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DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
EAR, NOSE AND THROAT DEVICES PANEL

IMPLANTABLE MIDDLE EAR AMPLIFICATION DEVICES

Friday, June 18, 1999

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P A R T I C I P A N T S

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Renee A. Middleton, Ph.D.

Industry Representative:

William H. Duffell, Ph.D.

Guest Expert:

Peter Uhthoff, M.D.

FDA Staff:

Harry Sauberman, Acting Executive Secretary

Ralph Rosenthal, M.D.

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

2 DR. PATOW: Good morning. I would like to call to
3 order this meeting of the Food and Drug Administration
4 Center for Devices and Radiological Health, Ear, Nose and
5 Throat Devices Panel.

6 Today's meeting will be on the subject of
7 implantable middle ear amplification devices. I am very
8 pleased to see the number of you who are here and interested
9 in this topic today.

10 The purpose of this meeting and the purpose of
11 this panel is to discuss, on a generic level, issues of
12 safety and efficacy that are related to implantable middle
13 ear amplification devices. The information generated at
14 this meeting will be used in the development of a guidance
15 document that manufacturers can follow when preparing
16 submissions to the agency.

17 At this time I would like to have each of the
18 members of the panel briefly identify themselves and their
19 affiliation. Let me start with myself.

20 My name is Carl Patow, and I am with Health
21 Partners in Minneapolis, Minnesota.

22 DR. CAMPBELL: Emmett Campbell. I am in private
23 practice in otology in Garden City, New York.

24 DR. KHAN: I am Anjum Khan. I am in private
25 practice, otolaryngology, Silver Spring, Maryland.

1 DR. WOODSON: I am Gayle Woodson. I am a
2 professor of otolaryngology at the University of Tennessee
3 at Memphis.

4 DR. ROSENTHAL: I am Ralph Rosenthal, and I am the
5 Division Director for the Division of Ophthalmic Devices,
6 which includes ENT, and which will be named appropriately
7 this summer.

8 DR. UHTHOFF: I am Peter Uthhoff. I am from
9 Health Canada.

10 DR. DUFFELL: I am Bill Duffell. I am the
11 industry representative. I am currently with Cyberonics in
12 Houston, Texas.

13 DR. MIDDLETON: I am Renee Middleton, and I am the
14 consumer representative and an associate professor at Auburn
15 University, Auburn, Alabama.

16 DR. KILENY: I am Paul Kileny. I am a professor
17 of otolaryngology at University of Michigan and a director
18 of audiology at the same institution.

19 DR. SHELTON: I am Clough Shelton. I am an
20 otologist at the University of Utah.

21 DR. SININGER: I am Yvonne Sininger. I am an
22 audiologist at the House Ear Institute.

23 MR. SAUBERMAN: I am Harry Sauberman. I am the
24 acting executive secretary for this meeting this morning.

25 DR. PATOW: Just a few housekeeping details.

1 The washrooms are located out this door and to
2 your right.

3 For all our presenters, we would ask that copies
4 of all your presentations and slides be given to the summary
5 recorder and the transcriber.

6 The third housekeeping detail that I think is
7 extremely important today is time management. We have a
8 very, very tight schedule and there are many of you who wish
9 to present information related to this topic. In the
10 interest of having everyone get ample and equal time, we
11 will be monitoring time very carefully and closely, so just
12 please try to stay within the prescribed time frames, and we
13 would like to get through the opportunity for everyone to
14 speak today.

15 At this point, Harry--

16 MR. SAUBERMAN: Thank you, Dr. Patow. I was just
17 reminded, if everybody can speak fairly close to the
18 microphones, this will enable everybody in the audience to
19 hear much better, and I would like everybody to try to
20 remember that if they can.

21 At this time I would like to take a few moments to
22 introduce a special guest that we have with us at the panel
23 today, and it is a pleasure to welcome the participation of
24 Peter Uhthoff, M.D., at this panel meeting. Dr. Uhthoff is
25 a medical reviewer. He is also a biomedical engineer, and

1 he is a regulatory official of Health Canada. He is based
2 in Ottawa, Ontario.

3 The FDA believes that the interaction and
4 interchange with the Government of Canada in the matters of
5 medical device safety and efficacy is in the interest of the
6 public health. In this regard, the FDA and the Government
7 of Canada have been working together over the past three
8 years in a partnering venture that entails the exchange of
9 scientific and clinical information.

10 Our association with Canada and the Government of
11 Canada represents an important step in FDA's vision for
12 working closely together with other governments. It is a
13 step, we believe, towards the realization of global
14 harmonization.

15 Dr. Uhthoff is sitting with the panel this morning
16 in the capacity of a guest expert. We welcome Dr. Peter
17 Uhthoff.

18 DR. PATOW: Thanks, Harry.

19 I would like to now just present a few words about
20 our last meeting of the ENT Devices Panel. The last meeting
21 of the Ear, Nose and Throat Devices Advisory Panel was held
22 on May 21st, 1997.

23 At this meeting the panel reviewed and discussed a
24 pre-market approval, a PMA application, for the Advanced
25 Bionics multistrategy cochlear implant intended for use in

1 children between 2 and 17 years of age, or with a lower age
2 limit of 18 months for infants diagnosed with an ossified
3 cochlea. The panel vote was to recommend a conditional
4 approval for the PMA. Subsequently, the conditions were
5 satisfied and the company received marketing approval for
6 the device.

7 At this time, Harry, would you--

8 MR. SAUBERMAN: Right. I would like to enter into
9 the record the following statement of conflict of interest
10 regarding the constituency of this panel this morning, and
11 this announcement addresses conflict of interest issues
12 associated with this meeting. This announcement is made
13 part of this record to preclude even the appearance of a
14 possible impropriety.

15 To determine if any conflict of interest existed,
16 the agency has reviewed the submitted agenda for this day's
17 session and all financial reports by the committee
18 participants. Our conflict of interest statutes prohibit
19 special government employees from participating in matters
20 that could affect their or their employer's financial
21 interests. However, the agency has determined that
22 participation of certain members and consultants, the need
23 for whose services we believe outweighs the potential
24 conflict of interest involved, is in the best interests of
25 the government.

1 We would like, therefore, to note for the record
2 that the agency has taken into consideration certain matters
3 reported regarding Drs. Paul Kileny and Yvonne Sininger.
4 Each of these panelists has reported past and/or current
5 interest in firms at issue, but in matters that are not
6 related to the agenda for today's session. And since their
7 interests are unrelated to today's agenda, the agency has
8 determined that they may fully participate in today's
9 deliberations.

10 We would also like to note for the record that the
11 agency has taken into consideration other matters regarding
12 the participation of Dr. Paul Kileny and Dr. Cough Shelton.
13 Dr. Kileny has reported current interest, and Dr. Shelton
14 has reported past and current interests, in firms at issue
15 for matters related to today's discussion. Since the agenda
16 item for this session involves only particular matters of
17 general applicability, the agency has determined that these
18 panelists may also participate fully in the discussion
19 today.

20 In the event that the discussions involve any
21 other products or firms not already on the agenda for which
22 an FDA participant may have a financial interest, the
23 participant should excuse him or herself from such
24 involvement, and that exclusion will be noted for the
25 record.

1 Finally, with respect to all other participants,
2 we ask in the interest of fairness that all persons making
3 statements or presentations, that they disclose any current
4 or previous financial involvement with any firm whose
5 products they may wish to comment upon.

6 Thank you.

7 DR. PATOW: At this time we would like to have Dr.
8 Tom Shope make a brief presentation on the Y2K activities of
9 the FDA.

10 DR. SHOPE: Good morning. We are taking the
11 opportunity, last year or so, at each of our panel meetings
12 to briefly brief the panel on some of our activities related
13 to the so-called Y2K problem, the Year 2000 date problem.

14 If I could have the first slide, the purpose here
15 is just to familiarize the panel members with this activity
16 and perhaps provide an opportunity for some feedback to the
17 agency if there are issues that the panel would like to let
18 us know about related to this.

19 Next slide, please. I am sure by now everybody
20 has heard about the Y2K, the Year 2000 date problem.
21 Several years ago it was being described in lots of ways, as
22 "digital doomsday." The Director of Medical Affairs at the
23 Veterans Health Administration I think coined the phrase
24 "the millennium bug syndrome" so it would have a medical
25 tone. But there is a potential here for problems with

1 medical devices and for health care delivery in general, and
2 that is the reason that we are paying some attention to this
3 problem.

4 Next slide. These are a couple of quotes from a
5 couple of years ago, but it sort of put into context for us
6 here, I think, the need to pay attention to this problem.
7 As you are probably all aware, some of the older personal
8 computers, the basic input-output systems, the BIOS, and the
9 realtime clock have some problems if they aren't attended
10 to. PCs are used in many medical devices, particularly in
11 control or recordkeeping functions, and so there is a
12 potential for some of these medical devices to have problems
13 if the PC operating them has problems.

14 Next. Focusing not so much on medical devices but
15 on the information technology aspects of the health care
16 system, this is a quote actually from an ad from a very
17 large consulting firm looking for business, I think, but it
18 kind of put in perspective that hospitals and their
19 information systems, their information technology, had quite
20 a bit of work to do to get prepared for January 1, 2000.

21 Next. In simple terms, the problem is that many
22 systems used, of course, only two digits to represent the
23 year back when we weren't as smart as we are now and memory
24 was expensive. So it can lead to problems in any kind of
25 date calculation where you are trying to do a comparison or

1 a calculation involving, if the two digits are only 00, it
2 is difficult to tell 2000 from 1900 or any other hundred-
3 year period.

4 Next. There are clearly some medical devices that
5 can have problems due to this design, if in fact the
6 manufacturers designed them in this way. As I mentioned,
7 there are microprocessors or PC-controlled products that are
8 used. There are medical devices that are simply just a
9 software program.

10 A medical device can be something called a
11 contrivance under the law, and so computer programs are
12 medical devices in some circumstances. In fact, radiation
13 treatment planning systems which are used to plan radiation
14 therapy, we do have a couple of examples where those
15 products did have problems trying to do calculations for the
16 source strength of a radioactive source to be used in
17 delivering teletherapy.

18 There is a lot of devices that interface to
19 databases or to each other and do recordkeeping, and there
20 is a problem there if the dates aren't handled correctly.
21 And the famous embedded chip problem, where many of these
22 devices only display the date or record the date but are not
23 actually used in the functioning of the device.

24 Next. We, for our purposes at FDA, adopted
25 basically the same definition that the Federal acquisition

1 regulations use for our current purchase of IT technology,
2 and basically it says in short here that you shouldn't have
3 a problem depending on the date and the functioning or
4 operation of the product.

5 These slides are in a handout that the committee
6 members have, and I am not going to cover all the slides in
7 that handout, but I will leave the latter part of the slides
8 for your review later. It is a little more detailed.

9 Next slide. Our request of the panel in these
10 discussions are simply to give you the opportunity and
11 request of you any advice you may have with regard to
12 devices in your area of expertise or your clinical domains
13 that have a potential for a problem, and we would like to
14 make sure we have addressed all those issues and paid
15 attention to them.

16 We have had staff here at the center for about two
17 years thinking hard about which products could be impacted,
18 which ones could present a lot of risk. In fact, in the
19 very near future we will be making a public list of the
20 kinds of devices we think have the highest potential for
21 direct patient risk or impact due to a date problem, and
22 will be focusing some of our activities more closely on
23 those devices.

24 So we are interested in hearing from you if there
25 are products that you think have specific or special

1 concerns that we need to take some actions to reduce risk in
2 the future.

3 Next. One of the things we have done, probably
4 the most active area has been in making information about
5 products available to the health care community, and we have
6 done this through our worldwide web side, which this is the
7 address for here. This is a database of information
8 provided by manufacturers.

9 If I could have the next slide, this is just the
10 introductory page to it, but here we have listed information
11 from manufacturers. Initially it was information about
12 products the manufacturer had determined that do have a
13 problem of some sort due to the Y2K or other date-related
14 problems, and the problems can not just be Y2K at January 1,
15 but it could be failure to address leap years properly,
16 failure to address other dates due to some kind of problem
17 in the computer system design.

18 Our web site now also has information on compliant
19 products. We have recently asked manufacturers of the kinds
20 of products that could be vulnerable to a date problem to
21 list those specific problems on our web site. We currently
22 there have almost 500 manufacturers listing over 5,000
23 compliant products, and we have upwards of 4,000
24 manufacturers that have given information about the status
25 of their products with relation to non-compliant problems.

1 And we also have links to most of the major manufacturers,
2 where you can go to the manufacturer's web page and see
3 their information.

4 Next slide. This is an example of some of the
5 information available if you search the web site and go to
6 information for consumers or health care, and you get a list
7 like this. All our guidance documents, all our letters to
8 the manufacturers, are available for review there.

9 Next. This is an example of our search page,
10 where one can go in, enter the name of a manufacturer, pull
11 up all the products from that manufacturer that have been
12 described as having a problem or not, or get a link to that
13 manufacturer's web site. You can search the web by
14 manufacturer name, by type of product, generic class of
15 product, or by model number. You can just put in a model
16 number, and this will tell you if that model number is in
17 our database with a statement from the manufacturer that it
18 is compliant, and if you find that, you are basically done
19 for that model number.

20 Next. What we have done here at CDRH is primarily
21 communicated with the manufacturers about the need to
22 address this problem, to assess their products, to develop
23 solutions where it is necessary. We have provided guidance
24 to manufacturers. We have done our database.

