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CENTER FOR DEVICES AND RADIOLOGICAL HEALTH
OFFICE OF DEVICE EVALUATION

DENTAL PRODUCTS PANEL

OPEN SESSION

Volume II

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PANEL MEMBERS PRESENT:

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E. DIANE REKOW, Ph.D., DDS
JANINE E. JANOSKY, Ph.D.
MARK R. PATTERS, DDS, Ph.D.
WILLIE L. STEPHENS, DDS
WILBERT C. JORDAN, M.D.
FLOYD LARSON
JAMES L. DRUMMOND, Ph.D., DDS
LESLIE HEFFEZ, DMD
ANDREA MORGAN, DDS
JOHN BRUNSKI, Ph.D.
GEORGE McCARTHY, DDS

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P R O C E E D I N G S

DR. GENCO: Good morning, ladies and gentlemen and members of the panel. I'd like to welcome you to this session on implants. First, Ms. Scott is going to give us some announcements.

MS. SCOTT: Good morning and welcome to the Dental Products Panel meeting. Again, my name is Pamela Scott and I serve as the secretary for the Dental Products Panel. If you have not signed in this morning, please do so at the sign-in desk just outside the room. Also, at the sign-in desk you will find agenda booklets for today, and also you will find information regarding obtaining a transcript for today's meeting.

Meetings are held only if there are applications or issues that FDA needs to or chooses to bring before the panel. Whether or not a meeting will be held is determined about two months prior to the tentative meeting date. When a decision is made, the information is made available through the FDA Medical Advisory Committee hotline. The phone number for the hotline is 1-800-741-8138 or 301-443-0572. The code for the Dental Products Panel is 12518.

At this time I would like to announce the future tentative dates for the Dental Products Panel. And if I

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could ask the panel, if you have your calendars with you, if you could pull out your calendars so that you can mark those dates and also let me know whether or not, particularly the voting members, if you will not be available on those particular dates.

March 10th through the 11th, 1998 is the next tentatively scheduled meeting. May 12th through the 14th, 1998; August 4th through the 6th; and November 3rd through the 5th. Again, those dates are March 10th through 11th; May 12th through the 14th; August 4th through the 6th; and November 3rd through the 5th.

Do any of the voting members at this time foresee any difficulties in their schedules with making those dates? Voting members, industry rep?

[No response.]

MS. SCOTT: If not, I'll give you time to look through your calendars the rest of the day and we may come back to this just to make sure that those dates are good for most of our members.

The next item of business are three statements that are to be read into the record. The Dental Products Panel meeting January 13th, 1998 conflict of interest statement. The following announcement addresses conflict of interest issues associated with this meeting and is made

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part of the record to preclude even the appearance of an impropriety. To determine if any conflict existed, the agency reviewed and submitted agenda and all financial interest reported by the committee participants.

The conflict of interest statutes prohibit special Government employees from participating in matters that could affect their or their employees' financial interest. However, under the final rule on 18 USC 208, acts affecting a personal financial interest, Title V, CFR Part 2640, published December 18th, 1996 in the Federal Register, Volume 61, No. 244, a special Government employee may participate in any particular matter of general applicability where the disqualifying financial interest arises from his non-Federal employment or from a de minimis stock holding.

Since the agenda items for this session involve only particular matters of general applicability, the agency has determined that Dr. Robert Genco, Dr. Elizabeth Rekow, Dr. John Brunski, and Dr. James Drummond may participate fully in the discussions.

We would like to note for the record that the agency took into consideration another matter regarding Dr. George McCarthy. Dr. McCarthy reported an interest, but no financial involvement, in a device at issue. Since there is

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no financial involvement, the agency has determined that Dr. McCarthy may participate fully in all discussions.

In the event that the discussions involve any other products or firms not already on the agenda for which an FDA participant has a financial interest, the participant should excuse himself or herself from such involvement, and the exclusion will be noted for the record.

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

Secondly, I would like to read into the record the appointment of temporary panel chairperson. I appoint Dr. Robert Genco to act as temporary chairman for the duration of the Dental Products Panel meeting on January 13th, 1998. For the record, Dr. Genco is a special Government employee and is a voting member of the Dental Products Panel. Dr. Genco has undergone the customary conflict of interest review. He has reviewed the issues to be considered at this meeting. Signed by Dr. Bruce Burlington, director for the Center for Devices of Radiological Health on January 6th, 1998.

Appointment to temporary voting status. Pursuant

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to the authority granted under the Medical Devices Advisory Committee Charter dated October 27th, 1990, as amended April 20th, 1995, I appoint the following people as voting members of the Dental Products Panel for this panel meeting on January 13th, 1998: Dr. Diane Rekow, Dr. Leslie Heffez, Dr. Andrea Morgan, Dr. John Brunski. For the record, these people are special Government employees and are consultants to this panel under the Medical Devices Advisory Committee. They have undergone customary conflict of interest review. They have reviewed the material to be considered at this meeting. Signed by Dr. Bruce Burlington, director, Center for Devices of Radiological Health, January 6th, 1998.

At this time I would now like to introduce our panel for today. Our acting chairperson for today is Dr. Robert Genco. He is distinguished professor and chair of the department of oral biology at the School of Dental Medicine at the State University of New York at Buffalo. Next we have Dr. Willie Stephens. He is associate surgeon with the division of maxillofacial surgery at Brigham & Women's Hospital.

We also have with us Dr. Andrea Morgan. She's the clinical instructor with the department of restorative dentistry at the University of Maryland Dental School. We have Dr. Mark Patters, who is the chair of the department of

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Periodontology with the College of Dentistry at the University of Tennessee. We also have Mr. Floyd Larson, who is the president of Pacific Materials and Interfaces, and he is our industry representative.

We have Dr. Diane Rekow. She's the chairperson for the department of orthodontics at the University of Medicine & Dentistry of New Jersey. We also have with us Dr. Leslie Heffez. He is professor and department head of oral and maxillofacial surgery at the University of Illinois at Chicago. We also have Dr. Janine Janosky. She is assistant professor with the department of family medicine and clinical epidemiology with the School of Medicine at the University of Pittsburgh.

We have Dr. George McCarthy. He is the chief of the Commissioned Officers Dental Clinic with the National Institutes of Health. We have Dr. John Brunski, who is professor of biomedical engineering at Rensselaer Polytechnic Institute. We have Dr. James Drummond. He is professor of restorative dentistry at the University of Illinois at Chicago. And our consumer representative is Dr. Wilbert Jordan. He is associate professor of internal medicine and family medicine, and the director of the AIDS program at the King Drew Medical Center at the Charles R. Drew University.

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We also have Mr. Tim Ulatowski, who is the division director for the Division of Dental, Infection Control, and General Hospital Devices.

Lastly, just to remind the panel that you have a folder before you that contains information pertaining to the issues to be discussed today. If by chance the panel should need any of the reference material that was sent to the panel, that can also be available, if you would like to refer to any of the submissions that were made to the panel. I remind you that certain information pertaining to the devices discussed must remain confidential. This includes manufacturing information and formulation. Please be careful when you are discussing the submissions not to make public any confidential information.

I will now turn the meeting back over to Dr. Genco.

DR. GENCO: Thank you, Pamela. I'm very much impressed with this panel with wide-ranging expertise and I look forward to a very productive day.

Today we will make recommendations to the FDA regarding classification of endosseous implants. Before presentations from FDA and industry, however, we will have an open public hearing. I would at this time like to ask anyone from the public who would like to address the panel.

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Is there anyone here who would like to address the panel?

Raise your hand, please.

[No response.]

DR. GENCO: It looks like there isn't anyone from the public who would like to address the panel. Therefore, what we'll do is proceed with the FDA presentation.

But before that I'd like to ask all of you who will represent industry later that when you do address the panel, if you could come up to the microphone and speak clearly, of course, as the proceedings of the meeting are recorded. In addition, if you could make sure that you disclose any interest that you have, financial or otherwise, in medical device companies.

Now I'd like to introduce Dr. Susan Runner, who is branch chief of the Dental Devices Branch, and she will be followed by Dr. Pei Sung, who will make FDA presentations. Dr. Runner?

FDA PRESENTATION

DR. RUNNER: Good morning. Today we will continue our discussion on endosseous dental implants. The issue, as you recall, is the reclassification of subgroups of various endosseous dental implants for partial or complete rehabilitation of the oral cavity.

As you recall from the last meeting, the initial

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panel recommendation for classification of endosseous dental implants was class III in 1987. At that time the panel felt that there was insufficient information to determine safety and effectiveness of this device based on the information that was available at that time.

Subsequently, the agency was petitioned to consider down-classification of all types of implants into class II. The panel again met and considered the issue and determined that the uncoated, screw type implant for use in the anterior mandible should be down-classified to class II. All other type and indications were to remain in class III.

At the last panel meeting, the panel was again asked to consider the information that is available, the scientific evidence that may allow reclassification of certain subtypes of endosseous dental implants. The last meeting was a beginning and today you will be presented with more information for your consideration.

At the last meeting on this issue the panel was given a grid consisting of the various types and indications of endosseous dental implants. The grid contained all presently known combinations of implant types and indications. The panel was asked specifically to consider if the information presented to them would allow grouping of any implant types for the purpose of reclassification.

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The panel was also asked to consider if implant location in the oral cavity should continue to be considered as a part of the indication for use. The panel was also asked if abutments should be classified separately from the implant fixture system, and they were asked as well what additional information would be helpful to the panel prior to the next panel meeting which we are holding today.

The panel had a wide-ranging discussion that included the various types of implants and indications. At the end of the previous meeting the panel had grouped the implants tentatively into the following groups, root form (cylinder and screw type), blade implants, implants with special retention features, and temporary implants.

A final conclusion as to whether the coatings should be considered in the implant classification was not reached as far as I could tell from reviewing the transcript. The panel also felt that implant location was not a component of the device's indication for use. The panel also felt that the abutments should be considered separately from the implant system for the purposes of classification.

The panel asked that the follows questions be answered before this meeting. They asked that the industry present information on implants that are indicated for

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special areas of the oral cavity. What data is there to support the use of these implants in these areas?

They also asked for information on failure data for endosseous implants and for data on hybrid types of implants.

We would like for you to consider the information that is presented today and recommend to the agency the appropriate regulatory classification for the various types of endosseous implants.

This summary that I just gave you is my reconstruction from the transcript of the proceedings. If you feel that that is incorrect or needs to be modified, please feel free to do so. That's just my summary from the transcript.

But before we go on with presentations from the industry we would like to have a presentation from Dr. Pei Sung, who is a materials engineer with the Dental Devices Branch. He will give a brief overview on the coatings that we see on the endosseous implants. He will discuss the methods that are available to FDA to characterize and evaluate the various coatings that we see.

DR. GENCO: Susan, before we proceed to Dr. Sung I'd like to ask the panel to answer your question. Does everyone agree with Susan's summary of the panel's

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discussion in November? The four types of implants that we recommended; that we recommended that implants and abutments be considered separately; and that there was no indication, at least from what we heard--maybe we'll hear something different today--that anatomic location made a difference. Is that pretty much in agreement with what we all remember or read?

DR. RUNNER: The only thing that was not quite clear, and there was a lot of discussion back and forth, was the issue of coatings. There was discussion as to coatings did not make a difference or they did, and I'd like that to be clarified some today.

DR. GENCO: I'm sure we'll hear about that today. Thank you, Susan.

This is Dr. Pei Sung, who's a material scientist with the Dental Divisions Branch of the FDA. Dr. Sung?

DR. SUNG: Good morning. My name is Pei Sung, materials scientist, dental branch. The purpose of this presentation is to provide some coating information that may assist you to make decisions. This talk is limited to porous and hydroxyapatite coated devices. I'm going to discuss the porous coating first, and hydroxyapatite coating later.

For porous coated implants, as indicated in this

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slide, there are sintered beads, fibers, and particles, and they are thermal sprayed, such as wire arced, plasma sprayed, and flame sprayed products.

The next slide indicates some additional methods of spraying of coated implants. Different coating techniques involve different temperatures and impact force of coated particles and will generate different coating morphology and bonding strengths between particle and substrate, and between particle and particles. For example, as indicated in this slide, the temperature generated for plasma spray process is more than 10,000 degree Fahrenheit.

This slide indicates some physical parameters for characterization of porous coating. The thickness of coatings usually ranges between 500 to 1,500 microns. The volume porosity is between 30 to 70 percent. The average pore size ranges between 100 to 1,000 microns. The pores are interconnected.

The following 35 millimeter slide are some examples of those coatings. This is sintered beads. You can see there's particle-particle contact, and it has a very good metallurgical bond sintered together. This slide is the metallurgy of sintered beads on the substrate. You can see there's good metallurgical bonding between beads and the substrate, and between particle and particle.

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This is typical plasma sprayed coatings. Usually in metallurgy we call it a sponge coating. This is titanium 64 substrate. Those are particles.

The last slide was not sintered. After coating then it goes through a sintering process. The particle and particle has better bondings. However, usually the plasma sprayed coating doesn't go through the sintering process.

There are many calcium phosphate compounds available as indicated in this slide. For example, hydroxyapatite with calcium phosphate ratio of 1.67; there are oxyhydroxyapatite, oxyapatite, and type A and B carbonate apatites. Certainly there are some others, tetracal and trical, tricalcium phosphate, both alpha-beta and amorphous phases.

The calcium phosphate coatings can be achieved by solution precipitations, plasma sprayed, and other techniques. However, the coating is usually carried out by using plasma sprayed techniques.

After the ultra high temperature spraying process, somewhere around 10,000 degree Fahrenheit, the composition of the porous hydroxyapatite can be changed to tricalcium phosphate, tetracalcium phosphate, amorphous calcium phosphate, and calcium oxide, as indicated in this slide. In here you have three samples here. The number one sample,

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before the coatings there was 83 percent hydroxyapatite. After coating it changed to 18 percent plus tricalcium phosphate, calcium oxide, and amorphous calcium phosphate, primarily amorphous calcium phosphate.

The number two sample before coating plasma sprayed was 95 percent hydroxyapatite, after coating it sharply dropped down to 23 percent, plus various other components. The same thing applies to number three sample, which before coating was 87 percent, after coating was 36.4 percent. This study was reported from the American Dental Association group in the National Institute of Science and Technology.

This slide indicates some typical analytical techniques used for characterization of hydroxyapatite coatings, such as calcium phosphate ratio, x-ray defraction, infrared, and solubility products. I'd like to remind you that a standard reference material 2910 for hydroxyapatite has been officially introduced by the National Institute of Standards and Technology this year.

One of the publications indicated that there is no clinical advantage of hydroxyapatite being added to a porous coated surface. This was based on the studies of 42 hips that were implanted with hydroxyapatite coating on the porous coated surface, and 42 hips had porous coated stems

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without hydroxyapatite coating. This publication was published in the Clinical Orthopedics and Related Research, No. 315, page 223, 1995.

My final suggestion for you is to put your emphasis on the clinical utility, safety, and effectiveness of devices that have been properly characterized. The clinical utility of these devices should be compared to control devices which were non-coated and clinically very well established.

Thank you for your time.

DR. GENCO: Thank you, Dr. Sung. Are there any comments or questions from the panel for Dr. Sung? Yes, Dr. Drummond?

DR. DRUMMOND: I have one question on this last study here. Femoral hips are going to be loaded immediately, whereas the dental implants are not going to be loaded. Is it fair to compare this study to dental implants?

DR. SUNG: The hydroxyapatite for the hip device is usually inserted in the femur. We allow to have a hydroxyapatite hip devices in class II categories because we allow it to claim as press-fit devices. It doesn't matter if the hydroxyapatite really achieves a biological fixation or not. But in the dental implant, yes, you coat it with

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hydroxyapatite, you automatically give people an impression that implant will achieve some sort of biological fixation.

DR. DRUMMOND: My question was the loading, not the implication of whether or not there's a biological interaction.

DR. SUNG: For the hip, there's certainly bone modeling process, and what the bone modeling process to do with the hydroxyapatite coating, there's no--as far as I know there's no good study at this time.

DR. GENCO: Further comments, questions? Yes, Mr. Larson?

MR. LARSON: Dr. Sung, you showed porous metal coatings with the suggestion that titanium plasma sprayed coatings, the one that you showed was a porous coating. I guess I'd like the panel to not forget that there's a distinct difference between the titanium plasma spray coatings that are used on dental implants and those that are used on orthopedic implants. The one that you showed I believe was an orthopedic implant coating.

DR. SUNG: That was dental.

