Appendix B) common
17 to all IMEHD devices?"

18 We look forward to a very interesting discussion
19 this afternoon and now I would like to turn the meeting over to
20 the Chairperson, Dr. Gulya.

21 CHAIRPERSON GULYA: Thank you very much. Well,
22 this is how I propose to address our discussion of the
23 questions. The way I see it, we really have five questions
24 before us. I think we can take the first two questions, give
25 each one of them about 20 minutes, and take what I assume will

1 be a badly needed 15 minute break at that point in time, and
2 then deal with the remaining two questions in 40 minutes, and I
3 think we should end up just about fine. Okay. Any objections
4 there?

5 Okay. Good. All right. First of all, I would
6 like to see if there are any questions for Teri before we dive
7 right into her questions. Anything that you need clarified, any
8 questions at all? Do we need any help?

9 I think that was a very nice presentation, and I
10 think you set us up real well. Okay. Dr. Blumenstein.

11 DR. BLUMENSTEIN: Yes. We are focused on the
12 questions that have been raised by you, I suppose, or the --

13 DR. CYGNAROWICZ: The branch, the division.

14 DR. BLUMENSTEIN: The division. I didn't know
15 what to call it. But I also noticed some additional things that
16 I would change -- wordings, phrases, and things of that nature.

17 I assume that we are not going to get into that here.

18 CHAIRPERSON GULYA: Well, you can certainly
19 address it on your letterhead and give it to Sally Thornton, and
20 they will submit it to the docket for you. Similarly, if there
21 are issues of concern to the members of the public that really
22 do not address the central focus of the discussion of the
23 questions, we certainly are very interested in hearing from you,
24 and entering those into the docket.

25 But perhaps in the interest of focusing on the

1 critical issues, if you similarly would submit your thoughts on
2 your letterhead and send it into the FDA, and you have to
3 indicate the docket number. What is the number, 4106?

4 MS. THORNTON: The docket number is 1406.

5 CHAIRPERSON GULYA: 1406. My dyslexia came
6 through again. Okay.

7 MS. THORNTON: I believe that is on the second
8 page of the guidance as it is printed out.

9 CHAIRPERSON GULYA: Okay. Thank you. All right.
10 So, Paul, you were supposed to be our summarizer and discussion
11 leader for this first question. Are you ready?

12 DR. KILENY: Yes, I am, and thank you very much,
13 and thank you, Teri, for preparing these questions for us. And
14 what I would like to do is to share with you some thoughts on
15 the matter of the role of animal research as a basis for our
16 discussion.

17 Implantable middle ear amplification devices are
18 surgically placed with a prostheses, typically coupled to a
19 component of the ossicular chain of the middle ear.

20 While the specific mode of attachment and the drive mechanism
21 and technologies differ, these devices share the principle of
22 directing driving the ossicular chain, the input being the
23 environment acoustic stimulation, including speech, delivered to
24 the microphone of the system.

25 All the devices also include processing stages

1 where the input signal is conditioned in a variety of ways. Due
2 to the nature of these devices, I believe that animal studies
3 may contribute significantly to determine the safety and
4 effectiveness.

5 I would like to divide my remarks into two areas,
6 the first area being applications related to safety issues
7 related to the biological system, or the auditory system in our
8 case.

9 Following safety related issues associated with
10 the biological system -- middle ear, external ear, temporal bone
11 -- may be investigated through appropriately designed and
12 controlled animal studies.

13 Number 1, biocompatibility of materials used to
14 construct the device. This would be appropriate in particular
15 if in future designs new materials would be used, including
16 looking at concerns regarding prolonged contact of these
17 materials with living tissue that have not been previously
18 investigated.

19 Number 2. The risk of tissue remodeling, such as
20 bone erosion or resorption in response to prolonged contact with
21 the device; mounting hardware may also be investigated.

22 Additionally, in those cases where the ossicular
23 chain is temporarily or acutely decoupled, it would be possible
24 to investigate the possible long term effects of ossicular
25 joints to determine whether phenomenon such as ankylosis or

1 discontinuity might occur, and how does that affect aided and
2 unaided hearing.

3 Number 3. Animal studies could also contribute
4 to investigate whether there is increased susceptibility to
5 microorganisms or other pathogens that may promote or trigger
6 the transmission of infection.

7 Number 4. Animal studies may also afford
8 investigations of the effects of the surgical technique on the
9 maintenance of the integrity of the conductive mechanism to help
10 predict whether if necessary a patient with an implanted middle
11 ear amplification device may transition back to conventional
12 hearing aids in an effective manner.

13 And, Number 5, in this area, another important
14 issue that may be investigated through appropriately designed
15 and controlled animal studies is the risk of acoustic over-
16 stimulation, resulting in noise induced hearing loss when
17 activating the implantable middle ear amplification device over
18 a longer period of time at peak output levels.

19 This, of course, would avoid the development of
20 noise in this hearing loss. The second area that I would like
21 to address, and in which I believe animal studies might be
22 useful would be applications of such studies related to device
23 effectiveness.

24 Number 1, it is important to determine fatigue
25 and wear properties of the device. This may be investigated by

1 bench top testing through accelerated multi-cycle activations.
2 A more natural way would be to apply those principles to a
3 device implanted in an animal model, where stress, fatigue, and
4 wear properties may be investigated. This way the effects of
5 the biological environmental on the device and its specific
6 component materials may also be investigated. The maintenance
7 of seal or hematicity of the device can be evaluated in this
8 fashion as well.

9 Number 2. Animal studies may be used to
10 determine the long term in vivo reliability of the various
11 implanted components.

12 Number 3. In those cases where the device is
13 totally implanted, including the microphone, the maintenance of
14 the integrity of the implanted microphone may also be determined
15 in this fashion.

16 Number 4. Animal studies will also provide the
17 opportunity to investigate various versions of the same design
18 in terms of gain and frequency response.

19 Number 5. In those cases where devices may be
20 constructed in such a way that they can be later retrofitted
21 from a semi to a totally implanted device, animal studies may be
22 extremely valuable to investigate effective coupling methods and
23 the effects of a second surgical procedure on the implanted
24 device, as well as on the conductive mechanism in terms of
25 safety and effectiveness.

1 In summary, animal studies may be of particular
2 importance in the following cases. First of all, if the surgical
3 approach is very different from currently used approaches, these
4 studies may provide the opportunity to study the effects of the
5 surgical technical and approach on the maintenance of the
6 integrity of the conductive mechanism. When placement of the
7 device requires an acute or chronic modification of the
8 ossicular chain, such as a temporary decoupling of one of the
9 joints, or in some cases a chronic discontinuity of the
10 ossicular chain, or the permanent removal of one of the
11 ossicles, animal studies may be very useful to study the effects
12 in such cases.

13 Finally, animal studies will also be critical in designing and
14 bringing to market the devices that are totally implanted in
15 terms of the maintenance of microphone integrity, which I have
16 mentioned before, and to have the ability to investigate battery
17 life, battery integrity, in a biological system, and battery
18 replacement techniques, as well as transcutaneous charging of
19 batteries in the long term.

20 I would like now to open this for discussion. If
21 any of my colleagues on the panel would like to comment on any
22 of these statements. I am sure that there are many more that
23 many of you can add. I will start with Dr. Walden and kind of
24 move over this way.

25 DR. WALDEN: I was interested in your number four

1 under effectiveness as measuring variations in gain and
2 circuitry response to the implanted device, both from a point of
3 view of quality control of the product and also variations as it
4 is implanted across different animals. How would you measure
5 the output? What would you use as a --

6 DR. KILENY: Well, obviously this would involve
7 some type of objective physiological measure of hearing, such as
8 a cochlear nerve action potential, or an auditory brain stem
9 response, or perhaps some other objective measure.

10 DR. WALDEN: Are there ways to physically look at
11 the vibrations and look at the movements? In the document it
12 mentions one technique which I am not really familiar with. But
13 are there ways to actually look at the movement, and is this the
14 sort of thing that you could do in an animal model, or does this
15 require a temporal bone or cadaver, or that sort of thing?

16 DR. KILENY: Well, I think that there are also
17 ways to objectively look at the mechanics of the system in
18 function with various kinds of techniques, such as a laser
19 vibrometry, for instance, would be one of them, or some type of
20 doppler type of measurement.

21 I am personally not proficient in carrying out
22 these measurements, but I am aware of them, and I think that
23 they are fine-tuned enough that you can do that. Brenda.