25 We are continuing to monitor and assess the

1 situation with regard to product performance, and we are
2 also very concerned and interested and paying attention to
3 the ability of manufacturers to stay in business, to keep
4 their automated manufacturing lines running, to make sure
5 that we don't have a shortage of an essential or critical
6 medical supply.

7 I think my impression from meetings that were held
8 just a week or so ago with the industry, the industry is
9 making good progress to being prepared. I don't think we
10 have to worry about everybody needs to get an extra six
11 months of everything in their hospital to last out the
12 duration. I think the industry is taking this seriously and
13 making steps to get prepared.

14 And, lastly, we are now undertaking some
15 activities to better educate the clinicians and the public
16 about this issue.

17 Next. And if you have suggestions, comments or
18 concerns, we would invite you to give them to Harry
19 Sauberman, the executive secretary for this panel, or you
20 can communicate with me or anyone else here at the Center,
21 for that matter. I am sure it will get passed along.

22 And with that I will conclude, and will be glad to
23 answer any brief questions if you have the time for that.

24 DR. PATOW: Thank you. Are there any questions
25 from the panel?

1 I am sure the panel members would be interested in
2 reviewing that list of devices and providing any input they
3 could.

4 DR. SHOPE: Yes. Our plan is to--we have done a
5 lot of internal review. We will post that on the web site
6 and invite public comment on it. It is a little bit of an
7 urgency here to get it out, get it reacted to, because we
8 are using it for several other things. The manufacturers of
9 those products will see a little additional oversight from
10 us in terms of what they have done. So we need to get
11 started on that. So I would invite your comments on that
12 list when it does get put up on the web.

13 DR. PATOW: Thank you very much.

14 MR. SAUBERMAN: There was a question.

15 DR. DUFFELL: Yes, just one quick question. I
16 recently read something in one of the industry trade sheets,
17 that FDA was looking into possibly mandating or requiring
18 recalls of products that hadn't been certified as Y2000
19 compliant. Is there any truth to that? And if so, how
20 would it be rolled out? I mean, if the manufacturer hasn't
21 responded back to the agency?

22 DR. SHOPE: No. We would only do a recall if the
23 problem with that product looks like it is not being
24 addressed by the manufacturer appropriately, and the level
25 of concern one has to have to do a mandatory recall is quite

1 high under the Act. It has to really be a serious problem.

2 We are certainly under a lot of scrutiny to make
3 sure we are doing the right thing and paying attention to
4 manufacturers, and we do have plans for the next three or
5 four months to pay close attention to these high-risk types
6 of devices, to make sure that information about those is
7 available.

8 If there is a manufacturer that has not taken the
9 appropriate action to notify customers and users, then I
10 think FDA would use any of our legal authorities. Recall is
11 only one of them, and it is sort of the ultimate sort of
12 seizure. We can also seize products, though. I mean, I
13 think the press fixed on a list that was read of all the
14 kind of authorities we have, and the one at the end of the
15 list which sounded the most ominous, I think, made the
16 story.

17 DR. PATOW: Thank you very much.

18 Just a reminder to panel members and also to
19 anyone who comes to the microphone, please identify yourself
20 each and every time you speak. The reason being that this
21 meeting is being transcribed, and unless we identify
22 ourselves as being the speaker, it will be impossible for
23 the transcriptionist to know who is making the comment.

24 I would like to now introduce Dr. Tom Gross, who
25 will be speaking for Dr. Larry Kessler. He will be making

1 comments on the post-market surveillance activities of the
2 FDA.

3 DR. GROSS: Good morning. I am Tom Gross,
4 Director of Division of Post-Market Surveillance in the
5 Office of Surveillance and Biometrics, and I would like to
6 take a few minutes this morning to talk to you about post-
7 market evaluation at CDRH. We in the Office of Surveillance
8 and Biometrics think it is important that the advisory
9 panels are aware of post-market programs and activities that
10 we conduct, since they are likely to be directly related to
11 your deliberations about a product's safety and
12 effectiveness.

13 The objectives of this presentation are threefold:
14 one, to describe a few of the key methods of device post-
15 market evaluation; two, to present challenges in better
16 accomplishing post-market evaluation; and, three, to
17 describe the pivotal role that advisory panels can play in
18 this arena.

19 This slide, entitled "From Design to
20 Obsolescence," makes three key points. One is, it depicts
21 the natural history of medical devices from design, lab
22 bench testing, clinical testing, FDA review, and
23 importantly, post-market evaluation.

24 Secondly, it depicts the fact that there are
25 continuous feedback loops throughout this process, leading

1 to product improvements. Post-market evaluation has an
2 important part to play in that process.

3 And, three, the clinical community, and
4 importantly the advisory panel, have an important part to
5 play in product improvements.

6 The rest of this talk will focus on three of the
7 post-market evaluation programs listed: the MDR program,
8 post-market surveillance under 522, and our post-approval
9 authority.

10 Now, as products are moved into the marketplace,
11 questions of potential public health interests may arise.
12 There may be concerns about a product's long-term safety,
13 about the performance of the device in community practice,
14 as it moves from outside the narrow confines of clinical
15 trials. There may be concerns about effects of changes in
16 user setting, for instance, moving a product from
17 professional to home use, or concerns about effects of
18 incremental changes in technology. Lastly, there could be
19 concerns about adverse events or unusual patterns of adverse
20 events.

21 Now let's talk about some of the post-market
22 evaluation programs, starting with the Medical Device
23 Reporting program or MDR.

24 Beginning in 1984 under the medical device
25 amendments, manufacturers were required to report deaths and

1 serious injuries to the FDA if a medical device may have
2 caused or contributed to the event, and they were also
3 required to report malfunctions. In 1990 under SMDA all
4 user facilities, and most notably hospitals and nursing
5 homes, had to report deaths to the FDA and serious injuries
6 to the manufacturers.

7 Beginning in 1973, we have received voluntary
8 reports. It was only in the early 1990s that we have
9 received up to and over 100,000 reports of adverse events
10 related to medical devices per year. These reports are
11 submitted on standardized forms and capture data on device
12 specifics, event description, pertinent date, and patient
13 characteristics.

14 Now, unfortunately, many of these reports often
15 have very limited information, but nonetheless they may
16 provide critical signals for FDA to take action.

17 Now, these are some of the actions that may be
18 prompted by the MDR program. They may result in directed
19 inspections of manufacturers or user facilities; ultimately,
20 in product injunctions or seizures, product recalls; patient
21 or physician notification, such as safety alerts or public
22 health advisories; and they may also prompt additional post-
23 market studies.

24 Now, let's talk about two authorities that we have
25 available for the conduct of post-market studies. One is

1 Section 522, referred to in the statute as post-market
2 surveillance, and one is our PMA regulatory authority,
3 referred to as post-approval studies.

4 Now, Section 522 was originally mandated in SMDA
5 1990, and was significantly changed in FDAMA 1997. The 1990
6 version actually had categories and lists of devices, the
7 manufacturers of which were required to do post-market
8 studies on. FDAMA has no such lists or categories; however,
9 it reserves the discretionary right that FDA has to impose
10 post-market surveillance on Class II or III products when
11 there are issues of public health interest at stake.

12 Now, post-approval refers strictly to PMA
13 products, and it is reserved for PMA products, and the
14 studies are noted as condition-of-approval studies. 522
15 extends our authority to Class II or III 510(k) products
16 whose failure may present a public health problem. Both
17 authorities are seen as a complement to our pre-market
18 efforts to continually assure the safety and effectiveness
19 of marketed products.

20 Now, in implementing post-market surveillance
21 under 522, we publish criteria in the form of guidance to
22 help guide our considerations on when to impose post-market
23 surveillance on Class II or III products.

24 The principal criterion is that there needs to be
25 a critical public health question. It may arise from a "for

1 cause" situation such as unique adverse events. It may be
2 linked to new or expanded conditions of use, moving a
3 product, say, from professional to home use. There may be
4 concerns about safety related to the evolution of the
5 product's technology.

6 The second criterion is that there should be
7 consideration of other post-market strategies. Implementing
8 522 may not be the right post-market strategy to address the
9 public health question. Perhaps an inspection or quality
10 system changes can more adequately address the question.

11 Thirdly, the conduct of the study should be
12 practicable and feasible, and a related issue is, how will
13 the data be used? This is particularly important for
14 rapidly changing technologies. By the time we get the data,
15 they may be obsolete because the product has changed several
16 generations.

17 And, lastly, there is a priority consideration.
18 We have limited resources. In implementing and overseeing
19 these studies, we need to take into account the magnitude of
20 the risk and the benefit.

21 Now, once we decide to impose post-market
22 surveillance, there are a variety of post-market
23 surveillance study design approaches that we can choose
24 from. We should choose the least burdensome approach to
25 address the particular public health question at issue.

1 The approaches listed go from the more simple to
2 the more complex. We may only rely on a detailed review of
3 the complaint history or literature to address the public
4 health question. Or we can turn to non-clinical testing the
5 device, use of existing data sets, simple telephone or mail,
6 postcard follow-up of patients, or do something more
7 sophisticated, such as use of product registries, case
8 control studies, and very rarely, randomized trials.

9 Now, in implementing particularly the SMDA 1990
10 version of 522, we experienced several frustrations in the
11 conduct of these studies, and these challenges still exist
12 today. The rapid evolution of technology, as stated before,
13 may make studies obsolete. There may be lack of incentives
14 for industry.

15 Industry may view these studies as providing only
16 negative information about their product. I think the
17 paradigm has to be changed. We have to make it interesting
18 and worthwhile for industry to participate in these studies.

19 There may be lack of interest in the clinical
20 community. Clinicians may be only interested in studying
21 cutting-edge technologies, and not so interested in studying
22 mature technologies that may have some safety issues
23 surrounding them.

24 And there may be lack of specified public health
25 questions. This was the case in the 1990 version of 522,

1 where certain products were required to be studied whether
2 there were pertinent public health questions or not.

3 Now, what is the challenge to the advisory panel?
4 It is a really a challenge, it is a challenge to us all.
5 When considering post-market studies, whether they are post-
6 approval or 522 studies, we should ensure that these are of
7 primary importance, keeping in mind the resource
8 considerations and keeping in mind whether they are
9 practical and feasible. Clearly specify the public health
10 question.

11 And, lastly, note the clinical or regulatory
12 relevance of answering the question: What will we do with
13 the data? Will they be there to reassure us that the post-
14 market arena is similar to what we see in the pre-market
15 data? Are they there to answer residual questions about the
16 products? Can they be done in a timely fashion, so that the
17 data will not be obsolete?

18 And, lastly, just a picture into the future of MDR
19 and post-market surveillance. With regard to medical device
20 reporting, we are moving further away from individual
21 reports and more toward summary reporting as a more
22 efficient review of the reports. We are planning on
23 instituting a sentinel reporting system, whereby we take a
24 subset of the universe of hospitals to provide us high-
25 quality and timely reports. We are moving towards

1 electronic interchange, the electronic submission of
2 reports. We are trying to integrate our efforts with the
3 quality systems regulation. And we are also exchanging
4 reports internationally.

5 With regard to post-market surveillance, I
6 mentioned before that we are employing a wider variety of
7 design approaches. We are intent on collaborating more with
8 industry and the clinical community in the conduct of these
9 studies. And we are also having expanded access to
10 different data sources, such as registries.

11 That is it, and I will entertain any questions.

12 DR. PATOW: Are there any questions from the
13 panel?

14 DR. DUFFELL: Just one.

15 DR. PATOW: Can you identify yourself, please?

16 DR. DUFFELL: Yes, Bill Duffell, the industry rep.

17 Could you clarify again, what is the difference
18 between a condition of approval and post-market
19 surveillance? Are they one and the same or are they
20 separate entities?

21 DR. GROSS: Well, currently we use PMA authority
22 for post-approval studies. Those are Class III PMA
23 products. Since that authority exists under the regulation,
24 under the PMA regulation, we defer PMA Class III products to
25 that authority. Post-market surveillance exists for Class

1 II or III, 510(k) products.

2 DR. DUFFELL: So then the condition of approval
3 would be considered a post-market surveillance. It is just
4 restricted to the Class III products.

5 DR. GROSS; Yes.

6 DR. DUFFELL: Which is what we are looking at
7 today, I believe, in these--

8 DR. GROSS: That is right. It is under the PMA
9 authority. It is referred to as conditions of approval.

10 DR. DUFFELL: Okay.

11 DR. PATOW: Thank you very much, Dr. Gross.

12 At this time we will move to our open public
13 discussion. There are a few comments I would like to make
14 about this part of our meeting.

15 Presenters today are members of the public who
16 have an interest in addressing the panel on today's topic or
17 related matters. Each of the presenters are asked to state
18 their affiliation, any consulting arrangements or financial
19 interest with medical device firms; if travel expenses were
20 paid and by whom; and be aware of the time limit for each
21 presentation.

22 Since our break is at 10:15 and it is now almost
23 9:15 and there are six speakers; we will have exactly 10
24 minutes per speaker, so please be aware of that so that we
25 can get everyone in in a timely fashion.

1 To afford the opportunity for everyone to speak,
2 we have a time monitoring system, and it will be set for 10
3 minutes for each speaker, and you will be able to--I believe
4 on the podium there will be a flashing light.

5 MR. SAUBERMAN: I believe the yellow light will go
6 on at eight or nine minutes and then you will have one
7 minute to wrap up, but we will hold--we will be very strict
8 on time in order to give equity to all the presenters here.

9 DR. PATOW: And, once again, copies of all
10 presentations and slides must be given to the summary
11 recorder and to the transcriber.