MR. LARSON: The sponge, titanium?

DR. SUNG: Yes.

MR. LARSON: But it explicitly had porosity, whereas most coatings that are used on dental implants are

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coatings that are intended for the purpose of roughening the surface and do not have interconnected porosity. They certainly wouldn't be defined by 21 CFR 888.3358.

DR. SUNG: Yes, you are right.

MR. LARSON: You need to make that distinction.

DR. SUNG: You are right in that category.

They're surface-roughed devices, and also there's devices intended for bony ingrowth. Plasma sprayed products came out about 11, 12 years ago. At that time it was intended for bony ingrowth. So the people have a tendency to coat it as porous as possible so that FDA can grant substantial equivalence to those bead coated devices.

However, after time to time at the porous coated, this means sponge coated devices, the particles are pretty loose. So the industry has tried to coat it as dense as possible, and as dense as possible to such a degree that almost there's no interconnecting porosities. So if those devices--how you achieve bony ingrowth, that's a very questionable state.

There's another type of device was designed for surface roughness. The surface roughness is usually carried out, for example, by sand blast, by groove, or by some sort of coating. But for the purpose of the surface roughness purpose, the coating--if it is achieved by coating, the

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coating should be non-porous and it should be as thin and loose as possible.

What I mean thin, because dental implant, the diameter is very small. You don't want the whole dental implant to be manufactured by plasma spray or wire arc sprayed products. I'm talking about loose means that they should not have particle-particle contacts, and the mechanical products should be as good as non-coated and non-roughed implants.

Did that answer your question?

MR. LARSON: Not completely. I guess I just wanted to make sure that we maintained that distinction, that we were aware that the vast majority of dental implants today that are titanium plasma coated are plasma coated for the purpose of surface roughening and are not porous.

DR. SUNG: I believe that the plasma spray coated for the purpose of surface rough, and if the coating is thin, and if there is no particle-particle interactions we should be treated as the same as non-coated devices. What I'm talking here today is primarily for bony ingrowth and biological fixation devices.

MR. LARSON: Right. And as I mentioned last time, the issue there is the claims that are made.

DR. GENCO: Thank you. Other questions? Yes,

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John? Dr. Brunski.

DR. BRUNSKI: One question. One of the slides you showed, the slide that showed three specimens that had been coated I wasn't clear, they were plasma spray coated with HA? Where you were talking about the percent HA in the feedstock as opposed to the coating?

DR. SUNG: Yes.

DR. BRUNSKI: Were they representative samples of commercial type coatings?

DR. SUNG: My answer is yes, because there's lots of process. So after coating there's lots of process to improve the amount of hydroxyapatite and the methods. There are methods to increase the crystallinity of hydroxyapatite after coating.

Those three samples, that slide which I showed you was published and presented by the American Dental Association group in the NIST, National Institute of Science and Technology. They were looking at the hydroxyapatite powder. One powder was their own powder, I believe. And they asked a very reputable dental company to plasma spray on the titanium 64 alloy, then they performed the analysis. For the detail, I refer you to Dr. Min Tung of American Dental Association in the NIST.

DR. GENCO: Floyd?

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MR. LARSON: May I address the same data? Those data, while I'm not questioning the data explicitly but I'm saying I've never seen data with HA contents as low as those by any analytical technique that I'm familiar with and would recognize. As you're aware, there is no recognized standard for x-ray defraction of HA. There are a lot of techniques that are fairly similar and the ASTM task group that I head has been trying for a long time to develop a standard, and I'm sure that Dr. LeGeros will also refer to her method.

But by any of these methods that I'm aware of, I've never seen commercial product with those compositions. Even the starting powder was lower than I would--typically starting powder is fully sintered HA and is at least 95 percent HA.

DR. SUNG: You are right, it depends on the analytical technique. They are using the x-ray defraction method. As far as I know it measures half-widths of the peak. And they're doing a very careful job. That's why their initial HA contents is slightly lower than the usual industrial reported.

However, there is standard reference materials came out in the NIST, 2910, and that material has been properly studied by using x-ray defraction, infrared, rama, and solubility products. You certainly can have any product

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right now in comparison with that standard reference material. I believe that the value of that report is compared to those original studies.

MR. LARSON: But it's a fully crystalline material so it really can't serve as a standard unless you mix it with fully amorphous material.

DR. SUNG: For the detail of that study I refer you to ADA people.

MR. LARSON: I'm sorry, I don't mean to belabor this technical point, but I guess just to say that's not typical.

DR. SUNG: Any other questions?

[No response.]

DR. GENCO: Thank you very much, Dr. Sung.

We'll now proceed with the presentations from industry. And I'd again ask you to give your relationship to the device company that you're working with or for and any financial or other interests.

The first company is Sulzer-Calcitek and the presenters are Mr. Kermit Stott, Dr. Steven Guttenberg, Dr. Rachel LeGeros, and Dr. John Davliakos. Mr. Stott?

MR. STOTT: Thank you. Good morning, I'm Kermit Stott, vice president of operations and regulatory affairs, Sulzer-Calcitek. I'd like to thank the panel and the FDA

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for again providing Sulzer-Calcitek time to present its data and views.

At the last panel meeting Sulzer-Calcitek recommended that endosseous dental implants coated with hydroxylapatite should be down-classed into class II as long as special controls are established to reasonably assure continued safety and effectiveness. Sulzer-Calcitek has demonstrated the success of our HA coated implants in clinical studies and numerous journal articles.

Additionally, we have established stringent controls and testing standards to ensure the quality of our HA coatings. These standards and tests have shown to be both reliable and reproducible.

However, we have not evaluated other companies HA coatings. We cannot attest to their clinical safety and effectiveness. Sulzer-Calcitek recommends that the following special controls be used to provide reasonable assurances of safety and effectiveness of the coating. These special controls include control of coating adhesion, strength, trace elements, and coating compositions.

Concerning this last item, there may have been some confusion concerning our requirement of 70 percent crystallinity for HA coatings. We propose that this is only a starting point until further valid scientific evidence is

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presented. If additional clinical data demonstrates HA safety and effectiveness are available for a lower percentage crystallinity then the special controls should also reflect a lower percentage of crystallinity. In other words, we propose 70 percent crystallinity as a clinical documented starting point.

Due to the late notice of the last panel meeting we were unable to present all of our clinical data. Today we have three short presentations. Dr. Steven Guttenberg will be presenting our remaining clinical study data and his own clinical study of HA implants. Dr. Guttenberg is a board certified oral and maxillofacial surgeon who practices the full scope of that specialty in Washington, D.C.

Our second speaker is Dr. Rachel LeGeros. Dr. LeGeros is the director of laboratory for calcium phosphate and calcified tissue research. She is a world-renowned expert in the are of calcium phosphate materials and is published widely on the subject. Dr. LeGeros will identify certain characteristics of HA coatings that must be present and the special controls necessary to provide reasonable assurance of safety and effectiveness.

Dr. John Davliakos will conclude our presentation with a clinical overview of HA coated implants, his clinical experience and the desirability for clinicians to have a

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choice on implant surfaces. Dr. Davliakos is an assistant professor in the post-graduate prosthodontic program at the University of Maryland. He also maintains a private practice in Annapolis, Maryland.

Dr. Guttenberg?

DR. GUTTENBERG: Good morning and thank you very much. I'd like to thank the panel very much for the brief time I have available to discuss this issue. Even though I'm speaking on behalf of Sulzer-Calcitek, I have no financial interest in the company. I've not been offered, nor have I asked for, any remuneration for the presentation that I'm making today.

What I'm going to do in the brief time available to me is just to review three university studies which have investigated the use of the HA coated Sulzer-Calcitek implants as well as four individual investigations by myself and my partner who are in private practice in downtown Washington.

First of all, the University of Chicago study, Dr. Toljanic is the principal investigator in that study. They took a look at 50 patients, 275 implants, all of which were placed into the maxilla. As you can see, their cumulative success rate after four years based on life table analysis was 98.1 percent.

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In the study at the University of Manitoba with Dr. William Love as the principal investigator, they took a look at 90 patients, a little bit over 300 implants, about 25 percent of those implants were in the maxilla and the remainder in the mandible. As you can see on the right-hand screen, their cumulative success rate based on life table analysis after five to six years was 97.6 percent.

At the Ohio State University, Ed McGlumphy was the principal investigator of their study, and they saw 121 patients, 428 implants. Once again with the division between maxilla and mandible, about three times as many in the mandible as in the maxilla. After their five to six-year time span again their cumulative success rate was out to 91.8 percent.

I am now going to present four individual investigations made by myself and my partner, Dr. Robert Emery, in a different sort of setting, a private practice sort of setting where we didn't have the controls that perhaps one has in a university sort of situation. That is, we received patients from a large number of private practitioners as opposed to a small number of restorative dentists and prosthetic specialists in the university setting.

In our study, the model number of patients that

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we'll see is 553 patients, 1,490 implants. I should point out that we do not use only HA coated implants in our practice. We also use titanium implants as well. But in this particular study just using just the Calcitek HA coated implants we had, as you can see, something which is a little bit different than the university studies in the fact that approximately 48 percent of our implants were placed into the maxilla with 52 percent placed into the mandible. Of the 553, 271 were males and 283 were females.

As you can see on the right-hand screen this was--the last time that I've actually done a life table analysis was the implants that were restored out through 11 years, through 1996. As you can see, our cumulative success rate has been 94.5 percent. I think it's also important to notice that it's been pretty much of a flat curve, as you can see. Especially if you take a look at this area here for the last four years where some individuals have perhaps anticipated a marked increase in failures in HA coated, we have found that actually to be just the opposite the case. That we seem to reach a steady state and we have been able to show a 94.5 percent success rate.

Now I'd like to just show you the four individual studies that we have complied. The first one which was done in 1991, perhaps some individuals might call that our test

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or trial zone. We had had at that point up to 88 months of experience with this implant. The implants that did not integrate, we only had 10 implants which failed to integrate at the time of abutment placement. That turned out to be about 1.4 percent of the implants did not integrate.

We just mention this at this point because you'll see through the following three studies that the failure to integrate continued to drop down each time, perhaps due to familiarity with the system.

But out of the 690 implants that we had placed by that time our survival rate was 660 implants for a 96.5 percent success rate. In 1993 we had placed 931 implants. As you can see, our failure rate to integrate had dropped down slightly to 1.4 percent, and our overall survival was 96.9 percent.

By 1996 we had placed 1,210 implants of which our failure to integrate had dropped down now to 1.1 percent and our overall implant survival was 96.52 percent. And in our current study we now have 1,490 of these implants at this time that we have placed. Out of these, only 1.01 percentage points had failed to integrate. We had lost another 2.42 percent for an overall survival rate after 56 months of mean follow-up and 144 months of long term follow-up of 96.58 percent.

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I took it upon myself, just to let you all know, that we looked at numerous factors in each of these studies to compare success rates between maxilla and mandible, between men and women, position in the jaws, and we really found no difference, statistical difference in the success rates amongst those different groups.

What we did find however in the evaluation, as you can see here we found no difference by the diameter of the implant; 3.25 millimeter implants actually had a numerically higher success rate, 96.8 percent, than did the 4 millimeter implants at 96.4 percent. But there's not a statistical significance. We don't have enough of the 5 millimeter implants of longer time in place, but I can tell you anecdotally that we so far have a 100 percent success rate with the 5 millimeter diameter implants.

But what is important that I wanted to show here with these two slides is that the shorter implants, 8 and 10 millimeters, had a success rate of 91.6 and 92.7 percent, but the longer implants, 13, 15, and 18 millimeter implants had success rates, survival rates between 98.1 and 100 percent. This is just shown graphically on the right-hand screen.

I compared these numbers to numbers from very well done, nice studies by individuals who have placed or who

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have reviewed titanium implants which have already been classified to class II. Certainly in an Adell study, very nicely done study at the International Journal of Oral Surgery in 1990. In his developmental stage, they had seven years developmental stage, anterior mandibular implant success was 66 percent and the maxillary success rate was 54 percent. Following that they had a five-year, what they call a routine portion of their study, anterior mandibular success rate was 90, maxilla was 81 percent.

Dr. Wayne O'Rourke in the International Journal of Oral Implantology in 1991 reviewing the work by a large number of individuals found that the maxillary success rate for titanium implants was 78.3 percent. Zarb and Schmidt in Canada found in their five to nine-year studies that maxilla and mandible combined success rate was 83.7 percent with titanium implants. And Jamie Lezada finally, in California, reporting in 1993 found that the integration rate for titanium screws was 85 percent and 67.3 percent.

I only give these numbers just to compare these to the success rates or failure rates, however you'd like to look at them, of the HA coated implants that I've just presented.

So once again, a very brief presentation, but my read on it is that the Sulzer-Calcitek HA coated implants

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that I've been able to use and evaluate from others have been shown to be clinically and statistically successful, and safe, because we've not had any dramatic failures in their ability to integrate to bone and to support prostheses over long periods of time.

Once again, I'd like to thank the panel for this opportunity to speak before you.

DR. GENCO: Thank you, Dr. Guttenberg. Any questions from the panel?

DR. HEFFEZ: It appears that your criteria for success that you were looking at primarily was failure to integrate; is that correct, or were there other criteria that were considered?

DR. GUTTENBERG: No. Perhaps I did not make that clear, Dr. Heffez. I showed two criteria up there. I showed the short term did not integrate, failure to integrate rate, which ranged between 1.01 percent failure rate to 1.4 percent failure rate. The remainder of the cases were cases which were late failures, and that, obviously, ranged higher since I had success rates of about 97 percent. So there were about 2 percent of the implants which went on to fail later. So it was not just on failure to integrate, it was the long term success rate, sir.

DR. HEFFEZ: But long term success rate, again, is

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interpreted as failure to--complete loss of the implant as opposed to success as being interpreted as being able to maintain the implant despite the fact of loss of significant bone attachment to it? In other words, what specific criteria of success--

DR. GUTTENBERG: That's a good question. The specific criteria for success obviously is, is the implant still there is number one? If the implant is lost that's clearly a failure, whether the--if the implant is loose, that's a failure. If there is a substantial bone loss that will clearly require the imminent removal of that implant, we have put that into the failure range.

If the implant--for example, if we have a 15 millimeter implant that we put in 10 years ago, and it's lost three millimeters of bone and it's still functioning to support an abutment and a crown, and it's controllable--patient does not have active periodontal disease or perimplantitis, if you wish, around that implant, we consider that a successful implant, not a failure.

DR. HEFFEZ: Maybe you can say that in a different way. How many implants required secondary procedures in order to preserve them? Do you have some data to say that?

DR. GUTTENBERG: I only have anecdotal data. There certainly have been implants that we have gone back,

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and I'd say that probably ranges to be about maybe 40 or 50 implants out of that 1,490 that we've gone back and done procedures to curet inflammatory tissue from around the implant. The particular technique that I use is to use a citric acid to remove a surface layer of decontamination from the HA, and then I ordinarily place a bone graft material, whether it be a bioactive glass or freeze-dried bone or autogenous bone around the implant to save it. And we've been able to, in that manner, save the vast majority of that approximately 50 implants that we've addressed.

DR. GENCO: Further comments or questions of Dr. Guttenberg? Yes, Dr. McCarthy?

DR. MCCARTHY: You remarked that in your practice you used both coated and uncoated implants. What's your basis for making a decision when the patient presents to you?

DR. GUTTENBERG: My basis of decision is one based on reality as a private practitioner. If the referring dentist asks me to put in a titanium implant, I put in a titanium implant. If they don't have a preference or if they leave it up to me, I put in an HA coated implants because of the great success rate we've had.

DR. GENCO: Dr. Brunski?

DR. BRUNSKI: Just to follow-up on that. You do

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use titanium implants in your practice?

DR. GUTTENBERG: That's correct.

DR. BRUNSKI: Do you have any comments on your own success rates with that style in comparison with the HA?

DR. GUTTENBERG: Yes, our success rates are slightly less favorable using titanium than with the HA coated implants.

DR. BRUNSKI: Do they more or less square with the other studies that you noted by Adell and Lezada and some others where--

DR. GUTTENBERG: They're closer to the Zarb and Adell secondary studies than they are with the HA coated studies, yes.

DR. GENCO: Further comments or questions?

[No response.]

DR. GENCO: Thank you very much, Dr. Guttenberg.

DR. GUTTENBERG: Thank you, Dr. Genco.

DR. GENCO: Dr. LeGeros?

DR. LeGEROS: Mr. Chairman, and panel members, guests, thank you for this opportunity to share with you some of our studies and also to provide some information that I think are important for the area of coated implants.