24 DR. LONSBURY-MARTIN: Brenda Lonsbury-Martin. I
25 agree, Paul, that for biocompatibility studies that animal

1 studies would really be fit for that application. But I am
2 wondering, as part of what you said was to test the
3 effectiveness in an animal model, and unless you use the actual
4 device that you are going to use clinically, then I think there
5 is some inference problems. If you have to miniaturize it down
6 to a guinea pig, you are going to have a whole different system
7 than in the real world. So what you are suggesting is something
8 like higher order animals, like primates. Otherwise, I think
9 there is going to be a big leap of inferences, and it is going
10 to be awful difficult to assess in an animal model.

11 DR. KILENY: Well I think that it is possible to
12 test the various principles associated with these devices and
13 not necessarily the original device which is scaled for the
14 human temporal bone. Obviously, those would work in a primate
15 model, but it would make it way too cumbersome and expensive to
16 do.

17 But I do believe that the technical principles
18 underlying these devices could be investigated in mammalian
19 models, with a different size and anatomy of the middle ear
20 mechanism, and leave space, and one can then probably
21 extrapolate at least to some extent from those measurements to
22 the full scale human size device. I actually think that if
23 these are done appropriately, one could have a fair amount of
24 valuable data before going to clinical trials, which would make
25 clinical trials more effective and perhaps even less cumbersome

1 in the long run.

2 DR. LONSBURY-MARTIN: Well, I understand with a
3 device that was much more complex, in terms of like a cochlear
4 implant, where there is lots of encoding strategies, and basic
5 information that some of the early animal studies really
6 provided for that field. But the middle ear, granted, we don't
7 know everything about the subtleties of middle ear function, but
8 relatively speaking, it is a much more simple mechanical system
9 to understand than was the transduction at the hair cell level
10 into a code that the brain could understand. So it seems like
11 that it wouldn't be gaining that much information to have a
12 small animal model, assuming that it was supposed to be a
13 laboratory model of some sort. That you have all of the little
14 intricacies of difference in species -- you know, differences in
15 the middle ear ossicula chain and the attachments. And the
16 tendons, the muscles, all these things are quite different for
17 primates between rodent models, for example.

18 I just don't know if I agree that the classic
19 beginning or knowledge base in a small laboratory animal is
20 going to be a model that is really going to buy a lot in this
21 particular problem.

22 DR. KILENY: Linda.

23 MS. HOOD: Linda Hood. Yes, I was thinking
24 somewhat along the lines of what Brenda was, and the importance
25 of defining whatever model was used. I think for purposes of

1 biocompatibility and such, there are many different species that
2 could be used effectively.

3 But I am thinking about in terms of cochlea
4 damage, and differences in the ossicular motion and force on the
5 cochlea that really would give us something comparable. Perhaps
6 there is a way to work out some of those differences across
7 species. I don't know if that is something that is possible or
8 not, The other question I had was I noticed in the document
9 that there is some discussion of electromagnetic fields and MRI,
10 and the effects specifically on the hardware.

11 I am wondering if there would be a role at all to
12 look at the effects of magnetic field in vivo, in terms of
13 whether there is any susceptibility to dislodging or things like
14 that, or if that would be an issue.

15 DR. KILENY: Yes. I mean, I think that could be.

16 I just think that those are issues that probably would lend
17 themselves to in vitro studies. For instance, if there is
18 concern about the effects of magnetic field, as in a magnetic
19 resonance imaging, one could attach these devices to the human
20 temporal bone and place them in the magnetic field in the same
21 position as one's head would normally be in, and that certainly
22 would make it more realistic. But certainly that is another
23 option to do it in an animal model. Dr. Jenkins.

24 DR. JENKINS: I would agree with my colleagues to
25 my right here about the biocompatibility issues being very

1 important to use an animal model for. You mentioned surgical
2 techniques to be worked out in animal models, et cetera. That
3 is not a very good place to work out surgical techniques for
4 implanting in humans. First of all, just techniques alone, we
5 have cadaver temporal bones which are much more effective, and
6 you are actually working in the real structures.

7 But such things as taking apart the ossicular
8 chain and then reversing that and putting it back together, we
9 have been doing that for the last 40 or 50 years, and there is a
10 lot of information in the literature that you take apart that
11 ossicular chain, and how much gain you can get back, et cetera.

12 So I think that really alters very little to use an animal
13 model for the system.

14 DR. KILENY: What about the information regarding
15 disarticulating the ossicular chain and then loading it with
16 something, and then what happens in the long term? Is there any
17 information on that?

18 DR. JENKINS: Well, we load it with various
19 prostheses currently, and we know the type of results that we
20 get with that, you know, and putting a magnet on it, there is
21 really not that type of information there.

22 DR. KILENY: The issue of cochlear effects. I
23 agree that it might be difficult to make a translation from
24 cochlea effects in an animal model to human, but we do actually
25 have an opportunity now, because we have two approved devices

1 out there, and of course we have the benefit maybe of time
2 effects, looking at time effects in those devices, and relating
3 gain to changes in cochlear function. As we see, for example,
4 the emergence of asymmetric sensual function in these
5 individuals, it tells us a great deal, and I put that out there
6 because it may be something that we need to look at through the
7 branch.

8 DR. TUCCI: Debara Tucci. Paul, I noticed that
9 in the past -- I think it is laser vibrometry, which I don't
10 know a lot about, has been used in cadaver specimens to assess
11 functional gain. I wonder what you think about doing that, and
12 if you think that that might be as or more appropriate than some
13 of the animal models for assessing functional benefits of these
14 hearing aids.

15 DR. KILENY: I think if you know -- if you have a
16 target for a ossicular chain displacement, and if that is
17 specifically worked out as to what sort of target ossicular
18 chain displacement there ought to be to achieve a certain amount
19 of gain or hearing correction, yes, that would be the case.

20 But I think given -- and I think that is still a
21 very valuable measurement at a certain stage. But given the
22 variety of coupling mechanisms, and driving mechanisms that
23 these devices have, I am not sure that that would be something
24 that we could come up easily with that type of a target.

25 Maybe a target could be arrived at, but you need

1 to know the transfer functions to the target as they might be
2 different from one type of device to another type, and there are
3 going to be devices out there that we have yet to see. And they
4 maybe are on somebody's computer design program and have not
5 been conceived of yet. So I think that these could be at least
6 in my opinion complimentary.

7 DR. SOLI: Sig Soli. I don't have a lot to add
8 to what the panelists have already said, but I would just add or
9 make a couple of observations. It seems to me that these middle
10 ear devices are intended primarily to transfer energy into the
11 cochlea that causes hearing. And they are meant to substitute
12 by using laboratory input for air conducted acoustic energy. So
13 when you look at a system like that, it is a mechanical system,
14 and its mechanical properties depend on its geometry, its size,
15 its orientation, the method by which the stimulator is affixed
16 to the ossicles. All of those things are different from one
17 species to the next. So I guess I would question beyond a
18 certain point how much information we could get about the real
19 function of the device in animal models.

20 The other thing I would add is that since we are
21 substituting laboratory input for air-conducted sound input, we
22 need to know how the system responds to sound as a calibration
23 or as a reference so that we can interpret the information from
24 the laboratory interface appropriately. And if that information
25 is available in animal models, there may be an opportunity to

1 use an animal model in that respect.

2 DR. EDDINGTON: Don Eddington. It seems to me,
3 Paul, that stapes displacement is something that can be measured
4 reliably, and quite accurately, and in general, at least in
5 terms of the animal models with which I am familiar, can be
6 related directly back to equivalent SDO as a function of
7 frequency. And that seems to be a part preferable methodology
8 over some evoked responses it seems to me.

9 I would like to take a step back a little bit.
10 You have a very interesting list that is fairly long, and each
11 one of those projects is a relatively large project in and of
12 itself. I am wondering if you could try to rank order them, or
13 give us a feeling for whether you are suggesting that each and
14 every one of these ought to be done before some sort of approval
15 is provided, or whether there is some that might be more
16 important in here in your view than others?

17 DR. KILENY: That really was not my intent to
18 suggest that all of these should be done before clinical trials
19 begin. I merely tried to assemble a variety of applications
20 where one could take advantage of an animal model. And
21 certainly there are some that might be more relevant and higher
22 priority than others. Everybody around the table mentioned
23 biocompatibility issues. I think that the integrity of the
24 device within a biological system and its response to contact
25 with a biological system might be some of the most important

1 ones. One can definitely investigate the effects of the
2 mounting hardware or the contact with ossicular chain, and those
3 effects on the integrity and well-being of the ossicular chain
4 where it is mounted.

5 I think it is also important to find out whether
6 the device has the required longevity, and this is especially
7 true for those devices that have many rather intricate
8 mechanical moving components, or maybe likely more wear and tear
9 than other ones that are relatively more static.