12 Our first speaker this morning is Dr. Michael
13 Glasscock of the University of Tennessee Health Science
14 Center. Dr. Glasscock?

15 DR. GLASSCOCK: Thank you. My name is Mike
16 Glasscock. I am a retired otologist, and I am currently
17 living in Austin, Texas. I am a consultant for St. Croix
18 Medical, and my expenses were paid here today.

19 Any time we stand on the threshold of a new ear in
20 medicine, I think it is very important that we consider the
21 ethics of where we are and where we are headed.

22 And the reason that conventional hearing aids are
23 not used as much as they should be--there are probably 25
24 million people that are candidates for a hearing aid but
25 only about 20 percent of that number wear them--and I think

1 the reason for that is that even though conventional aids
2 are greatly improved in the last few years, particularly
3 with the digital and programmable ones, they are greatly
4 improved but there is still discomfort for the patient.
5 There is feedback a lot of times, particularly with severe
6 hearing loss, and the ear canal is occluded.

7 There is a certain stigma of wearing a hearing
8 aid. It indicates a handicap. It is a cosmetic problem for
9 some people. Individuals say "It makes me feel old, makes
10 me look old." And so there is a certain stigma that goes
11 with wearing one of these regular devices.

12 DR. PATOW: Dr. Glasscock, could we ask you to
13 speak up just a little bit?

14 DR. GLASSCOCK: Sure. Sorry.

15 DR. PATOW: Thank you.

16 DR. GLASSCOCK: I have that Southern voice. It is
17 a little low sometimes.

18 The implantable devices, as they become available,
19 will either be partially or totally implantable, and this
20 will depend on the device. And the technologies that are
21 currently being studied are the electromagnetic and the
22 piezoelectrode.

23 Now, these devices will require operating on the
24 ossicular chain, either attaching something to the ossicular
25 chain or in some cases disarticulating the ossicular chain.

1 Either way, this requires operating on a normal ear,
2 basically, a normal middle ear. Now, what are the ethics of
3 this? How do we justify this?

4 Well, first we have to make sure that it is safe
5 and effective, and by "safe" that means that the patient
6 should be able to wear it for years with no injury to
7 themselves, to their inner ear or their middle ear. And it
8 has to be effective. In other words, it has to be better or
9 at least as good as a conventional hearing aid. And it
10 should be, if they work like we think they will, because it
11 should do away with feedback, the hearing should be more
12 clear, there won't be anything in the ear canal in most
13 instances.

14 So how do we justify operating on a normal middle
15 ear? Well, if we go back in history and think about the
16 surgery that we do and have done over the years, many times
17 in order to get to an end, in other words to improve the
18 patient in some way, we may operate on essentially a normal
19 ear. So in fenestration surgery for otosclerosis, we do a
20 mastoidectomy, remove an incus, open up a normal
21 semicircular canal. And in stapes surgery we are opening up
22 a normal inner ear, we are operating in a normal middle ear,
23 and the surgery is not even necessary, it is elective. The
24 patient chooses to have stapes surgery.

25 And in--I can't make this thing go backwards--but

1 in rhinoplastic surgery, for instance, the nose may be
2 functional, normal and work well, but it doesn't please the
3 patient, so it is a cosmetic consideration and that is a
4 patient choice. If a patient would rather have a totally
5 implantable middle ear hearing device, it may be purely on a
6 cosmetic consideration. And so if they have a little hump
7 on their nose or their nose may be a little wide for them,
8 it may be a completely normal functioning nose, and yet they
9 choose to have it operated on.

10 In shunt surgery, we operate on a normal mastoid.
11 In doing cochlear implant surgery, we operate on a normal
12 mastoid, operate on a normal middle ear cavity.

13 So where we stand at this point, in summary, is
14 where I think we were back in about 1971. They had a
15 meeting at the University of California in San Francisco in
16 the fall of 1971, and all of the researchers from around the
17 country were there, and they made a point of saying that it
18 was impossible to stimulate the eighth nerve and that
19 cochlear implants would never work, and that that work
20 should be abandoned.

21 Well, Dr. William House did not abandon the
22 cochlear implant, and the FDA I think was very courageous in
23 working with him at that time to let him develop the
24 cochlear implant, and of course now thousands have been
25 benefitted by that type of device. And I believe that in

1 the future when implantable devices have been proved safe
2 and effective, that in the future millions of people will be
3 benefitted from these devices.

4 Thank you very much.

5 DR. PATOW: Thank you, Dr. Glasscock.

6 Our next speaker this morning will be Dr. Lorenz
7 Lassen and Dr. Maureen Hannley of the American Academy of
8 Otolaryngology.

9 DR. LASSEN: Hello. I am Dr. Lorenz Frederick
10 Lassen. I am in the United States Navy as an
11 otolaryngologist. I work at Portsmouth Naval Hospital. I
12 am currently on leave, and I represent the Academy. I am
13 getting no remuneration from anyone for this.

14 I am Dr. Lassen, and I represent the American
15 Academy of Otolaryngology-Head and Neck Surgery, which is a
16 professional organization of over 12,000 physicians who
17 specialize in treating disorders of the ear, nose and throat
18 and related structures of the head and neck. As you all
19 know, otolaryngologists have been leaders in the medical
20 profession in diagnosing and treating persons with hearing
21 loss and deafness for over 100 years.

22 I am chairman of the Academy's Subcommittee on
23 Implantable Hearing Devices, and I am pleased to have the
24 opportunity to assist this panel in its consideration of
25 implantable hearing devices. In the time available to me, I

1 would like to address issues of patient safety, patient
2 benefit, and efficacy of such devices in a broad, general
3 way.

4 Over 28 million Americans are believed to be
5 hearing-impaired. Levels of hearing impairment may range
6 from mild to more severe. Most important, people with
7 hearing loss can have hearing loss in either low frequencies
8 or high frequencies, most often the high frequencies. The
9 number of hearing-impaired people in the United States is
10 expected to increase as our population increases, our aging
11 population increases.

12 Some types of hearing impairment can be treated
13 medically, some surgically, but most must be managed with
14 amplification systems, either hearing aids or cochlear
15 implants, and rehabilitation measures. Between 6 to 8
16 million Americans who could benefit from amplification
17 either do not have a hearing aid or own but do not use one.

18 What contributes to this situation of non-use are:
19 cosmetic considerations and social stigmatization;
20 unsatisfactory quality of the amplified signal due to
21 limited frequency range and undesired distortion; further
22 modification of the signal by the ear canal occlusion effect
23 in many patients; acoustic feedback with high amplification
24 levels; and cost.

25 Considerable progress has been made in the

1 technology of hearing aids and auditory protheses. Digital
2 and programmable aids with improved signal processing
3 capabilities have enabled customization of hearing aid
4 characteristics to satisfy many individual needs, and
5 various noise reduction schemes have been incorporated into
6 new models. Microchip technology has resulted in hearing
7 aids that can be worn invisibly within the ear canal, the
8 so-called "completely in the canal" hearing aids.

9 Even with these advantages and advances, however,
10 some fundamental disadvantages of conventional hearing aids
11 persist. These disadvantages are related to the acoustics
12 of sound transmission to the outer and middle ear, as well
13 as to certain technical barriers.

14 Persons with moderate to severe cochlear hearing
15 loss offer a special challenge. They are ineligible for
16 cochlear implantation because of their residual good nerve
17 hearing. They nonetheless often experience limited benefit
18 from conventional hearing aids because that same residual
19 hearing is not functional without high levels of
20 amplification, and these levels result in feedback, sound
21 distortion, and unfavorable conditions for frequency
22 transfer. Additionally, patients who have occluded ear
23 canals with hearing aids can have problems with external
24 otitis and wax buildup. Thus, we have a category of
25 hearing-impaired persons for whom cost of the latest hearing

1 technology buys very little benefit.

2 In order to overcome some of these disadvantages,
3 and to provide amplification options for the full range of
4 hearing-impaired persons, a significant amount of research
5 has been directed at developing surgically implantable
6 electronic hearing devices. Because otolaryngologists are
7 committed to helping all our hearing-impaired patients
8 regain the richness of the world of sound through as many
9 means as possible, we support the continued development and
10 use of these devices.

11 The benefits of implantable hearing devices have
12 been documented in the literature. Some of the more
13 important features include: Improved sound quality and
14 speech intelligibility. By leaving the ear canal
15 unobstructed and the natural resonance undisturbed, a more
16 natural sound quality is obtained over a broader range of
17 frequencies, and the user's ability to understand speech is
18 expected to be greater. The benefit of an unobstructed ear
19 canal, underestimated in the past, is crucial, allowing the
20 patient to use his or her own low-frequency residual
21 hearing.

22 Moreover, the status of the tympanic membrane can
23 introduce unwanted and uncontrolled modifications to the
24 amplified signal before it reaches the cochlea, a variable
25 which is eliminated in devices that act directly on the

1 middle ear structures. Both the piezoelectric and
2 electromagnetic transducers have the advantage of very broad
3 frequency responses with low linear and non-linear
4 distortion, leading to patient reports of better
5 understanding, and even appreciation of music.

6 Elimination of acoustic feedback is important.
7 Since implantable hearing aids do not require an earmold and
8 thus effectively separate the microphone from the speaker,
9 they do not generate the disconcerting and annoying acoustic
10 feedback of high-gain instruments used with an earmold.

11 Improved sound localization. Users seem to be
12 able to appreciate the acoustic sound environment, identify
13 specific sounds and their source, and differentiate sounds
14 from background noise. The superior speech understanding in
15 noise achieved with implantable hearing aids is an important
16 feature not uniformly available with conventional aids.

17 Improved comfort, reliability, and aural hygiene.
18 There is no earmold inserted in the ear canal, resulting in
19 increased comfort for users as well as improved reliability.
20 Since none of the hearing aid's components are seated within
21 the ear canal, the reliability problems caused by wax and
22 moisture are eliminated and the susceptibility to otitis
23 externa related to an occluded ear canal is reduced.

24 Ease and longevity of use. These devices may make
25 hearing aids more accessible to persons with physical

1 limitations or special needs, since there are no miniature
2 controls, and there is no necessity to change properly
3 oriented small batteries and no necessity to insert an
4 earmold. This is particularly important with our elderly
5 population, who have a difficult time with these small
6 little hearing aids. Users can have the benefit of
7 amplification while swimming, bathing, and even sleeping.
8 Rechargeable power sources provide substantially longer
9 operation than the batteries used with conventional hearing
10 aids.

11 As physicians and surgeons, otolaryngologists
12 naturally are concerned about the safety of products they
13 may use to treat their patients. Those that will be
14 implanted deserve special close scrutiny. Again, the
15 pioneers of this technology have scrutinized and measured
16 potential sources of hazard, especially the power source,
17 the force output of the transducer, biocompatibility and
18 biostability of the materials, and the potential risks of
19 the electromagnetic field, and concluded that these devices
20 are safe, effective and beneficial.

21 Patients electing to have middle ear hearing
22 devices implanted would of course have the generally known
23 risks of anesthesia and surgery which are common to other
24 middle ear and mastoid type operations. Because the
25 implantable hearing devices are a relatively new

1 development, there is limited longitudinal data on the risks
2 of deteriorating materials or their long-term effects on the
3 middle ear structures to which they are coupled. As you
4 know, however, clinical trials with several different
5 devices have been conducted for a long period of time in
6 Japan, Germany, and the United States with no serious
7 consequences.

8 In summary, the American Academy of
9 Otolaryngology-Head and Neck Surgery supports the concept
10 and utilization of implantable middle ear hearing devices.
11 They have been shown to offer an important new option to a
12 category of hearing-impaired persons who have been able to
13 derive little benefit from conventional hearing aids. They
14 have eliminated some common problems which have frustrated
15 or discouraged hearing-impaired persons from using personal
16 amplification systems, and their efficacy and benefits to
17 patients have been documented through careful psychoacoustic
18 and audiologic studies.

19 There are certain risks common to all types of
20 surgically implanted devices, but the current thoughtfully
21 engineered, rigorously tested implantable middle ear hearing
22 devices may represent a very real new millennium in hearing
23 health care.

24 Thank you very much, and I would be happy to
25 answer any questions.

1 DR. PATOW: Are there any questions from the
2 panel?

3 DR. KHAN: Could you state some risks?

4 DR. PATOW: Can you identify yourself, please?

5 DR. KHAN: I am Dr. Khan from Silver Spring,
6 Maryland.

7 DR. LASSEN: Sure. The risks would be the same
8 sort of risks that you would have with any type of operative
9 procedure involving the middle ear and mastoid, and they
10 include bleeding, infection, nerve damage. The nerve damage
11 that could occur with an operative procedure of the middle
12 or inner ear would include damage to the cochlear nerve, the
13 vestibulocochlear apparatus, the balance nerve, and of
14 course the possibility of residual pain.

15 DR. CAMPBELL: Dr. Emmett Campbell. The facial
16 nerve also?

17 DR. LASSEN: Yes, sir.

18 DR. PATOW: Any other questions?

19 Thank you very much.

20 DR. LASSEN: Thank you.

21 DR. PATOW: Our next speaker this morning will be
22 Dr. Sigfrid Soli from the House Ear Institute.

23 DR. SOLI: My name is Sigfrid Soli. I am the
24 Director of Hearing Aid Research at the House Ear Institute.
25 I would like to disclose several different affiliations with

1 industry.