We have been involved in calcium phosphate materials, whether they're in calcified tissues or in

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synthetic materials like bone graft, coatings, and orthopedic and dental implants.

My relationship with Calcitek is that we have analyzed some of their coated implants, just like we have analyzed other people who have requested us, and we have also analyzed other people just out of our own curiosity.

We have also analyzed coatings on orthopedic implants from Osteonics, for example. We have used different methods of analysis, x-ray defraction, infrared, SEM, TEM, and chemistry.

We all know that for the implants to be successful there are several factors, some of which we have control over and some of which we cannot control. For example, there's the clinical skills, there's the patient quality of bone and compliance, and then there are factors that are relating to the implants. These factors include coating composition, crystallinity or purity which means trace element concentration, and adhesion strength which relates to substrate coating interspatial strength. Now these factors the manufacturers of implants can control.

For adhesion strength, ASTM has made a recommendation of 5,000 psi, so at least that is a control. The reason that the adhesion strength is important is that if the adhesion is not optimal then the implant can fail due

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to unloading, that the coating can separate from the substrate. After implantation, if there are micro-motions, again the coating can separate from the substrate because the bonding of the coating to the bone is stronger than the bonding of the coating to the substrate, as you can see here.

About trace element concentrations, again ASTM has made some standards about this. We know that some trace element, for example, arsenic, aluminum, iron, cadmium, lead, et cetera, have been known to be toxic, carcinogenic, or cause pathologies. In addition, some of these elements interfere or suppress the formation of apatites, which is the mineral phase of bone.

In this x-ray defraction here you have apatite which is formed without aluminum being present and apatite formed in the presence of aluminum. Clearly, the presence of aluminum inhibits or suppresses the crystal growth of apatite. So that adverse trace element concentration can compromise the safety and efficacy of good implant coating.

As Dr. Pei Sung said, although I didn't agree with one table--but anyway the idea here is that you start with almost pure HA. What we have looked at the commercial HA that are being used as starting materials is at least 95 percent pure HA. Because of this process you end up with HA

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and ACP, which is the amorphous calcium phosphate, as the principal components, and then you have minor components like alpha and beta TCP, and sometimes you have TTCP, and sometimes you also have calcium oxide.

It is important that the right technological methods should be used. Actually, not only one method but maybe a combination of methods, to measure crystallinity. Crystallinity, as we will mention later, should actually be better defined than it has been. When manufacturers talk about percent crystallinity, you never know really what they're talking about. Sometimes I don't know if they know what they are talking about.

For example, when they say a coating is 95 HA, what they really mean is that it is 95 percent of the crystalline phase. Now the crystalline phase may only be 40 percent of the total coating. So sometimes I don't know whether it's from ignorance or from intent that they say these things. But I think that FDA should regulate honesty in reporting crystallinity.

Another thing that manufacturers do is that they coat a coupon at the same time they're coating the cylinders and assume that the coating on the coupon will be representative of the coating on the implants. Now our studies show that that is not so. This is the starting

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material, the HA, this is the coating on the coupon, and this is the coating on the implant. So that therefore the coating on the coupon cannot be used to determine the coating on the implant.

Another method is to determine the coating on the coupon by scraping it and powdering it or by just analyzing it without scraping it. This is analysis that is without scraping it, and this is analysis by scraping and powdering it. Again you can see some differences here.

We have also shown that the inner and outer layers of the coating can be very different so that if you are analyzing the surface it is very important that you analyze the coating while it is sitting on the implant and not after you scrape it.

So, realizing that John LeGeros actually developed a system so that you can analyze the coating that is on the implant--and the details of this is presented in the ASTM in 1994--our analyses have shown that the percent crystalline phases, that means HA, less all of these phases, but mostly HA, can vary from 30 percent to 66 percent. And the amorphous calcium phosphate component can vary from 34 percent to 72 percent. And that is this amorphous background here and that is the crystalline HA and other components, TCP, TTCP and everything.

So, it is very important that analysis of the coating composition and crystallinity be adhered to. Here in this, for example, we are saying here that the HA in most of these analyses is 95 percent of the crystalline component. And as I said, previously, the crystalline component can be as low as 28 percent.

So, in summary, there is variability among manufacturers as far as the coating composition and crystallinity. We have also observed variability in the same manufacturer from the different lots. And, of course, its variability and composition would be related to the dissolution properties and, therefore, the stability of this coating.

Very briefly, we determined the solution as the amount of calcium released in the buffer with time. Here are coatings from different manufacturers, manufacturer A, B and C. A and C are pretty consistent with different lot numbers; B is not. One is dissolving in this manner and the other in this manner.

Here is, again, the extent of dissolution with time. Here is implant A, implant B, implant C. And when we compare it with our mixtures of only HA, this is HA, and only ACP, amorphous calcium phosphate, that is D, and C is 30 percent amorphous, 70 percent HA. B is 50-50. So, the

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more amorphous, as you would expect, the higher the amorphous concentration, the higher the extent of dissolution.

And what happens when the implant coating is exposed into acid is shown here. This is before exposure to acid and this is after. As you can see the amorphous component and the more soluble components like TCP have been preferentially dissolved.

Well, maybe that is good, but then morphologically it is really not so good. Because this is the morphologically exposure to acid and this is after. And you can see that some of these craters have been created by the preferential dissolution of the amorphous calcium phosphate. So, these things, particles can float out of the coating.

So, the importance of coating composition is that the higher the HA, the less soluble and, therefore, the more stable the coating, and the high ACP component affects integrity of the coating.

So, what is the acceptable coating? Should it be 70 percent crystalline, 60 or 50? And I think that only the clinical data could support it. But, more or less, you can, I guess, speculate that something with better low crystallinity would have a very low stability in vivo.

I, in summary and in recommendation, I would

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recommend that manufacturers take the responsibility of controlling the coating composition, the purity and adhesion strength using reliable and reproducible methods and they should have honesty in reporting.

Thank you.

DR. GENCO: Thank you, Dr. LeGeros.

I would like to ask Mr. Stott recommended a 70 percent crystallinity and I see that in some of the 510(k)s that is reported but from your analysis you did not have any that were 70 percent. The highest was 66 percent.

So, what is your recommendation to us with respect to crystallinity?

DR. LeGEROS: Well, like I said, I think that it should be supported by clinical studies. But I think it is very important to have the both of them: a complete characterization of the coating and clinical study. Then you know whether--it may be even 50 would be okay, but that has to be supported by clinical studies.

DR. GENCO: And then the other consideration was a percent of that crystal structure that was hydroxyapatite.

DR. LeGEROS: Hmm-hmm. Yes.

DR. GENCO: Comments, questions from the panel?
John?

DR. BRUNSKI: I just have to get something

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clarified because I am still a little bit confused. Your question was relating to one of the slides where you showed some analysis where in a given coating experiment, of the total amount of calcium phosphate material that was on the surface a certain percentage was crystalline?

DR. LeGEROS: Right.

DR. BRUNSKI: All right. That is one kind of measure. Now, of that percentage that is crystalline, when we see statements that 70 percent is a desirable crystallinity, are we talking about 70 percent of that already crystalline material or--

DR. LeGEROS: No. I think 70 percent of the total.

DR. BRUNSKI: Okay.

DR. LeGEROS: So, that is an honest reporting. But when somebody says 95 percent crystalline or 95 percent HA, they are talking of 95 percent of the crystalline.

DR. BRUNSKI: This is really just one other comment because you started with a slide that had a reference to some bite force numbers. And I thought I just wanted to clarify one thing that, you know, when we look at coating adhesions strength measured in stress units, that is different than a biting force on an implant. And I think just for our panel deliberations the stress has the

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significance in the sense of an interfacial strength requirement that develops because of a force on the implant.

But the fact that the strength might be 5,000 psi in a biting force is, I don not know, 50 pounds. There is not necessarily a close relationship between those two numbers.

DR. LeGEROS: No. But I thought since I am not familiar with this kind. I know you are and you will explain it to the panel. But I thought that the ASTM requirement of 5,000 is really way above the forces that you had mentioned. And I do not know where the ASTM people, what was the basis of their decision for it, 5,000 and not 3,000 and not 2,000 or 10,000.

DR. BRUNSKI: Well, just to clarify. I mean forces are in pounds.

DR. LeGEROS: Yes.

DR. BRUNSKI: Strength as quoted here is in pounds per square inch.

DR. LeGEROS: Okay.

DR. BRUNSKI: So, that the stresses that develop at an interface are a strong function of the geometry of the implant--

DR. LeGEROS: Exactly.

DR. BRUNSKI: --the amount of bone that is around

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and the force and direction. So, I mean it is a little bit misleading to, to connect the 5,000 psi with a bite force.

DR. LeGEROS: Okay. I will take away that slide.

DR. GENCO: Okay, thank you, Dr. LeGeros.

Any further comments or questions?

Yes, Floyd.

MR. LARSON: I just wanted to point out to the panel that there is an FDA guidance document that covers a lot of this territory. Recognizing the difficulty in the analytical method--and, by the way, I do agree with Dr. LeGeros regarding the misuse of the term, crystallinity, I would like to banish it entirely and just refer to the percent HA content. But the term, crystallinity is used in the FDA guidance document and the number is 62 percent. So, that is the number that has been used in terms of submissions to FDA up to now.

DR. GENCO: Thank you.

Further comments? Yes, Dr. Drummond?

DR. DRUMMOND: I know this is probably a loaded question; do we have any clinical studies relating the amount of crystallinity versus the success or failure rate with HA integration?

DR. GENCO: Does anybody from the audience want to answer that? Did you hear the question?

[No response.]

DR. GENCO: The question is directed to Dr. LeGeros' suggestion that we have or the field has information relative to clinical success as compared to--I hate to use this term, crystallinity, as Floyd has told me it should not be used but--percent hydroxyapatite or percent crystallinity, whatever way it is expressed?

[No response.]

DR. GENCO: Apparently, at least the group here is not aware of anything, the clinical studies related to that. Any further comments or questions?

DR. HEFFEZ: Just one.

DR. GENCO: Oh, yes, Leslie.

DR. HEFFEZ: In your studies, you had actually studied different manufacturers' hydroxyapatite. I just would like to have your comments concerning the process of developing the hydroxyapatite. Is it a uniform--once--does it have to be stringently adhered? Do the company's coatings of hydroxyapatite vary from implant to implant?

DR. LeGEROS: The starting material that we have examined are usually very much, very close to each other, the starting material. But, you know, there are several parameters in the plasma spraying process that causes the variation in the composition from one manufacturer to

another and even from the same manufacturer from one lab number to another.

So, the first time in 1991 when we presented our first results of comparative composition, one gentleman from FDA came to me and said, it is amazing, I never realized that there was such variability. And I said to him, you should be ashamed of yourself that you approve everything.

And he said, well, we believe in the honor system. If they tell us it is HA coated, it is HA coated. But HA coated is not HA.

DR. HEFFEZ: Well, within even one manufacturer producing hydroxyapatite there can be a tremendous variation in the implants that are produced, is that correct?

DR. LeGEROS: Yes.

DR. HEFFEZ: In other words, certain, some of the implants produced by that company may have, to use the word crystallinity, 90 percent crystallinity but not 90 percent, 70 percent.

DR. LeGEROS: Okay, yes.

DR. HEFFEZ: Let us say 70 percent and then another batch of those implants could also be 30 percent.

DR. LeGEROS: Well, it depends on the manufacturer. This is what I mean. That is why they have to analyze it by batch by batch. If they change

technicians, who will change parameters, then they will get different coating compositions.

DR. HEFFEZ: And our companies typically evaluating it by batches, their hydroxyapatite.

DR. LeGEROS: I think we have to ask them that. We have analyzed other people who have asked us to analyze it for them to compare it with their analysis. We have also analyzed other people's who did not ask us to analyze it for them, just to compare for our own curiosity.

DR. HEFFEZ: And, again, we do not know the clinical significance of all these variable factors.

DR. LeGEROS: Well, that is true. That is why we say we need clinical support for the crystallinity that is being reported. But I think there have been some reports where some coatings have failed but then there was no analysis of the coating so you do not know.

For example, what Dr. Pei Sung presented here that there was no difference between coated or uncoated. Well, I do not know what was the coating of the coated, you know?

DR. HEFFEZ: Thank you very much.

MR. STOTT: Let me just comment on your question. There can be variability in the spraying process. I will put my manufacturing hat on. You need to look at not just the crystallinity but also the tensile. And you can vary

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the tensile and the crystallinity, let us say, by moving the gun in or out or varying the amount of gas flow with it.

But in a controlled process you are testing each slot. You are testing the raw material that is coming out to make sure it complies with your specifications, and then in the finish spray process you are also testing it, too. So, you are ensuring that you have a consistent process and it is reproducible. And that is what we find at Sulzer-Calcitek.

DR. HEFFEZ: Are you testing the implant or are you testing material that was sprayed with the hydroxyapatite?

MR. STOTT: We are testing the implant. Now, you cannot test the tensile on an implant. We are testing a substrata on the tensile but for crystallinity, we are testing the implant through X-ray diffractometer.

MR. STOTT: Thank you.

DR. GENCO: Thank you.

Okay. Dr. Davliakos, we apologize for the fact that you have been up at the podium three times now. And we will not interrupt you but we will ask you to keep it short. Thank you.

DR. DAVLIAKOS: Thank you.

Good morning, everybody, Mr. Chairman, panel

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members, consultants and guests. I have no financial relationship with any implant manufacturer whatsoever. I was presented this opportunity to present to you today. Although Sulzer-Calcitek has agreed to reimburse me for any travel expenses or out-of-pocket expenses that I would submit if needed.

It is a privilege to be able to present a clinical interpretation or understanding to the research material shown by Dr. LeGeros and Dr. Guttenberg.

I plan to show a perspective of implant treatment that has resulted in successful surgical and prosthetic outcomes for the patients I have been fortunate to treat.

My formal education is that of a prosthodontist, responsible for the restorative procedures, long-term follow-up and observation of the patients that I treat. My ultimate goal, as a practitioner, is to restore a patient to the proper function and aesthetics in the most practical method without undue damage or future compromise.

Following my prosthetic in 1986, I was fortunate to be accepted in a very progressive and prestigious fellowship in oral implantology at the University of Pittsburgh. This allowed me exposure and education in the surgical prosthetic and laboratory phases of implant dentistry.

I worked with many types of dental implants. The primary endosteal dental implant we used at that time, between 1984 and 1987, was a commercially pure titanium screw. This began my exposure to dental implants and I have been involved with their use in patients for over 14 years.

Early on, we learned that the skill, technique and judgments of placing a titanium screw implant was very critical. This is supported by Dr. Branemark's group, themselves, having the need for a developmental period or group in their initial research.

We learned that Dr. Branemark's research data was applicable primarily to only the mandibular anterior portion of the jaw due to the type and quality of the bone. For, as we placed implants in other areas of the oral cavity, we experienced initial surgical losses of approximately 10 to 20 percent. This later correlated with the published results of Dr. O'Dell, along with Drs. Jappen and Berman who had similar decrease success rates following stage II uncover surgery.

They published a 35 percent failure rate in five years in the poorest quality of bone, the type of bone usually found in areas other than the mandibular anterior region. This is why we must keep in mind that Dr. Branemark's research was not to preclude that other

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bio-compatible materials would not work as well or even better than titanium, but that a stable bone to implant interface surrounding and resulting in the non-mobile implant was our goal in oral implant reconstructive therapy.

In light of this concept, attempts to improve this osteon-integration have been developed and offered to the dental profession. Examples of these being titanium plasma sprayed, HA coated and recently micro-abraded and/or edge-titanium surfaces. These were all developed to improve the amount of bone in direct contact with the dental implant.

It is shown in current dental implant literature that HA coated implants have been and are at least as safe and effective products as titanium implants. They exhibit equal to or better stage II surgical uncovering success rates compared to titanium implants where an implant is placed randomly in any region of the oral cavity.

To support this literature I have been involved with the ADA approval study for HA coated, screw-type implants with a spline prosthetic interface developed by Calcitek. As of January of 1998, I have enrolled 22 patients in the study with a total of 47 implants placed. I have performed second stage uncovering surgery on 16 of these patients, having uncovered 31 implants. I have not had any

implant failures or complications to date.

This increase in the direct bone to implant surface using HA coated implants is supported by research performed by Dr. Buser at the University of Berne in Switzerland. Dr. Buser's paper on the influence of surface characteristics on bone integration of titanium implants, published in 1991, showed that HA coated implants exhibited a 60 to 70 percent implant to bone contact while the titanium implant showed a 20 to 25 percent.

