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. BRENTE 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
C-O-N-T-E-N-T-S

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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 It is good to see a number of you who are interested in today's meeting regarding the draft guidance document for implantable middle ear hearing devices.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
agency, we ask that those of you with cell phones and pagers
read the pink signs on the door, and either turn them off, or
put them on vibration mode while you are in this room. We
certainly would appreciate it.

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

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

Dr. Hood is a professor at the Kresge Hearing
Research Laboratory of the South, in the Department of
Otorhinolaryngology, at Louisiana State University Health
Dr. Jenkins is the Chairman of the Department of Otolaryngology at the University of Colorado Health Sciences Center in Denver.

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

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

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

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

Our remaining voting members, who continue to serve us faithfully, are Dr. Howard Francis, who is an Assistant Professor with the Division of Neurotology and Skull Base Surgery, in the Department of Otolaryngology, Head and Neck Surgery, at the Johns Hopkins University School of Medicine, in Baltimore, to my right. And also to my right is Dr. Paul Kileny, who is a Professor of Otorhinolaryngology and Director of the Division of Audiology and Electrophysiology at the University of Michigan School of Medicine in Ann Arbor.
I would also like to extend a special welcome and introduce to the public, the panel, and the FDA staff, six panel consultants who are new and with us today for the first time.

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

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

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

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

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

And Dr. Brent Blumenstein is a biostatistician
and clinical trialist who is being shared from the FDA's General
Hospital and Plastic Surgery Devices Panel. We are grateful to
him for his willingness to do double-duty today. Welcome to you
all.

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

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

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

The waiver allows this individual to participate
fully in today's deliberations. Copies of this waiver may be
obtained from the agency's Freedom of Information Office, Room
12A15 of the Parklawn Building.

We would like to note for the record that the agency took into consideration other matters regarding Dr. Soli. This panel has reported interests in firms at issue, but in matters that are not related to today's agenda. In the event that the discussions involve any other products or firms not already on the agenda, for which an FDA participant has a financial interest, the participant should excuse him or herself from such involvement, and the exclusion will be noted for the record.

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

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

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

We have 30 minutes for this session, and from the
handout here, it appears that we have one speaker, Dr. Christopher Turner, from the University of Iowa, scheduled. Dr. Turner.

DR. TURNER: I have a couple of overheads.

(Discussion off the record.)

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

(Discussion off the record.)

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

I have been trying to think about how to evaluate these devices, and I have a lot of experience in hearing aids and some experience in Cochlear implants, and this has been a lot of fun for me, because there are some issues that are very different than what I am used to. And maybe the panel is already familiar with these, but I thought that I would just bring them up, because there are some things that I think we
might need to take into consideration. Can we start the
overheads there?

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

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

So this leads to a couple of things that I guess
I would like to just ask the committee to consider, and maybe
they are already thinking about these things, but when they
draft the guidelines for evaluation, there is some new issues
and maybe opportunities here that I just want to make sure that
we are all kind of aware of. Can I have the next one, please.

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

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

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

Another thing that comes up from the industry all
the time is that 80 percent, or some 70 to 80 percent of people
with significant hearing loss refuse to wear a hearing aid, because they don't want to have something hanging outside their head. And this device, you know, may not fall into that category. There may be some people that don't or wouldn't mind having an invisible device. In that case, you know, I see that the guidelines have in there unaided condition as one of the controls to measure against. And that might actually be a valuable condition, because that might be the only other alternative that people would consider. You know, they might say that I want nothing on my head, and so I want to compare to unaided. I don't care if this really compares to a hearing aid or not. So that is something that you might want to consider.
The next one, please. And here is what we have sort of come up with as a list at one of our times when we sat down on how to measure the utility of these devices.

Of course, there is the traditional ones like bandwidth and gain, and those of you who know my research in hearing aids know that I don't necessarily believe that more bandwidth and more gain is always a good thing. We have shown that when you get a severe hearing loss in the high frequencies that sometimes an additional gain up there doesn't really help you. So I don't think that these devices should be evaluated strictly in terms of bandwidth and gain. At some point, it is diminishing return.
Speech recognition, of course, is the traditional method, and I don't think anybody would find any fault with that. But we were thinking of some other ones along the line, and quality of life measures are probably going to be important when you have a device that falls into a whole new category like this.

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

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

These are some things that we think could potentially be benefits of totally implantable devices that may be the measurements that we are looking at that you might want to take into consideration if there are measures that could
incorporate this. No microphone wind noise, no ear canal irritation, and there are probably going to be some advantages in having the ear drum as a microphone, because you can use the whole pinna in the ear canal then in a way that it is naturally. So maybe there is going to be some test in terms of localization in the vertical plane, and localization tests that may really be around, and that might be something that we want to take a look at, and it might be a real advantage in a device like this. No daily maintenance. This thing has -- their device has a 7 or 8 year battery. So that is not going to show up in a speech recognition test, but it certainly would be an advantage, I think, for people who want to wear them.

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

CHAIRPERSON GULYA: This is your two minute warning.

DR. TURNER: Okay. The next one. We are almost done. The only other thing we thought about in the draft that we thought we might at least ask about is that it wasn't quite certain when they did want to compare it to a hearing aid, we used the words "state of the art hearing aid." We were sort of thinking that if the patient has their own hearing aid that it
meets the NAL or some program standards that are out there, it is probably a good enough comparison.

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

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

So it might lead to something that the committee wants to consider, and that is all that I really wanted to say.
CHAIRPERSON GULYA: Thank you very much, Dr. Turner. I guess I will let the panel have an opportunity to ask Dr. Turner -- Dr. Turner, don't leave so quickly. I will see if any of the panel members have any questions for you. Why don't we start towards Dr. Walden, and then maybe work our way around. Paul. Dr. Kileny.

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

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

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

Brenda.

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

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

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

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

CHAIRPERSON GULYA: Dr. Tucci.

DR. TUCCI: Yes. Dr. Turner, since this is totally implantable, I was just wondering how the power issues
were addressed. I remember that orange rule.

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

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

DR. TURNER: Oh, sorry.

CHAIRPERSON GULYA: Dr. Soli.

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

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

DR. SOLI: How can you measure functional gain if
the ossicular chain is disarticulated?

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

DR. SOLI: How can you measure unaided?

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

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

CHAIRPERSON GULYA: Can you identify yourself, please.

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

DR. TURNER: I think it is about the best that people can do these days. I mean, the NAL, the most recent version of NAL is what people tend to say as being the best job.