2 The House Ear Institute is currently conducting
3 clinical trials for two implantable hearing aid devices,
4 Symphonix and Otologics. In addition, my laboratory has a
5 research contract with Otologics, and a portion of my travel
6 on this trip has been paid under that contract. I have also
7 in the past had research contracts with Advanced Bionics,
8 been a consultant to Cochlear Corporation, and have had a
9 research contract with Starkey Laboratories, a hearing aid
10 manufacturer. The House Ear Institute is also the developer
11 of the Hearing In Noise Test, which I will mention later.

12 Today I would like to address several comments to
13 the safety and effectiveness of middle ear amplification
14 devices, and in beginning these comments I would like to
15 harken back over 15 years ago to the first middle ear
16 implants performed by Dr. Yanagihara in Japan at Ahima
17 University. Dr. Yanagihara did not have the benefit of a
18 group such as this to advise him in his efforts, but I think
19 that we have learned in those ensuing years that perhaps the
20 primary concern for evaluation of these devices has to do
21 with their efficacy, and I would like to address most of my
22 comments today to the question of efficacy.

23 Let me begin by offering a definition of
24 effectiveness or efficacy. I would suggest that a middle
25 ear implant, if it is to be effective, must be functionally

1 superior to air conduction hearing aids, and that needs to
2 be demonstrated. Functional superiority falls in several
3 categories: audibility and loudness, speech communication,
4 the clarity and quality of sound, and the ability to
5 localize sound and to listen selectively or to hear
6 directionally, which is a binaural hearing ability.

7 I think effectiveness must be defined in terms of
8 two different modes of use, both monaural use, that is to
9 say the implanted device in the implanted ear by itself, and
10 binaural use, when it is used in conjunction with an air
11 conduction hearing aid in the other ear. Many of the
12 patients who may be indicated for implantation with this
13 device have moderately severe to severe hearing loss and
14 will benefit from the use of an air conduction device in the
15 unimplanted ear, so part of the effectiveness will depend, I
16 believe, on the function of the implant in conjunction with
17 an air conduction device in the other ear.

18 How do we achieve this effectiveness? The device
19 must ensure audibility, loudness, clarity and quality, as
20 follows directly from my previous slide. That means that
21 the implant system must generate vibratory displacements of
22 the ossicles that produce sensations ranging from threshold
23 to UCL or upper comfort level at all frequencies, with low
24 distortion, and that span the desired audio bandwidth.

25 To achieve this goal, we have to attend, I

1 believe, to the various transformations of energy that occur
2 in the use of an implanted hearing aid. I have tried to
3 summarize these on this slide.

4 The first transform is that of the transmission
5 system, from the electrical input of the transmission system
6 to its electrical output which serves as the input to the
7 stimulator or the transducer. The second transform is
8 electromechanical transformation from the electrical input
9 of the stimulator to the mechanical output it produces when
10 it vibrates the ossicles. And the third transform, and
11 perhaps the most important one, is how those displacements
12 translate into audibility and loudness, the auditory
13 phenomenon. These transforms I believe must be known if we
14 are to establish the effectiveness of these devices.

15 Now, it is also important in characterizing these
16 transforms to consider the wide range of variability that
17 might impact them and that will also impact effectiveness.
18 As you know, thresholds and UCLs differ between subjects,
19 they differ as a function of frequency, and they can differ
20 over time longitudinally within the same subject.

21 There is also variability in the mechanical
22 coupling of the stimulator to the ossicle. Not all of the
23 energy that is put into the mechanical stimulator is
24 necessarily transformed in an appropriate vector into
25 displacements of the ossicles that produce auditory

1 sensations.

2 There may be variability, as well, in the
3 sensitivity of the transducers. That can probably be
4 handled at the time of manufacture. And there is
5 variability in the alignment and separation between the
6 transmitter and the receiver. So all of these will affect
7 these transforms.

8 Now, these transforms in the dynamic range of the
9 device must be known if we can establish its effectiveness.
10 If you add all those up that I showed you on the two slides,
11 and you take into consideration the variability, make some
12 assumptions about how wide that might be, I think the system
13 dynamic range requirements may exceed 100 dB from the lowest
14 threshold to the highest UCL, and including the variability
15 in mechanical coupling and transmission system.

16 Moreover, the minimum vibratory displacements at
17 threshold, say the threshold is down around 20 dB SPL, are
18 on the order of Angstroms. These requirements I think
19 significantly challenge current hearing aid technology and
20 RF technology. So I think it is very important, in
21 establishing effectiveness, to examine these closely.

22 How do we demonstrate effectiveness? I think it
23 begins with appropriate patient selection. Clearly the
24 thresholds and UCLs measured with air conducted sound must
25 be within the achievable dynamic range of the device, with

1 an extra margin for the unpredictable variability that is
2 only known after the device is implanted.

3 And I believe that it is extremely important that
4 there should be pre-implant baseline trials with state-of-
5 the-art air conduction hearing aids, because there is an
6 alternative therapy in the case of these individuals,
7 namely, air conduction hearing aids. This should monaural
8 evaluation of the implant ear and binaural evaluation with
9 two air conduction hearing aids, and you will see why in a
10 moment.

11 The signal processing that is used in the air
12 conduction aids and the implant ideally should be
13 comparable, and the fitting strategies should be comparable.
14 That is the only way to ensure appropriate comparisons. It
15 is also important, in evaluating effectiveness, to use
16 reliable norm-referenced outcome measures.

17 I think it might be appropriate to follow the
18 example of the cochlear implant community in this regard and
19 define a minimum set of measures for use in all trials.
20 Those measures might be used with whatever other measures
21 are appropriate for the particular device. The Minimum
22 Speech Test Battery for Adult Cochlear Implant Users is
23 comprised of two speech tests, the Hearing In Noise Test
24 which measures speech intelligibility in quiet and in noise,
25 and the Consonant-Nucleus-Consonant or CNC test which

1 measures word intelligibility. So I would encourage the
2 panel to consider the adoption of some type of a minimum set
3 of measures.

4 Okay. Post-operatively, I think it is important
5 in documenting or demonstrating effectiveness to include, of
6 course, monaural assessments comparing the implant ear to
7 the monaural baseline with an air conduction aid, using the
8 same fitting and signal processing if possible.

9 And post-operative binaural assessments, as well,
10 should compare the implant plus the air conduction aid,
11 post-op, to the binaural baseline with two air conduction
12 aids. These evaluations and assessments, to really
13 determine the binaural effectiveness of the implant together
14 with an air conduction aid, should include some measures of
15 directional hearing and/or sound localization, and again
16 using same fitting and signal processing.

17 Finally, I would like to mention that I believe
18 that despite the positive implications and strengths of
19 implantable devices, there are some practical limitations
20 that need to be considered as well. I mentioned before that
21 the efficiency of the vibratory energy transfer from the
22 stimulator to the ossicles may be unpredictable. The
23 ossicles vibrate in different modes at different
24 frequencies. The stimulators in use today may not be able
25 to produce those types of displacements, so the impact of

1 that energy, the efficiency of that transfer, needs to be
2 examined carefully.

3 Of course the ossicular loading of the device can
4 affect the audibility of air conducted sound, since hearing
5 with air conducted sound in some cases is possible after
6 implantation. Despite what the previous speaker said, I
7 know that acoustic feedback can occur with these implanted
8 devices. If the tympanic membrane is vibrated by an
9 implanted stimulator, it creates sound pressure that finds
10 its way back to the microphone, so that is a potential
11 practical limitation. Clearly it is not as severe as with
12 air conduction hearing aids, however,

13 And, finally, I think it is important to consider
14 the way in which acoustic stimulation via air conduction
15 sound at the TM and the mechanical stimulation produced by
16 the implant might interact with each other, since there are
17 two sources of energy activating the middle ear. This is
18 especially true at high sound pressure levels if you are
19 using a compression amplifier in your implant device.

20 So these are all things that I think can have an
21 impact on effectiveness, and I thank you for the time to
22 present this information to you today.

23 DR. PATOW: Thank you.

24 Do you have a question?

25 MR. SAUBERMAN: Yes. Thank you, Dr. Soli. Do you

1 have copies of your slides?

2 DR. SOLI: Yes, I do.

3 MR. SAUBERMAN: Good. Okay.

4 DR. PATOW: Are there any questions from the
5 panelists? Please identify yourself?

6 DR. KILENY: I am Dr. Kileny. I have a quick
7 question. Could you speculate on the effects of surgical
8 variance in terms of coupling those devices that are
9 mechanically coupled to the intact or the disarticulated
10 ossicular chain on this energy transfer that you have
11 discussed previously? There might be some minute ways that
12 these devices may be attached. How would those affect the
13 energy transfer?

14 DR. SOLI: Well, certainly the method of fixation
15 will affect energy transfer. Whether you--the variability
16 associated with methods of fixation, at this time I am not
17 prepared to speculate, but it is something that I think
18 could be established, for example, in animal studies prior
19 to implantation in humans.

20 DR. WOODSON: This is Gayle Woodson from Memphis.
21 You specified that we should test this, verify its efficacy
22 against air conduction aids. You didn't mention bone
23 conduction aids. I was wondering what your comments would
24 be on that.

25 DR. SOLI: Bone conduction aids. Well, I limited

1 my comments to the selection criteria I am familiar with,
2 which are sensorineural hearing loss rather than mixed or
3 conductive losses, so for those cases a bone conduction aid
4 would probably not be used. However, if there is an
5 effective alternative for conductive and mixed losses
6 involving bone conduction stimulation, then, yes, I believe
7 it should be--that could define an appropriate baseline.
8 The appropriate baseline is whatever gives the patient the
9 best performance pre-implant.

10 DR. PATOW: Thank you, Dr. Soli.

11 Our next speaker this morning is Dr. Henry J.
12 Ilecki of the American Speech-Language-Hearing Association.
13 And Dr. Ilecki will be introduced by Ms. Evy Cherow of the
14 American Speech-Language-Hearing Association.

15 MS. CHEROW: Thank you. Dr. Patow, Dr. Rosenthal,
16 Mr. Sauberman, and members of the Ear, Nose and Throat
17 Devices Panel, good morning and thank you for the
18 opportunity to offer comments on the safety and efficacy of
19 middle ear amplification devices. I am Evelyn Cherow,
20 Director of the Audiology Practice Policy and Consultation
21 Unit of the American Speech-Language-Hearing Association. I
22 have no relationship with manufacturers. We have had no
23 support for travel today.

24 The American Speech-Language-Hearing Association
25 is the professional and scientific organization that

1 represents over 96,000 audiologists, speech-language
2 pathologists, and hearing and speech scientists. The
3 Association encourages the development, evaluation and
4 implementation of procedures, programs and technologies
5 holding promise in the areas of identification, evaluation
6 and treatment of individuals with hearing loss. The work of
7 the Food and Drug Administration in this regard has been
8 highly constructive and beneficial to the public health, and
9 there is every anticipation that this record will be
10 extended into the newly expanding realm of implantable
11 hearing aids.

12 At this time I would like to introduce a new
13 member of ASHA's staff, Dr. Henry Ilecki, Director for
14 Audiology Practice in Industry and Private Practice, who
15 will provide ASHA's recommendations on this topic.

16 DR. ILECKI: Thank you, Evy. Good morning, panel
17 members. My name is Henry Ilecki. As you have just heard,
18 I am employed by the American Speech-Language-Hearing
19 Association. I have no commercial affiliations. My travel
20 expenses are nil, since I am a local resident, living in
21 Rockville, although I should mention that free parking was
22 provided by the Food and Drug Administration.

23 In the promising and emerging area of implantable
24 hearing aids, the American Speech-Language-Hearing
25 Association recommends that, at the least, five broad areas

1 of investigation be included during the Food and Drug
2 Administration's deliberative process. These are, one,
3 analysis of the safety and efficacy of the technology; two,
4 compatibility with other amplification and
5 telecommunications technologies; three, cost-benefit
6 analysis; four, consideration of candidacy criteria; and,
7 five, the essential need for comprehensive pre- and post-
8 implant audiological evaluation and treatment.

9 First, technology safety and efficacy. The
10 preeminent concern of the FDA when reviewing a new
11 technology is the short- and long-term safety of the
12 technology to its intended beneficiaries. ASHA is confident
13 that the technology and process of implantable hearing aids
14 will undergo the critical scrutiny of the Food and Drug
15 Administration in all aspects of its implementation related
16 to the issue of safety, comparable to its work with the
17 development and distribution of cochlear implants.

18 However, no matter how safe a procedure may be, it
19 is not a course worth pursuing if it is not judged to be an
20 efficacious one. In its examination of the efficacy of
21 implantable devices, it is ASHA's view that it would be
22 useful for the FDA to review the issue from the following
23 five perspectives:

24 Number one, etiology and type of hearing loss.
25 The heterogeneous effects that conductive and sensorineural

1 hearing loss have on such conventional measures as
2 audiometric configuration, speech perception, speech
3 reception, and speech recognition in quiet and background
4 noise are well known. Similarly, hearing loss type has a
5 profound influence on the clinician's plan for medical and
6 audiological rehabilitative intervention.

7 The indications for consideration of implantable
8 middle ear devices doubtless will be influenced by the type
9 of pathology causing the patient's hearing loss. A
10 desirable outcome of the panel's work would be a description
11 of the types of hearing loss and related etiology or
12 etiologies most expected to benefit from this type of
13 technology. Conversely, a description of contraindications
14 is equally desirable.

15 Two, degree of hearing loss. While surgical
16 intervention and high technology, namely cochlear implants,
17 are typically restricted to individuals with severe to
18 profound degrees of hearing loss, it is postulated that
19 middle ear amplification devices will have a broader base of
20 application. This is an important distinction to make, as
21 there would appear to be growing numbers of patients with
22 comparatively moderate losses of sensitivity seeking
23 benefits heretofore unavailable with conventional devices
24 and traditional follow-up procedures. The determination of
25 the extent to which implantable hearing aids can

1 successfully treat a variety of degrees of hearing loss
2 would be a useful outcome of the panel's work.