In correlation with this, Dr. Allen Carr of Ohio State University's paper on reverse torque failure of screw shaped implants in baboons, published in 1995, showed that on average it took 74 Newton centimeters of reverse counterclockwise torque to remove an integrated titanium implant, while it was necessary to use 186 Newton centimeters in removing an HA coated implant of the same design and manufacturer.

These papers I feel to be the indicators of an implant's ability to transfer the occlusal load or force to the supporting osseous structures. Dr. Eugene Roberts stated in 1988 in the Journal of the California Dental Association that the mechanical properties are directly related to the proximity and mineral content of the bone intimately contacting the endosteal surface. And Dr. Carl

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Misch states in his text, Contemporary Implant Dentistry, that the greater the surface area of bone to implant interface the better the support system for the protheses.

This is why these factors are of utmost importance for the longevity and stability of a restored implant prothesis.

However, in the late 1980s to the early 1990s, many different compositions and types of HA coatings were available. There was no definition to what HA coating meant to the dental profession. As a result of a lack of understanding and subsequent unregulation of this term, the public and the dental profession were served an injustice and subsequent fears resulted. At that time in the profession, in my opinion and to my knowledge, there appear to be two dental implant manufacturers with a stable HA coated implant with published clinical results. These being Calcitek and Steross.

Dr. LeGeros' research sheds the light on why these products have shown to be successful over time and why there is the need to implement the special controls she mentioned to call an implant HA coated. This is necessary for the safety of the public and the confidence of the dental profession.

It has been my experience that when these controls

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are met there is every reason to believe that an HA coated implant will perform as well or perhaps better than a similar titanium implant. We should not wait for a manufacturer to voluntarily withdraw a product due to coating inferiority.

For example, an HA coating of less than 20 percent crystallinity was shown by Dr. Buser to have signs of resorption and he felt this to be biologically unstable. This was the original IMZ HA coating.

I have personally placed over 1,000 dental implants in my professional career with 60 to 70 percent of these implants being HA coated type implants. There is no doubt in my mind that if the special controls as proposed are followed or exceeded that these products are, indeed, as safe and effective as the pure titanium screw type implants.

Therefore, it is important that as a clinician we have equal access and availability to either titanium or HA coated implants depending on what we feel to be the proper indication or choice for our patients. If I wanted to remove an implant at a later date, the titanium screw type implant would be my implant of choice.

Once an implant integrates and demonstrates a bio-compatible and stable bone to implant interface, the long-term prognosis depends on many factors. The

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biomechanical stress transfer to the supporting tissues determines the implant longevity.

This is dependent on the skills, the techniques, the judgments of the implant surgeon, restorative doctor and laboratory technician. It has been published by Dr. Paul Binan in the International Journal of Prosthodontics that the precision of the prosthetic interface connection is critical to decrease complication and improve long-term implant restorative success.

This is the next area in need of regulation for further safety to the public and assurance to the profession.

We will never know for each patient what is the stress threshold of each individual implant but our understanding is that a stable interface with the opportunity to have the greatest bone to implant surface contact will be the most preferred type of implant for longevity and ultimate success for our patients.

This, in my opinion, is achieved through an HA coated titanium implant with the special controls mentioned. It has been shown to be safe and effective to both our patients and the dental profession.

Thank you for your time.

DR. GENCO: Thank you very much.

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Comments or questions from the panel?

[No response.]

DR. GENCO: Okay, thank you very much, John.

Okay, let us proceed to the Nobel Biocare presentations. The first presenter is Dr. Loreen Langer and then Dr. Irene Herrmann.

DR. HERRMANN: My name is Irene Herrmann. I have been working for Nobel Biocare. I am now their consultant so I am here on their behalf. And after the meeting last time we had the discussion, what is a failure, and I would like to bring up some of the issues about this, statistical, how you can compare success rates from different implant systems. So, I am referring to the material we have sent in.

Okay. What is a failure? It depends on the baseline how the patient looked when you started and expectation. In the industrial world we talk about the product claims. If we move on to talk about statistics, statistics are like a bikini. It is the user who decides how much they want to reveal. They always keep the important parts covered.

Let me give you some examples. Because this has been discussed for 10 years now and FDA has given guidelines on study design. So, if we have, for instance, 1,000

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implants placed in the interior and posterior sides and we have 50 failures, that would mathematically easily give you 5 percent failure rate which would be transferred to be 95 percent survival rate.

If you get more information, and you learn that 900 of those implants were placed in the anterior region where you have no failures, the success rate in that group would be 100 percent.

And the rest of the implants, the 100 implants would be placed in posterior sides. There you might have 50 failures. The survival rate would be 50 percent in posterior sides. So, now, we have revealed more.

Let us continue this discussion about statistics because when we talk about cumulative success rates, it is important to know what has not been revealed from the beginning. So, look at this cumulative success rate here. We have a very nice line here with success rate on 96.1 percent shown at the bottom.

If you start to read and ask for more information, the important part is how many implants were actually considered at the end of this study? Not 1,000, 15 implants.

So, statistically it's correct to draw the cumulative success rate at 96.1 percent. But if you make a

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conclusion that the ones that you don't know the fate of are failing instead of like using the statistical method where you are judging them to have the same fate as the ones you know, you could call that the worst case scenario, right, that all are failing. Then we have a curve that looks like this.

This area are definitely safe. We know that. The area between the red, worst case scenario, and the green, cumulative success rate, when you have so little information on the data claiming to be 9 to 10 years, like 15 implants, are uncertain.

So, the truth are lying somewhere in between those two lines.

Then we did also discuss what kind of success criteria do we have? Then you have to be reminded that you don't take X-rays like every year; you take them at certain intervals. So, the ones that are actually checked according to the claimed success criteria, which are a radiographical and clinical exams, are even less.

It does not have to be like this. If you would follow guidelines given by FDA or the standards in Europe you would start to do prospective clinical trials where you have control on most of the implants. Like if you start with a 1,000, you end up with 750 after 10 years. You must

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accept a certain number of drop-outs, otherwise, you're violating the Helsinki Declaration because patients are allowed to drop out.

And now, you see, the area where you have the true known fate of the implants is much more, it's much greater and the gray zone between the red and the green line is less. So, the important part is to look at how many implants were actually there on the final checkup.

Okay. Let us now consider this on published data. I have, from the data that was sent out for this meeting, selected two studies; one by Buser and one by Sullivan. They are published in 1997, so they are very fresh.

The one by Buser is concerning 2,359 implants at the start of the study. He is claiming a 0 to 8-point follow-up period. And he is claiming a failure rate at 5 years on 5.5 percent. That is what we are discussing and comparing.

But if you read and analyze the data a little bit more, you will find that less than 10 percent of these patients are evaluated at the end of the study. So, if we consider and apply the worst case scenario, you would have a possible failure rate at 64.8 percent instead at five years.

With Sullivan's study, it is even worse. You start off with 147 implants and the claimed follow-up period

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is 0 to 36 months. He calculated statistically correct success or failure rate of 3.4 percent but since so few are followed, less than 10 percent at 2 years here, the possible failure rate in this study could end up with 93.2 percent.

I am not claiming that that would be the case but it shows you that we have an uncertainty that we are talking about. So, what we have to do is to have a risk/benefit analysis. So, if you introduce new implants systems that have not been in use for a long time you do introduce unknown risk and then the scale will weigh over for the benefits which could only be things that are really proven.

You also have to do a failure analysis on what you see. I mean any kind of tissue loss on the patient is extremely serious because once you lose tissue, it won't come back. Implant failure, you have to know how the implant failed, if you should discuss the failure analysis, and then you move up to abutment screw fractures, gold screw fractures, veneering material fracture, with all failures that you could take it easy, at least, from this point.

So, we need FDA and the dentist, the clinician's responsibility to supervise and report effects on both new and old products. The industry's responsibility is to do failure analysis, find out causes for failures on the implant systems, on the uses, they might need more

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information, and also on how to select patients. From that we can do improvements.

So, we have a total responsibility to the patients here from FDA through the industry and through the dentist back to FDA.

Published and unpublished data is what we had to add up because who wants to publish failures? That is why we have so few failure reports. Everyone wants to publish their success. So, when we draw prognosis we have prognosis on both published and unpublished data, on implant types and also on the indications. This way we will get an increased knowledge. With that increased knowledge we can develop implants and put the right product claims on them, for instance, Zygomaticus or Onplant, for the Branemark system.

Onplant is an HA-coated subperiosteal implant for temporary use as an orthodontic anchorage placed in the palate to be removed after one to two years. An investigation that has been performed are dog studies on four dogs, very limited number; a monkey study on five monkeys, a study on four females who are actually the pilot cases. But what we do know is that HA has been used on 1,000 patients and 5,000 implants in human studies and they have shown how HA works and that it works well for the first year. Complications usually occurs after that and how the

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complications occurs are also well documented.

So, we do the same risk analysis on Onplant. We do have a lot of benefits if we can use an implant for orthodontic treatment instead of a head gear where you are having to risk with eye injuries. The risk with Onplant is that it might fail since it is not integrated into the bone, just on the bone, the tissue loss will be limited. So, the risks are limited and they are well-known.

So, we would strongly recommend to keep Onplant in class II.

For Zygomaticus, it is a different situation. Here we are talking about the real oral invalids as Professor Branemark started his research. These are patients that due to very little bone with poor quality may end up with very low success rate as has been mentioned before. In those patients, you could graft them but still they do have less success rate.

This new implant has been designed. It is the same material as the Branemark system, it is the same design except that it is longer, it is the same surface. It is prosthetically similar, surgically similar, but the site is different and to [unintelligible] [?] the site it is a different procedure. So, you might need more experience to use them.

What is important to see here, even if like I told you before look for the final numbers that are followed, is that the success rate here is extremely good and these patients cannot be treated with anything else.

So, if we look at, once again, the risk/benefit analysis, the benefits, even if they are just prognosis so far, are very great compared to the risk with those patients and the risks are known and should be addressed, of course.

So, I strongly recommend that they will remain in the class II as they have achieved a 510(k) today.

Thank you for listening to me again.

DR. GENCO: Thank you very much, Dr. Herrmann.

Are there any questions from the panel?

[No response.]

DR. GENCO: Or comments?

Yes, Dr. Patters?

DR. PATTERS: Excuse me, could I see the next to last overhead?

DR. HERRMANN: That's the figures on the Zygomaticus study, yes.

DR. PATTERS: But what I want to ask is, why you didn't apply the same worst case scenario analysis to those data as you applied to Buser and Sullivan?

DR. HERRMANN: Yes. You can do that definitely.

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So, that is why I pointed at it because you only have, you have a very big gray zone which I did address. So, it is just prognostic values here. The prognosis seems to be good but we do not have the definite answer on a long-term basis.

On the short-term, as well as in the Buser and the Sullivan article, it seems very promising. Absolutely correct.

DR. PATTERS: Thank you.

DR. GENCO: Further comments or questions?

[No response.]

DR. GENCO: Janine?

DR. JANOSKY: Thank you for going through the two parts of sort of analyses and how you can present them and how one might be appropriate in one circumstance and one might be appropriate in another. Actually the issue is looking at proportions as opposed to survival analyses and you had spent some time explaining those two to us.

Why in the survival analyses results that you are presenting are you presenting them like proportion results and not the step-down that we typically see for survival?

So, even though you have spent a nice presentation showing us the difference of the two and why censoring needs to be taken into account, when you presented the data for these two sponsors you also went back to the proportion

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response?

DR. HERRMANN: Yes. Because that is the data that is available today. Why I presented it afterwards and not ahead? Why I presented it is going back to the bikini discussion. As long as you know what you are looking for you can see that very easily yourself that not all of them are followed the entire period. We do not have that long-term follow-up on all of them as yet.

It is limited documentation here. But the need for those patients are so great, so, that's why we want to have them released.

DR. JANOSKY: So, in terms of presenting failure data for implants, are you advocating for using survival analyses with censored data or proportions reporting like we had seen earlier today?

DR. HERRMANN: No. I definitely prefer censored data, of course, so you really have the definitely study design where you decide when you censor your data, what kind of success criteria you apply. And that all implants should be followed for the period that you are claiming that you have follow-up on.

DR. JANOSKY: Okay. One of the issues I have and I think you had mentioned today is that the follow-up period is varied, given that we have open enrollment for any study.

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So, in presenting data in terms of straight proportions and not using censoring for survival data we are missing a fair amount of the picture.

DR. HERRMANN: Yes, yes. That was the point I was trying to make that you cannot compare results from one study to another one if you do not look at all of the data.

DR. GENCO: Thank you. Further comments or questions?

[No response.]

DR. GENCO: Okay. Thank you very much, Dr. Herrmann.

We now have Dr. Loreen Langer.

DR. LANGER: Good morning.

I think it is nice to be here. The topic, of course, is one that no one likes to talk about. Failures, as Irene said, and we have not heard much about failures yet but we will now.

And as I said, we really, no one likes to talk about this. It is a subject that no one likes to publish on but there are published reports. So, what I am bringing you are some of my clinical information having a practice, and I have to dis--you know, my disclosure is that I am not paid by any implant company, I am not sponsored by any implant company and I am in private practice as a practitioner who

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pays for implants. I am a customer, okay?

When asked to lecture if a society wants to ask Nobel Farmer [?] to pay for me, I say, no. They have to come up with the money themselves. I have wanted to keep it this way for these last 12 years while I have been placing implants so that I could be as unbiased as possible and not feel that if I wanted to switch that I could not switch at some time without feeling that I owed somebody something. And I do not owe anybody anything.

Okay. So, we will talk about failures. What I have seen and I brought you charts not only slides. These are not just slides, these are not just published reports, these are people, we are talking about. These are people who have been damaged and these are people who have been damaged repeatedly. And I think we have to really take that into consideration that that is what we are talking about when we are talking about failure. It is not just, did we fail as a dentist or are we having a bad day, but what happens to the patient and what happens to them on a long-term basis?

And what I have seen is that different implants fail differently. They do not all succeed the same, although they all seem to publish 96.6 success rate, and they do not all fail the same. The failures are different

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and quantifiable.

This is a classic case in point. If you want to say that different all implants, all root-form implants are generically the same, this is a perfect case to illustrate that they are not. These are all placed by the same dentist. They are all placed in the same patient. So, the host is the same. The bacteria is the same. The clinician is the same. The implants are different.

We have some HA-coated cylinders here. We have some cylinders here. We have some titanium screws in the center. These have massive bone loss. All of these. These three and these two. The only ones that have no bone loss are the two in the center.

I think this is a very strong point for that they do not all fail the same. Because as I said, this is the same patient.

What is it that we did not like about implants before 1982? Unpredictable results. Radiographs that were unreliable. They were unable to be free-standing. They had multiple infections. But the most important thing is that when they failed, they destroyed a large quantity of bone, leaving patients worse off than when they started.

We had things like this, blades that did not look too bad, radiographically, but the radiographs were

unreliable because this was loose and infected and when it was removed, the bone loss was so severe that even making a removable partial denture was almost an impossibility.

This is not an uncommon picture for subperiosteals. Massive infection eating away the mandible. This is not all subperiosteals, but this is not uncommon and we all knew that. This is why these methods were not taught in most dental schools and was not accepted by the American Academy of Perio.

The same. This lady came in. If you wanted to count this as survival, you could count this as survival. This is a 10-year survival of two subperiosteals. However, the reason I got to see her is she came into me because there is a diner next door to one of my offices, and she could not eat because this had perforated through the floor of the mouth. She can now wear it as an erring.

So, we had a criteria for success in 1979. It is all we had. And it was what we had from--let me just go back to get that focused--it was all that we had from the NIH conference, basically, that you could have mobility, less than one millimeter in any direction. You could have radiologically observed radiolucency, graded but no criteria defined. Bone loss no greater than a third of the vertical height of the implant.

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This was implant survival. But this was also 1978. NIH recommended at that time, at that conference, that we have better controls, that we have longer term studies, we do animal and clinical trials. That was 1978.

In 1988, they recommended the same thing. And in the last 10 years, nothing has changed. It seems that we still do not have long-term clinical trials.

Thank you.

The difference is criteria of success. The difference is it just is not focused and I do not think there is a focus button on these. There might be on this one but that does not help the other one.