I mean, people don't know what exactly the right formula is,
but NAL seems to have the most validation studies done of any
formula, and so I am going to guess that that is about the best
one. I am sure that the committee agrees or disagrees, but NAL
seems to be the only people that have done any validation on
that stuff.

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

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

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

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

DR. HALL: Joe Hall. Do we know the implications
of using the eardrum as the microphone for the frequency
response of the eardrum?

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

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

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

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

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

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

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

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

Before I turn this meeting over to our new ENT branch chief, Dr. Eric Mann, who I will formally introduce in a few moments, I have a couple of specific announcements that I would like to make, personnel announcements.
The Director of our Office of Device Evaluation, Dr. Bernie Statland, will be leaving the Food and Drug Administration at the end of next week. Dr. Statland has supported our division while he has been here, and we want to thank him for his support and his generosity to our division while he has been here. He will be leaving and he will be taking up residency in Minnesota, where he is going to pursue his law degree there. So we wish him well on that.

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

Dr. Schultz received his medical degree from the University of Pittsburgh in 1974. Upon graduating, he entered the Public Health Service, serving in hospitals in the west and southwestern United States, where he was involved in general practice, a surgical residency, and a pediatric surgery fellowship. He also served as the chief of surgery at the Sante Fe Indian Hospital in New Mexico. Dr. Schultz came to the FDA in 1994 as a medical officer in the general surgery devices branch in the Office of Device Evaluation. He was promoted to
the chief medical officer in the Division of Reproductive, Abdominal, and ENT Radiology Devices Division, and eventually became Director of that division in the year 2000. Some of you may remember Dan, or have worked with Dan, when he was the division director when ENT was under that division. And as I said, Dan is currently serving as the deputy director for clinical and review policy, and device evaluation, and we congratulate him on his new appointment.

Now, last, but not least, I would like to introduce to you our new Chief of the ENT Branch, Dr. Eric Mann. Eric has been with us since November of 2001, and it is truly has been a baptism of fire for that man since he has been here. Eric received his MD and his Ph.D. degree in Immunology from the Medical College of Pennsylvanian 1988. He did his residency in Otolaryngology, Head and Neck Surgery, at the University of Connecticut Health Center in 1993. Eric served on active duty in the United States Army at Walter Reed Army Medical Center until 1997, where he later joined the Public Health Service and served as a Medical Officer in the Division of Anti-Infective Drug Products with the FDA until 1999. He then accepted a position as Senior Staff Otolaryngolist in the Otolaryngology and Speech Section at NIH, where he worked until November of 2001, when we made him an offer that he couldn't refuse. We stole him from NIH, and we made him our chief of the ENT branch. He is probably having second thoughts about accepting that
position at this time, but we are certainly grateful that he accepted it, and certainly proud to have him as our new chief. So, Eric, you've got the floor.

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

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

So moving on to the approvals, I will first cover the implantable middle ear hearing devices. Next slide.
The month following our last panel meeting, the Vibrant Soundbridge was approved in accordance with the panel's recommendation for the intended use of providing a useful level of sound perception to individuals via mechanical stimulation of the ossicula. Next slide. It consists of an externally-worn audio speech processor here which converts sound into an electromagnetic signal, and it is transmitted across the skin to an implanted internal receiver.

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

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

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

The Direct Drive system is a bit different from the Vibrant Soundbridge in that you have an externally worn processor again, but this in-turn connects to an ear mold coil.
assembly, which is located in the ear canal. This assembly generates an alternating electromagnetic field, which drives a small magnetic implant, which is attached at the ossicles at the incudostapedial joint as shown here in the illustration.

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

Regarding Cochlear implant devices, since the last panel meeting, we have also had a number of these approved. The COMBI 40 Plus Implant System by MED-EL Corporation received approval almost exactly one year ago from today.

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

The COMBI 40 Plus device, as indicated for patients or for adults with bilateral severe to profound sensory neural hearing loss, with limited benefit from amplification, and limited benefit is defined as hearing in noise test scores less than equal to 40 percent in the best aided condition. In pediatric patients, it is approved for bilateral profound sensory neural hearing loss, with lack of benefit from
amplification defined as lack of auditory skill development in younger children, and is less than a 20 percent score on the multi-syllabic lexical neighborhood test, or the lexical neighborhood test.

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

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

Now as an extension of their cochlear implant technology, the Cochlear Corporation has also developed and received approval from the FDA for the first auditory brain stem implant device, and this was back in October of 2000. Its intended use is to restore useful hearing via electrical stimulation of the cochlear nucleus. A body worn speech processor delivers the electrical signal to the implant.
receiver/stimulator shown here, and it looks very similar to
that of the nucleus cochlear implant, and then the signal
travels along the electrode array here to terminate in a 21
electrode brainstem array. And as shown here in the diagram the
electrode lead traverses the temporal bone and terminates here,
and the brain stem over the cochlea nucleus. Next slide,
please.

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

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

Finally, I would like to conclude the branch
update by reading a brief statement on the recently publicized
issue meningitis in cochlear implant recipients, and I would
also refer you to the FDA website on this issue, which is at the
bottom of the slide, for further details on this. I would point
out that this website is administered by the Office of
Surveillance and Biometrics, and that is OSB if you were a
little confused about that terminology during the closed
session.
So I will now read the statement about meningitis in cochlear implant recipients. The FDA has recently become aware of a possible association between cochlear implants and the occurrence of bacterial meningitis. We have received more than 25 reports from the United States, and more than 20 reports from abroad, of bacterial meningitis associated with cochlear implantation.

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

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

A small percentage of deaf patients may have congenital abnormalities of the cochlea or inner ear which predispose them to meningitis even prior to implantation.
Patients who become deaf as a result of meningitis are also at an increased risk of subsequent episodes of meningitis compared to the general population.

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

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

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

The FDA believes that cochlear implant candidates, as well as those already implanted, may benefit from vaccinations against organisms that commonly cause bacterial meningitis, particularly streptococcus pneumoninae, and
Hemophilus influenza. The immunizations status should be ascertained for all candidates for cochlear implants prior to surgery, as well as for those with an existing implant. We would again refer you to the FDA website on the screen for specific vaccination recommendations. In some of the reported cases of meningitis in cochlear implant recipients, patients may have had overt or subclinical signs of otitis media prior to surgery, or before the meningitis developed. Physicians are encouraged to consider appropriate prophylactic perioperative antibiotic treatment, and to diagnose and treat otitis media promptly in patients with cochlear implants.