3 Item three, other audiometric and related factors.
4 While type and degree of hearing loss are primary
5 determinants in hearing aid candidacy and management
6 decisions, they are not exclusive. Several other factors
7 come into consideration, including tolerance problems
8 related to loudness recruitment; non-auditory tolerance
9 issues, for example, allergic reactions to hearing aid
10 material; audiometric configuration effects; unilateral
11 versus bilateral fittings, et cetera. The extent to which
12 these and other considerations are factored into surgical
13 decisions for implantable hearing aids is another critical
14 area of study.

15 Item four, perceived disability and quality of
16 life. In reviewing desired outcomes, the question must be
17 posed as to what extent do implantable hearing aids alter
18 recipients' perception of disability and their sense of
19 quality of life? What differences, if any, are there
20 between recipients of implantable hearing aids and users of
21 traditional amplification devices?

22 Item five, history of amplification use. Not
23 surprisingly, experienced hearing aid users typically have a
24 set of expectations regarding amplification that is
25 different from that of inexperienced users. In addition,

1 reported satisfaction rates are higher among experienced
2 users. Any study of the efficacy of implantable hearing
3 aids should include an accounting of recipients' outcomes,
4 expectations, and levels of sophistication, in general terms
5 and specifically with regard to hearing aid usage.

6 The second broad area of study recommended by ASHA
7 concerns the vast array of existing assistive technology in
8 the marketplace and in use by myriad users of conventional,
9 that is to say wearable, hearing aid devices. Assistive
10 listening devices range in size and cost from the simple
11 strap-mounted, battery-powered telephone amplifier to FM or
12 infrared devices used to enhance the signal-to-noise ratio
13 of stage material broadcast to compatibly equipped hearing
14 aid users in the audiences of concert and lecture halls.

15 The extent to which the implantable hearing aid
16 obviates the need for this technology or, more likely,
17 utilizes existing assistive technology in special listening
18 circumstances, needs to be investigated.

19 A cost-benefit analysis of middle ear
20 amplification devices is ASHA's third broad recommendation.
21 A procedure or device that exceeds by many times the cost of
22 traditional intervention should be reasonably expected to
23 provide appreciable and measurable advantages over the
24 referent technology. Useful to this process would be a
25 description and implementation of universal outcome measures

1 applied to the new and referent technologies.

2 Four, ASHA encourages, urges the panel to consider
3 a general recommendation recognizing the essential role
4 performed by the audiologist as a critical hearing care
5 professional in candidacy consideration and the
6 rehabilitative process. Decisions relative to the
7 implantation of middle ear amplification devices should
8 relate to auditory status and auditory processing
9 information derived through a comprehensive pre- and post-
10 implantation audiologic evaluation performed by an
11 audiologist.

12 And, five, certainly in the area of cochlear
13 implants but as well in all device-based forms of
14 intervention, the critical component to successful patient
15 outcome has been shown to be dependent upon regular,
16 intensive, and quality post-surgical orientation,
17 counseling, and rehabilitation by the audiologist. Areas of
18 audiologist participation would include determination of
19 candidacy, pre-operative counseling, and post-operative
20 audiologic rehabilitation.

21 In summary, the review and regulation of medical
22 devices such as hearing aids and implantable amplification
23 devices is the critically important function of the Food and
24 Drug Administration. It is the view of the American Speech-
25 Language-Hearing Association that in evaluating emerging

1 technologies and applications, the FDA recognizes and
2 promotes the value of a concomitant audiologic component to
3 ensure the eventual clinical acceptance, utility, and
4 successful outcomes with these new devices.

5 I ran a little bit over. I am sorry.

6 DR. PATOW: No problem.

7 Any questions from the panel for Dr. Ilecki?

8 DR. MIDDLETON: I paid particular attention to--

9 DR. PATOW: Can you identify yourself, please?

10 DR. MIDDLETON: I'm sorry. Renee Middleton,
11 consumer rep. Your comments regarding client expectations,
12 particularly with respect to perceived disability and
13 quality of life, just making sure I understood you
14 correctly, that your belief is that individuals who are
15 experienced hearing aid users may have a different set of
16 expectations and knowledge base compared to those who have
17 never been aided with any device in the past. Is that--

18 DR. ILECKI: I believe that the experience of the
19 user does enter into the equation, and clearly the
20 expectations of those two groups of people are very much
21 different.

22 DR. MIDDLETON: And so, in looking at the
23 feasibility of using the middle ear implantable devices,
24 would you then suggest some type of comparison between the
25 two--

1 DR. ILECKI: I am saying that is a factor that you
2 would have to control. You wouldn't want to compare, for
3 example, the experience of one group with one technology to
4 another group with a different technology if the experience
5 bases were somewhat different, because the experience bases
6 I think influence the outcomes that you observe.

7 DR. MIDDLETON: Thank you.

8 DR. PATOW: Thank you very much.

9 Our next speaker is Ms. Brenda Battat from Self
10 Help for the Hard of Hearing.

11 MS. BATTAT: Good morning, members of the panel.
12 I am very pleased to be here and have the opportunity to
13 present to you. I am Brenda Battat. I am Acting Executive
14 Director of Self Help for Hard of Hearing People, which is
15 the major consumer organization for people who are hard of
16 hearing and want to use their residual hearing. Over 80
17 percent of our members use hearing aids, and an increasing
18 number are being implanted with cochlear implants, so my
19 comments are directly related to the user and the concerns
20 that we have from the consumer perspective.

21 DR. PATOW: Before you proceed, could you just
22 mention if you have had any industry sponsorship, any
23 sponsorship from a device manufacturer.

24 MS. BATTAT: Oh, from device manufacturers? Yes.
25 In terms for our--

1 DR. PATOW: Travel or--

2 MS. BATTAT: --convention and related activities?

3 DR. PATOW: Well, if you in your travel here, or
4 if you have a grant or any sponsorship.

5 MS. BATTAT: Oh, no, no, no. No, no. I came
6 completely independently. No.

7 Assuming a consumer is eligible for this device,
8 they may select or make a decision based on cosmetic reasons
9 only, and that is their right. They may also have the
10 perception, given that it is a surgical intervention, that
11 it will be a lot better than conventional hearing aids, so
12 that we feel that it is critical that listening advantages,
13 disadvantages, should be reviewed for all potential
14 candidates, and that realistic and truthful expectations be
15 delivered up front so that the consumer understands exactly
16 what the expectations might be.

17 For both hearing aids and cochlear implants, we
18 have found rehabilitation following fitting is critical to
19 ensure successful use of the devices. We want to make sure
20 that rehabilitation will be a major part of the fitting
21 procedure and will be available following implant of the
22 implantable hearing aids. It is critical for their
23 successful use.

24 Hearing aids are subject to electromagnetic
25 interference from environmental sources such as computers

1 and fluorescent lights and motion detectors, security
2 systems, microwave ovens and digital wireless telephones,
3 just to mention a few sources. We want to make sure that
4 these devices have been thoroughly tested to make sure that
5 they have a high immunity to such interference, because this
6 can be extremely difficult for people who are using
7 conventional hearing aids.

8 A significant portion of our daily life is spent
9 on the telephone, and these devices must be suitable and
10 usable successfully with all kinds of telephones. For
11 people with severe hearing loss, we have found that being
12 able to couple their hearing aid directly, inductively with
13 a hearing aid compatible phone improves performance on the
14 telephone. Will these devices allow such coupling for
15 people with more severe levels of hearing loss?

16 Cochlear implant and hearing aid wearers still
17 find situations where they need to augment their implant or
18 their hearing aid, for example when there is a long distance
19 from the speaker, and I can give you an example myself
20 today. I wear two behind-the-ear hearing aids, power aids,
21 but I am not able to follow the discussion here without an
22 assistive listening device.

23 So that we want to make sure that these
24 implantable devices will be able to be used with assistive
25 listening devices in those situations where they will be

1 necessary. That is a very important aspect of the design in
2 terms of successfully being able to participate in a variety
3 of situations.

4 And of course we are very concerned about the
5 testing, which I know that the FDA is going to be monitoring
6 closely to make sure of the safety and the actual surgery,
7 including things such as rejection, breakdown, and
8 malfunction.

9 I wanted to keep my comments short, but these are
10 all concerns that we have from the consumer perspective.

11 Thank you very much.

12 DR. PATOW: Thank you. I appreciate the speakers
13 staying on time this morning. I think that will help our
14 meeting to proceed in a timely way.

15 Our final speaker for this open discussion is Dr.
16 Stanley Baker of the Otologic Medical Center in Oklahoma
17 City, Oklahoma. Dr. Baker.

18 DR. BAKER: Thank you. Good morning, members of
19 the panel, FDA, industry representatives and interested
20 parties. My name is Stan Baker and I live in Oklahoma City,
21 where I am privileged to work at the Otologic Medical Clinic
22 and have a private practice in otology and neuro-otology.

23 I am a co-investigator in the clinical trial of
24 the Symphonix Vibrant Soundbridge, and have performed six
25 implant procedures with the Symphonix device and one

1 revision procedure. I have no financial arrangement with
2 the manufacturer other than for reimbursement of travel
3 expenses related to this meeting.

4 In the private practice of otology and neuro-
5 otology, I have had the opportunity to develop significant
6 mastoid and middle ear surgical experience, and regularly
7 perform cochlear implants in children and adults. This
8 morning I will address the issues related to the surgical
9 procedure, risks and benefits associated with performing
10 such operations in normal middle ear anatomy. And while
11 what I am presenting is in specific reference to my
12 experience with one of these middle ear implantable hearing
13 devices, I believe that the surgical issues may be common to
14 more than this one particular implantable hearing device.

15 There is a technique, a bone dissection technique
16 issue at play here that I want to touch on briefly, and that
17 is, while surgically entering the middle ear through the
18 facial recess for this type of procedure, it is important to
19 remember that this is a normal middle ear anatomy and with
20 residual or native hearing that must be protected.

21 While creating a posterior tympanotomy through the
22 facial recess, a diamond burr must be used instead of a
23 cutting burr with the drill system, and care must be
24 exercised not to touch any part of the ossicular chain with
25 the spinning burr. The use of the diamond burr is strongly

1 preferred in order to protect the cochlea from acoustic
2 trauma.

3 Use of the diamond burr should minimize the
4 possibility of inadvertent contact with the ossicular chain,
5 and should such accidental contact occur, the use of the
6 diamond burr will minimize the consequences. Preservation
7 of the patient's residual hearing is a primary concern, and
8 preservation of the chorda tympani nerve is also advisable.

9 Any potential long-term negative effects of an
10 implant in the middle ear should be minimized by ensuring
11 that the device is designed not to interrupt blood supply to
12 the ossicles. Patients who have undergone revision surgery,
13 including the one that I have had the occasion to do, have
14 been found to have remarkably healthy middle ear mucosa and
15 a normal appearance of the ossicular chain.

16 In general, an implant device and procedure that
17 does not structurally alter the middle ear anatomy is
18 desirable.

19 The weight of middle ear implants can have a
20 significant effect on residual hearing by virtue of adding
21 mass to the ossicular chain. The effect of this has been
22 well documented in the literature for over 20 years.
23 Attention should be given to not exceeding 50 milligrams
24 with the weight of the middle ear component of an implanted
25 hearing device.

1 In general, it is desirable to have a device
2 configuration that allows for the possibility of revision
3 surgery. Additionally, that revision surgery should pose no
4 greater risk than the original implant operation.

5 Any middle ear implantable hearing device and its
6 attendant implant surgery should allow for the possibility
7 that the patient may need or want to return to the use of a
8 conventional acoustic hearing aid in the future. This would
9 be best achieved if the procedure were in fact reversible,
10 in that the patient's post-surgical residual hearing is
11 substantially equivalent to the pre-surgical hearing. This
12 would allow the use of an acoustic hearing aid to be easily
13 resumed, should that be necessary.

14 An adequate post-operative healing period should
15 be allowed before the initial device activation. This
16 period of time allows for mucosal healing and for resolution
17 of middle ear fluid to occur, so that the expected temporary
18 post-operative conductive hearing loss will resolve and
19 allow appropriate device programming.

20 The use of a semi-implantable device affords the
21 patient the opportunity of upgrades, processing
22 improvements, and technological enhancements as they
23 develop. And while this technology is in its infancy,
24 patients are best served by a device that offers the
25 flexibility of a semi-implantable configuration.

1 And, finally, because of the routine use of MRI
2 scans in medical diagnosis and concern about the possible
3 incompatibility of electromagnetic devices with MRI
4 scanning, this issue of theoretical and real limitations on
5 future MRI scanning for this group of patients needs to be
6 addressed in detail with each implantable middle ear hearing
7 device.

8 Thank you for your time and attention. I would be
9 glad to take any questions.

10 DR. PATOW: Yes, Dr. Shelton?

11 DR. SHELTON: Dr. Shelton. You mentioned that you
12 have done a revision surgery on one of these cases. Can you
13 elaborate on the reasons to need to do the revision and what
14 you found at that revision?

15 DR. BAKER: Well, there are at least two parts in
16 answer to that. There was a device situation, that you may
17 want to address the company about the particulars about it.
18 I might mention that it did obviously present a unique
19 opportunity to reinspect the status of the middle ear and,
20 with the microscope, inspect the mucosa and the ossicular
21 configuration, and they appeared to be normal.