10 I can certainly sit down and go over my list and
11 rank order what I have listed, but the idea wasn't that you have
12 got to do everything. these are just options.

13 Roberto.

14 DR. CUEVA: I am Roberto Cueva. One of the
15 things that I think would be appropriate for animal
16 investigation would be the topic of hermicity and not so much
17 the initial manufacturer, which can be fairly well controlled,
18 but after the battery change for some of the totally implantable
19 devices, where the seal would be broken, and you would have to
20 then bring in the -- you would need an electricity source, and
21 any kind of moisture is going to affect the duration of the
22 function of that battery.

23 I am sure that some of this has been worked out at the level of
24 pacemakers and that type of thing where they have to change the
25 device or change the a battery periodically. But that would be

1 one concern where you wouldn't change the entire device, but
2 just the battery, and how do you ensure that good dry seal
3 again.

4 DR. KILENY: And as a I mentioned just earlier, I
5 think the retrofit issue might also be something that could be
6 investigated in an animal model from a semi-implantable to a
7 totally implantable device, and I think that does also address
8 your comments regarding the maintenance of the hematicity of the
9 package.

10 MR. CROMPTON: I am Mike Crompton, Industry Rep,
11 and frankly GOP animal studies are one of the most burdensome
12 aspects that we face. They are time consuming, and very costly,
13 and although industry does agree that at times they are
14 appropriate to determine maybe the safety profile of the device,
15 to date there really has been little or no contribution of these
16 studies to the potential of performance characteristics for
17 effectiveness of the device.

18 And it really is the issues that the panel has
19 discussed this afternoon; what animal model is appropriate. The
20 first device that was approved used a bovine model. A sham
21 control surgery device was -- APR measurements were taken, but
22 they were inconclusive. It did demonstrate, I think, some of
23 the positive tissue remodeling, and so I think those issues were
24 addressed and those were novel for the device at that time.
25 Biocompatibility, frankly, is addressed through internationally

1 recognized standards, and so unless there is a novel biomaterial
2 to go back into the animal is frankly very burdensome.

3 So I think that industry does recognize for
4 safety that it does make sense, and the effectiveness is the
5 crux of the matter. What animal really works. The primates,
6 again, are a very expensive model, but also the ossicular chain
7 is very different. So we tend to follow the lead that Dr. Soli
8 was talking about, and we can model this system as a mechanical
9 system as long as we can characterize the input and measure the
10 effect of output using a human temporal bone, there is
11 variability from bone to bone, to bone, but with a sufficient
12 sample size you can certainly characterize the device.

13 The key, I think, for industry that we are
14 struggling with is how do we use a representative unit so that
15 among the devices the panel could have an equivalent dB sound
16 pressure level output, and I think that is frankly something
17 that industry is struggling with now.

18 We can all start with the same acoustic
19 measurement, and we can use laser developed Doppler vibrometry
20 to look at the transducer output, but that transfer function
21 does vary between the devices. So that is something that
22 industry, frankly, is working towards right now. Thank you.

23 CHAIRPERSON GULYA: Okay. Paul, would you like
24 to summarize.

25 DR. KILENY: Well, I guess I can summarize this

1 discussion that there appears to be support and interest in
2 certain aspects and certain contributions of animal studies in
3 investigating and ultimately bringing to market middle ear
4 implanted amplification devices. In particular, in terms of
5 biocompatibility, in terms of the maintenance of the integrity
6 of the device within a biological system such as maintenance of
7 hematicity. Certainly the emphasis of effectiveness seems to be
8 of more interest than some of the other issues, some of the
9 safety issues that I have brought up.

10 There have been suggestions that mechanical
11 measurements on human temporal bones with the device attached,
12 using laser Doppler vibrometry may be as effective as
13 physiological measurements in animals. One of the concerns is
14 the ability to compare ossicular chain motion and the anatomy of
15 the ossicular chain across species, and certainly to extrapolate
16 from a small mammalian model to the human temporal bone.

17 I guess in terms of the effectiveness or
18 usefulness of animal studies in investigating surgical
19 techniques, it appears that those are best worked out in a human
20 temporal bone, in a cadaver model. Well, help me out here if I
21 am missing anything in my --

22 CHAIRPERSON GULYA: What I will do, Paul, is ask
23 Teri and Eric if they have anything else, or if we have answered
24 their questions for them, or if they have still some
25 information, or if they are happy with what we have done so far.

1 DR. CYGNAROWICZ: I think you have pretty much
2 covered the whole spectrum of pros, cons, areas, the different
3 devices, et cetera.

4 CHAIRPERSON GULYA: Fine. Great. Thanks a lot,
5 Paul.

6 DR. KILENY: Thank you.

7 CHAIRPERSON GULYA: Next we will have Dr. Sig
8 Soli address questions -- and this is getting almost legalistic
9 -- 2(a)(i) and (ii).

10 DR. SOLI: This is Sig Soli. What I would like
11 to do is summarize quite briefly a few of my thoughts and
12 observations regarding those items that you just mentioned.
13 There are many people on the panel who I am sure can contribute
14 substantially to this discussion, and I will leave time for them
15 to do that.

16 First off, I would like to try to perhaps
17 rephrase a little bit of the terminology that is used in the
18 question as it is posed here under 2(a), because I would have
19 phrased it a little bit differently. I would say that there are
20 hearing aid fitting targets. They are not really algorithms
21 necessarily.

22 They are targets and they are targets that are
23 expressed in terms of the amount of amplification or gain that
24 is to be provided to the patient when the hearing aid is in
25 their ear. So they are based as the question states on real ear

1 measurements, and these targets then -- they don't really
2 predict gain. They recommend a particular amount of gain, and
3 often time the gain that is recommended is dependent on the
4 level of the signal at the input, and on the frequency of the
5 signal. The reason that this terminology is so important is
6 because the amount of gain as a function of level and frequency
7 is very important to the benefit of hearing aid devices to their
8 users.

9 We heard Dr. Turner a little earlier talking
10 about the importance of a certain gain prescription called NAL.

11 That is just one example. Now, having said that, it seems to
12 me that the importance of these gain targets and procedures for
13 achieving them in hearing aids underscores their potential
14 importance for use in implantable hearing aid devices. And the
15 reason that I say that is because these devices are indicated
16 for the same population, the same characteristics of sensory and
17 neural hearing impairment.

18 So the short answer to question 2(a)(i) or
19 2(a)(ii), is should the manufacturers be responsible for
20 developing algorithms to achieve fitting targets, and I would
21 say yes, because of the evidence that we have of the benefit of
22 using those targets in the same population when people are
23 fitted with air conduction hearing aids.

24 Number 2(a)(ii) is a little harder in my mind,
25 because common units of measurement. Again relying on Dr.

1 Turner's earlier comments, we are stimulating a system now where
2 we cannot measure its output in an acoustic coupler. We are
3 measuring it in situ, in the human subject.

4 Ideally, I would like to see some means, and I am
5 not sure I know what that means is, some means by which we could
6 know that when we deliver a certain signal to the transmitter
7 that is used with these systems that a certain amount of
8 laboratory force or displacement is created in the middle ear,
9 and measured in neurons or some unit like that.

10 If we could do that, then we could also have some
11 knowledge -- we also need knowledge to relate that displacement
12 to hearing level, or to sensation level for the patient. If we
13 had the ability to do that, then we could talk about common
14 units. We could talk about the output of these devices as we
15 could measure them electrically, and we could relate that to the
16 hearing levels and the sensation levels of the patient who might
17 use them.

18 Again, that is what has been done with hearing
19 aids, and there are international standards that describe the
20 procedures for taking those measurements. And having
21 information like that, I think would be useful to clinicians in
22 selecting devices for patients.

23 Again, once the device is in, it is not something
24 that you can return in 30 days and get a different one as you
25 can with a hearing aid. So the match of the output

1 characteristics of the device expressed in meaningful units for
2 the hearing of the patient, the match of those output
3 characteristics to the need of the patient I think is very
4 important.

5 I will just stop at that. I am sure that there
6 will be questions.

7 DR. CUEVA: Bob Cueva again. Maybe expressing a
8 little bit of my ignorance, but if one of the ways to say
9 measuring the totally implantable device is where you don't have
10 a way to do a sound coupler, what role would it be -- cochlear
11 microphonic play as a kind of internal reflection?

12 Is it gain dependent, or is it the louder you
13 make the sound input, and does the cochlear microphonic reflect
14 that?

15 DR. SOLI: I am probably not the best person to
16 answer that question. There are a number of physiological
17 measures, and our friends over on this side will weigh in right
18 away, I bet.

19 No, there are a number of physiological measures,
20 like the auditory brain stem response, and perhaps the cochlear
21 microphonic. There are reflex measurements that can be taken.