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

A team of experts from various offices within CDRH has been formed to assess this issue and we are working closely with manufacturers and collaborating with our colleagues at the CDC to gather complete information on all cases that have occurred within the United States. Although the FDA is carefully investigating these reported cases of meningitis, we recognize that cochlear implantation has been a highly effective
procedure to restore hearing function in over 20,000 patients in
the United States, and approximately 60,000 patients worldwide.

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

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

(No audible response.)

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

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

It is always a disadvantage to be after lunch,
because listening to anything is always -- it is just hard to
stay awake, and it is also difficult because I have been so
close to this project that I can't see the forest or the trees,
and of course I have gotten to the point that I think it is all
very boring. But I think that it is a very important area, and
it is an exciting device area that I have been involved in for
quite some time now, probably since the very beginning of it.
And I think that it is important for me to give you some
background as to what went into the development of this document
that is before you today.

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

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

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

This slide highlights the areas of concern that
we brought before the panel in 1999. Simply put, we asked
questions regarding safety, i.e., how much benefit justifies performing surgery on an oftentimes perfectly normal middle ear. We also asked questions related to the broader issue of risk versus benefit of these devices, and how best to evaluate the effectiveness of the IMEHD. We specifically asked the panel about the comparative control condition and measuring changes in residual hearing. Next.

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

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

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

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

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

Also, last September, the FDA approved the second IMEHD PMA for the Soundtec Direct System. Next. Which brings me to today. The draft guidance document before you has been publicly available for comment since June 12th, 2002. The 90 day comment period ends on September 12th, at which time we will take into consideration and address all written comments, revisions to the document, if necessary, will then be made, and the final guidance will be published shortly thereafter.

Today, we ask next that you review and discuss the guidance. You will notice via the table of contents that there are seven sections and two appendices. The goal here was to prevent areas that the FDA would want to see in a pre-market notification, or pre-market approval application. Excuse me. This information, unique to the IMEHD, includes device description, manufacturing information, pre-clinical testing, clinical trial details, including unique aspects of the clinical protocol, and clinical results. The appendices provides areas of importance regarding informed consent and labeling. You can scroll down. Next. In developing this guidance and during the review of proposed clinical trial protocols, and applications for PMA approval, there have been repeated areas of concern that continue to arise, both in the pre-clinical and clinical studies.
Today we have asked you to address and discuss three questions we have that will assist us in ensuring a quality document. We sincerely appreciate your assistance.

Next.

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

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

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

"What is the role of animal studies in the
development of an IMEHD? When should preclinical animal studies be performed to support the safety and performance of an IMEHD?"

That is question number one.

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

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

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

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

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

Question Number 2(c): "Previous clinical studies with two approved IMEHDs showed enhanced patient satisfaction
with these devices despite the fact that objective hearing assessment results were similar to those using conventional hearing aids. What additional assessments, if any, could be used to demonstrate an enhancement in hearing performance to account for a subjective improvement in patient satisfaction?"

Next.

And lastly, Item 3, "Conventional hearing aid labeling includes performance characteristics based on standardized measurement methodology, i.e., ANSI S3.22 1996."

Until we get another one out.

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

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

CHAIRPERSON GULYA: Thank you very much. Well, this is how I propose to address our discussion of the questions. The way I see it, we really have five questions before us. I think we can take the first two questions, give each one of them about 20 minutes, and take what I assume will
be a badly needed 15 minute break at that point in time, and then deal with the remaining two questions in 40 minutes, and I think we should end up just about fine. Okay. Any objections there?

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

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

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

DR. CYGNAROWICZ: The branch, the division.

DR. BLUMENSTEIN: The division. I didn't know what to call it. But I also noticed some additional things that I would change -- wordings, phrases, and things of that nature. I assume that we are not going to get into that here.

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

But perhaps in the interest of focusing on the
critical issues, if you similarly would submit your thoughts on
your letterhead and send it into the FDA, and you have to
indicate the docket number. What is the number, 4106?

MS. THORNTON: The docket number is 1406.

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

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

CHAIRPERSON GULYA: Okay. Thank you. All right.

So, Paul, you were supposed to be our summarizer and discussion
leader for this first question. Are you ready?

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

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

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

All the devices also include processing stages
where the input signal is conditioned in a variety of ways. Due to the nature of these devices, I believe that animal studies may contribute significantly to determine the safety and effectiveness.

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

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

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

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

Additionally, in those cases where the ossicular chain is temporarily or acutely decoupled, it would be possible to investigate the possible long term effects of ossicular joints to determine whether phenomenon such as ankylosis or
discontinuity might occur, and how does that affect aided and unaided hearing.

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

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

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

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

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

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

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

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

Number 5. In those cases where devices may be constructed in such a way that they can be later retrofitted from a semi to a totally implanted device, animal studies may be extremely valuable to investigate effective coupling methods and the effects of a second surgical procedure on the implanted device, as well as on the conductive mechanism in terms of safety and effectiveness.
In summary, animal studies may be of particular importance in the following cases. First of all, if the surgical approach is very different from currently used approaches, these studies may provide the opportunity to study the effects of the surgical technical and approach on the maintenance of the integrity of the conductive mechanism. When placement of the device requires an acute or chronic modification of the ossicular chain, such as a temporary decoupling of one of the joints, or in some cases a chronic discontinuity of the ossicular chain, or the permanent removal of one of the ossicles, animal studies may be very useful to study the effects in such cases.

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

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

DR. WALDEN: I was interested in your number four
under effectiveness as measuring variations in gain and
circuitry response to the implanted device, both from a point of
view of quality control of the product and also variations as it
is implanted across different animals. How would you measure
the output? What would you use as a --

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

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

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

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

DR. LONSBURY-MARTIN: Brenda Lonsbury-Martin. I
agree, Paul, that for biocompatibility studies that animal
studies would really be fit for that application. But I am wondering, as part of what you said was to test the effectiveness in an animal model, and unless you use the actual device that you are going to use clinically, then I think there is some inference problems. If you have to miniaturize it down to a guinea pig, you are going to have a whole different system than in the real world. So what you are suggesting is something like higher order animals, like primates. Otherwise, I think there is going to be a big leap of inferences, and it is going to be awful difficult to assess in an animal model.

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

But I do believe that the technical principles underlying these devices could be investigated in mammalian models, with a different size and anatomy of the middle ear mechanism, and leave space, and one can then probably extrapolate at least to some extent from those measurements to the full scale human size device. I actually think that if these are done appropriately, one could have a fair amount of valuable data before going to clinical trials, which would make clinical trials more effective and perhaps even less cumbersome
DR. LONSUBY-MARTIN: Well, I understand with a device that was much more complex, in terms of like a cochlear implant, where there is lots of encoding strategies, and basic information that some of the early animal studies really provided for that field. But the middle ear, granted, we don't know everything about the subtleties of middle ear function, but relatively speaking, it is a much more simple mechanical system to understand than was the transduction at the hair cell level into a code that the brain could understand. So it seems like that it wouldn't be gaining that much information to have a small animal model, assuming that it was supposed to be a laboratory model of some sort. That you have all of the little intricacies of difference in species -- you know, differences in the middle ear ossicula chain and the attachments. And the tendons, the muscles, all these things are quite different for primates between rodent models, for example.