22 I am not sure that answers exactly what your
23 question was, though.

24 DR. SHELTON: So the connection of the device to
25 the ossicular chain--this is the Symphonix device?

1 DR. BAKER: Yes.

2 DR. SHELTON: That appeared normal in that
3 location?

4 DR. BAKER: Yes, it was remarkably normal, and
5 even with a higher power on the magnification, the mucosa
6 appeared intact and there was no sign of what you will see
7 with a stapedectomy prosthesis sometimes in terms of incus
8 changes. That was not visible.

9 The patient had had the implant in place for seven
10 months and was actively using it at least 18 hours a day for
11 five months.

12 DR. SHELTON: Very good.

13 DR. PATOW: Dr. Campbell?

14 DR. CAMPBELL: This is Dr. Campbell. In your
15 experience with the fixation on the incus, do you see any
16 potential problems or are you anticipating potential
17 problems of blood supply to the incus and loss of the incus,
18 the distal portion of it, by blood supply? In stapes
19 surgery there seems to be no problem with this, but do you
20 see any from this situation here?

21 DR. BAKER: The theoretical concern is there, and
22 that is why it was gratifying to be able to see this
23 particular patient. Theoretically there is that possibility
24 and it needs to be attended to, and I suppose there are
25 different ways of watching for that particular outcome in

1 terms of residual hearing, if there is any degradation of
2 that over time. I am not aware of that having happened with
3 that particular device or any of the others at this point.
4 But, yes, theoretically that concern is there, and
5 specifically for each device that needs to be watched, using
6 whatever modalities are available to watch for that
7 possibility.

8 DR. CAMPBELL: The other question is, what is
9 your--what do you think about consideration of the
10 experience of the surgeon and his experience with the facial
11 recess and training?

12 DR. BAKER: That might should be the topic of a
13 separate meeting, but that is an issue, and that is an issue
14 for virtually any kind of delicate microsurgical procedure.
15 The experience of the surgeon in general, and specifically
16 with the device and that particular anatomy and the
17 variations of anatomy, are at play. And the safety and
18 efficacy of a device is going to be dependent on several
19 things, and one of the major considerations will be the
20 experience of the surgeon. That is right.

21 DR. CAMPBELL: Thank you, Mr. Chairman.

22 DR. PATOW: Other questions from the panel?

23 Thank you, Dr. Baker.

24 DR. BAKER: Thank you.

25 DR. PATOW: I would like to thank each of the

1 speakers this morning for the valuable information they have
2 provided to the panel, and for their taking time and making
3 the effort to be here today.

4 We will now take a break until 10:30, and we will
5 start promptly then with the open committee discussion at
6 10:30. Thank you.

7 [Recess.]

8 DR. PATOW: This will start our open committee
9 discussion portion of today's program, if I could ask you
10 all to have your seats, and we will have an opportunity now
11 between 10:30 and lunch at 12:30 to have presentations
12 during the open committee discussion.

13 Prior to the presentations, Mr. Sauberman will be
14 presenting the charge to the panel.

15 MR. SAUBERMAN: I just want to mention first,
16 there will be another break this afternoon, midway through
17 the afternoon. Dr. Patow, what time will that be? About 3
18 o'clock.

19 At this time I would like to give the charge to
20 the panel before this meeting. Good morning, ladies and
21 gentlemen. This panel meeting is being convened to review
22 and discuss the pertinent issues of safety and efficacy for
23 the class of products known as implantable middle ear
24 amplification devices. These products, as you have seen,
25 represent a new application of technology for the hearing

1 impaired.

2 We seek your input and your advisory
3 recommendations on the nature and substance of the
4 information that should be provided by manufacturers to the
5 FDA for these devices when they are submitting an
6 application to the FDA for an investigational study or for
7 marketing approval. Your information to us will be of great
8 value, as the agency will use it to develop a guidance
9 document that the manufacturers can follow.

10 We plan to keep you connected as we proceed with
11 our development of a guidance document, and this meeting is
12 our first step. As versions of the document are drafted, we
13 will forward these to you and ask for your comments and
14 review. The information that will ultimately reside in the
15 guidance document, however, should not be seen as being
16 retroactive. We would like the guidance to reflect updates
17 in our knowledge as we gain understanding of the significant
18 issues relating to safety and efficacy.

19 At this meeting, we will not be asking you to vote
20 or to give a regulatory opinion on any submission.
21 Likewise, we will not be reviewing or examining the data
22 from any particular study that may be ongoing at this time.
23 We ask that this meeting be generic in content and generic
24 in all of your discussions.

25 Middle ear amplification devices have emerged on

1 the scene after many years of exploratory research and
2 development. These devices are of various designs, with
3 many having unique characteristics, and they are the
4 products of newly formed companies, from academic
5 institutions, and from international research centers.

6 Today we have invited the sponsors of these
7 organizations, all that we are aware of, to describe their
8 devices, explain how they operate, and to discuss the
9 features of device safety and efficacy. We ask that you
10 take an assessment of these products in a generic sense and
11 identify the areas where you believe meaningful and
12 significant data on safety and efficacy needs to be
13 collected and submitted.

14 A set of questions has been developed to
15 facilitate your discussion, and these questions were posted
16 on the FDA's web page. We believe there will be added value
17 to the questions when they are accompanied with a short
18 narrative. As a result, we have asked our medical officer,
19 Dr. Sid Jaffee, and our audiologist, Ms. Teri Cygnarowicz,
20 to provide this short narrative.

21 We have asked Dr. Clough Shelton and Dr. Paul
22 Kileny of the panel to lead the panel discussion on the
23 questions. The first set deals for the most part with
24 issues of safety and the second set deals with issues of
25 device efficacy and risk-to-benefit ratio.

1 We are aware of the vast benefit that your
2 expertise brings to this meeting. In this regard, we
3 encourage you to also raise whatever additional questions
4 you deem appropriate for discussion. We have asked Dr.
5 Patow, our panel Chair, to facilitate the discussion
6 regarding any additional questions.

7 The FDA is very pleased to have the participation
8 of this most distinguished panel in this important device
9 area. We look forward to your discussion.

10 DR. PATOW: Thank you, Harry.

11 At this time we will have scheduled speakers
12 present in the open committee discussion. I would like to
13 ask each of the speakers to limit their presentations to
14 about 12 minutes each, and that should leave adequate time
15 for the panel members to have questions for each of the
16 presenters.

17 Our first speaker this morning will be Jonathan
18 Spindel from the University of Virginia Center for Sensory-
19 Neural Engineering, Charlottesville, Virginia. Dr. Spindel?

20 DR. SPINDEL: Thank you, Dr. Patow, and thank you,
21 the committee, for giving me the opportunity to talk today.
22 As he said, I am Dr. Jonathan Spindel at the University of
23 Virginia with the Center for Sensory-Neural Engineering.

24 What I would like to do today is, first, restate
25 the problem that has been stated over and over again this

1 morning; discuss some of the issues associated with
2 implantable hearing device transduction; talk about our
3 particular approach at the University of Virginia, namely,
4 the round window electromagnetic approach; and then talk a
5 little more generally about some experimental evaluation of
6 implantable devices and how that data may be used.

7 Again, to reiterate, hearing loss affects over 27
8 million Americans. For greater than 80 percent of those it
9 is not correctable through medical or surgical intervention.
10 Hearing aids provide for partial rehabilitation and, though
11 effective, a majority of people choose not to use them.

12 They choose not to use them for a variety of
13 reasons, partly due to the problem of acoustic feedback or
14 "squeal" which requires a tight-fitting earmold, as well as
15 things that come along with that, such as introduced
16 distortion, long-term wear comfort, problems with ear canal
17 infections, difficult-to-fit anatomies, as well as
18 effectiveness with background noise. Again, some of the
19 inherent problems with conventional hearing aids come from
20 this issue of dealing with feedback and the associated
21 problems of that.

22 Basically, we have a microphone, amplifier,
23 processor and speaker, and the speaker sends amplified
24 acoustic energy into the ear canal. Now, we seal that into
25 the ear canal to avoid feedback, but essentially that is

1 like sending "very loud sounds into a very small space"--
2 very loud sounds into a very small space--which has a
3 tendency to distort sound and cause all sorts of other
4 issues, as listed here.

5 So over the last several decades a number of
6 researchers have worked on developing implantable hearing
7 approaches to circumvent many of these problems. And of
8 course when we start thinking of implantable hearing devices
9 or implantable devices at all, the first thing that comes to
10 mind, of course, is our friend Steve Austin, the six million
11 dollar man, the bionic man, but actually Steve Austin
12 himself didn't have a bionic ear. It was actually Lindsey
13 Wagner, the bionic woman, who had the implantable hearing
14 device.

15 And what you can see here, pulled off of the
16 bionic man/bionic woman web site, on the left hand side is
17 the actual schematic diagram, which I think really has to
18 set the threshold that we look at when we look at these
19 things, especially when we realize that the amplification on
20 this device is 1400 dB with only .001 distortion, max. Now,
21 obviously the image is a little clouded, so it is hard for
22 us to reverse engineer that, but you can see the surgical
23 approach is pretty straightforward. You just drop a hearing
24 aid battery in the ear canal, and away it goes.

25 But the reality is, what is an implantable hearing

1 device? Namely, an implantable hearing device is a hearing
2 amplification device in which vibrational energy is
3 delivered to the ear using implantable components. Again,
4 this is different from a cochlear implant in that residual
5 cochlear function is utilized, and so the implantable
6 hearing device sensation is "sound-like."

7 Now, the improvements that many people have
8 discussed already this morning and you will hear about this
9 afternoon is, over conventional acoustic transduction, is
10 that it removes the extra transduction step. Generally, you
11 have a direct vibrational drive. There is no distortion
12 from a small speaker element.

13 It eliminates the need for an earmold in many
14 cases. Potential to fit anatomic anomalies is present, and
15 you can use several of these devices to deal with
16 problematic conductive losses. It increases the long-term
17 wear comfort issues, improves signal processing and noise
18 management and, as was mentioned already, it is an
19 alternative device for non-compliant patient populations.

20 Now, the overall goals of all of us in the field
21 working this is to target basically moderate to severe
22 hearing impaired patients or those with significant
23 inoperable conductive losses. However, again it is clear
24 from the statistics, given the fact that hearing aids only
25 have about a 20 percent market share of that 27 million, so

1 roughly 5 million people wearing hearing aids, that there is
2 an incredible amount of dissatisfaction and non-use of
3 conventional hearing aids, and so implantable hearing device
4 technology may offer things that attract that population
5 sort of back into the amplification fold.

6 Now, implantable transducers take a wide--well,
7 take a variety of forms. Some of the ones that are out
8 there are piezoelectric, electromagnetic, and electrostatic.
9 Of the three here, electrostatic is the one that is probably
10 least developed at this stage, due to some limitations.

11 Piezoelectric, of course, taking advantage of the
12 deformability of crystalline material and the use of that in
13 both changing vibrational energy into electrical energy and
14 reverse, taking electrical energy and changing it back into
15 vibrational energy. Electromagnetic, based on the idea that
16 you can attract and repel a magnet by putting it in close
17 proximity to a coil. And there are technical issues
18 associated with both of these predominant means.

19 In the piezoelectric, or what they call
20 piezokinetic, this is a very reliable and controllable
21 design. However, in many of the approaches that are
22 proposed, there are some issues with regard to
23 disarticulation or restriction of the ossicular chain which
24 make the application of this type of an approach somewhat
25 problematic.

1 In the electrokinetic or electromagnetic
2 approaches, the advantage is that this is a non-fixed
3 driver. In other words, it doesn't necessarily, depending
4 on design, tie down the ossicular chain. However, the
5 application of it is that it is very unfocused. For anyone
6 who has worked in the field, they realize that the power of
7 an electromagnetic device drops off with the cube of the
8 distance, so it is very unfocused in that regard.

9 Now, some of the downsides is that it is a
10 potential for loading or movement-driven damage to the
11 system. Again, that is still an issue that is being
12 investigated and is still to be confirmed or denied.

13 But, however, when you are dealing with any sorts
14 of innovation, you know, people have said innovation is one
15 part inspiration and nine parts perspiration. My personal
16 view is, innovation is one part inspiration, four parts
17 perspiration, and five parts desperation. When you get a
18 problem, you solve it, and that is where the innovative
19 solutions come from.

20 A variety of research teams, both academic as well
21 as corporate, have been looking at trying to solve those
22 problems and solve the problems of conventional hearing
23 devices, some of which are here, some of which were here and
24 are gone now. The main thing is, is that we do have a wide
25 variety of different types of implantable approaches out

1 there: Symphonix, St. Croix, Otologics, SoundTec, Implex,
2 and then of course the approach that I have taken. The
3 approach that I am taking at this stage in the game is not
4 currently within a corporate structure. However, we are
5 hoping to move that way at some point.

6 So what is the program goal? What I would like to
7 do now is just briefly talk about the round window
8 electromagnetic approach. Our goal was to develop an
9 implantable hearing device which overcomes problems inherent
10 to conventional hearing aids while circumventing some of the
11 issues encountered with other approaches.

12 Now, to do this we have taken the approach of
13 saying we can put a magnet onto the round window membrane
14 and use the fact that it doesn't matter how you get
15 vibrational energy into the cochlea itself; the basal
16 membrane is still going to ring the same way, the traveling
17 wave is going to do the same thing. And so rather than work
18 on the ossicular side, on the TM side, we take advantage of
19 the round window membrane's presence and use this to develop
20 an implantable transducer that does nothing to interfere
21 with or manipulate the ossicular chain.