22 The fact that those cannot be used to fit air
23 conduction hearing aids in an accurately acceptable way would
24 cause me to wonder whether they might have any use of that type
25 in this application. Although my physiologist friends might

1 have something else to say about that. Brenda.

2 DR. LONSBURY-MARTIN: Actually, I think Paul
3 would be a great guy to start this discussion off. I mean,
4 when it comes to routes and lights, I can really put out here,
5 but I will save my comments.

6 DR. KILENY: I think that the problem with using
7 the -- for instance, the cochlear microphonic, or the cochlea
8 nerve action potential recorded the minimally invasive methods.

9 The problem is that you are dealing with an auditory system
10 that has been impoverish, in terms of innovation, and so you are
11 beginning with an auditory system that you may not really have a
12 measurable cochlear microphonic with these non-evasive methods,
13 but we can measure them in our patients.

14 And so I think that is where the problem begins,
15 and with any kind of physiological measure. Another idea would
16 be -- and as I was listening to Dr. Soli and to my colleagues
17 here, is in terms of developing fitting algorithms or some kind
18 of an objective measure.

19 What about incorporating in these devices some
20 type of a telemetry measurement, which then can be obviously
21 measured with some type of surface recordings and use that as an
22 indicator, the telemetry being in terms of the telemetry in
23 terms of the displacement of the ossicular chain, or of the
24 device that is mounted on to the ossicular chain? I think that
25 would be far more accurate and would not be dependent on either

1 the current neurological status of the auditory periphery, or
2 the future status, because there could be more loss of afferent
3 nerve fibers, hair cells, et cetera, et cetera.

4 DR. LONSBURY-MARTIN: Well, Paul, I think that is
5 an interesting idea., but in a sense, wouldn't the very best
6 measure be a functional gain that the patient can report through
7 some psychophysical measure, or reaction time, or some
8 behavioral response? I mean, in the end, you want to equate the
9 movement of whatever you are applying to the system to some
10 output, and in the very best situation, you would want to have
11 an output that was measurable in the real world.

12 DR. SOLI: If I could jump back in. Yes, the
13 functional gain measurements are --

14 CHAIRPERSON GULYA: Let's help out the
15 transcribers, and let's just remember to identify ourselves. I
16 think he might be getting lost.

17 DR. SOLI: Sorry. Sig Soli. Functional gain
18 measurements can certainly be made, except perhaps in the case
19 where you do a disarticulation, but maybe you can use a
20 preoperative reference for that. The thing about functional
21 gain measurements is that it is not a measurement that you can
22 take independently of the patient, or you cannot take it in a
23 calibrated way.

24 I was trying to think of some way around that,
25 and the only thing I could come up with is to use the analogy of

1 a bone vibrator and how you calibrate that when you do bone
2 conduction hearing tests. There is a device called an
3 artificial mastoid, and you load the bone vibrator on that
4 mastoid in a specified way, and you can measure the core
5 response between electrical input and laboratory output
6 according to a standardized procedure.

7 It is conceivable that maybe we should consider
8 some type of an artificial loading system that could be used to
9 calibrate the output of middle ear transducers as well. There
10 are artificial ears, and there are artificial mastoids, and
11 there are artificial skulls, and I guess we could have an
12 artificial ossicular chain or something comparable to it as
13 well.

14 DR. EDDINGTON: This is Don Eddington. This is
15 one thing that I was going to suggest in the question session
16 that I was supposed to at least start the discussion on, and
17 that is it seems very feasible given our understanding of the
18 middle ear system and the cochlea load.

19 That a system, a mechanical electric or a
20 mechanical optic system, be made that basically translates the
21 output of these devices to a stapes displacement, which can be
22 then translated to equivalent SPO at the input. And it seems
23 like that is just crying to be done and is something that will
24 be important in trying to determine the degree to which these
25 devices produce the predicted output as a function of the load

1 bearing. So a simulation may be better than in some cases than
2 in using a fresh temporal bone, because one can manipulate the
3 characteristics of the load. And in the case of the fully
4 implantable device, the same thing goes for the implant
5 transducer.

6 So what one would like to have is a system where
7 an acoustics signal is delivered, and the equivalent SPL
8 measured at the output is given, and that is what audiologists
9 use all the time in current acoustic hearing aids. So in terms
10 of it being a clinically useful system, that is something that
11 they will be able to understand, and relate to their past life
12 experience. So I think that would be an important thing to
13 consider.

14 DR. LONSBURY-MARTIN: This is Brenda Lonsbury-
15 Martin. Would that not be an unreasonable burden to ask a
16 manufacturer to develop a system like that?

17 DR. EDDINGTON: I discussed, at least on a very
18 superficial level, this with colleagues of mine who are experts
19 in the middle ear and cochlear load, and their initial reaction
20 is that is probably something that could be done relatively
21 straightforwardly. And if the industrial community
22 got together to do this as a team, it seems like it would
23 benefit them all, and there are individuals with the expertise
24 to do that.

25 DR. WALDEN: Brian Walden. I just wanted to

1 follow up on that notion; that we are talking about technology
2 that doesn't exist, and if we think about prescriptive methods,
3 and real measures, there are ways of predicting something else.

4 And that is sort of predicting how the patient is going to do
5 with issues like speech recognition and how much gain is the
6 person or the device providing.

7 And I am wondering if functional gain in measures of speech
8 recognition at this point are a more reasonable standard.

9 Secondly, when you are going to compare an
10 implantable device to a standard air conduction hearing aid, you
11 have to have units of measure that are going to be comparable
12 there if that is where you want to go with it, as opposed to if
13 you go to the other end, which is how is the patient
14 functioning, in terms of the functional gain that is being
15 provided by the device, or speech recognition, you are after
16 that point. So you kind of see the effect of both devices, and
17 you sort of avoid that problem.

18 DR. SOLI: You can compare apples and apples if
19 you use functional gain, but I think -- and Don sort of took a
20 page out of -- we both had the same pages of notes here, I
21 think, and so that's good.

22 But you get more from what he is proposing than
23 from what I am proposing, because not only do you need to know
24 the functional gain, but you also need to know the vibratory
25 output of this device, and what the corresponding sound pressure

1 level or hearing level might be created with that output to
2 ensure that those levels are safe.

3 DR. WALDEN: Yes.

4 DR. SOLI: But that is something that you know
5 acoustically with a hearing aid, but those numbers aren't known,
6 at least to me, from vibratory output in the middle ear.

7 DR. WALDEN: I think it is important though to
8 distinguish between when you are using measurements to document
9 the outputs in a sort of input-output relationship, which we
10 were talking about earlier, and when you are trying to document
11 user benefit in a more general sense. I think in the one case
12 this may be very applicable, and in the other case, I am not so
13 sure that we need to solve that problem right now, or that we
14 should expect the manufacturers to solve that problem given what
15 these devices do.

16 DR. SOLI: Joe.

17 DR. HALL: Yes, Joe Hall. I just want to chime
18 in on that. I also feel that way, that perhaps the functional
19 gain sensation level base measures something to work with the
20 patient, and to achieve the best outcome is perhaps a front
21 burner thing that should be done fairly immediately.

22 Whereas, the very interesting and important methods
23 related to determining stapes output are perhaps down the line a
24 bit.

25 DR. SOLI: Well, I am not sure that I would agree

1 with that, as long as you know that the stapes output is safe,
2 and as long as you know that it is predictable. Another issue
3 we really have not talked about directly is the efficiency of
4 energy transfer into the middle ear.

5 As you know the middle ear vibrates in a very
6 complex manner, with module displacements and patterns that are
7 both frequency and level dependent, and the way that most middle
8 ear implant actuators function is as a piston. You know, sort
9 of as a one-dimensional vector so to speak.

10 And it may well be that we could measure
11 functional gains that looked just great compared to hearing
12 aids, but we are putting huge amounts of energy into the middle
13 ear to achieve a level of -- a hearing level beyond -- we are
14 putting energy in beyond what we would normally want to see in
15 the middle ear, because of the efficiency of energy transfer.
16 And that is a question that I think needs to be addressed at
17 some point.

18 MS. HOOD: Linda Hood. A couple of things.
19 First of all, I think looking at as Sig was saying both the
20 energy loss, as well as the gain from this, what we really need
21 in terms of the patient is the ultimate outcome, and whether
22 sound is audible to them or not. And I think we can achieve
23 these things through many of the behavioral sorts of measures
24 that we have. I am interested in what Dr. Eddington said about
25 the stapes displacement and integrity. I am wondering if that

1 maybe down the line would also facilitate some kind of system
2 integrity test as an external check of that.