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

DR. KILENY: Linda.

MS. HOOD: Linda Hood. Yes, I was thinking somewhat along the lines of what Brenda was, and the importance of defining whatever model was used. I think for purposes of
biocompatibility and such, there are many different species that
could be used effectively.

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

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

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

DR. JENKINS: I would agree with my colleagues to
my right here about the biocompatibility issues being very
important to use an animal model for. You mentioned surgical
techniques to be worked out in animal models, et cetera. That
is not a very good place to work out surgical techniques for
implanting in humans. First of all, just techniques alone, we
have cadaver temporal bones which are much more effective, and
you are actually working in the real structures.

But such things as taking apart the ossicular
chain and then reversing that and putting it back together, we
have been doing that for the last 40 or 50 years, and there is a
lot of information in the literature that you take apart that
ossicular chain, and how much gain you can get back, et cetera.
So I think that really alters very little to use an animal
model for the system.

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

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

DR. KILENY: The issue of cochlear effects. I
agree that it might be difficult to make a translation from
cochlea effects in an animal model to human, but we do actually
have an opportunity now, because we have two approved devices
out there, and of course we have the benefit maybe of time
effects, looking at time effects in those devices, and relating
gain to changes in cochlear function. As we see, for example,
the emergence of asymmetric sensual function in these
individuals, it tells us a great deal, and I put that out there
because it may be something that we need to look at through the
branch.

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

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

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

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

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

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

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

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

DR. KILENY: That really was not my intent to suggest that all of these should be done before clinical trials begin. I merely tried to assemble a variety of applications where one could take advantage of an animal model. And certainly there are some that might be more relevant and higher priority than others. Everybody around the table mentioned biocompatibility issues. I think that the integrity of the device within a biological system and its response to contact with a biological system might be some of the most important
ones. One can definitely investigate the effects of the mounting hardware or the contact with ossicular chain, and those effects on the integrity and well-being of the ossicular chain where it is mounted.

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

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

Roberto.

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

I am sure that some of this has been worked out at the level of pacemakers and that type of thing where they have to change the device or change the battery periodically. But that would be
one concern where you wouldn't change the entire device, but just the battery, and how do you ensure that good dry seal again.

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

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

And it really is the issues that the panel has discussed this afternoon; what animal model is appropriate. The first device that was approved used a bovine model. A sham control surgery device was -- APR measurements were taken, but they were inconclusive. It did demonstrate, I think, some of the positive tissue remodeling, and so I think those issues were addressed and those were novel for the device at that time. Biocompatibility, frankly, is addressed through internationally
recognized standards, and so unless there is a novel biomaterial
to go back into the animal is frankly very burdensome.

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

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

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

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

DR. KILENY: Well, I guess I can summarize this
discussion that there appears to be support and interest in certain aspects and certain contributions of animal studies in investigating and ultimately bringing to market middle ear implanted amplification devices. In particular, in terms of biocompatibility, in terms of the maintenance of the integrity of the device within a biological system such as maintenance of hematicity. Certainly the emphasis of effectiveness seems to be of more interest than some of the other issues, some of the safety issues that I have brought up.

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

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

CHAIRPERSON GULYA: What I will do, Paul, is ask Teri and Eric if they have anything else, or if we have answered their questions for them, or if they have still some information, or if they are happy with what we have done so far.
DR. CYGNAROWICZ: I think you have pretty much covered the whole spectrum of pros, cons, areas, the different devices, et cetera.

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

DR. KILENY: Thank you.

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

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

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

They are targets and they are targets that are expressed in terms of the amount of amplification or gain that is to be provided to the patient when the hearing aid is in their ear. So they are based as the question states on real ear
measurements, and these targets then -- they don't really predict gain. They recommend a particular amount of gain, and often time the gain that is recommended is dependent on the level of the signal at the input, and on the frequency of the signal. The reason that this terminology is so important is because the amount of gain as a function of level and frequency is very important to the benefit of hearing aid devices to their users.

We heard Dr. Turner a little earlier talking about the importance of a certain gain prescription called NAL. That is just one example. Now, having said that, it seems to me that the importance of these gain targets and procedures for achieving them in hearing aids underscores their potential importance for use in implantable hearing aid devices. And the reason that I say that is because these devices are indicated for the same population, the same characteristics of sensory and neural hearing impairment.

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

Number 2(a)(ii) is a little harder in my mind, because common units of measurement. Again relying on Dr.
Turner's earlier comments, we are stimulating a system now where we cannot measure its output in an acoustic coupler. We are measuring it in situ, in the human subject.

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

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

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

Again, once the device is in, it is not something that you can return in 30 days and get a different one as you can with a hearing aid. So the match of the output
characteristics of the device expressed in meaningful units for
the hearing of the patient, the match of those output
characteristics to the need of the patient I think is very
important.

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

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

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

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

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

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

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

DR. KILENY: I think that the problem with using the -- for instance, the cochlear microphonic, or the cochlea nerve action potential recorded the minimally invasive methods. The problem is that you are dealing with an auditory system that has been impoverish, in terms of innovation, and so you are beginning with an auditory system that you may not really have a measurable cochlear microphonic with these non-evasive methods, but we can measure them in our patients.

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

What about incorporating in these devices some type of a telemetry measurement, which then can be obviously measured with some type of surface recordings and use that as an indicator, the telemetry being in terms of the telemetry in terms of the displacement of the ossicular chain, or of the device that is mounted on to the ossicular chain? I think that would be far more accurate and would not be dependent on either
the current neurological status of the auditory periphery, or
the future status, because there could be more loss of afferent
nerve fibers, hair cells, et cetera, et cetera.

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

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

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

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

I was trying to think of some way around that,
and the only thing I could come up with is to use the analogy of
a bone vibrator and how you calibrate that when you do bone conduction hearing tests. There is a device called an artificial mastoid, and you load the dong vibrator on that mastoid in a specified way, and you can measure the core response between electrical input and laboratory output according to a standardized procedure.