The main difference is that our standards should have changed by now. In this ensuing 20 years, they have raised the bar. Branemark raised the bar and said, okay, an implant to be considered successful has to be immobile when tested clinically. A radiograph cannot have any evidence of peri-implant radiolucency and the vertical bone loss should be less than two-tenths of a millimeter annually.

So, now, the standard was set in 1986. This is 1998. Where are we?

Well, the American Academy of Perio, of which I am a member, became interested in implants only after Branemark. Why? Because he described a long-term well

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researched recipe for placing, restoring and maintaining a specific type of implant in a steady state of health. And all of these articles from Adell, Lecomte, Coxin, [unintelligible], Albertson, Chader [ph], show that after the first year where one millimeter of bone can commonly be lost that it maintains a steady state over time. Bone levels stay the same.

The AAP then at the World Workshop in 1999 [sic] unanimously agreed that these criteria of success were acceptable and they actually made it even more stringent saying that progressive attachment losses measured by probing from a fixed reference point.

And what are we talking about and why is it important? Because we are dealing with patients like this, patients who if we create more damage to, this is their last chance. They are really on their last legs dentally. As Irene was talking about, the dental invalids.

So, we have to have something that will maintain their bone, not destroy it. And the controversies, of course, that we have come to talk about are bone contact and peri-implantitis and what can we learn from the literature?

Well, this is an often quoted article by Jappan and Berman, "Excessive Loss of Branemark Fixtures in Type IV Bone: A Five-Year Analysis." They place 90 percent in type

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I, II and III bone for a 3 percent failure rate. They place 10 percent in type IV bone for a 35 percent failure rate. This was the worst case scenario, the worst published data on a Branemark implant failure rate. So, I am giving it to you as it is.

The learning curve, it was their learning curve but the most important thing is that they used glow-discharge sterilization which was a method not recommended by the manufacturer and has now fallen out of favor and I do not think anyone uses glow-discharge sterilization any more as far as I know.

So, they had altered the surface of the implant. Most of their implants were lost prior to or at stage II. This was not a loading problem. This was not after they were restored. This tends to be a surgical problem. They have tried HA cylinders. They have gone back to screws.

This paper was mentioned a few moments ago, the Weindlander paper. And it is very interesting. It is a dog mandible, three-months, non-loaded. The titanium screw had less bone than the IMZ cylinder, which both had less bone contact than the integral cylinder.

But the authors, themselves, pointed out that the implants were evaluated prior to loading and the results are not a reflection of bone apposition around implants

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functioning in the clinical environment. And said that future studies must look at the long-term stability of HA coatings, which is what we are here today to do, because there is evidence that the surface of some HA-coated implants can be resorbed after implantation.

Gottlander [ph] and Albertson [ph] compared IMZ cylinders. 75.6 contact with HA-IMZ; 59.6 with TPS-IMZ. They were used in rabbit leg, six months again, not loaded, but Axel Kirsch stopped using it, using the HA coated, even though there is clearly better bone contact experimentally in animals around the HA as opposed to the titanium plasma sprayed.

In the Lyon Conference in 1992, and at the Ten Year Anniversary in 1993, he stated, there is sufficient histological and clinical evidence to say that HA-coated implants should not be used in patients and he stopped manufacturing them.

Gottlander pointed out one of the problems that may have occurred is that we had a lot of six-week studies and in six-week studies the HA certainly had more bone contact than the titanium. But if we carried the study out a little bit longer to 52 weeks, the HA lost some of its bone contact and the titanium increased.

And this graph, I think, is very important because

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this makes plain what is going on with the early studies and why they are so different from the later, long-term studies.

So, we accept that HA is bioactive. That is the good news and I think it is also the bad news, is that the bone likes it but the bacteria likes it also.

And unfortunately, we have both things that we have to deal with. So, how rough is good? How smooth is bad? We know that this totally smooth cylinder does not integrate. We know that this does integrate and we have thirty year's worth of well-documented research, long-term studies.

We know that these two integrate but we do not know what happens to them long-term because there are no real long-term studies with all implants followed consecutively placed.

But looking for something like this, early on this was one of the better studies. This was the Kent and Block study. Bio-integrated, HA-coated dental implants, five-year clinical observations. To the casual reader that means a five-year study. However, as Irene pointed out, if you look at this for any, just a little more than casually, you can see that all the implants that were placed in '89 cannot be five years, the ones in '88 cannot be five years, the ones in '87 cannot be five years. So, is this really a five-year

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observation?

And when they are dealing with 772 HA-coated implants and they had lost 29, that is not bad. However, as Ken states, not all implants have been in place for five years. Actually 717 out of 772 were restored for less than two years. So, this is really a less than two year study, not a five-year study.

And, additionally, if you apply the Albertson-Zarr [ph] criteria of success to the bone loss, you have an additional 78 that you have to add-in as failures because they have lost more bone than is allowed by that.

And if we look at the actual life table taken from the paper, you see in very small print at the bottom of the life table, not all implants have been in place for five years. Well, as we have been taught the way to read a life table is from the bottom up and if we look at this how many have been in from up to four to five years? Twelve.

So, out of the 745, actually only 12 have been in up to five years and only 12 have been in for longer than four years. So, this is not a long-term study.

However, Block did a follow-up study just recently in '96. Hydroxy-coated cylindrical implants in the posterior mandible, 10-year observations. 443 mandibular implants placed between July '85 and December of '91. Okay,

fine. And they were followed to '95. That is a good time frame.

He defined survival as an implant that has not been removed; non-morbid, which is a term that we do not use that often in dental implant literature. He says those that were removed or the ones that were still there but had greater than 2.5 millimeters of bone loss. So, this is adhering to the stricter criteria of success. They were evaluated annually, radiographically, from '88 to '95.

And 233 out of the 443 were followed for greater than five years. And 70 were followed for greater than eight years. Of survival, he had 79.3 percent. However, so, that is 20 percent failure. Non-morbid, he had 65 percent at 10 years. That means that if you added in the ones that had lost bone and you counted them as failures, you had a 35 percent failure rate. Or, I am sorry, 15 to 20 percent complications.

And what Block states publicly in all of his presentations is that these are--he no longer places cylindrical implants.

Golec and Krauser similar results. Since we are short on time. HA-coatings, not a long-term study but very good early success, 98.52. Described ailing, failing, and failed, which I think you are all familiar with. And in

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Implantology Update in 1993, the implants with greater than 5 millimeters of bone loss, which were in the at-risk category, all failed two years later. Those with 2 to 3 millimeter bone loss have moved into the at-risk group.

And he stated that, yes, the concerns are warranted and the failure rate is a gradually increasing one. The break down of the failure of the implant occurs in the steady state period.

One of these is a failed implant. The middle one. This is a Branemark implant. This is what those failures look like. This is mine. This is another failed Branemark.

But the damage to the bone is insignificant. You can remove this. You can put the patient back to the way they were before they came to you. They are less susceptible to bacterial pathogens than teeth or coated fixtures and they do not cause major amounts of bone loss.

Pari-implantitis was defined early in 1987 by Mombelli [ph]. Fully edentulous cases. He defined it as a site-specific infection, similar to periodontitis. Was he looking at HA-coated? No. He was looking at ITI hollow cylinders, titanium-plasma-sprayed surfaces, fully edentulous patients.

We will skip this for time. This is a case, a patient that I saw last year. This is the announcer for the

New York Yankees. He makes a living speaking. He could not work because he had infection in this area. He also had an infection in this area and he had an infection in this area.

I thought these might have been placed a long time ago. They had been placed one year prior.

So, what is the long-term evaluation? We mentioned this Buser study, an 8-year life table analysis, and the conclusion was solid screws are better than hollow cylinders. So, Buser is saying that screws are better than cylinders, but in reality only 55 of the 1,141 solid screws were in for five years. So, it is not exactly an 8-year study and very few of the implant that they seem to prefer have been evaluated for five years.

DR. GENCO: We are going to have to wrap this up soon in deference to the other speakers. We have a whole day of speakers.

DR. LANGER: Okay. I just thought you wanted to know about failures and there is a lot of information and we have not heard any yet. But if you want me to skip this and just get to the clinical cases?

DR. GENCO: Can you tie it up in a minute?

We have 20 minutes for each presentation. You are working on about 40 now for the Nobel Biocare.

DR. LANGER: Okay. I can stop right here if you

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want. I feel that this is information that I thought the FDA wanted to know. And that they really wanted to see the long-term studies. So far we have seen no long-term studies on failures. We have only seen successes.

DR. GENCO: We are going to have a presentation on failures by Dr. Krauser at 1:40.

DR. LANGER: Okay. So, what would you like me to do? I would like to bring them--

DR. GENCO: Can you just finish up in a minute summarizing in the next minute.

DR. LANGER: Okay. We are talking about peri-implantitis. We have Dr. Meffert telling us that poor home care and poor plaque control and HO credit [?] systems may make more at risk due to rough surface fostering plaque retention but this patient is not a patient for implant therapy anyway.

The problem is that most of the patients that we want to treat that need implants have poor plaque control, have advanced periodontal disease. These are the people who need implants. And if we look at this case that was treated for eight years, the patient did get a recurrence of periodontal disease. But he got it around his tooth not next to the implant next to it.

And I would like to--I have several of those

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cases--but I would like to skip forward to a recent advertisement that I think is very offensive that was in the Journal, in both Journals, Journal of Perio and the International Journal of Oral and Maxi-Facial Implants, this one.

This ad would give us hope because basically what it says is enhanced performance in poor quality bone: 96.6 overall success rate. So, you would think that for those cases that we have been talking about, the type IV bone, where the success rates have not been good, this should be an answer to that. And if you look at this asterisk it says way down here at the bottom, research on file.

So, I sent for the research. And what I got were the Buser and Wong [ph] articles which were on cylindrical implants, HA-coated, rip-blasted and acid-edged. Having very little or nothing at all to do with the implant that the advertisement was advertising.

These were miniature pig studies, three, six, and 12 weeks. The surfaces were different. And as the person before me spoke, the HA-plasma sprayed had a better success rate than the etched surface. So, if you are advertising an etched surface, it might be nice to have an article that has something to do with a purely etched surface.

The Sullivan article, in type IV bone, had 63.6

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success rate in their own article. If you look at this, this is the implant that was advertised, but this is not the implant that was discussed. This is the table of one-to-four bone quality; only less than 8 percent of the implants were placed in type IV bone.

So, they are making a claim that 96.6 success rate, overall cumulative success rate, less than 8 percent of the implants were placed in type IV bone. It depends because in the article it says it is .8 percent, but we have called them and they say that these two numbers have been transposed and that is a typo.

If we look back at what Keith Beatty spoke about at the San Diego Meeting, AAP, he talked about the same exact study, and I will finish with this, that 147 implants, 75 patients. However, he said the acid-edged surface went all the way to the top. In that picture that you just saw, it did not go all the way up to the top.

He said that this was the implant design initially developed and approved by the FDA. And that most of the implants had less than one year of post-loading. So, here are two reports of the same article, of the same material telling us different things. It is very hard to understand which one is accurate. Was this the implant that was used in the study? If it was, it was not available in '92 when

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the study started.

Was it etched all the way to the top, as he said? We do not know. So, the question is, how clinically significant is the rough surface? Does enhanced and admittedly more rapid contact in miniature pigs, dogs or rabbits for a period of three to six months have any relevance? And are there any reliable five-year studies to support any of these claims? I do not think so.

Why do we have to be constantly vigilant regarding not only spoken but published reports? Why do we have to do all the work?

Thank you.

DR. GENCO: Thank you very much.

There is no time for questions unless there is a burning question, Dr. Langer, from the panel.

What we are going to do is, we are running a little behind, so, we will take a ten-minute break and then Friatec is going to be up and we are going to try to give everybody their appropriate 20 minutes. I would ask each group to make sure that you condense your presentations to the allotted time in fairness to everyone who is on the program.

Thank you very much. We will see you back there at 10:30.

[Recess.]

DR. GENCO: We have a very full program.

Let me read the schedule. I guess this has not been handed out to you. We have it. And I guess it is unfair to you to surprise you that you are up and have to be speaking in 30 seconds.

We will start immediately with Friatec. And then at approximately 20 minutes later, it is going to be about 10:55, Reimplants; and then shortly after 11:00, Sargon Enterprises; and then around 11:30, Tronics Oral; and just before noon, Dr. Gerald Marlin; then we will take a break for lunch. And then Strauman after lunch, which might be something like 1:00 o'clock; and then Innova Corporation about 1:20; and Dr. Jack Krauser at 1:40; and then Dr. Victor Sendax [ph] at 2:00 o'clock.

Any questions?

[No response.]

DR. GENCO: Okay, good.

Let us proceed now with the Friatec presentation. Mr. Knox is up first and he is going to introduce Dr. Vizethum and Dr. Tarnow.

Dr. Knox?

DR. KNOX: Based on the last panel meeting, I believe Dr. Patters and several other members asked several

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questions and asked that this meeting, that further information be presented on immediate placement of implants following extraction of teeth. And with that in mind, we have asked that Dr. Vizethum present today and also Dr. Tarnow.

Dr. Vizethum, if you recall from past panel meetings, is a dentist and he is a graduate of the University of Freiberg, in Germany. He is both a dentist and an engineer and is also the General Manager of Friatec Worldwide.

Dr. Vizethum also has the distinction of being one of the principal developers of the Friatec II Dental Important System. Following his presentation, we have asked Dr. Tarnow to present here today. Those of you who may be familiar with Dr. Tarnow, he is the Chairman of Implant Dentistry at New York University and he has extensive clinical and published experience with immediate placement of implants following extractions and we have asked him to come and present to the panel.

So, with that, Dr. Vizethum?

DR. VIZETHUM: Good morning, ladies and gentlemen.

I am glad to be able to, in front of this panel, to make a statement according to FDA's request for information on immediate implantation, in the letter

following the panel meeting from November 4, 1997.

Immediate implantation is a method which has been described as early as 1975 by Schulte. But in a definition given by the DeHurt in 1985 that there is an implantation before healing of bone defect after extraction and gingiva defect, post-extraction to six days. So, it is a matter of some history.

After extraction this is the situation we have to face in the bone and this is the situation which we end up in many patients after several year of dentalism. So, this is a situation which has been described by different authors, describing the bone results following extraction and bone healing by Atwood, Johnson, Atwood and Coy, [?], Olam Solar [?] and others.

So, the atrophy of the bone is inevitable: a consequence of the extraction and the loss of the root and the probably not optimum load by the superstructure, by any means.

Now, if we talk about safety and effectiveness, it has been recorded by Barzilay and Becker that there may be some evidence that there is a prevention of bone atrophy by early implantation. This has been also the concept of the so-called tubing implant published in 1976 with, as early as, immediately after extraction, replacement of the root.

This is a case which shows the same case 12 years after implantation and there is very clear visible where the implants are there is still bone. Where there are no implants there is no bone. So, the atrophy seems to be related to the loading of the bone by the implants directly.

Now, referring to the safety and effectiveness, we have first to consider what are the differences following the treatment schedule of the patient. So, if you start with a patient evaluation, patient treatment planning and pre-treatment, we see that there is no major difference between late implantation and immediate implantation.

Then we have to go with implant surgery and prosthetic treatment recall. Starting with the first step, the implant surgery phase, we can see that there is one step, the extraction which we do not have in late implantation. Then we have a formation of a mucoperiosteal flap, which is in both procedures, and then we have an excavation of the alveoli cavity, which is not visible in the late implantation, but in the immediate implantation. But from this on, all following the same procedure.

Now, to describe very short the procedure. The first step is the pre-drilling so that the determination of the position of the implant and preparing the implant cavity

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with an increasing diameter, following the shape of the implant with a desire to fill up the recipient gap, especially the crestal bone level.

Now, the prosthetic phase, again. If we have to look after the reentry operation we see with the impression no difference between late implantation and immediate implantation, with the lab procedure it is the same procedure, restoration is the same procedure, and the recall, as well.

So, if you overlook all the procedure to restore a patient there is only two phases where there is a difference between late implantation and immediate implantation.

So, even in the second step operation it is all the same procedure compared to immediate and late implantation.

Now, the procedure has been referenced many years ago. So, in the studies of Shulte et al, histological results were by a mechanical shaped, [?] maxilla implants have been reported. These implants have been designed especially for the immediate implantation. Animal testing has been performed to develop the procedure and it has been shown first-time for these implants to develop an osteon-integration even after immediate implantation cases as early as 1984.

In 1981, Barzilay and others documented a study of immediate implantation. They found that there is no measurable increase in [?] depths, gingiva inflammation in the same degree than on natural tooth.