3 DR. EDDINGTON: Don Eddington. I guess the
4 problem that I see is how do you even begin to characterize
5 these devices unless you can effectively relate the output to
6 the input, and one can make various measures on the force of the
7 piston and that sort of thing. But I am not sure how much
8 relevance that has, because the actual stimulus that induces the
9 sensation at this level is the stapes displacement, and I am not
10 suggesting that we are always measuring the stapes displacement.

11 What I am suggesting is that we have a simulated
12 load, just like a cochlear, that tells you that. And once you
13 have that, then you can characterize the device. And until you
14 have something like that, what we are doing is using devices
15 that aren't really characterized. And from a safety standpoint,
16 I think as Sig was pointing out, and also from a functional
17 standpoint, if you don't have some confidence that over the
18 appropriate output level ranges that you are going to have a
19 reliable output delivery system, that seems a bit problematic to
20 me. I agree completely that in terms of performance that the
21 behavioral measures have the face value, and they are the bottom
22 line, and they ought to be pursued.

23 CHAIRPERSON GULYA: Sig, we have got like about
24 two minutes for this segment. So that is the your time.

25 DR. SOLI: To wrap up?

1 CHAIRPERSON GULYA: I think so, unless there is
2 some burning --

3 DR. SOLI: I think there was one other question
4 over here, I think.

5 MR. CROMPTON: Mike Crompton. Just one brief
6 comment. We are pleased to hear that the functional gain
7 measurements, the clinicals are significant to the results in
8 the patient population is what is key.

9 Previously, companies have investigated and come
10 up with relationships, but not consistent between manufacturers
11 of a known acoustic signal, and a known stapes displacement.
12 That is the challenge. I am pleased to hear Dr. Soli and Dr.
13 Eddington saying that there may be a model out there. We do
14 believe it would be unfairly burdensome for one manufacturer to
15 take on that burden, but for industry consortium or academic
16 group to come up with a model would be a great benefit for
17 everyone.

18 DR. SOLI: Okay. Well, I will try to summarize.
19 This is Sig Soli. First, I sense that there was, if not
20 agreement, at least no disagreement that fitting targets are
21 relevant because of the population for whom these are indicated.

22 It is important that manufacturers devise a means of achieving
23 these targets and verifying them as perhaps as functional gain
24 measurements. That seems to be the clinical method of choice,
25 and for many good reasons. Underlying that are issues about

1 safety and characterization of the system, in terms of its
2 input/output characteristics. We have suggested that perhaps
3 devising some kind of a mechanical coupler that would enable
4 calibrated measurements of that type to be taken.

5 I would just add an observation that generally
6 the time that is required to develop these instruments and the
7 standards that go with them is time well spent in the long run,
8 because you spend some time and energy up front, but it creates
9 efficiencies later on and you get it back over and over again.
10 And I guess implicit in what I am saying is what I sense in
11 agreement is that some common units of measurement, perhaps in
12 terms of stapes displacement ultimately, should be the objective
13 of this -- part of this endeavor.

14 CHAIRPERSON GULYA: Thank you very much, Sig.
15 Teri and Eric, do you have what you need out of this?

16 DR. CYGNAROWICZ: Yes.

17 CHAIRPERSON GULYA: Okay. Good.

18 DR. CYGNAROWICZ: It was a very interesting
19 discussion, and yes.

20 CHAIRPERSON GULYA: Okay. Great. Okay. I will
21 tell you what. We are about halfway through addressing these
22 questions. What I propose we do is take a 10 minute break,
23 because it actually takes 15 minutes to get everybody back here.

24 So we will be adjourned until 2:45, and we will probably really
25 get started at 2:50.

1 (Whereupon, at 2:29 p.m., the open session was
2 recessed and resumed at 2:46 p.m.)

3 CHAIRPERSON GULYA: All right. As I figured, it
4 would take a little bit for everybody to get in and settle down,
5 and Joe, and Paul. All right. Very good. I would like to call
6 the panel into order once again.

7 And I have the distinction of leading us through
8 two subquestions, 2(b), or I guess is the case, not 2(b), and
9 then 2(c). So 2(b). What control conditions should studies
10 with an implantable middle ear hearing device include.

11 MS. THORNTON: IMEHD.

12 CHAIRPERSON GULYA: Thank you. That will be
13 easier. Should it be state-of-the-art acoustic hearing aids?
14 If so, how does one define "state-of-the-art" or "Optimally fit"
15 if they are to be utilized in the controls?

16 Should the condition include a comparison to the
17 best aided condition, including binaural amplification?

18 And I think I am going to forego the summary, and
19 I think instead, I guess I will turn right to Brian Walden, and
20 ask him to give us his thoughts. And I am going to target each
21 one of the individuals as we go along, and so you can start
22 formulating your thoughts, because it will happen. Thank you.
23 Brian.

24 DR. WALDEN: Yes. I think that the appropriate
25 control condition or the appropriate experimental design depends

1 upon the clinical utility that you intend for the device, or
2 what your clinical goal is.

3 And quite frankly, I think that when you look for
4 -- the first time I read the document, I felt that it was a
5 little schizophrenic about that point. That it tended to
6 suggest that we had some of standard things that we wanted to
7 accomplish.

8 And so we compared it to the best fitting hearing
9 aid and so on, and we were going to concern ourselves with
10 speech recognition and all these other issues.

11 And I think that Dr. Turner has made an important
12 point, and that is that there may be reasons like acoustic
13 feedback, or the occlusion effect, or convenience, or quality of
14 life issues that could be equally or more important than even
15 cases where you might be willing to tolerate somewhat less in
16 terms of the traditional measures that we think of, that air
17 conduction hearing aids as accomplishing, to acquire these
18 benefits in these other areas.

19 On Section 6, in the second paragraph, I think
20 that actually gets to the point that it is really up to the
21 sponsor to decide what is the intended use or purpose, and
22 therefore, having stated that, that will be the standard to
23 which you will be held, assuming that the FDA agrees that that
24 is not a trivial goal.

25 And then that would dictate your experimental

1 design, your control conditions, and so on. But it may be
2 useful given the concern that Dr. Turner expressed, that that be
3 put up a little more forward in the document.

4 And that it be made quite clear that there may be
5 reasons other than very traditional reasons that a person would
6 want to go toward an implantable device, as opposed to a
7 standard air conduction device, and that it is up to the
8 manufacturer to make a clear case of what the product is
9 intended to do.

10 And then to design an experiment and gather data
11 to support those goals, assuming that the FDA has indicated that
12 is an appropriate goal, a useful goal from the patient's point
13 of view, the consumer's point of view.

14 CHAIRPERSON GULYA: Okay. Thank you, Brian,
15 Joe.

16 DR. HALL: I agree with what Brian just said, and
17 I think that things should be tailored to what the intended
18 benefit of the implanted hearing aid is, particularly in terms
19 of things like should we compare it to binaural hearing, and
20 that is optimally fitted binaural hearing aids.

21 And I think that is sort of idea might be
22 appropriate given the -- a particular tact that was taken in
23 terms of designing the protocol for the implanted aid.

24 But it might be totally inappropriate also, and
25 also in terms of -- for instance, things like compression, and

1 comparing to, let's say, a compression air conduction hearing
2 aid, might be highly appropriate if the implanted hearing aid
3 also has a significant compression component to it.

4 CHAIRPERSON GULYA: Okay.

5 DR. LONSBURY-MARTIN: I agree, too, that I think
6 the main goal here would be to have some comparison to the
7 optimally fit condition, and whatever that be.

8 I sort of think what Chris Turner was talking
9 about, he inferred that every patient would come with an already
10 hearing aid set, and I take it that these devices are more going
11 to people that won't wear hearing aids, no matter what.

12 So they might not come with their own device to
13 compare against, but whatever the optimally fit standard hearing
14 aid device does for these folks, and I would say, too, like Joe
15 said, that binaural conditions seems most natural.

16 But that is the target that you would want to
17 replicate, and then go from there. It seems to me that would be
18 the ideal control condition.

19 CHAIRPERSON GULYA: Okay. Linda.

20 MS. HOOD: Linda Hood. A couple of things.
21 First of all, I think that I agree with what Brian has said. It
22 depends on what the goal is in the device, and what their
23 ultimate goal is.

24 And I think some combination of performance and
25 satisfaction, and quality of life all figures into this.

1 Clearly if someone has a hearing loss, communication ability and
2 improvement of that has to be a goal.

3 So there has to be some way to meet that, whether
4 it be through comparison to current practices for overcoming
5 hearing loss and improving communication. That's important.