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

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

That a system, a mechanical electric or a mechanical optic system, be made that basically translates the output of these devices to a stapes displacement, which can be then translated to equivalent SPO at the input. And it seems like that is just crying to be done and is something that will be important in trying to determine the degree to which these devices produce the predicted output as a function of the load.
bearing. So a simulation may be better than in some cases than
in using a fresh temporal bone, because one can manipulate the
characteristics of the load. And in the case of the fully
implantable device, the same thing goes for the implant
transducer.

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

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

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

DR. WALDEN: Brian Walden. I just wanted to
follow up on that notion; that we are talking about technology
that doesn't exist, and if we think about prescriptive methods,
and real measures, there are ways of predicting something else.
And that is sort of predicting how the patient is going to do
with issues like speech recognition and how much gain is the
person or the device providing.

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

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

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

But you get more from what he is proposing than
from what I am proposing, because not only do you need to know
the functional gain, but you also need to know the vibratory
output of this device, and what the corresponding sound pressure
level or hearing level might be created with that output to ensure that those levels are safe.

DR. WALDEN: Yes.

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

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

DR. SOLI: Joe.

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

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

DR. SOLI: Well, I am not sure that I would agree
with that, as long as you know that the stapes output is safe, and as long as you know that it is predictable. Another issue we really have not talked about directly is the efficiency of energy transfer into the middle ear.

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

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

MS. HOOD: Linda Hood. A couple of things. First of all, I think looking at as Sig was saying both the energy loss, as well as the gain from this, what we really need in terms of the patient is the ultimate outcome, and whether sound is audible to them or not. And I think we can achieve these things through many of the behavioral sorts of measures that we have. I am interested in what Dr. Eddington said about the stapes displacement and integrity. I am wondering if that
maybe down the line would also facilitate some kind of system
integrity test as an external check of that.

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

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

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

DR. SOLI: To wrap up?
CHAIRPERSON GULYA: I think so, unless there is some burning —

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

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

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

DR. SOLI: Okay. Well, I will try to summarize. This is Sig Soli. First, I sense that there was, if not agreement, at least no disagreement that fitting targets are relevant because of the population for whom these are indicated. It is important that manufacturers devise a means of achieving these targets and verifying them as perhaps as functional gain measurements. That seems to be the clinical method of choice, and for many good reasons. Underlying that are issues about
safety and characterization of the system, in terms of its
input/output characteristics. We have suggested that perhaps
devising some kind of a mechanical coupler that would enable
calibrated measurements of that type to be taken.

I would just add an observation that generally
the time that is required to develop these instruments and the
standards that go with them is time well spent in the long run,
because you spend some time and energy up front, but it creates
efficiencies later on and you get it back over and over again.

And I guess implicit in what I am saying is what I sense in
agreement is that some common units of measurement, perhaps in
terms of stapes displacement ultimately, should be the objective
of this -- part of this endeavor.

CHAIRPERSON GULYA: Thank you very much, Sig.

Teri and Eric, do you have what you need out of this?

DR. CYGNAROWICZ: Yes.

CHAIRPERSON GULYA: Okay. Good.

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

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

So we will be adjourned until 2:45, and we will probably really
get started at 2:50.
(Whereupon, at 2:29 p.m., the open session was recessed and resumed at 2:46 p.m.)

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

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

MS. THORNTON: IMEHD.

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

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

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

DR. WALDEN: Yes. I think that the appropriate control condition or the appropriate experimental design depends
upon the clinical utility that you intend for the device, or what your clinical goal is.

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

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

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

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

And then that would dictate your experimental
design, your control conditions, and so on. But it may be useful given the concern that Dr. Turner expressed, that that be put up a little more forward in the document.

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

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

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

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

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

But it might be totally inappropriate also, and also in terms of -- for instance, things like compression, and
comparing to, let's say, a compression air conduction hearing aid, might be highly appropriate if the implanted hearing aid also has a significant compression component to it.

CHAIRPERSON GULYA: Okay.

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

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

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

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

CHAIRPERSON GULYA: Okay. Linda.

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

And I think some combination of performance and satisfaction, and quality of life all figures into this.
Clearly if someone has a hearing loss, communication ability and improvement of that has to be a goal.

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

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

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

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

CHAIRPERSON GULYA: Okay. Thank you, Herman Jenkins.

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

And you have demonstrated the efficacy in that, and it doesn't have to be against the best stated condition, and
that it is going to be better, or worse. That is not really the
condition that you are trying to prove when you are trying to
prove a device.

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

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

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

DR. HALL: You are not disagreeing with me.

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

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

And there is basically two categories of
patients. One category of patients would be previous hearing
aid users, who for whatever reason -- well, perhaps because
their hearing loss has advanced, and they are now seeking a new
amplification device, and this could be one of the choices.

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

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

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

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

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

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

DR. KILENY: I'm sorry?
CHAIRPERSON GULYA: That is going to be an additional question that we will be getting into, into quality of life issues.

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

CHAIRPERSON GULYA: Okay. Thanks, Paul.

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

CHAIRPERSON GULYA: Sure.

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

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

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

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

CHAIRPERSON GULYA: Correct. Right. Right.
Exactly.

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

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

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

CHAIRPERSON GULYA: Dr. Tucci.

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

I think that we need to be able to present our patients with some information about this is an implantable
device, and this is what you might expect the results to be.

This is the optimal conventional aided situation, and this is what you might expect.

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

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

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

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

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

So I think it is imperative that we use the best
binaural aided situation in these trials so that we have the
information to pass on, and also I think that there is an issue
with the optimal state-of-the-art situation, and what exactly
that is.

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

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

CHAIRPERSON GULYA: Brian Walden speaking.

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

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

So my thought would be that the patients who are
candidates for the implantable hearing aid should be tested in
that situation, but not necessarily should it be mandated that
they wear it for a certain period of time, although I do concede
that there are situations in which performance would be expected
to improve over that time.

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

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

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

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

So it might be easier to talk about appropriately
fitted devices. I think also that as I listen to some of the
discussion here that we are confusing a couple of different
things.
One is how an individual patient is going to be treated after these devices are approved at the end of the trial. The other is how do you design the best trial to arm the physician and the audiologist with appropriate information so that they can counsel patients?

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

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

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

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

So it seems to me that regardless of how you will
inform patients, and work with patients, at the end of the day, you need to have a baseline that gives you enough information to deal with any situation, and that includes monaural or binaural testing of appropriately fitting hearing aids, and unaided testing as well.

CHAIRPERSON GULYA: Thank you, Sig. Don.

DR. EDDINGTON: I think I --

CHAIRPERSON GULYA: Don Eddington.