22 Again, what are some of the advantages of this
23 approach? As with many of them, elimination of feedback and
24 no associated issues with the ear canal. It is a direct
25 vibrational input to the cochlea because you are actually

1 vibrating the cochlear fluid through the round window
2 membrane. It avoids the disarticulation or possibility of
3 erosion.

4 And what is interesting is, it opens the door for
5 the possibility of doing active noise cancellation within
6 the cochlea. The very issue that was brought up earlier
7 about normal sound coming into the ear could be used in
8 concert with a round window stimulus to both selectively
9 enhance as well as selectively degrade different parts of
10 the acoustic spectrum.

11 In our round window work thus far we have only
12 been in the animal investigation mode, in the animal
13 investigation stage. We have used the proverbial and actual
14 guinea pig model, with a magnet on the round window membrane
15 and a coil on the skin surface. What you see here is our
16 guinea pig magnet, which is the smaller magnet, and the
17 human size prototype, which is the larger magnet on the
18 penny. There is the guinea pig round window membrane.

19 And we have tested it using a variety of tests.
20 Most of what we did was electrophysiologic, and to that
21 extent experimental evaluation of implantable devices takes
22 the form of auditory brain stem response recordings;
23 otacoustic emissions; what we call reverse conductive
24 measures, meaning measuring acoustic events in the ear canal
25 in response to an implant; as well as laser vibrometry.

1 Our data from auditory brain stem response
2 recording shows that with our device the system seems to be
3 operating the same under acoustic stimulation as well as
4 round window stimulation. And these are the same kinds of
5 tools that can be used in many implant approaches. We also
6 did this work from a frequency specific standpoint, which
7 basically confirmed the same data across frequency ranges.

8 The reverse conductive pulse is the acoustic event
9 that you can measure in the ear canal in response to an
10 implant device being driven, and using that, we were again
11 able to use a first order approximation of a physical
12 measure of the way this device was working.

13 And, finally, I would like to touch on laser
14 doppler vibrometry because that is an issue that is key in
15 the field. Laser doppler vibrometry is basically a
16 physical, non-contact measure of displacement, velocity,
17 acceleration, basically vibrations. It allows displacements
18 to be measured easily in the audio range between .2 and 10
19 kHz all the way down to as much as 10 to the minus 6 microns
20 in movement.

21 It has extensively been used to look at the
22 tympanum, malleus, incus, stapes, footplate, round window
23 membrane. Significantly, this is the only true physiologic
24 measure we have to look at implant performance, and I think
25 it is an important thing for the panel to consider as it

1 looks at the approval process.

2 There are several different types, single point
3 systems that are under development, as well as scanning
4 systems which allow us to look at dynamic characteristics.
5 These video clips I have to give credit to Jeff Ball for.
6 These are some of his TM shots using scanner doppler laser
7 vibrometry to measure the system, and it allows for direct
8 comparison of different types of movement within the system.
9 This motion here is motion of the incus.

10 And so it is easy to see that this type of
11 measurement system can be used to evaluate and compare
12 acoustic movement of the ossicular chain and the TM and
13 structures of the middle ear as compared to implant-driven
14 movement.

15 So with that I just put up sort of our conceptual
16 diagram of where we would like to head ultimately, which is
17 a totally implantable hearing aid. And I would invite,
18 being that we are in proximity to University of Virginia,
19 anyone who would like to come down and take a look at our
20 facilities in the Center for Sensory-Neural Engineering, to
21 do so. Thank you.

22 DR. PATOW: Are there any questions from the panel
23 for Dr. Spindel? Dr. Sininger?

24 DR. SININGER: Yvonne Sininger from House Ear
25 Institute. You mentioned twice, but briefly, that the round

1 window device might allow you some way of improving noise
2 reduction, improving the signal-to-noise ratio. Obviously
3 that is a pretty significant improvement, and can you
4 elaborate on that a little bit, how that might happen?

5 DR. SPINDEL: Again, all of that is still in our
6 animal investigation work, and we are working on whether or
7 not that becomes a functional--

8 DR. PATOW: Could I ask you to come to a mike?
9 Thank you.

10 DR. SPINDEL: I don't want to push Iain out of the
11 way here. Jonathan Spindel.

12 Again, we are still in the animal investigation
13 phase of all of that and showing proof of concept on that,
14 but the idea would be that in theory if you drive the oval
15 window and the round window in phase, then you will have an
16 essential cancelling out of the vibrational energy
17 transported to the cochlea itself. If you drive them 180
18 degrees out of phase, then potentially you have the ability
19 to enhance.

20 So one of the approaches, one of the things that
21 we have enjoyed being able to look at with this type of
22 device is its use as a hearing assist device rather than a
23 hearing replacement device, a device that could actually be
24 used to, again, differentially enhance vibrational energy
25 into the cochlea.

1 DR. SININGER: But that is my point. You can
2 cancel signals, certainly, but you are going to cancel the
3 signal you want as well as the one you don't want, and how
4 can you differentially hope to cancel noise and not the
5 signal--

6 DR. SPINDEL: Again, that comes into the type of
7 noise that you put in and the type of noise--and the phase;
8 in other words, if you can selectively change the phase,
9 change the response of the sound that you are putting in
10 from one side to the other within certain frequency ranges,
11 within certain bands that you are interested in cancelling
12 out, while not changing phase in others. It boils down to a
13 signal processing problem.

14 DR. PATOW: Dr. Kileny?

15 DR. KILENY: Paul Kileny. Dr. Spindel, have you
16 looked at impaired guinea pig ears, or all of your studies
17 so far have been on normal ears?

18 DR. SPINDEL: Everything that we have done so far
19 has been in normal ears. There is no reason to assume,
20 however, from our standpoint, that the responsiveness would
21 be any different.

22 DR. PATOW: Dr. Campbell?

23 DR. CAMPBELL: Yes. Dr. Campbell. This is
24 anticipated in the future that this will be completely
25 implanted, a completely implanted hearing aid?

1 DR. SPINDEL: Yes, but I do have to qualify that,
2 that that is highly conceptual at this stage of the game.
3 Most of our research has been focused in at the transduction
4 level.

5 DR. CAMPBELL: Would it be middle ear only?
6 Middle ear only, or somewhere in the mastoid?

7 DR. SPINDEL: As far as placement?

8 DR. CAMPBELL: Yes.

9 DR. SPINDEL: No, it would be placed probably in
10 the mastoid.

11 DR. CAMPBELL: In the mastoid?

12 DR. SPINDEL: In the mastoid, that would be the
13 placement of the implant, electronics package.

14 DR. PATOW: Dr. Woodson?

15 DR. WOODSON: Yes. With regard to this laser
16 velocity measurement, are there packages that are
17 commercially available, that all investigators would have
18 access to, or is this something that specific investigators
19 have developed? How would you envision this to be
20 incorporated?

21 DR. SPINDEL: I think that is actually a very good
22 question because there are some commercial packages that
23 have been developed and have been evaluated, but it is very
24 key in this field that there is a tremendous--if you are--
25 the unsophisticated user or the user who opens the box and

1 tries to use things like single point or scanning laser
2 vibrometry without a very complete knowledge of exactly how
3 the system functions, may find themselves coming up with
4 data that is completely erroneous.

5 So as much as there are commercial packages out
6 there, it is very important that the operators of these have
7 a very clear understanding at a technical level as to how
8 this data is applied and how to analyze this data.
9 Otherwise, the information is relatively useless.

10 DR. PATOW: Thank you, Dr. Spindel.

11 Our next speaker this morning is Iain Grant, Dr.
12 Iain Grant from St. Croix Medical in Minneapolis, Minnesota.

13 DR. GRANT: Dr. Patow, members of the panel, my
14 name is Iain Grant. I am an otologist at the Ohio State
15 University. For two years now I have been actively
16 researching the field of active middle ear implantable
17 devices and the mechanics of the middle ear, and this
18 morning I am here representing St. Croix Medical, who have
19 paid my travel costs.

20 Pre-clinical investigation of implantable hearing
21 devices. Implantable hearing devices are here, they are
22 available commercially in some countries, not yet in the
23 United States, and are certainly experimentally available.
24 They have been talked about for many years. The 21st
25 century is almost here. They sound complex devices. In

1 concept, in fact they are not. They are really quite
2 familiar.

3 They consist of an input stage, similar to this
4 behind-the-ear microphone that we have here. This can be a
5 microphone or a sensor. They consist of a sound processor
6 which serves to amplify, compress and filter the sound; an
7 output stage that vibrationally drives the stapes, and
8 currently the favored output stages are piezoelectric or
9 electromagnetic. In addition, you need to power the device
10 with some form of battery, and you clearly need to control
11 it with some form of telemetric or other device control. So
12 conceptually they are not too complex.

13 When it comes to evaluating the performance of
14 these devices, there are two models that are presently
15 available. The first one is the cadaver temporal bone.
16 This is a freshly harvested human temporal bone. It
17 contains the intact tympanic membrane, external auditory
18 canal, the middle ear ossicles, and the inner ear.

19 Within that model you can test the sensor or the
20 microphone by affixing it to the ossicles or placing it
21 wherever it is surgically desired, and easily record the
22 frequency response and sensitivity of the device. You can
23 also test the driver or the output stage of the device.
24 This is done using the laser doppler vibrometer which Dr.
25 Spindel has outlined.

1 The LDV is an instrument that has been around for
2 some 20 years and commercially available for almost 10. It
3 is based on firing a laser beam similar to this laser
4 pointer at any sinusoidally vibrating structure. It is
5 relatively simple to use. A vibrating structure, based on
6 the mechanics of the vibration and the interference, the
7 doppler pattern reflected back from the structure results in
8 a voltage coming out of the instrument which can be easily
9 related to the displacement of the original structure. It
10 measures velocity, and from that information we can very
11 accurately derive displacement.

12 Using the LDV, we can measure the displacement of
13 the middle ear ossicles and obtain some very useful
14 normative data as to how the middle ear vibrates. We can
15 also place a driver, the output stage of these devices, and
16 quantify the power output of the driver and the frequency
17 response of it.

18 Finally, you can connect the sensor and the driver
19 to the sound processing unit and follow the acoustic signal
20 through the sound processor to the ultimate stapes
21 vibration, so it allows complete system testing of the
22 devices in an environment which is very similar to the live
23 surgical situation.

24 The alternative model is the animal model. This
25 is based on implanting device components into a convenient

1 animal model. You can implant the sensor or microphone,
2 record the sensitivity and frequency response. You can also
3 implant the driver, and this time, rather than measure
4 displacement and how much the stapes is moving, because the
5 animal model is living, you can use the more clinically
6 familiar measures of hearing, the electrophysiological
7 measures, brain stem response audiometry,
8 electrocochleography. However, this is fraught with some
9 extreme technical difficulty.

10 In addition, in some circumstances you may be able
11 to test the system, the complete device as intended for
12 human configuration. However, this is very limited, as the
13 animal anatomy is different, the frequency response of the
14 ear is different, the shape of the ear is different, the
15 resonant frequency of the ear is different, and the
16 sensitivity of the cochlea is different, and so this
17 frequently requires device modification.

18 If you are coming to assessing a model of
19 performance, it clearly needs to be a valid one. The
20 temporal bone has been validated in some studies by Dr.
21 Goode, who has been very active in this area. He looked at
22 umbo displacement in a cadaver model and also in living
23 temporal bones, in living human specimens.

24 Frequency is here, displacement on a log scale
25 along here, and the acoustic stimulus was 80 dB of sound

1 pressure level. Here we are measuring displacement of the
2 umbo, the umbo in a normal ear with the solid line, in a
3 temporal bone model in the dotted line. And as you can see,
4 the two measurements are within a few dB of each other out
5 to 10 kHz here, so there is good evidence that the umbo in
6 the temporal bone and the cadaver is vibrating in a very
7 similar manner.

8 Dr. Rosowski at Mass. Eye and Ear has also looked
9 at middle ear input impedances across frequency, and has
10 noted them to be similar or the same between cadaver and
11 temporal bone models.

12 The animal model has not been validated. It is
13 difficult to validate because clearly an animal is not the
14 same as a human. Devices, as I have mentioned, require
15 modification. The frequency responses are different.² And
16 in view of that, the animal model is a useful predictive
17 model, but in my personal experience of two major animal
18 implant trials and multiple minor experimentations with
19 cadaver animals, it has not quantitatively reflected any
20 useful data, as it does not relate to the human condition.

21 With that being said, I would like to compare a
22 number of parameters that I believe to be important in the
23 assessment of these devices between the animal and the
24 temporal bone model, and give some insight into the useful
25 information that can be gleaned from both of the models.

1 The first one I have touched upon is device
2 modification required to fit the model anatomy. In a
3 temporal bone of course the anatomy is the same as the live
4 human surgical situation, so no modifications are necessary.
5 However, in the animal model with a different middle ear
6 anatomy, different in middle ear frequency response, inner
7 ear sensitivity, it is quite different.

8 An example of this is one of my animal experiments
9 that involved building an output stage for a dog. We were
10 using piezoelectric drivers. To fit within the dog's
11 anatomy, we had to halve the length of the intended human
12 length. By halving the length, you quartered the power, so
13 you needed four times the battery voltage to get the same
14 loudness, and of course the circuitry was not designed for
15 that, so it became impossible to fit an animal driver into
16 the dog that related to the human condition.

17 I have mentioned the acoustic characteristics.
18 When it comes to assessing the various stages of these
19 devices, the sensor sensitivity, the microphone sensitivity,
20 in some cases you can get useful data in an animal model but
21 it is highly contingent on your sensor design. For the
22 temporal bone, using the laser doppler vibrometer and
23 measuring the outputs of the sensor, you can get accurate
24 sensor output across frequency.