6 Along that line, one question I have is if there
7 are people who do not use hearing aids, and never have used
8 hearing aids, is there need to mandate that, and I think that is
9 something that would have to be considered in designing a
10 clinical trial, depending on what the outcome was.

11 But I think communication ability clearly is one
12 thing, but then the other issue as Dr. Turner brought up has to
13 do with patient satisfaction, and having some validated method
14 of assessing that, and I think we get into that later.

15 But they are happy enough to actually use it, and
16 so I think we have to somehow balance these things.

17 CHAIRPERSON GULYA: Okay. Thank you. Herman
18 Jenkins.

19 DR. JENKINS: I am afraid that I have to disagree
20 with these people. You know, you are talking about an aid here
21 that is going to improve hearing, and that is what you want to
22 know. Do they get improvement over the unaided condition, and
23 if that is the case, then it is effective.

24 And you have demonstrated the efficacy in that,
25 and it doesn't have to be against the best stated condition, and

1 that it is going to be better, or worse. That is not really the
2 condition that you are trying to prove when you are trying to
3 prove a device.

4 You want to know is it effective in remediating
5 the disease process there, which is basically do they get
6 improvement over their unaided condition. Now, granted, we all
7 want to know is it better than the air conduction aid, or the
8 bone conduction aid, et cetera.

9 But that is not what you are really trying to
10 prove for this device. You want to know do they get improvement
11 and that is what they are claiming they are doing, and that is
12 your gold standard there.

13 It is not how they do against the junk aid or all
14 these other type things that you have available.

15 DR. HALL: You are not disagreeing with me.

16 CHAIRPERSON GULYA: All right. Paul. Dr.
17 Kileny.

18 DR. KILENY: Thank you. Paul Kileny. As I
19 think about this issue, I am really thinking of the next step,
20 and that is what kinds of patients will be seeking or are
21 seeking implantable middle ear devices.

22 And there is basically two categories of
23 patients. One category of patients would be previous hearing
24 aid users, who for whatever reason -- well, perhaps because
25 their hearing loss has advanced, and they are now seeking a new

1 amplification device, and this could be one of the choices.

2 And in those cases, obviously the comparison
3 ought to be made to their current amplification binaural, and
4 make a decision from there. So the patient comes in, and needs
5 a new hearing aid, is presented with two options; an implantable
6 mid-amplification device that requires surgery, et cetera, or go
7 on with conventional amplification.

8 The other patient category is patients who are de
9 novo seekers of hearing help, and again in those cases you also
10 present them with the two options.

11 And in that case, of course, it would be relevant
12 to compare the performance of the implanted amplification device
13 to an unaided condition. So I think that we need to look at it
14 in both ways.

15 I think we need to recognize these two kinds of
16 patient populations that will be seeking to receive these
17 devices, and have information both about comparison to existing
18 amplification, and conventional amplification, and to unaided
19 hearing.

20 And I certainly agree with everyone here. There
21 is are a variety of standardized quality of life instruments
22 that --

23 CHAIRPERSON GULYA: We will be getting into the
24 quality of life things, yes.

25 DR. KILENY: I'm sorry?

1 CHAIRPERSON GULYA: That is going to be an
2 additional question that we will be getting into, into quality
3 of life issues.

4 DR. KILENY: I don't want to mention it, but the
5 combination of those I think would be ideal. Thank you.

6 CHAIRPERSON GULYA: Okay. Thanks, Paul.

7 DR. JENKINS: Can I just ask a question before
8 you go on to the next person?

9 CHAIRPERSON GULYA: Sure.

10 DR. JENKINS: In addressing this question, are we
11 talking about what the labeling is going to be, or the package
12 insert, or are these the guidelines for the companies in
13 developing their implant?

14 CHAIRPERSON GULYA: This is the testing as I
15 understand it -- and correct me if I am wrong -- testing as to
16 what kind of studies need to be conducted to establish safety
17 and efficacy, and what kind of control groups we need in these
18 studies.

19 DR. JENKINS: So this is actually before it is
20 brought on the market, and so we are not presenting this to a
21 patient and you get this result with this air conduction, and
22 you get this with an implant.

23 This is really what the manufacturer has to go
24 through to prove efficacy; is that correct?

25 CHAIRPERSON GULYA: Correct. Right. Right.

1 Exactly.

2 DR. FRANCIS: I don't have a lot more to add. I
3 am Dr. Howard Francis. You pretty much summarized how I feel
4 about this and that there are two groups of patients, two
5 populations that are going to seek this device.

6 But I do think that in order to test a null
7 hypothesis that it is important to be as consistent as possible
8 across the subjects. I mean, it is impossible to have everyone
9 having the same hearing loss and the same response to hearing
10 aids in a controlled situation.

11 But I do think that the consistency of our best
12 aided condition, regarding best aided condition, is beneficial,
13 at least for that group that are hearing aid users currently,
14 and are looking to consider upgrading or side-grading, or
15 whatever you want to call it, to an IMEHD. So I think I do -- I
16 am with you on that.

17 CHAIRPERSON GULYA: Dr. Tucci.

18 DR. TUCCI: Debara Tucci. I think that it is
19 very important, in terms of the initial clinical trials that are
20 conducted with these implants, for the companies to provide some
21 information about what the optimal situation is with binaural as
22 it stands now, state-of-the-art amplification, which is likely
23 to be a moving target in the future.

24 I think that we need to be able to present our
25 patients with some information about this is an implantable

1 device, and this is what you might expect the results to be.
2 This is the optimal conventional aided situation, and this is
3 what you might expect.

4 I don't think it is really important to be able
5 to say that you are going to do better with an implantable
6 hearing aid, because there are intangible factors that have been
7 alluded to today that some patients will weigh more heavily than
8 others.

9 And I think that some patients, given this
10 information, will go one way, and some patients will go another.

11 But I think given that with implantable hearing aids that you
12 have a situation where you are putting the patient at some
13 surgical risk, and that varies according to the implant.

14 There is a much higher cost involved in doing an
15 implantable system than with a conventional hearing aid, and
16 there are all sorts of issues, such as -- and depending upon the
17 device -- whether you cause more of a hearing loss in that
18 person than they had to begin with.

19 So in some ways it is an irreversible situation,
20 and so I think you need to provide the patients with as much
21 information as possible. And we are not talking now about the
22 fitting situation. We are talking about the clinical trials
23 that are going to provide the information that we use to counsel
24 our patients.

25 So I think it is imperative that we use the best

1 binaural aided situation in these trials so that we have the
2 information to pass on, and also I think that there is an issue
3 with the optimal state-of-the-art situation, and what exactly
4 that is.

5 And I think we need to keep in mind for the
6 future how the fitting should proceed if the patient should be
7 required to go through some sort of a trial with a conventional
8 aid like we do with cochlear implant candidates. I personally
9 don't think that that is important in this situation.

10 DR. WALDEN: Point of clarification. What if the
11 patient --

12 CHAIRPERSON GULYA: Brian Walden speaking.

13 DR. WALDEN: -- has been fit with -- you know,
14 following accepted procedures, and they don't want to wear the
15 hearing aid because of acoustic feedback, or occlusion, in what
16 sense then is it an appropriate comparison to this air
17 conduction hearing aid if in fact they are not going to wear it
18 under any circumstances?

19 DR. TUCCI: Well, I don't think they need to wear
20 it at all. For our cochlear implant candidates, what we do is
21 assess them and get their test scores with optimal -- in the
22 optimal aided condition, and then compare that with what are the
23 criteria for cochlear implantations.

24 So my thought would be that the patients who are
25 candidates for the implantable hearing aid should be tested in

1 that situation, but not necessarily should it be mandated that
2 they wear it for a certain period of time, although I do concede
3 that there are situations in which performance would be expected
4 to improve over that time.

5 I think that is probably just a little bit much
6 to ask to bring them back, and then retest them after they have
7 had a chance to use the aids.

8 DR. SOLI: Sig Soli speaking. I think Debara has
9 summarized a number of the points that I wanted to make very
10 well. I would like to comment a little bit on language in here
11 again, and then maybe elaborate a little on what she and the
12 others have said.

13 I would suggest that you not use the term "state-
14 of-the-art." I would say use a well fit and appropriately fit
15 air conduction hearing aid, because I don't have any idea what
16 "state-of-the-art" is, and if I did today, it would be wrong
17 tomorrow.

18 The same with optimally fit. I would say
19 appropriately fit, because if you ask for an optimally fit air
20 conduction hearing aid, then you should compare it with an
21 optimally fit MET. What does that mean? I don't know.

22 So it might be easier to talk about appropriately
23 fitted devices. I think also that as I listen to some of the
24 discussion here that we are confusing a couple of different
25 things.