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

I agree that state-of-the-art is not a good term. It seems like what you are doing is you have a patient coming in and the fitting of the hearing aid is going to depend on the experience of the audiologist, and training of the audiologist.

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

But given their clinical expertise, what is the best situation for this patient. And then I agree with
something that Chris Turner said, or at least wrote in his
handout, and that is that the patients ought to have a
significant experience with that if it is substantially
different than what they walked in with.

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

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

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

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

And so given those caveats, I think I agree with
the last two talkers.
CHAIRPERSON GULYA: Thank you, Don. Bob.

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

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

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

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

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

And so it is not an inconsequential surgical risk. There is a real surgical risk, and so that risk bar is
raised, and to be honest, most of the manufacturers are claiming
an advantage, audiologic advantage, to conventional hearing
aids, and is it really there. So we need to compare it to
hearing aids as well.

CHAIRPERSON GULYA: Brent. Dr. Blumenstein.

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

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

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

I don't have much of an opinion about that,
because I am a statistician, but it seems like to me that some
of the things that we have discussed here could be addressed by
this guidance directly allowing for mentioning the possibility
of a non-inferiority design.
And what that means is that instead of specifying that the hypothesis is that this new device, or this new intervention, be superior to the pre-intervention, and that it be not worse than, or that the goal be to show that it is not worse than the pre-intervention.

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

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

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

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

DR. GARCIA: Catalina Garcia. Thank you very
much for that inclusion. As I sat here this afternoon as someone not in this field my eyes were glazing over at the technicality of it.

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

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

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

CHAIRPERSON GULYA: Thank you.

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

But the best aided condition with an appropriately fit hearing aid is something that certainly we can
support to the NAL as targets, and allow the professional
audiologists to say yes, this hearing aid condition is the best
aid condition for that patient.

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

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

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

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

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

We have also heard a real emphasis on the safety
being attested to and being evaluated. How did we do there?

Are you okay now with these questions? Can we move on to (c)?

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

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

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

DR. FRANCIS: Okay.

CHAIRPERSON GULYA: And then we will go around.

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

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

You can look across basically all interventions
and make some kind of comparison about what or how the population values a particular outcome for a given intervention, and make some comparisons that way.

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

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

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

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

DR. SOLI: Sig Soli speaking I am not familiar with HUI. I assume it is a self-report. I have a general question that sort of underlies this question, is how does one
validate a self-report quality of life measure, and are there such validated measures out there? Maybe that is what you were saying a moment ago, that there aren't perhaps.

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

DR. SOLI: Okay.

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

CHAIRPERSON GULYA: Brian.

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

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

And if their needs and expectations are outside of the realm of hearing performance as we traditionally define them, they could be quite satisfied with the device.
So in a sense, I think that leads us to an assumption, or it makes an assumption which probably was not intended at all, but it misleads us. I think we need to make or keep that separation, and I think it is important that we demonstrate that it is at least as good or perhaps in the ballpark as being as good in terms of hearing performance.

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

CHAIRPERSON GULYA: Joe.

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

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

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

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

CHAIRPERSON GULYA: Brenda.

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

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


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

And, one, having had an operation, there is a strong psychological effect to like I have got to be better. So
there is that part of it. The other side of it is a very real aspect of what was mentioned in lifestyle consideration, having spent most of my life wearing glasses and not being able to wear contacts.

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

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

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

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

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

But not the preclusion of looking at other
effects, like the residence in the canal, and other auditory
effects that maybe the implantable hearing aid can give you.

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

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

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

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

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

And I don't think it is particularly difficult
given the state of knowledge of some people in this field to
actually develop a load that simulates the drive that these
systems connect to, or the load that these systems connect to.

And in fact as a first approximation, I don't
think one has to take into account the ossicles that the
cochlear load will be the main factor there, which I think is
fairly well known and described.

In the case of the totally implantable, there is
another factor that has to be taken into account, and that is
the input part. And it seems to me that the right way to go in
this specific case, and I don't think it need be so difficult
that one would expect it to take a year or two years, and amount
to a tremendous development effort, to actually specify the
input to the device, in terms of acoustic input, and be able to
relate the output of the device to an equivalent acoustic input.

And be able to directly therefore compare it to hearing aids,
and use the specification standards that are already developed
for hearing aids that have been tried and true over many years.

In addition, it provides comfort for the
clinicians, in a sense that they know what that stuff means, and
may have used it in their clinical lives for many years, and are
adept at using that information to fit devices.

So my question is why now take advantage of what
we have, and specify the device in a way to me at least make
sense, and is a complete specification, and provides consistent
units across devices.
And I didn't warn anyone that I was going to call on them first, and so I will take volunteers. If I don't see any, then I will exercise my prerogative as a discussion starter. I don't see any brave individuals.

DR. WALDEN: Well, I was sort of a half-volunteer.

DR. EDDINGTON: I thought it was a nervous twitch.

DR. WALDEN: Maybe it was, but really out of my area, but I just wonder how many audiologists -- I mean, the quality of the signal processors that are built into hearing aids now are so good that I wonder in terms of sort of the basic measures that we are talking about here do audiologists really take these into consideration in fitting devices, in terms of dynamic range, and distortion, and that sort of thing, which is what I think we are talking about here.

As opposed to the question earlier about prescriptive formula and so on. And my guess would be probably not a whole lot, and I am wondering if computer models or mathematical models would suffice, as opposed to actually looking at or requiring mechanical movement and measuring the mechanical movement.

And that is a question, and I don't know the answer to that, but I just wondered.

DR. EDDINGTON: I think that is a very important -- I think you have raised two very important issues, and I
should obviously let the audiologists respond. As I poll the audiologists at the infirmary, they are dying for that kind of step.

Granted, they don't use them all, but because systems have become so complicated, you really do need very tight specifications for how to make the measurements.

So when you have these highly compressive aids, for instance, with automatic gain controls, it is extremely difficult to characterize those devices. And those issues have been faced already, and at least the audiologists that I talked to at our institution have tremendous confidence, and know what that means, and when they start looking at how the IMEHDs or whatever we are calling them, they don't know where to begin.

Your other point about models was an excellent one, and that would be wonderful. I had the feeling that in terms of developing and validating those kinds of models that is a longer process than simply having what is in a sense a model, a simulated load that is analogous to the coupler.

But I would be interested in what others have to say. I think those are two very good important issues, and you may want to respond before we open it up to others.

DR. WALDEN: Well, I think your point about specifying output, in terms of advanced processing algorithms, and noise suppression, directional hearing aids and so on, is a very good one. And I wonder how that fits into this discussion
given that we can't do it very well right now with the technology that we have available to us with air conduction hearing aids.