25 Similarly, the driver. In an animal model, to

1 measure the power of the output, if you were able to implant
2 it, using ABR it is very difficult to get estimates of
3 growth of loudness. And so it is a poor model for driver
4 output power, while the laser is a linear output model, it
5 gets very useful indication of output power across
6 frequency.

7 Feedback is going to be an issue with these
8 devices. They are active devices. They are providing gain
9 between the input and the output stages. To quantify
10 feedback in an animal model, the different temporal bone, it
11 provides no useful quantitative data. The LDV provides an
12 excellent model of quantifying feedback. It gives not only
13 very useful information on amplitude, but crucial phase
14 related information, so it is a good model for providing
15 feedback that relates directly to the human condition.

16 When we measure these devices, we want to know how
17 well they function at low sound levels. If you can fit a
18 sensor or a microphone into an animal, it may provide some
19 good information. With the current sensors that I am
20 working on, it is technically not possible. In the temporal
21 bone model, at low threshold levels you are approaching the
22 noise floor of the laser, so the measurement is a little
23 restricted in this area. However, you do get some
24 information.

25 More importantly, rather than functioning at

1 threshold, these devices provide gain, and we need them to
2 function at conversational and high listening levels within
3 the available dynamic range of the patient. The animal
4 model gives no information on this. However, the laser
5 doppler vibrometer in the cadaver temporal bone provides
6 accurate information that relates clearly to listening
7 levels and is frequency specific.

8 How accurate are these devices? In an animal
9 model, you can often get a threshold using ABR, or
10 clinically within 10 or 15 dB of the patient's threshold,
11 and so you may get some threshold information, but at poor
12 conversational levels. The temporal bone model is pretty
13 accurate at conversation on high levels, although limited at
14 thresholds. The limitation of the temporal bone is the
15 range of normal human variation, which is moderate, and in
16 view of that there must be a band of acceptable
17 displacements within the temporal bone.

18 Speech discrimination information is the preserve
19 of human implantation. Unfortunately, we have no pre-
20 clinical model that provides useful speech discrimination
21 information.

22 I think as an investigator, as a scientist, I
23 really need to be able to compare devices on a level playing
24 field, and the temporal bone provides a very good model for
25 comparing devices. It allows comparison between particular

1 devices, between the results of particular institutions, and
2 even between specimens within the same lab, so there is a
3 huge availability of comparative data so we can perform on a
4 level playing field.

5 The animal model comes into its own when it comes
6 to histology. It is a living model and you can see
7 histological changes at the transducer-ossicle interface.
8 However, animal ossicles, depending on your models, are
9 often much more fragile, and it can be technically very
10 difficult to implant and get that information. The temporal
11 bone model is poor in the issue of histology. It gives no
12 useful information.

13 Long-term potential cochlear damage is a potential
14 issue with these devices, purely dependent on the output or
15 the dose of sound. In an animal model it is very difficult
16 to quantify the dose of sound, while in the laser doppler
17 vibrometer temporal bone model it is easy to know exactly
18 how loud the sound you are presenting, at what frequency it
19 is, and on the basis of the safe OSHA levels of safe sound
20 dosimetry, we can extrapolate to the safe outputs and safe
21 limits of the device.

22 Toxicity is an issue, and the animal model is
23 proven in that arena.

24 MRI compatibility is also a major issue. MRI
25 utilization is again increasing, and it is becoming the

1 preserve of the family practitioner in many respects as an
2 investigation of first choice that is cost-effective for the
3 diagnosis of many problems. I allude in particular to soft
4 tissue injuries of the knee, low back pain. MRI is very
5 much the investigation that is most cost-effective. We need
6 a good model to be able to prove MRI compatibility. An
7 animal model will give us good information. So will a
8 temporal bone model.

9 So, in conclusion, these two models are
10 complementary. The animal model provides some qualitative
11 data. It is technically very difficult to implant often
12 because of the variations of animal anatomy, and it is often
13 limited to partial system implantation. It does not give
14 quantitative data. Its major strengths are tissue response
15 and toxicity effects.

16 The temporal bone model is a quantitative and a
17 qualitative model. It relates directly to the human
18 condition. It can be used by surgeons in wet labs for
19 practice and verification of surgical competence on
20 implantation, and it gives reliable performance information
21 when combined with laser doppler vibrometry.

22 Thank you very much.

23 DR. PATOW: Thank you.

24 Are there questions from the panel? Dr. Woodson?

25 DR. WOODSON: Yes. I am just wondering about how

1 you extrapolate from knowing how the model performs in terms
2 of displacement, as to how that then is perceived in how
3 effective it is in the patient hearing sound.

4 For example, let's say you determine that the
5 implant has a very good linear response in terms of
6 amplitude, and maybe you have a patient who has a cochlear
7 hearing loss where there is some recruitment and maybe you
8 don't want a linear response. Maybe you would want
9 something that wouldn't be linear. I am just wondering, in
10 terms of when you test something in a temporal bone model,
11 how do you know what would be the optimal displacements and
12 characteristics of the device?

13 DR. GRANT: That is an extremely good question,
14 and to do that within a temporal bone model, obviously
15 patients' hearing losses are widely variable, and there is a
16 huge differentiation in terms of dynamic range available to
17 the patient, in terms of the frequency responses available
18 to the patient. And to optimize that in a hearing device
19 setting is wholly dependent on the flexibility of the
20 hearing aid circuitry, its ability to offer multiple levels
21 of crossover, multiple different frequency response bands,
22 and also the compression, where that kicks in, the
23 kneepoints of the compression, the compression ratios. And
24 so that is very much the preserve of the flexibility of the
25 electronic circuitry.

1 The temporal bone model comes into its own,
2 clearly temporal bones don't have hearing losses, but the
3 model allows us to give a known input and measure precisely
4 a known output which we can relate to a known loudness in a
5 human situation. Knowing that response to be linear, then
6 based on the flexibility of the electronic circuitry, you
7 can tailor the output to the available dynamic range of the
8 patient.

9 DR. PATOW: Thank you very much, Dr. Grant.

10 Our next presentation will be by Mr. Jose Bedoya
11 from Otologics in Boulder, Colorado.

12 MR. BEDOYA: Good morning, distinguished panel
13 members, invited guest, and fellow industry colleagues.
14 Thank you for the time, for allowing me to present
15 Otologics' perspective on the questions before the panel. I
16 will focus my talk on the specifics of clinical trial
17 design, the risks of surgery, and the benefits and claims
18 that we may derive from this.

19 One of the most important issues in designing a
20 clinical trial will be in establishing a baseline for the
21 measurement of a benefit. In this particular case we have
22 elected to use a conventional hearing aid as our baseline.
23 We have also attempted to use the same rationale and
24 approach in fitting this acoustic aid with that of the
25 implant, so that appropriate measurements can be made. In

1 looking at the patient population group that we have, we
2 need to establish appropriate assessment, outcome assessment
3 measurements so that we can compare the baseline and the
4 implant performance in an equitable fashion.

5 In utilizing the conventional hearing aids, we
6 have seen that there is a tremendous variability between the
7 aids with which the patients arrived at the clinic, and we
8 have experienced a 75 percent demonstration of benefit of
9 these patients when we installed new, modern baseline
10 hearing aids, versus that of their own aids; which means
11 that had we not taken the time and the effort to install a
12 modern, well-fitted aid, patient measurements or the
13 validity of any claims that we would have would be highly
14 suspect. So we would recommend that this is something that
15 should be looked at very carefully.

16 There are many reasons for that. Their own aids
17 may be of an old technology, they may be linear peak
18 clippers, they may be malfunctioning, aging, or they may be
19 poorly fitted. So this essential element of introducing a
20 modern hearing aid into the evaluation is--it cannot be
21 overstated. It should be a multi-channel signal processor
22 of the best modern technology available to us.

23 Other factors that we need to consider in
24 measuring benefit, I think it is appropriate to look at the
25 single subject as a design, for control, and to look at the

1 group analysis for overall benefits. As stated previously
2 in other discussions, monaural and binaural testing, and the
3 binaural condition having a conventional hearing aid in the
4 other ear, is critical. This is realistic. This is what
5 the patient will be confronted with once he leaves the
6 clinical trial. Again, the same outcome measurements need
7 to be applied to both the baseline and the implant. If they
8 are not, then results will be highly suspect.

9 The type of outcome measurements that we need are
10 speech recognition tests. They need to be very sensitive
11 and have high reliability. They need to be validated and
12 they need to be normed; and they need to be conducted in
13 real environments, such as in quiet and in noise.

14 Functional gain is an important outcome that we
15 need to understand. However, when comparing the functional
16 gain of the implant versus a conventional aid, we need to
17 consider that they are using the same rationale, that one is
18 not a linear fitting versus another one that is a
19 compression fitting. The differences between that could
20 skew the results of one or the other, so similar rationale
21 for fitting of that aid is essential.

22 I think another measurement of outcome is aided
23 loudness judgments and comfort levels. These will allow us
24 to determine whether the patient perceives the implant to be
25 sufficiently comfortable or compare it to that of his

1 acoustic aid.

2 Electromechanical versus electroacoustic
3 parameters need to be well understood for both the acoustic
4 condition and the implant condition. That goes into
5 frequency response, overall gain, distortion, and others.

6 Subjective outcome measurements, it has been
7 reported, with the experience of all these implants, that
8 patients perceive a marked improvement in perceptual sound
9 quality. However, we must consider the possible bias due to
10 belief in new technology, and that these results may depend
11 on expectation of the patients. We have to be very careful
12 in considering that.

13 Questionnaire data and magnitude estimators are
14 good tools but they are somewhat unreliable, and they should
15 be well validated and well normed before they are used in
16 any of the criteria for approval. Comments like "more
17 natural," "richer," "easier to listen to" are very important
18 benefits, but improved sound quality should not be the only
19 criterion for market approval.

20 Complications with the surgical procedures are
21 very much device dependent. The more exposure or proximity
22 to the facial nerve, the dinner ear, the vestibular system
23 or the stapes footplate, the more similar the risks will be
24 to cochlear implant and stapes surgery. However, these
25 devices, many of them are really not proximal to the

1 cochlea. They do not penetrate the cochlea, so there
2 complications cannot be directly linked to those such as
3 stapes surgeries.

4 One of the limitations and risks that may be
5 evident, and it is dependent on the design, is that when
6 installing these implants we cannot and we should not
7 decrease the residual air conduction hearing by more than a
8 10 to 12 dB range in the speech range. This is, I think
9 this is something we should all strive for, and it should be
10 set as an objective for all these implants.

11 If possible, the implanted patients should be able
12 to use a conventional hearing aid if desired. If there is a
13 malfunction, if in fact there is a deterioration, they
14 should have that opportunity. The implant should be
15 designed so that they have that alternative available to
16 them.

17 Performance of the implant electronics, these must
18 be well defined. We must understand what is the full range
19 of gain and output and frequency response and distortion
20 that these devices provide. They have to be predictable.
21 We have to be able to go into surgery and provide the
22 targeted benefit that the surgeon and the patient are
23 seeking. They have to be reliable. They have to be
24 sustainable over time. That performance cannot degrade.

25 They have to accommodate the long-range potential

1 deficit of the patient. We cannot go in with an implant
2 that satisfies the patient's need today, and then tomorrow
3 when his hearing deteriorates, the implant no longer has the
4 capacity to provide amplification needed for him to
5 communicate and act effectively in society.

6 Long-term safety, there are some issues with these
7 implants. Primarily it boils down to the attachment to the
8 ossicular chain. How do we drive the system? It must
9 induce minimal or no damage to these ossicles and be proven
10 in long-term in vivo tests. This is the crucial Achilles
11 heel of all these implants. Binaural implantation should
12 not be allowed until all these long-term issues are well
13 resolved and well defined and well understood.

14 If we look at a graphical representation of the
15 anatomy of the ossicles, we can see that the ossicles are
16 very unique in that they are--their nutrients are supplied
17 through a vascular membrane on the surface of the ossicles.
18 When we attach a clip, such as in stapes surgery, or we
19 disrupt this vascular membrane in some way, the possibility
20 of a necrosis of the ossicle is evident.

21 I mean, we have seen that with stapes surgery,
22 that over a number of years that there are significant
23 instances of fracture. This must be considered in design.
24 Clips such as that of a stapes would not be something that
25 we would want to implant in a person who is going to receive

1 a device and expect it to function for a period of 20 years.

2 Reversibility. It is not if a device will fail,
3 it is when it fails. We need to be able to go in and
4 replace that device without the risk of further damaging or
5 impairing hearing altogether. There are going to be adverse
6 effects, and in the future hopefully there will be upgrades
7 that we will be able to provide these patients. So our
8 devices need to be reversible. They need to be able to be
9 explanted and upgraded if necessary.

10 Candidacy issues. In our particular study we have
11 focused on the moderately severe to severely hearing
12 impaired, and we look in particular to the middle to higher
13 frequencies, which are those which are commonly seen in this
14 patient population.

15 We look for two or more years of relative
16 stability in their hearing thresholds. This is so that we
17 do not introduce patients that will later be necessitating
18 other surgeries.

19 Sensorineural hearing loss with normal middle ear
20 function. This is, of course, particular to our device.
21 Others that do not have normal middle ear function will
22 obviously have different criteria in this area.

23 But at the end of the day we have got to be able
24 to predictably claim a benefit. To claim this benefit, we
25 have got to demonstrate substantially that the benefit