And 58 percent of the implant's embedded links was in direct contact with bone. Another animal study with stereos implants showed from periodontal in '93 that bone contact in mandible was around 60 percent; bone contact in maxilla was around 46 percent. A study of 1,800 in 1993, found that there is an average bone contact around the implants of 50 percent. There are numerous more studies available.

If you go to clinical studies, there was just recently published paper of Schwartz et al which referenced more than 50 different papers of different quality from case reports to perfected studies. So, I just have to limit it to some of these studies. Crummet et al in 1991 has 11 patients against the control group of 35 patients; 41 is immediate implant, 154 is control group. The result was success rate of 92.7 percent; the control group showed a success rate of 98 percent.

Tallman et al, in a six-year follow-up study, has showed a survival rate of 99.3 percent in Branemark implants. [?] et al in 1991, reported about 290 implant

with 427 patient--sorry, 290 patients with 427 implants with a maximum observation period of 144 months. And he viewed a bone [?] per year in the first year of 0.6 millimeter and in the second to third year of 0.3 to 0.2 millimeter, in the fourth to seventh year of 0.05 millimeter.

Shulte, in 1993, presented a paper of 69 patients with the two implant system with a major observation period of 24 months. Gelb, early 1993, presented a paper of Branemark with 35 patients and 50 implants with a survival rate of 98 percent.

Wazek et al, reported in a retrospective study, a success rate of 97.7 percent for Einzep [ph] and Branemark implants with a mean observation period of 27 months, with a minimum of four months and a maximum of 83 months.

Rosenquist et al, in 1996, presented a paper where he described the results of 51 patients and 109 implants with Branemark implants with a mean observation period of 30 months, minimum one month, maximum 6 to 7 months, with a success rate of 92 percent and a survival rate of 93 percent.

And Archet, early 1997, presented a case report of four patients with five implants and he reported no complications during the procedures.

Gomez et al, presented in 1997, 86 implants,

really two implants with a minimum observation period of three months and a maximum of 60 months and the survival rate of these immediate implants he reported as 98.

He described that single tooth replacement was performed in 42 percent of all his cases. Of these, 22.4 percent were placed immediately following extraction.

The overall success rate was found to be 96, using Kaplan and Meyer statistical analysis.

With the risk evaluation, we have to start with the non-loaded situation. So, in the first and the second clinical procedure with implantation and the reentry operation, if we go through the clinical observations, then we have the inter-operative bone defect which may occur in late implantation due to the atrophy of the bone, but in immediate implantation it is a clear part of the procedure because we have to close the crestal gap which is there.

Then there is, in both cases, the situation that there may be a lack of primary stability. There may be an infection and there may be perforations of the gingiva.

If we continue with the loaded situation then we have a loosening of fastening screws, fracture of the abutment and crown, gingiva inflamed, implant mobile. So the same risks as we have in late implantation we can also envision in immediate implantation.

Now, regarding the risk management, we have to consider that the surgical challenge with immediate implantation is the obliteration of the recipient gap. So, with just using any implant, it has to be the goal to close this gap at the crestal part of the bone.

So, for these closures, there are different opportunities available today: selection of the root and implant diameter to fill up these crestal gaps, closure of mucoperiosteal flaps or support by membrane technique or augmentation techniques.

Gomez described in his article the anatomic situation created when some implant systems are delivered to the anterior maxilla as an immediate implant. Several diameters are needed to prevent a crestal gap.

The clinical observation with immediate implantation and intra-operative bone defects leads to the consequence that especially vertical defects along the interface have to be closed. But due to this situation with three wall defects, which we find around these implants, show a high regeneration probability which was described by Gelb in 1993 and by DeHurt in 1991.

As a matter of fact, this shows the equity of the root diameter and the implant diameter and you can see that it is possible to close, especially in this crestal area,

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the recipient gap very nicely.

So, risk management. And there was a nice article also presented by DeHurt in 1991, has also evidence of the fact that when he analyzed 1,054 patients, with 1,592 implants and when he analyzed those implants who failed, he found that in 66 percent of the failed implants, so the cases with implant failure, show the same volume of the outer [?] ridge as at the time of implantation.

So, referring to the question which was just opened by the former speaker, Ms. Langer, we can say that in 66 percent of the cases following that study there was no change in bone volume compared to the situation as the root has been lost at that time.

So, in the summary, the immediate implantation is based on the same principle as late implantation. It offers shorter treatment to the patient. It prevents bone atrophy. It is a potential use of longer or wider implants due to the lack of initial bone atrophy.

Animal and clinical studies show similar success compared to late implantation. Risk is similar as in late implantation and performed risk management is the same as after failure of a late implant.

Thank you very much for your attention.

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DR. GENCO: Thank you.u.

Are there any questions, comments?

[No response.]

DR. GENCO: If not, thank you very much.

We will go to the next presentation then.

Dr. Tarnow?

DR. TARNOW: Thank you.

My name is Dennis Tarnow. I have been paid today to come down by the Friatec group. I am also of interest that they asked me to discuss the clinical aspects of immediate socket placement. And it is kind of interesting that they asked me to do that because in lecturing I usually wind up discussing the pros and cons of this, and in many respects I talk about the delayed socket placement. Because you will see that histologically at the top of the implant is my biggest concern and that is what I want to discuss with you.

But I also want to show you that placing it immediately, apparently based on clinical data and most of it by case report, as you will see, as well as animal research, there does not at this point seem to be the risk that I was once concerned about, although I still have some concerns if you do not obliterate the socket or graft it. I

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think that will come out in a moment.

I also want to mention that although Friatec Industries is bringing me down here today, I had a personal conversation with two other presidents of major companies, Stereos and Three III before this presentation as of yesterday. And both of them also feel the same way as the Friatec group and I am sure that most of the implant companies, although I cannot speak for them and I am not trying to, would say that placing implants into immediate sockets is something that they feel the FDA should allow for the systems that are approved. They do not feel that that should be a limitation. As a clinician, I feel that we should have that option and you will see why in a moment.

I think that when it comes down to the bottom line, we have clinical data and histological data. As a clinician, myself, I always like to see something that works and is predictable. However, being trained by Sigman Stahl as a fine histopathologist, I am always thinking histologically and I want to know what is going to happen on a wound-healing basis.

So, if we take that scenario we have to look at whether or not the question that we have to ask, is there a critical width or distance between, or gap, between an implant surface and the bony wall beyond which the bone will

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not bridge?

For example, in this diagram as you see here, here there is a membrane placed over it, but if you look at this distance between the crest of the bone and the implant, is there a distance whereby this bone will not bridge this gap without fibrous tissue in between? And I think that is the bottom line in terms of the histological aspect.

Clinically, I want to emphasize this to the panel, clinically--and you will see this and I will even show you a human histological core before I finish this morning--that this bone down in this area here where you have direct contact is absolutely the same as in delayed placement to a completely healed socket. So, that is not of any concern whatsoever. And I think that should be as clear as day when we finish this discussion, if that was not before.

The question really is just whether or not you can obliterate the space with the use of wide body implants? As you saw by Dr. Vizethum, and well-known by other implant systems, you will see that you can obliterate the space in many cases. If you cannot at the top, in order to prevent fibrous tissue from going between the implant and the healing bone of the socket, you have to place a membrane.

Whether or not, if it is inside the bone like this, whether or not just to otogenous bone chips may work

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is still open to discussion and has not been shown in the literature.

However, what has been shown is that the use of a membrane by many different researchers--once a membrane is placed on top--this gap seems to be able to fill in with bone, with or without grafting material underneath it. And I think Waror Godfritz [ph] certainly showed that in the early '90s and there has been a series of papers to discuss it since.

Two papers stick out like sore thumbs when it comes to this gap distance. And that is the work of Carlson which was done on a Branemark type implant, a machine titanium implant. And they were looking at a space between the titanium implants and the bone cannot be predictably bridged by new bone if the space is greater than .35 millimeters.

And Knox, Caudill and Meffert, using HA-coated implants, found something very similar. Their's was between .3 and .8. And, so, when you get to one millimeter, the distance did not close unless you had a membrane there. And I think that is important and I think that is the critical gap distance that we have established by two different researchers, two different systems, but the gap distance is clearly there. And I think that is an important point.

Recently, Dr. Schwartz just published a paper in the Journal of Periodontology and she reviewed the literature from 1979 to 1996. It is an excellent review and I deliberately took this page so that you could not read it. I deliberately show you that to show you how incredible the number of research--this is animal as well as human reports. Now, some of the reports, the animal ones, are more standardized and general. Almost all of the human data is case reports.

So, I took out the human data so that you would not get bleary-eyed. I took out the human data longer than one year. And if you start to look at the number of implants, all different types of implants, different surfaces of implants, you start to look at anything from one-to-six year data and you start to realize that most of the data is up to six years, and there is actually quite a number of implants that have been placed in humans. Probably close to 600-some-odd, 648 implants if you want to look at the number exactly, seems to be about the number that has been out there and with an incredibly high success rate.

Now, this is a survival rate. This is not talking about bone loss or anything like that. But most of them are showing quite high levels of bone height radiographically

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but the survival rates, if you start looking at these numbers, this is the original Tubigen [ph] which has now been changed to the Frialit. But if you look at all the others, you will see that the high percentage of bone, I mean survival rate of these implants.

The only mistake on this was when I had this, this was Lange and not Branemark. I do not think that he--I am sorry for Klaus. I hope you extend my apologies to Klaus, those of you here from ITI. That was ITI. Klaus Lange at ITI. But look at the high percentage of success.

So, we know that this is at least comparable to delayed in most situations.

The Frialit work by Gomez was just reported. And what was interesting is that this is one of the few reports starting at least to look at one-to-five year data longitudinally. And what is of interest that they talk about immediate and delayed as well as very late, like nine month or greater. And that, I think, is one of the first studies that I have seen. If you look at just case reports, like the beautiful reports by David Gelb that is now updated up to almost, most of the cases that he showed in that original article, in 1993, are now over five years.

He still has over a 95 percent success rate. But he is grafting. He is doing all different types of things

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at the top. He's an excellent surgeon and we see enough of this now to realize that this is a process that can work. So, if you look at the Gomez article, he compared a few different things, not just immediate placement, all right?

He had immediate implants. The failure rate was 1.16. The delayed was, that was within up to nine months, of seven days to nine months was .6. And the late or the re-ossification cases, meaning greater than nine months, typical of a perfectly healed ridge, was 3 percent.

So, you can see at least in the smaller population, this number was quite high. And even using the Kaplan-Meier statistical analysis, which this group certainly is familiar with and I think that's a high standard to hold yourself to, is a 96 percent overall success rate.

Clinically, just to show you a few things of where we are with this, when you have a smaller type defect with taking a root out and placing an implant in, what you are looking at especially when all the walls are there, you can do almost anything with this and it seems to clinically work. Becker has certainly shown this. But we still like to put a membrane on.

For small defects you might even use a resorbable membrane. This is open to discussion. For bigger defects,

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as you will see, we go with a membrane that is non-resorbable and that has some shape to it.

You can see here we just placed a demineralized, freeze-dried bone. We placed a membrane, a resorbable membrane on top and placed it over it. I hiked up the flap to get closure as you see here. And this case was done about five years ago. This is the immediate post-op. You can see how innocuous this was. This is only 10 days later. And here you see the ridge healed at six months and you can see that we have a very nice ridge and here is the final crown. And this crown, by the way, this is a three-year post-op.

So, we have an excellent ability to take and do immediate sockets. It certainly is something that can be done and can be done quite effectively.

When we start dealing with bigger defects like this, we have to start being concerned about how long the membrane is in place. I think we have to realize that the membrane should be in place for a minimum of four to six months and this is not just filling a defect with some material and closing it. Ideally this should be closed with a membrane. This one does not seem to close readily based on so many research, Lecombe, Becker and so on, in animals. We know that this is something which has to have a membrane.

Now, you can use different grafting materials. We now have gone more to mineralized freeze-dried bone, but certainly people have had great success with demineralized freeze-dried, as well as synthetic bone grafts. I will show you just two cases. This one was with mineralized bone graft material. You can see the bone graft placed.

I then placed a titanium reinforced membrane over the top of this, as you see here, closed. And if you see the before and after at six months, you can see that this now becomes a rather predictable outcome when you start to see the before and you start to see the after with the use of membranes and bone grafts.

Another case, it looks identical but it is different. You can see the large defects. When we have large defects with no buckle plate at all, we graft, and this one I grafted with HTR. You can place different materials under here. The key is the membrane. Put the membrane over the top and ideally it is otogenous based on Buser's work. But we also see the same success if the membrane stays in and is covered properly for six months, we see success with all of these graft materials. Here you see the membrane, I am taking it out. And here you see this similar kind of before and after kind of effects.

And here you see the before and after from the

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occlusive surface, not just height, but we also have width of the buckle plate restored. And this is today. You have all seen material like this.

This is rather routine and I just want to emphasize to the group, to the panel, that this is something that we can expect today rather routinely. That if you obliterate the socket, number one, you get bone deposition just like any other implant.

If you have a space then you can graft it. If you have a wider implant, as most of the companies have today, you can obliterate the space. If you obliterate the space it becomes basically just like any other implant when the bone is contacted. Because if you think about it, you really have, if you have direct bone contact you can have, it is almost, it is guided bone regeneration.

Because what you have done is you have blocked--it is really by contact inhibition--you have basically, instead of putting a membrane on top, you have direct contact of an implant to a socket, as you see in this case, like right here, in these cases of lower anteriors, if you get an implant to block out the complete extraction socket you basically cannot have fibrous tissue and epithelium going down here by contact inhibition. The bone stops it from growing down between it. So, you do not get fibrous

encapsulation.

I will show you this case lastly. This was a case in France, by a good colleague of mine, Dr. Tadeo, in Grenoble and he was kind enough to share this with me. He had taken these hopeless teeth out. He placed three implants. He then was going to look at this implant histologically six months later. He placed these implants in as you see here. He hiked up the flap in this case.

We are going to look at this implant. It happened to be immediately loaded also but that is not part of our discussion. I just wanted you to look at the histology of the bone so that you know when you obliterate the socket at the bottom this is the kind of bone integration six months later. This is human histology. So, this is not an animal. This is human histology verifying that you can get clear ossea-integration with remodeling and the haversian systems as you see here so beautifully documented in this particular case report.

So, do we know that this works? Yes. The key is histologically dealing with the top space. If you can obliterate the space at the top, it is just like any other delayed socket type of healing. If you do have a space, certainly greater than a millimeter, the question is just a matter of choosing which bone graft and which membrane do

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you want to use. But it is safe, it seems to be effective. And the 95 to 97 percent of most case reports that have been documented seem to hold this up at least on the one-to-five year data.

Some of them are approaching five to seven years now, and showing a similar high success rate. So, I think we are fairly safe in dealing with this.

I want to thank you for giving me the opportunity to present this to you.

DR. GENCO: Thank you very much, Dr. Tarnow.

Are there any comments or questions from the panel?

[No response.]

DR. GENCO: Thank you, Dennis.

We will now proceed to the next presentation by the Reimplants USA.

Oh, I'm sorry. John, did you have a question?

DR. BRUNSKI: Yes. Just a short question if I could ask Dr. Tarnow?

I think the panel is going to be faced with thinking about different kinds of implants and different kinds of indications. Do you have any comments on the immediate placement and the role of different implant configurations and designs and materials? Is there any choices to be made

there?

DR. TARNOW: I am presently doing research with eight different implants. So, I am familiar with utilization of most of the main systems today. I will tell you that when used properly they are all, at this point with early data, working very similarly in terms of their, their high success rate. I think the standardization of technique today is so well done and the machining and the parts and the drilling that I think that this, in the hands of any fairly experienced clinician, with moderate experience even, can handle this quite effectively.

We are seeing that long-term I do not have that kind of data. As you see most of this is case reports. So, longitudinal data greater than five years on immediate sockets is rather limited. Lazara's [ph] article in 1989, putting an implant, in this case it was a Branemark implant, putting a Branemark implant with Gortex over the top and submerging it for two months and then taking the Gortex out or at least placing it and taking the Gortex out at two months was the first use of a membrane, at least, with immediate socket placement.

This is in today's modern dentistry. The point that I am making here is that most of the implants seem to be successful. Most of the clinicians who have been using

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different systems, let us say only one system for years, John, have been doing it successfully or else they would have stopped. They would have stopped clinically. I think the key is how well it is done and also choice of case.