How would we expect to do that with something where what we are trying to measure is movement, as opposed to an acoustic signal?

DR. EDDINGTON: Well, what I am saying is that we could do it at least as well as we can with the acoustics. But that is my opinion, and others may have other opinions.

DR. SOLI: Sig Soli. Brian, I understand what you are saying about advanced signal processing in a hearing aid, but I don't think that is the point where we are at in this issue. The issue is what are the output levels and how do they correspond to hearing levels, and are they safe in terms of the amount of energy they are putting into the middle ear.

When you do advanced signal processing that brings up a whole range of other questions. But if you have a model or a calibrated reference receiver that you can put your device that would normally transmit to the middle ear, if you have an appropriate model that is calibrated, you can -- when you put your device and you come to these higher level questions, you might have a chance of answering them then is the way that I would view it.

DR. CUEVA: Bob Cueva. I would agree. I think
there needs to be some way I guess to calibrate the mechanical
output of the devices, correlate it to a X-decibel level. So
that when you come to program it, it is not okay, tell me when
it hurts, and how loud does it get. And then we back off from
there, and it has to be a little more refined than that
certainly.

DR. EDDINGTON: Right, and unless you have that,
how will you measure the amount of distortion that may vary its
function without the level?

DR. KILENY: Thank you. Paul Kileny. I just
wanted to get back to what I said before and I do agree that you
do need to be able to characterize the output if you want to
approximate some of the current hearing aid standards.

And I was actually a little bit amused listening
to the discussion about functional gain measurements, because
those had fallen into disfavor many years ago, and I don't think
anybody around the table here uses them routinely to securing
aids.

But those are actually pretty good measures, but in this case,
if you want to make some kind of an analogy between current
prescriptive methods for hearing aid fitting, I need to
reiterate that some type of -- the ability to telemetrically
measure the output when the device has been placed, I think that
is really the only way to do that. Coupled with the knowledge of
what the output is in some kind of a low simulator that has a
known load, I think that is the way to go. And then you can in fact mimic or copy those prescriptive measures if you have a telemetry measure of ossicular chain displacement.

DR. LONSBURY-MARTIN: Could you explain that a little bit more, Paul? This is Brenda Lonsbury-Martin. In the sense, do you mean like actually have a transmitter that is sitting in there with a device in the middle here?

DR. KILENY: Right. Yes. Basically what we call back telemetry, measuring -- if there is some kind of a component of the electronics that is within the device, which would allow you to measure either transcutaneously or in some other way, the actual output of the -- your input, you know, and you can measure that, especially in a totally implantable device, which does use the ear canal as the input. The microphone is sitting there someplace, and then how do you measure the output? Well, you measure the output by this back telemetry, measuring the actual mechanical information coming back from the ossicular chain.

And how do you do that? The device is riding on your ossicular chain, or rather displacing the ossicular chain, and you get that measurement back from the device.

DR. EDDINGTON: Yes. Can you state your name?

MS. HOOD: This is Linda Hood, and I didn't know if you were going to respond to Paul, or if I should change the --
DR. EDDINGTON: No, I am going to try to stay out of it now since I put in my two cents.

MS. HOOD: Then I will change the topic.

DR. EDDINGTON: And reduce the likelihood that I will say something stupider.

MS. HOOD: I was just going to say from a clinical audiologist standpoint relative to labeling, and characteristics, the standard characteristics of hearing aids, I think that is something that we want to be assured that those exist, and that they are -- you know, what the variation is, and what the expectation is there. And to the degree that it can relate to what clinical audiologists use now with acoustic hearing aids, I think that would make a transition into this for many clinicians smoother.

DR. EDDINGTON: Are there comments? I have got to imagine that our industry representative must have several on the tip of his tongue.

MR. CROMPTON: Just a few. Mike Crompton again. Again, I don't think that there is widespread opposition to the concept of developing a model. Again, we do view it as the next sponsor to come down the pike to have to bear that burden would be an extreme challenge, believe me.

With the first approved IMEHD, attempts were made, and we know for a fact that other sponsors and developers are working on models, and Dr. Soli presented a model two years
ago. So, it could work, and I think we would like that to be maybe industry wide or academically-led exercise, where we could have a reference standard if you would.

I think it is an obligation of industry to try to convey the information for these devices and relate them to in a language that the audiologists can understand. But to have a one-to-one comparison to state-of-the-art hearing aid frankly is an impossible task. Both sponsors of the PMAs faced this challenge when they started their trials. The first sponsor faced a challenge of the advent of the digital hearing and the widespread use of that device was not even contemplated when the study was designed. We had to go back and review and enroll additional subjects, and whole new questions were raised.

So we kind of chasing a moving target there. So I have been very pleased with the discussion around this. A model would be a value, and also I think just to echo one comment that Dr. Blumenstein made; the non-inferiority design for the clinical trial. Certainly with a totally implantable system, where there could be some other advantages may not be exactly equivalent to the state-of-the-art hearing aid or whatever that is. But there are intangible and tangible benefits for patients, and so to encourage sponsors to take that risk I think some flexibility in experimental designs would be advantageous.

DR. EDDINGTON: I have got maybe a question for
the FDA officials here, and that is to what extent is it possible that in cases like this some joint effort between the - it is not the National Bureau of Standards now. What is it called now, NID, but the FDA, the manufacturers, might provide some impetus there.

MR. WHIPPLE: There is a good chance. A very good chance.

(Laughter.)

MR. WHIPPLE: Both Teri and I are members of the CDRH standards task groups. I chair the Ophthalmic one, and Teri chairs the ENT one, and we recently have been given the opportunity to propose projects that can be brought forward to new standard development organizations, where existing standard development organizations for new projects.

Several of the things that were discussed here today would make great projects for them, and we are very much in touch with these standards organizations, and we can propose them, and I have already mentioned to several panel members here already that I thought this has been a fruitful discussion for standards groups if they are listening anywhere, and we will definitely take it forward.

DR. EDDINGTON: Maybe the rock has been cut out of the mountain. Sig, did you have --

DR. SOLI: I would like to -- at the risk of going back to a previous issue, since you brought up this thing
about non-inferiority designs, I would like to comment on that for a moment.

I am certainly comfortable with the idea that there might be non-biological or audiometric variables that provide or characterize benefits for the device. But in my mind it is extremely important when you go to the self-report measures to be certain that you are not dealing with cognitive dissonance and Hawthorne effect, and things like that, because those are very, very real. I have seen them myself many times, and so I would like to go on record that if those types of self-report measures are to be used, there is a pretty substantial burden of proof on the user to show that they are objective, that they are valid, that they have acceptable reliability, and that we can feel comfortable in interpreting them.