1 One is how an individual patient is going to be
2 treated after these devices are approved at the end of the
3 trial. The other is how do you design the best trial to arm the
4 physician and the audiologist with appropriate information so
5 that they can counsel patients?

6 And I would argue that you really must consider
7 baseline measures that include unaided hearing tests and hearing
8 tests with an appropriately fit pair of hearing aids. And the
9 testing should assess both monaural and binaural benefits.

10 And the reason that I say that is that at the end
11 of the day you will have patients who come in who are either
12 currently hearing aid users, and those are people either who
13 want to hear better, and so you have to know whether they are
14 going to hear better according to the standard well control
15 measures of the speech and intelligibility, and things like
16 that.

17 Or people who have non-audiological issues --
18 cosmetic issues, feedback issues, and things like that, and so
19 you have to know whether this device treats those as well, or
20 ameliorates those as well.

21 And you are going to have non-users, people who
22 are not currently hearing aid users, and you want to be able to
23 tell them what the benefit of this device is, and whether these
24 benefits would also prove from just using well fit hearing aids.

25 So it seems to me that regardless of how you will

1 inform patients, and work with patients, at the end of the day,
2 you need to have a baseline that gives you enough information to
3 deal with any situation, and that includes monaural or binaural
4 testing of appropriately fitting hearing aids, and unaided
5 testing as well.

6 CHAIRPERSON GULYA: Thank you, Sig. Don.

7 DR. EDDINGTON: I think I --

8 CHAIRPERSON GULYA: Don Eddington.

9 DR. EDDINGTON: Don Eddington, sorry. I think I
10 agree with almost everything the last two speakers have
11 articulated. Let me just say a couple of places where I might
12 disagree.

13 I agree that state-of-the-art is not a good term.

14 It seems like what you are doing is you have a patient coming
15 in and the fitting of the hearing aid is going to depend on the
16 experience of the audiologist, and training of the audiologist.

17

18 And that audiologist, given everything that they
19 know, needs to be given the opportunity to give this person the
20 best aid situation that they can. That might be binaural, and
21 in some cases it might be monaural in others, and I don't think
22 we should try to specify a standard by which they get these
23 devices.

24 But given their clinical expertise, what is the
25 best situation for this patient. And then I agree with

1 something that Chris Turner said, or at least wrote in his
2 handout, and that is that the patients ought to have a
3 significant experience with that if it is substantially
4 different than what they walked in with.

5 And certainly the audiologist in our clinic in
6 infirmary tell me that some patients come in with real trash,
7 and that they deserve the opportunity to find out what they can
8 accomplish with the best fitting these professionals can give
9 them.

10 There will be some cases where they won't wear
11 it, and can't wear it, and in that case it seems like unaided
12 may be appropriate, although I think most people can get fairly
13 interesting measure with headphones in the clinic, if that is
14 the best that can be done in that regard.

15 It seems like the measure that we want is to what
16 extent will a person do better quantitatively with that aid,
17 that they have been given the best opportunity to hear well with
18 after having become accustomed to it, and how much better or
19 differently will they do with the implantable.

20 And I agree with Chris that people will trade
21 that off. That should not be the determining factor, but I
22 think they at least ought to have the opportunity to know how
23 much they are losing or gaining by going with the implantable.

24 And so given those caveats, I think I agree with
25 the last two talkers.

1 CHAIRPERSON GULYA: Thank you, Don. Bob.

2 DR. CUEVA: Roberto Cueva. I would echo Dr.
3 Soli's comments. Again, we are really focusing on safety and
4 effectiveness. I think we need to measure both unaided, and
5 then best aided, whether it is monaural or binaural.

6 Somebody may come in with perfect hearing in one
7 ear, and just have one ear that needs to be aided. So the
8 binaural may not be as indicative as the monaural in that
9 circumstance.

10 Once it is approved, it is free game. I mean,
11 people do off-label uses of FDA things all the time, and you may
12 have a very wealthy individual who comes in and says, listen, I
13 don't want anything out. Implant this thing, and they need to
14 know how is it going to perform.

15 And whether it is unaided, or aided, and other
16 people who are going to make a value judgment as to how much is
17 it worth to me to have this device implanted so that I don't
18 have to fuss with a hearing aid.

19 And whether the risks are -- you know, what is
20 the risk-benefit ratio. And there is risk. You know, every
21 time you operate on an ear -- death, facial nerve, and with
22 these things, we are making a big facial recess, or gaining
23 access to the attic, there could be a cephal leak.

24 And so it is not an inconsequential surgical
25 risk. There is a real surgical risk, and so that risk bar is

1 raised, and to be honest, most of the manufacturers are claiming
2 an advantage, audiologic advantage, to conventional hearing
3 aids, and is it really there. So we need to compare it to
4 hearing aids as well.

5 CHAIRPERSON GULYA: Brent. Dr. Blumenstein.

6 DR. BLUMENSTEIN: Well, as a statistician -- this
7 is Brent Blumenstein. As a statistician, I looked at this and
8 first noticed that there was not a requirement for a randomized
9 clinical trial, and I started wondering about that.

10 And it became obvious with a little thought that
11 you really are talking about an intervention with surgical,
12 versus comparing to do non-surgical. It doesn't preclude the
13 possibility that some day somebody is going to want to compare
14 surgical to surgical.

15 I think that should be added to the guidance, and
16 I have stated that. But there is a couple of other features of
17 the study designs being specified in this guidance, and this is
18 basically a pre-post comparison, and pre is what we are talking
19 about, and what do you select as your control intervention in
20 the pre-period to compare to the post-period.

21 I don't have much of an opinion about that,
22 because I am a statistician, but it seems like to me that some
23 of the things that we have discussed here could be addressed by
24 this guidance directly allowing for mentioning the possibility
25 of a non-inferiority design.

1 And what that means is that instead of specifying
2 that the hypothesis is that this new device, or this new
3 intervention, be superior to the pre-intervention, and that it
4 be not worse than, or that the goal be to show that it is not
5 worse than the pre-intervention.

6 This would address the kind of thing that we
7 heard this morning about the fully implantable device, which
8 might have significant advantages relative to other measures
9 other than performance that you could even, if you go back and
10 consult the literature on --and the literature is incorrectly
11 called proving the null hypothesis.

12 That is old language, and nowadays we call it
13 non-inferiority, but if you go back to that literature, you will
14 see that you can actually offset and design to show not
15 significantly worse than where you allow for a little worse
16 than.

17 And it gets kind of technical and so forth, but
18 you could do that. So it is possible that the example that was
19 used this morning of accepting a little less visual acuity to
20 get certain other advantages could be actually built into these
21 designs.

22 That may be getting too technical, but the idea
23 of introducing the concept of non-inferiority into this would
24 really I think be a big help.

25 DR. GARCIA: Catalina Garcia. Thank you very

1 much for that inclusion. As I sat here this afternoon as
2 someone not in this field my eyes were glazing over at the
3 technicality of it.

4 But part of the problem is that I had become
5 concerned that we were going to stifle development of different
6 implantable devices if we continue to make our standards so
7 rigid. Perhaps it is my age group, but I am around a lot of
8 people now who have deaf patients, and trying to get these
9 people in to be looked after is very difficult.

10 They don't want to have to wear things. They
11 don't want to have to learn things. But if we can stress the
12 safety of these issues, I would like to see us stressing that
13 EMC testing, MRI testing, the electrical testing, and the stress
14 and fatigue, I would like to see that to be our main focus.

15 And I think then we will have a lot more people
16 hearing, because these implantable devices then will be safer,
17 and I think ahead of efficacy, safety I think is the place we
18 ought to be focusing on.

19 CHAIRPERSON GULYA: Thank you.

20 MR. CROMPTON: Mike Crompton, Industry Rep. Dr.
21 Soli stole some words from Industry again. Again, the state-of-
22 the-art, the hearing aid is problematic, and optimally fit, very
23 problematic.

24 But the best aided condition with an
25 appropriately fit hearing aid is something that certainly we can

1 support to the NAL as targets, and allow the professional
2 audiologists to say yes, this hearing aid condition is the best
3 aid condition for that patient.

4 But to pick up on what Dr. Jenkins and Dr. Kileny
5 mentioned, truly what we are talking about is comparing to the
6 unaided condition. A huge population do not -- they are in the
7 drawer users if you will with their hearing aids.

8 By analogy, there is no eyeglass requirement,
9 even though I see around the room that we are wearing them.
10 before you get involved in a clinical trial for laser eye
11 surgery. Now, there is a lot more experience now with laser eye
12 surgery. You know, we have several years now.