I think if you have pus coming out of an infected tooth and there is drainage and huge infections coming out, most people would agree that that is not a good selection of a case. But when you just have a fractured tooth or a non-separative lesion, these kind of lesions or some regular periodontitis or periodontal disease where the tooth is coming out, rather chronic inflammation, that kind of thing, this can be debrided very effectively and utilized.

We have also done it with acute infections with pus even coming out and still had success in many of these cases if you do full debridement, irrigation. But I think that pushes the limit again and is of higher risk.

But at this point, we do not see a difference yet clinically. Long-term with the integration we might have to look at that but that is five and 10 years down the road. But certainly it all seems to be working quite effectively now.

DR. GENCO: Any further comments or questions?

[No response.]

DR. GENCO: Thank you, Dennis.

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Okay. Next is the Reimplants USA, Inc., Mr. Phil Watkins.

MR. WATKINS: My name is Phil Watkins. I am part owner of Reimplants USA, Incorporated. We are in the midst of our 510 application and primarily why I am talking to you today is to show you an overview of our system. It is fairly unique and does not really fit the classification of the other systems that you have been evaluating, and, so, we would like to be included in your consideration for classifications as class II.

Reimplant is also an immediate extraction site implant. However, unlike the Friatec system this implant is a cad-cam milled duplicate copy of an extracted tooth. Essentially the application for this implant would be a situation where you have endo failure, a cracked tooth, limited periodontal concerns, advanced decay, something where you would be extracting a tooth but you would still have a respectful amount of cortical bone remaining.

It requires an a-traumatic extraction of the root and you have to be very careful not to fracture the cortical plate, obviously to maintain as much of that as you possibly can.

The surgical procedure rarely requires a flap. Generally you are just extracting the tooth and debriding

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the socket and reimplanting the implant. You will notice the little notch on the buckle of the tooth, that is to prevent confusion when the implant is placed back into the socket.

In addition, we take a small round burr and create a series of dimples to mark level of the alveolar bone immediately after extraction, like so. Then the tooth is replaced in the socket and using one of a series of different diameter probes the dimension of the space that has been occupied previously by the periodontal ligament is measured.

The coronal portion of the tooth is cut off at a 90 degree angle to the root and the remaining root is sent to the manufacturer to be made into a titanium implant. The canal space is enlarged so that a mounting jig can be placed into the tooth. The remaining root then is painted with a reflective lacquer so that the laser can read the surface of the extracted root.

It is then mounted onto a milling machine and the laser is activated. It reads approximately 80 points per revolution, four revolutions per millimeter. The computer then creates a schematic and at that point you have the ability to go in and adjust the dimensions of the implant to compensate for the periodontal ligament space so that you

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can enlarge the coronal portion of it to create more of a tight fit with the alveolar bone.

At that point the information is inputted to the milling machine and the milling machine creates the appropriate dimension implant out of this grade II titanium.

So, here it is as it is finished from the milling machine. You can see the faceted surface to give you increased surface area for better bone apposition. The surface is also grit-blasted to make it even a greater surface area with 500 micron alunus [ph] oxide.

At that point, the portion that will be coronal to the alveolar crest is finished down. And a crown margin is fabricated on which the restoration will sit. The coronal part is protected while the implant is cleaned to make it ready to ship it. You can also, if you choose to at this time, make a custom healing abutment for this implant since it is a one-stage surgery. However, that is not really necessary. If there is no flap procedure involved and there is no subsequent soft tissue damage, the propellate [?] maintains very well during integration.

This handle is attached to the implant. The implant is thoroughly cleaned. It is packaged in an autoclave pack and delivered to the dentist for implantation. The turn-around time is generally 72 hours,

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however, if infection is present you can go up to two weeks prior to implantation.

At this point the dentist after he has sterilized the implant will thoroughly debride the socket. Using a titanium forceps, take the implant to the mouth, it is tapped into position for primary stabilization and then allowed to integrate for the same period as conventional implants, six months in the maxilla, three months in the mandible.

As one-step surgery it does not require a membrane ordinarily and you do not have to close the site. The abutment system is very simplified. It is a series of preable posts that the doctor can place and prepare as he would a normal tooth preparation. At which point he will impress it and send it to the laboratory.

And here is the restored restoration. It is simple to do roots that have curvature to them. It is fairly, by the way you align the milling machine, it is not a problem. You can also do multi-rooted teeth. You have to block out in between the roots and create a fin there so that the laser can read the entire surface and then come back later and fit the implant to a matrix to get it back to the proper proportion.

They also have a ball attachment that you can

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utilize in situations like silver, you want to do a partial denture, for example.

In summary, I would like to say that I think thoroughly primary advantages of this, obviously, is that it is an extremely conservative procedure. And the alveolus and the surrounding soft tissue for the most part is unmodified.

As I said before, it rarely requires a flap. Very simplified restorative procedure, ideal emergence profile. As far as potential downside for the patient if the implant should fail it is generally due to a fibrous encapsulation that leaves the socket pretty much as it was before. At that point another implant can be placed or you may go to a conventional implant if you choose.

I think it is a system that finally is designed to fit the bone morphology rather than trying to make the bone fit the implant.

DR. GENCO: Thank you very much, Mr. Watkins.

Any comments or questions from the panel?

Yes, Leslie?

DR. HEFFEZ: Can you tell me what long-term, how many years you have been doing this?

DR. TARNOW: Yes. The technology was developed in Germany. They do have a three-year, multi-clinical study

that is showing a success rate of approximately 96 percent.

DR. HEFFEZ: How many years would you say?

DR. TARNOW: Three.

DR. STEPHENS: What is the cost of these implants relative to most other implants?

DR. TARNOW: We feel it could be comparable to an existing implant system, possibly a little less expensive but not very much.

DR. GENCO: So, for the panel's consideration, you are making the point that this could be grouped within one of the root-form types that there is no need to consider it any different?

DR. TARNOW: Exactly. It is not a coated implant, it is a grit-blasted surface.

DR. GENCO: Further comments, questions?

[No response.]

DR. GENCO: Okay. Thank you very much.

DR. TARNOW: You are welcome.

DR. GENCO: We will now proceed to Sargon Enterprises. Dr. Sargon Lazarof will make the presentation.

DR. LAZAROF: Good morning, ladies and gentlemen. I thank you for this opportunity. My name is Sargon Lazarof. I am the President of Sargon Enterprises and the developer of the Sargon Immediate Load Implant. I am a

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professor, clinical professor at the University of Southern California.

Last meeting you received a presentation from Dr. Hassan Nazari [ph], which was basically presenting the clinical aspects and the research aspects of it. I felt like there were some questions that were not properly answered because he did not have as long, as much knowledge on this implant. Since I am the developer I have the longest term clinical experience with this implant. So, I would like to address some of those questions.

Initially when I came here I was hoping that I would make an argument to include this implant as a root-form implant but judging from all the sparks that were flying earlier I do not know if I want to be in that category.

Essentially this implant is made of titanium alloy. It is an expandable screw implant. And basically all it does is it expands to custom-fit the prepared site. It eliminates that space between the implant and bone at times zero. And our research has shown that by eliminating that space between the implant and bone you can not only immediately load this implant but have better success at it.

This is basically a picture of the implant. As you can see, it is a screw implant and the top portion is

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the abutment. The implant can be expanded and we feel like this is the ultimate root-form implant because in anterior region of the jawbone where bone is harder it does not have to expand as much, so it acts as a single-rooted tooth. As you move posteriorly, it expands and acts as a up to five-rooted tooth.

It makes it possible for us to now perform this kind of treatment. I have done over 2,000 implants of this kind. Presently there is 5,000 implants that we have tracking of. And 15,000 implants have been sold but we have 5,000 implants that we have tracked because basically whoever we train has a requirement that they have to submit 10 cases after the initial course to get certified.

There is a three-year research at the University of Southern California which basically the initial one was a pilot study and then the second one is a prospective study which includes microbiology, immunology, and histology.

What we can do with this implant basically after extraction you can see the top left, if there is a pointer. At the top left portion you can see the tooth is extracted, the implant is placed and it is immediately provisionless. So the patient walks out of the office in this condition in full function.

There is no special diets or requirements that we

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give to the patient. This is the before. This is five years. This is five year clinical.

Now, what is very exciting about this implant is if you notice the top portion of this implant, the bone loss. Now, we talked about success criteria. One of the major concerns that we have with all present implants is the initial cratering that occurs. And our research shows that the reason crater occurs is not bacteria or perio-implantitis, it's basically implant design.

Any time you take a cylinder and put it under lateral forces, the lateral forces are concentrated at the crest. That is why the minute an abutment goes on a regular screw cylinder implant you get that initial crater and that initial crater is about a couple of millimeters added to the tissue depth. It is a periodontal pocket which there is always bacteria in.

So, if you go looking for bacteria in that pocket you will find it but we feel like it is a mechanical reason that causes that.

And just by reversing the mechanics of this implant and making the implant wider at the apex the entire mechanics of the system are changed and the lateral forces are transferred apically. So, we routinely do not see any crestal changes.

In some cases the ridge is really thin. You might surgically burn out the buckle lingual blade. You might see initial crater that occurs but we do not see progressive bone loss which I think this is more exciting than the immediate loading factor of it.

This is a posterior region. As you can see the implant reacts basically to the quality of bone. So, as an instrument it will tell us what type of bone we are dealing with. Depending on the amount of expansion, the amount of turns that you internally turn to expand it or radiographically we can site-type bone to either I, II, III or IV and the implant communicates to us to whether load it or not.

So, clearly, type I, type II and type III bones we immediately load and type IV, when the implant is fully expanded, is telling us there is hollow bone here, do not load it, so, we do not.

Also, the reason we hear about 100 percent success rates with this implant from university is very simple. The reason implants do not integrate is that micro-mobility that initially occurs and that happens in the initial two to three weeks.

Just because the implant is buried for four to six months that is when we find out when we uncover it. But

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that problem occurs in the initial two to three weeks. Now, we have a protocol that we followed this implant with. The initial two to three weeks are a very strict protocol that the patient has to come back once a week for a check. If there is any micro-movement present in the implant, if you percuss the implant you will see some sensitivity. And all you have to do to save this implant is to expand it further and restart the whole process.

So, we can save an ailing implant. If you place these implants and you never looked at them again, you loaded them and you never saw the patient, you would have about 70, 80 percent success rate. But we can increase that success rate by following the criteria and the protocol and save all those implants that are not being integrated.

Also, we have areas of type III bone, where it is basically a borderline between III and IV. If this micro-mobility occurs a second time, basically the bone is telling us, I cannot handle this load. So, we unload it. We expand it further, establish contact with bone. We unload it and we wait. So, our worst scenario is waiting for an implant to integrate.

This is what is exciting. As you have all seen the minute the implant is loaded, you get bone loss to the first threat. Now, the industry has accepted that. And

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patients have been going around accepting that. But what is exciting here is after seven years of loading--this is five years but we have a seven-year follow-up on this--we see bone growth past the collar, past the abutment joint which should be impossible. We do not know the answers why. We are doing research to find out.

Most of the research that is aimed--there are six research centers right now doing research on this. In April in Monte Carlo there will be a big news release and all these research centers will be releasing their data. They are focused not to find out whether this implant works or not because it clearly has shown itself to work; they want to find out why it works so well, why is it that we are getting bone growth through the margin of the crown and not bone loss?

So, it is true that we do not have 20, 30 year's experience with this implant. But if we have an implant that is in place for seven years and after seven years shows more bone or the same amount of bone it started with, there is a pretty good chance that the implant is going to be around.

We are not introducing any new chemicals, new surfaces or anything. It is basically a mechanical design that enables us to establish immediate contact with bone and

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maintain it. And that, after all, that is the whole ballgame, trying to integrate. The definition of integration is contact of bone to metal and we establish it as time zero.

Histological studies at the University of Indiana, again, formally they will be released in April. They clearly show that this is an osteon-integrated implant and we get osteon-integration both inside and outside the blade, increasing the surface area of osteon-integration to double the size of the same size of screw.

So, we can easily load this implant, a 10-millimeter implant, in the molar region with a molar, with a full force of a molar and it handles it much better. Again, here, this shows osteon-integration both outside and inside of the blades.

So, in conclusion, if this is an osteon-integrated implant, with the same materials and no new chemicals, we feel like it should be categorized as a root form implant.

Any questions?

DR. GENCO: Are you finished

MR. WATKINS: Yes.

DR. GENCO: Thank you very much.

You make the point that this should not be special retention? Why not?

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MR. WATKINS: The way we categorize implants, if I may suggest, at the University we look at implants at three categories. One, osteon-integrated; two, bio-integrate; three, fiber-integrated.

And osteon-integrated are implants that establish bone to metal contact directly. Now, whether they are grit-blasted or rough-end it does not matter. The bio-integrated implants have an intermediate layer which could be a HA coating, and then we have the fiber-integrated implants which basically can function with fibrous attachment.

Obviously a blade implant would fall under that. And then if you take a blade implant and make it a two-stage then it would fall into a category of osteon-integrated implant.

So, this implant basically all it is, it is a root form implant. Although it looks a little different it is a root form implant and it is a screw type expandable screw with the same material and I feel like it should be in the same category as the root forms.

DR. GENCO: Willie?

DR. STEPHENS: Can you tell me again what the success profile of this implant is?

DR. LAZAROF: My success rate because I am the

developer and I have had all kinds of experiences with this thing is lower than the clinical studies that are being done which are three year long at the University. My success rate, because I have tried placing it in the sinus, I have tried loading it immediately in type IV bone and I have failed, my success rate is somewhere around 85 percent with 2,000 implants.

But after developing the protocol and seeing that type IV bone cannot be loaded and you have the three week protocol and presenting it as such to the University, they have had us do, as you have heard from Dr. Nazari, they have had 100 percent success rate. And I know it sounds too good, but since the implant gives you a second opportunity for osteon-integration, even in case of failure you can save it, clearly that can be achieved.

DR. STEPHENS: Have you had any failures of the implant, itself, fractures in the body or--

DR. LAZAROF: Yeah. The implant is designed to expand within the memory of the metal, okay? So, when you collapse it, it can be fully collapsed. We have had a couple of cases that the blades were fractured but these, in placement of the implant you cannot tap bone with it. So, the surgeon assumed that the placement of this is similar to a screw type implant and did not tap the bone. So, he used

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the implant as the tap, so, tried to turn it and distorted the blades. So, he had to reverse it and replace, you know, place a new one.

But in function, we have never had an implant fracture.

DR. GENCO: Are there situations where you cannot use the implant? For example, if you had type IV bone and you had full expansion and it still was not tight, what would you do?

DR. LAZAROF: Okay. We feel like in type IV bone when it is fully expanded even in that situation where it is delayed loading it is much better to have a five-rooted implant trying to osteon-integrate than a single rooted implant.

But in the worst case scenario, let us say, the osteon-integration did not occur. If there is no attachment, the implant is fully reversible. You collapse it and you pull it out and the healing is exactly like an extraction socket, extracting a tooth.

DR. GENCO: So, those situations, let us say, mandibular posterior region where you may have type IV bone, hollow, if you fully expand it and it still is not firm, you would take it out and--

DR. LAZAROF: Oh, definitely. But we hardly--

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DR. GENCO: So you would not use it in that situation?

DR. LAZAROF: No. But we hardly have cases like that because this implant can double in its diameter. So, 3.8 millimeter implant and once expanded it goes to 6.8. So, it does anchor.

In the previous scenario you had the screw that you were looking for some opposite side cortical bone to anchor it to, and basically even if you got osteon-integration, was basically on top and bottom of the implant, and after loading it you found out that it came out.

But this implant, by compacting the surrounding bone--now, we have plenty of data that shows--this is not pressure this is compaction of the surrounding bone just like in osteon-tone, [?], compaction of surrounding bone causes direct osteoblastic activity. And if you can see there is one other case that I showed. Routinely we see increased density around the implant after loading.

Now, we have--and the University of Renn [?] is definitely doing studies to find out what causes this increased density but we do see it clinically and they are going to show [?] slides showing it in April, why this occurs.

DR. GENCO: You have a narrow space, let us say, a maxillary lateral incisor. Is there any risk or have you had this happen where you actually would impose upon the adjacent tooth's ligament, the perineal ligament?

DR. LAZAROF: The implant never goes where the previous tooth was. If you see the anatomy of anterior teeth, the apex of the anterior teeth are always very close to the buckle plate. And if you followed up with the root preparation, [?], we always take a palatal angulation to these. So, we just move them two or three millimeters and take a palatal direction so the implant is always apical and palatal to the adjacent teeth.