DR. BLUMENSTEIN: Brent Blumenstein. When I spoke about non-inferiority design, I was talking more about the performance measurements of the device, and the difficulty that one has when one is designing a trial with two kinds of end-points, two disparate types of end-points, such as patient satisfaction types of end-points, and performance types of end-points, is putting a weight on those two, a utility function if you will. And that is nearly impossible to do, and so the way that we usually work in clinical trials is that we will focus on the performance end-points, measure them, and so forth.

So a non-inferiority type of design may be
appropriate to say, okay, the performance is roughly equivalent, or something like that, but the context in which everything is put together, and interpreted, that is where your comments directly apply. Because if you then have a whole bunch of these other touchy-feely type measurements that are subject to all of these kinds of things, this makes a very difficult interpretation of what those things mean, but nonetheless, it has to be done.

CHAIRPERSON GULYA: Don, I think we need to have your summary and wrap up, please.

DR. EDDINGTON: I guess the way that I would summarize it is that to the extent that it is possible, and I think there needs to be work done to determine whether it is possible in the short term, but maybe with some collaborative effort among the various agencies and the manufacturers, we could develop at least simulated loads and sources in one case that would allow common specification of inputs/outputs. Therefore, performance characteristics or specifications for these devices.

CHAIRPERSON GULYA: Well, I thank all of my host chairs here for taking on these questions. They relieve my burden considerably. FDA, how did we do? Any other questions that now pop into your head? Have we answered the questions to your satisfaction?

DR. MANN: Yes. I would like to thank all of the
panel members. We have had a very thoughtful, educated discussion of all of the questions that we had raised. There has been consensus on some of the questions, and on questions where there were varying viewpoints, that perspective has been very helpful to us as well, and we appreciate all the time and effort that you all have put into preparing for this meeting.

CHAIRPERSON GULYA: Okay. Great. So we will now go to our second open public hearing session. This again is our opportunity to hear from public and industry representatives. The same rules as before. Please state clearly for the record your name and affiliation, interest in the topic at hand, and any consulting arrangements or financial interests with medical device firms, and if travel expenses have been paid, by whom. We have allocated 30 minutes for this segment. I don't exactly see anybody running to the microphone though. Going once -- yes?

MS. ARTHUR: Debara Arthur. I was before this panel two years ago, and I am the vice president of regulatory and clinical affairs for Symponics Devices. What I wanted to do was mention two things, most of it in support of the trend of your conversation over the last hour.

In looking at performance measures of these patients, we found with almost 100 patients implanted worldwide that patient expectations will never be appropriately met if these patients for the most part don't have a good acoustic
hearing aid experience, or trial prior to implantation. There are certain exceptions and usually these are medical exceptions, but for the most part, if these patients aren't fit with an appropriately fit device, we find that expectations are very difficult to manage post-operatively. And we have had that experience here and in Europe.

The second point I would like to make speaks to the issue of having some sort of a common denominator or a common measurement tool so that we can describe the output of these devices across manufacturers. I think with the fact that we are dealing with electromagnetic, as well as piezoelectric, and whatever new ones will come up in the end transducers, the confusion that we are seeing in an audiologist already is resonating. They are having a very difficult time understanding when we come in with laser Doppler vibrometry measures and take millivolt, and talk about equivalent SPL, they are very confused. I think the motion to have this set before a standards committee is an excellent one, even if it takes 2 or 3 years. The fact is that these devices are continuing, and we are going to see more of them in the next 2 years or 3 years, 5 years, and to know that we have something like that in the future as manufacturer to work towards would be very, very helpful for us.

And I think for the audiologists and audiologists, that we are trying to understand how these
products fit into their practice, and the hearing health care
management of their patients, it would really be a valuable
asset. So I encourage you to go down that road. Thank you.

CHAIRPERSON GULYA: Thank you. Any other
presenters? Thank you very much for your comments. I think I
would like now to turn to Mr. Whipple. If he would give us a
little bit of an overview as to what the next steps are for this
guidance document for the FDA, and where we might take it from
here.

MR. WHIPPLE: Sure. Thanks. I want to thank
you, too, for the great discussion today. It is going to be
very helpful. And it will also determine how quickly we can
get this guidance out.

As Teri mentioned in her presentation, the docket
will close on the 12th of September, and any comments that are
in that docket, along with the discussion here at this panel, we
will take all those comments back and we will sit and evaluate
them.

We will bring in the appropriate people that we need to discuss
and make the appropriate changes to that guidance document. The
process and how it gets out of the agency is a longer one than
some of the other documents that we usually deal with.

This is because this is a Class III PMA, level one, guidance
document, is what we call this. It is the highest level of
guidance that issues from the agency.
So it has to come out of not only the branch, and then the division, and then the office, but also the center. So it takes it up all the way to Dr. Feigal's level, and then through his office. Sometimes that can take a long time, depending on what policies, and what new things are being proposed, but this is a pretty specific guidance. This is one that is dealing with the specific device type. It is not changing the way the Food and Drug intends to regulate all medical devices in any way, shape, or form.

So I don't anticipate it being a difficult process to get through the center. It will be just more of a scientific issue of us coming to conclusions and making the right changes. Without being held to any specific due date or time frame, what I have heard here and in some of the discussion, and knowing the process, I would like to see this out before the end of the year, and anything earlier than that would be wonderful.

CHAIRPERSON GULYA: Well, taking the Chairman's prerogative here, I would like to thank all the panel members for all their thoughtful comments and hard work, in addition to the effort that they took to be here, and help us run on a timely schedule.

I would like to thank the FDA staff for their informative presentations, and all the hard work they have evidenced in putting together this meeting. It is much
appreciated. And unless there is any other pressing issue, I would call this meeting adjourned. And Sally has one thing.

MS. THORNTON: One thing. I just wanted to announce to the panel, and to the public, and the staff, that the October 17th-18th, 2002 tentatively scheduled ENT-THAL meeting has been canceled, and we will go forward toward the December 12th and 13th date, and I will let you all know by mid-October what the status of that meeting date is. I will be coming out with a new calendar for the panel probably sometime in September that I will be able to get that together. So I thank you very much for your time and for your attention, and it has been very nice meeting all of you for the first time, and I welcome you to the panel.

We have a lot of new talent and new expertise, and we are very grateful that you are willing to take time away from your busy schedule to work with us. Thank you.

CHAIRPERSON GULYA: Now we are adjourned.

(Whereupon, at 3:51 p.m., the open session was concluded.)