13 But we will be there with the IMEHDs in the next
14 several years. So what population should we target? Should we
15 take Dr. Kileny's lead and design trials where we have an
16 unaided population that desires to have access to new
17 technology? Maybe that is a different design than what we would
18 do compared to a hearing aid.

19 CHAIRPERSON GULYA: Thank you. And in brief to
20 sum up, I think we heard that in large the controls will be
21 dependent upon the purpose of the device at hand.

22 We have heard strong pleas for both an unaided
23 control, as well as for an amplified control, with avoidance of
24 the terms "state-of-the-art" type of design.

25 We have also heard a real emphasis on the safety

1 being attested to and being evaluated. How did we do there?
2 Are you okay now with these questions? Can we move on to (c)?

3 I guess I do 2(c) also. This one is previous
4 clinical studies with the two approved IMEHDS showed enhanced
5 patient satisfaction with these devices, despite the fact that
6 objective hearing assessment results were similar to those using
7 conventional hearing aids. And here we are getting into the
8 quality of life issues, I believe, in addition to other issues.

9 What additional assessments, if any, could be
10 used to demonstrate an enhancement in hearing performance to
11 account for a subjective improvement in patient satisfaction?

12 Now, I warned Dr. Francis that I was going to
13 call on him first, and I am going to follow through on that
14 warning.

15 DR. FRANCIS: Okay.

16 CHAIRPERSON GULYA: And then we will go around.

17 DR. FRANCIS: That sounds good. Well, there are
18 a few pretty well accepted instruments to measure your quality
19 of life, and health utility indexes is one of those that is
20 commonly used.

21 And the output measure essentially places the
22 perception of the effect of the hearing aid in this case on
23 quality of life, and on the same scale as, for example, an
24 output of cochlear implantation, or heart surgery.

25 You can look across basically all interventions

1 and make some kind of comparison about what or how the
2 population values a particular outcome for a given intervention,
3 and make some comparisons that way.

4 The only problem is that it may not get to the
5 specifics. The questionnaire may not get to the specifics of
6 this particular patient population, and the issue of occlusion
7 effect, or as was discussed earlier, you know, the ability to
8 swim with the device, versus not being able to, and these little
9 sort of other issues related or are very specific to hearing aid
10 use.

11 There are a couple of other instruments that
12 might also provide a way in which to assess that are specific to
13 hearing, but they are not as well standardized, and there are a
14 few that come to mind that I can discuss later.

15 But I think that essentially this is something
16 that still needs to evolve, and we still don't have the best
17 questionnaires, but the standard quality of life assessment
18 could be of benefit as an adjunct, and certainly not in my
19 opinion shouldn't be valid to the extent that the function
20 outcomes, but should be strongly considered.

21 CHAIRPERSON GULYA: Thank you, Howard. Any other
22 discussion?

23 DR. SOLI: Sig Soli speaking I am not familiar
24 with HUI. I assume it is a self-report. I have a general
25 question that sort of underlies this question, is how does one

1 validate a self-report quality of life measure, and are there
2 such validated measures out there? Maybe that is what you were
3 saying a moment ago, that there aren't perhaps.

4 DR. FRANCIS: Well, this mechanism has actually
5 been validated.

6 DR. SOLI: Okay.

7 DR. FRANCIS: And it was validated in the
8 Canadian population, and several hundreds, or I forget how many
9 people were actually studied, and they looked at the effect, and
10 so it has been validated, and it is very well accepted
11 statistically as a good mechanism.

12 CHAIRPERSON GULYA: Brian.

13 DR. WALDEN: I would like to kind of go back to
14 the point that I tried to make separating between performance
15 and satisfaction, and I maybe would take exception to the
16 question of what additional assessments, if any, could be used
17 to demonstrate an enhancement in hearing performance to account
18 for a subjective improvement in patient satisfaction.

19 And I don't think that improved patient
20 satisfaction is necessarily dependent upon enhanced hearing
21 performance. The patient satisfaction depends upon whether or
22 not their needs and expectations are being met by the device.

23 And if their needs and expectations are outside
24 of the realm of hearing performance as we traditionally define
25 them, they could be quite satisfied with the device.

1 So in a sense, I think that leads us to an
2 assumption, or it makes an assumption which probably was not
3 intended at all, but it misleads us. I think we need to make or
4 keep that separation, and I think it is important that we
5 demonstrate that it is at least as good or perhaps in the ball
6 park as being as good in terms of hearing performance.

7 But that there may be other issues that cause
8 these people to be very satisfied, which are unrelated to
9 hearing performance, and are very valid.

10 CHAIRPERSON GULYA: Joe.

11 DR. HALL: Joe Hall. Yes, I have sort of a
12 different slant on that, or another way to look at that, and
13 that is that patients that might be involved in these hearing
14 aids, that is, comparing an air conduction hearing aid, versus
15 an implanted hearing aid, may have some very important
16 psychological variables.

17 And the psychological magnitude of dealing with
18 the implanted aid may be quite high, and larger than that
19 associated with the air conduction aid. And there may be
20 important things like things related to psychological cognitive
21 dissonance things, or Hawthorne effect, or type things.

22 So in a way, even though patient satisfaction is
23 extremely important, actually getting a valid measure of it in
24 that sense may be quite difficult. And in that sense, I kind of
25 like part of the question that deals with other ways of

1 assessing what may be going on.

2 And someone spoke earlier today about effects
3 related to ear canal residences, and effects related to the
4 auricle, and to possible cues related sound localization, which
5 I think are quite exciting and interesting, and may actually be
6 tied into things like patient satisfaction.

7 CHAIRPERSON GULYA: Brenda.

8 DR. LONSBURY-MARTIN: This is not my area of
9 expertise, the self-evaluation instrument, but I believe -- and
10 my audiology colleagues would know more about this, but in the
11 tinnitus field that Jacobson and Newman have developed some test
12 instruments that are meant to evaluate the performance
13 effectiveness of like maskers and different treatment effects.

14 And I don't know if something like that could be
15 molded to this particular use, like a treatment effect, and it
16 is really aimed at the patient satisfaction with other things
17 that are very hard to measure to do with hearing.

18 CHAIRPERSON GULYA: All right. Okay. Bob.

19 DR. CUEVA: Certainly if that is addressing some
20 of or one of the things that was brought in the document about
21 patients who, even though they are audiologic, pre-and-post-
22 implantation criteria were not that different, or maybe even a
23 little bit worse after implementation.

24 And, one, having had an operation, there is a
25 strong psychological effect to like I have got to be better. So

1 there is that part of it. The other side of it is a very real
2 aspect of what was mentioned in lifestyle consideration, having
3 spent most of my life wearing glasses and not being able to wear
4 contacts.

5 And having had Lasik surgery in December, I can't
6 tell you how great it is not to have to wear glasses and do all
7 the things that I couldn't do with glasses on.

8 So thinking about a totally implantable hearing
9 aid, because that is what I tell my patients who are reluctant
10 to wear hearing aids, is that they are glasses for the ears as
11 glasses are for my eyes. that would be a very strong impact.

12 And I think using some of the lifestyle or
13 quality of life measurements which have been validated in a
14 variety of different ways, and it may be just picking the one
15 that seems best fit toward this area, would be the way to make
16 an additional way to judge the -- not really the effectiveness,
17 but the impact on the patient, which will help temper the
18 determination.

19 CHAIRPERSON GULYA: Okay. I think to avoid
20 trotting any more on Dr. Eddington's time, I will wrap this up.

21 And it seems to be that there is an interest in having some
22 measurement of the intangibles in terms of efficiencies and
23 effectiveness beyond just hearing improvement, with general
24 quality of life.

25 But not the preclusion of looking at other

1 effects, like the residence in the canal, and other auditory
2 effects that maybe the implantable hearing aid can give you.
3 Okay. So does that get it for you guys? Perfect. Okay. Don.

4 DR. EDDINGTON: I am suppose to start this
5 discussion on to what extent there should be other measures to
6 basically define the device, input-output characteristics, et
7 cetera.

8 And I thought that a lot of what was in the
9 guidelines is good, and I came back to the thought that these
10 are hearing aids, and there has been -- there have been many
11 years of experience in specifying hearing aids.

12 And all of that or much of it is included in
13 several ANSI standards. So the question that I would have and
14 that I would like to pose to the panel, is there any reason to
15 do anything different than that.

16 And I would like to put that in perspective a
17 little bit. So there are two things that have to be done
18 differently. One is the outputs of these devices are unique in
19 a sense, at least as compared to acoustic aids.

20 And so there needs to be some way to relate their
21 output to the output of hearing aids, and here we come back to
22 the point that I raised earlier and Sig did, that actually I
23 think is very doable.

24 And I don't think it is particularly difficult
25 given the state of knowledge of some people in this field to