So, even radiographically it might look like it is overlapping, it can never do that because it is weighted cup palatal.

DR. GENCO: Diane?

DR. REKO: Have you ever had a situation where you have expanded your implant and you have gotten osteon-integration around one of the wings that or the extensions that you have but not the others and subsequently had to remove the implant? I mean I can imagine.

DR. LAZAROF: Yes. If that happened, I would not be able to tell if it was osteon-integration around one blade or not. This could basically fall into a category of

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non-osteon-integration. If the osteon-integration was around one blade, obviously it would not handle the occlusal loads.

DR. REKO: But then you could not collapse it either to extract it either, could you?

DR. LAZAROF: Yeah. If there is no osteon-integration, you could collapse it.

DR. REKO: Right.

DR. LAZAROF: But if it is osteon-integrated the worst scenario is that in soft bone where the implant is wide expanded, let us say it is osteon-integrated and it is expanded and you want to remove it for some reason, which I have never had to, but if you wanted to remove it the defect from coring this out is a 7-millimeter defect, which is much smaller than the extraction of a molar bicuspid.

DR. REKO: But in the anterior portion 7 millimeters would be rather remarkable.

DR. LAZAROF: In the anterior region hardly ever you need that expansion because you can see it hardly expands because you have real dense bone.

DR. GENCO: Leslie?

DR. HEFFEZ: Just to follow-up on Dr. Reko's statement. Is it possible--you are assuming uniform expansion of that screw. If you achieve, if the expansion

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reaches a certain part of the bone which is already fairly compacted, that part of the screw will not permit the other portion to expand?

DR. LAZAROF: Correct. Correct.

DR. HEFFEZ: Just to finish the point completely, so, really what you end up doing is expanding the screw to where one surface of the implant is touching bone that no longer permits it to expand it any further?

DR. LAZAROF: Correct.

DR. HEFFEZ: It does not infer that the other surface is closer to the apposition.

DR. LAZAROF: Yeah. What happens in situations like that if one blade limits the entire implant expansion, the following week you find out that there is slight resorption and the following week you can expand the entire implant. Because that small contact on the implant was not enough to support the occlusal load. So, you will find that you can expand it further. That small load becomes like an orthodontic pressure and resorbs that area and then you can later expand it fully.

So, it has to have a full equilibrium in all surrounding implant for this to work.

DR. GENCO: Diane?

DR. REKO: Is it possible then that you could

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perforate the bone slowly?

DR. LAZAROF: Okay. Perforation of bone, if it is drilled, okay, if it is--

DR. REKO: No, no, not with the drilling. But as you are expanding your wings if you get some local resorption because of the pressure and then you do not think that you have it in solid enough and you expand it again, is it possible that you could come--

DR. LAZAROF: Not through the cortical bone. That would happen--like the instructions that we have it is full of very high pressure. It is not light pressure. So, if you are really close to the outside surface of the bone, possibly. But really to perf out through the cortical plate, that would be really difficult.

DR. REKO: No. I do not mean immediately with the pressure that you are doing it but--

DR. LAZAROF: Essentially? You know--

DR. REKO: --slowly because of the osteoblastic activity like in orthodontic appliances.

DR. LAZAROF: If you were to put light pressure at all times you would be able to do that. But the instructions are to go ahead and compact. The situation that the gentleman described as a hypothetical situation which basically I have not seen but the instructions are you

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go and compact one just like an osteon [?] would. So, there is a real compaction of the bone.

DR. GENCO: Further comments, questions?

[No response.]

DR. STEPHENS: One last question. How much of the threaded part of this implant is vented? How far does the splits, the wings, do they--

DR. LAZAROF: It is close to 50, half of the implant.

DR. GENCO: Okay. Further comments, questions?

[No response.]

DR. GENCO: Okay. Thank you very much.

DR. LAZAROF: Thank you.

DR. GENCO: We will now go to the Tronics Oral, Incorporated. And Dr. Raymond Schneider is going to make the presentation.

DR. SCHNEIDER: I will be working in combination with Barbara Ingalls. I am Dr. Raymond Schneider from Green Bay, Wisconsin, home of the Superbowl Champions again, hopefully.

What I am here to talk about is really that we, that the Board does not move implants, one-stage implants into, they maintain in a group, in group II. And I point out as an interest I am really not funded by Oral Tronics.

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It is Tronics Oral. It could be their future marketing in the United States will be to bring in an implant called the bi-cortical screw. It is a one-stage screw.

And I want to point out that it is site specific and that there is a risk in making limitations to the public for the public interest to, as a whole, not to restrict one-stage implants that would be under three millimeter, when they are under three millimeters if they would be considered class III.

Barbara?

MS. INGALLS: When you are reconsidering reclassifying to class II device, we are asking you not to make a restriction on the size of the one stage screw implant. The one-stage screw implant preceded the root form. Its design and protocol is most effective in the partially edentulous anterior arch and anterior fresh extraction site. The progress of dental health service to the public may be set back.

Our basic treatment options will be limited and doctors and the dental profession may not move forward in developing treatment for the partially edentulous patients and those needing transitional implant care. This will necessitate more grafting and enlarging surgical sites which will be detrimental to patients.

Doctor?

DR. SCHNEIDER: We are really talking about minimum treatment for maximum benefit and in that way the safety for the general public. I want to point out our basic tools that we know as a two-stage--

DR. GENCO: Excuse me, you have to be at the microphone.

DR. SCHNEIDER: I am pointing out here that we have basically two-stage implants and one-stage implants. And I am also pointing out there that we have a situation where we have a partially edentulous mouth and not a fully edentulous mouth. And what I am again looking at the design.

It is definitely in the design. It is not just surfaces we have been talking about much, it is also the length and the diameter of the implant in which I am referring to. There is a site-specific area and I would say we are not only talking about fresh extraction sites, we are talking about anterior versus posterior implants. Most of the implants that I saw today were put in the posterior unless they happened to be in a atrophic mandible.

There is a missing area, a missing link in the United States' treatment and that is that we are not designing implants that are narrow enough to treat the

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anterior portion of the mouth in a partially edentulous situation.

Barbara?

MS. INGALLS: The bi-cortical screw implant is a unibody, one-stage, non-coated, pure titanium, self-tapping dental implant. It is designed with apical load-bearing support in basal bone. Occlusal forces through the implant are directed to cortical anterior, inferior border of the mandible and the superior, cortical borders of the maxilla.

Therefore, it is a site-specific implant where length and bi-cortical support can be achieved in the anterior region.

The uni-body design is a one-stage surgery and a one-piece ready for prosthetic placement. This allows no micro-gaps for microbial contamination, no loosening of screws, smaller crestal width protecting bone in narrow proximal areas.

Site-specific indications for forces and anatomy of anterior narrow edentulous sites where cortical, apical or basal bone can be reached with long, narrow osteotomies and not endanger nerves or sinuses.

It was developed for edentulous ridges and fresh extraction sites of narrow anterior, single-rooted teeth. The osteotomy, fixation and load-bearing surface occurs

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below the apex, so leaving the delicate crestal bone and blood supply minimally traumatized.

Bi-cortical support is deemed gained below the crest. Success is not dependent upon grafting or primary closure. Only that the transfer of the post-operative load can be controlled through splitting on functioning natural teeth. This will permit healing of sockets with neighboring bone or teeth in the narrow anterior regions.

The problem is anterior and posterior teeth and bone anatomy differ. Posterior teeth are wider, mesial and distally. Anteriors are 5 millimeter average. Posteriors average 8.5 millimeters. This dimension critically decreases for anteriors lingually and apically but basically there is no change for the linear plane of posteriors.

This is not critical for over-dentures or multiple edentulous sites when teeth are not replaced one for one, however, in single tooth replacement, it is critical.

Doctor?

DR. SCHNEIDER: What we are seeing here is that the anterior portion of the mouth, as we know, is on a curve. Therefore, you have the anterior portion, there is greater width than there is on the lingual portion. Dr. Medford points out that when we place an implant in this area that we need approximately two millimeters on either

side so that we do not jeopardize the adjacent teeth.

This is not a consideration when you have an edentulous mandible maxilla because we are not confined to the restrictions that are opposed by teeth on either side.

When we are looking at this situation it is different. On the lower mandible, which Dr. Medford points out in the recent Journal of the American Dental Association, that he was pointing out in the article, "Single Tooth Implants," that rarely are implants placed in the lower mandible. The interesting thing is most implants are placed in the lower mandible but not in a partially edentulous situation.

The reason, he points out in this article, is because there is not adequate mesial and distal link that you are damaging the adjacent teeth. In a situation where you have a two-stage and a need for a two-stage implant, that in its design is required to have a wider diameter to encompass the component parts that rise above that point.

And in this design by having a uni-bodied design we are able to maintain strength and restrict that distance in not damaging adjacent teeth.

Other implants we are seeing as in Europe and this is where much of my training along with the International Congress of Implantology has come from, from Dr. Hans

Graffman in Bremen, Germany, where this implant has been and is designed. And its intention is to solve this particular problem of anterior extraction sites or anterior areas where we have narrow mesial distal component.

The difference in an anterior is that we have less force, we have longer bone, and basically narrow situations. So, the restriction on being narrower would restrict our possibilities of improving the industry of implant dentistry as it relates to single-tooth replacement.

MS. INGALLS: In the NIH of 1988, the National Institute of Health, consensus was the fewer teeth that are missing the more likely that an implant placement or failure could risk adjacent teeth due to the trauma to supporting tissues. The more teeth that are present in the arch the more the loads can be transferred to the natural teeth before and after treatment. This allows the design of the implant to be modified to protect adjacent teeth which is a different design than a root form or a plate form for edentulous arches.

Anterior single-tooth implant requirements are different than posterior. They are narrower and have more apical bone. The American public has shifted their attitude from implants replacing dreaded dentures to the attitude that implants are to be used to replace any missing tooth.

The public understanding and trust is this: If I lose a single tooth I can replace it with an implant. The teeth that are most important to them is, as they see it, their front teeth but the blade and the root form are not suitable for this area as they risk damaging the adjacent teeth.

DR. SCHNEIDER: Root forms basically and their smallest diameter now is near 3 millimeters. Where here the bi-cortical screw we are really looking at the trans-mucosal extension of a one-stage implant which would be, excuse me, which would be 2.25. But the strength of that we find there is clinically in my own experience of over 300 implants placed, that we do not have a fracture problem. We find that as the first, you know, the first interest, is it strong enough?

And the next issue is what is safe and effective? One of the things that we find safe and effective for a patient is when you are looking at a partially edentulous patient, for instance, a child, if we can eliminate in a congenitally missing tooth, if we can place an implant that does not have removable components to it, we reducing, which we now is the greatest problem is loosening of screws and parts.

I mean certainly a bridge, I think today there is

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very few implants on the market that I would recommend for my child that would be a two-piece because of their clinical complications with maintenance in the long-term. If we can eliminate those component parts then we can eliminate and make the implant safer and more effective. It is not always possible, of course, to remove those and in my clinical experience is that we do have certainly need for two-stage that is not my point. My point is that in a one-stage implant we can have a narrow transition and that we can maintain strength and safety and more effective implant.

At this time I did present to the panel some X-rays from a patient and I said this is typical. It was replacement of a single lower anterior tooth and at another time I will present all our statistics but at this time I wanted to ask the panel to not make a decision, that my thought was and I had heard that you would make implants that are under the three point diameter, the 3.3 millimeter diameter, that you would put that in a category of class III and I am asking that you not do that. That they maintain in a class II because of their safety and effectiveness.

Any questions from the panel?

DR. GENCO: We will go to Mark and then Willie.

DR. PATTERS: Dr. Tarnow was very concerned about the interrelationship between the implant and the coronal

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aspect of the socket in a one-stage direct implant into an extraction socket. You seem to have no concern whatsoever. What is the difference?

DR. SCHNEIDER: Okay. There, I am concerned about that area and what I am concerned about is I would want an area that I can treat just like a natural tooth. It cannot last forever. And the point I am trying to make is if we have to go and retreat that area I want an area that can be closed, it is this uni-body closed component in the trans-mucosal area. This implant gives me that and we find that really primary healing shown in other implant systems that if we can have a non-submerged implant the first healing around that collar is our best.

So, if we can achieve, when it is possible to achieve one-stage healing that is our best tissue component. Is that what you are referring to?

DR. PATTERS: Well, you have a 2.25 millimeter diameter implant going into a 5 millimeter diameter hole.

DR. SCHNEIDER: Yes.

DR. PATTERS: Therefore, you have minimally a millimeter all the way around the implant between the bone at the coronal aspect of the socket and the implant.

DR. SCHNEIDER: Yes.

DR. PATTERS: Dr. Tarnow thought that was of very

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serious concern and he was placing bone grafts and using membranes in order to get bone fill in that anything greater than one millimeter.

DR. SCHNEIDER: Yes. Well, our finding is that as long as it is disturbed, when you remove the inflammatory process in a single tooth, you are removing the inflammation that is caused by the bacteria, caused by the lack of--I am talking about we removed a tooth, put a fresh implant in that as you have seen in the panel, we have stopped that movement and the inflammation at the crestal bone. And without any grafting, without any additional procedures, that that crestal bone continually heals, that that defect is corrected because of you now no longer have that mobility component there that was in the natural tooth.

Does that answer your question? We do not have to graft and I am not saying that grafting is not necessary but in a situation where it was caused from the original defect, we removed the cause which was the ailing tooth and we replace it with an implant that we find that the bone regenerates to the height that is mesial and distal to the greatest height. It will resume its natural alveolar height.

DR. PATTERS: And it will bridge an area greater than a millimeter in your opinion?

DR. SCHNEIDER: Oh, it does, clinically there is evidence that it does. And it does in nature, too, if we would extract a tooth and leave it alone it would rise up to a certain level. Because it is scaffolded by the remaining bone on either side. So, on osteon-ostomy is now above the crest, it is all down below the crest and we allow it to heal up to the point of the undisturbed bone.

DR. PATTERS: Thank you.

DR. GENCO: Willie?

DR. STEPHENS: Yes. Can you tell me just three things. How long are the implants, one? Do they always go to the inferior border? And the third is, are you recommending that these implants be used in children?

DR. SCHNEIDER: Number one, do they always go. What you want to have is bi-cortical support. One of the principles of implant dentistry, not just compared, its trade name is bi-cortical. So, we are getting cortical support. And the reason for cortical support is because we want to anchor the apex because once again as one of the speakers noted that we are finding out if we have apical support, we have less crestal movement and, therefore, we are not losing that bone.

And because at the apex we have greater cortical bone. As Branemark pointed out that the quality of the bone

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was one of the main reasons his implants failed. Well, we are seeking out the highest quality of bone in that area.

So, to answer your point, what we want to do is go to the, we want to engage cortical plate. Sometimes, most often when you have a fully edentulous mandible you will see on radiograph that you are hitting the inferior border. When you have natural teeth you also hit the inferior but it would be more lingual too. So, on radiograph it does not appear like you are hitting the bottom but the protocol for osteon-ostomy is very narrow implants use very narrow drills. What happens we do not generate very much heat because of the smallness and we are bisecting the medullary plate. So, point is, yes, we intentionally in the protocol tap and sound the cortical plate on the other side to engage as best as possible bi-cortical support. That is why they are site-specific, they are meant for anterior to the sinus and anterior to the mentoferina [?].

DR. STEPHENS: On the mandible, how long are these implants?

DR. SCHNEIDER: That is a good question. They are 30 millimeters, the implants that are sold are 26 millimeters and 30 millimeters.

DR. STEPHENS: And you are recommending them for children?

DR. SCHNEIDER: Oh, when you say, child, I was talking about it cannot be a mixed intition [?]. Are we recommending them for children that have a fully developed intition? Yes. As is so is the National Institute of Health in that particular, where our guidelines are in the same instance. So, you have to define what the age of a child would be.

DR. GENCO: Further comments, questions?

[No response.]

DR. GENCO: Okay, thank you very much, Dr. Schneider.

DR. SCHNEIDER: Thank you.

DR. GENCO: We have next Dr. Gerald Marlin, who will make a presentation.

DR. MARLIN: I am Gerald Marlin. I am a practicing prosthodontist here in Washington and the President of Universal Implants Systems.

And as in the last panel meeting, I will be presenting as a manufacturer as well as a clinician. Universal produces a vediohex [?] implant restoration system which is an abutment that is designed to be used on a variety of different types of implants.

I appreciate the opportunity to present and address the issue of what constitutes appropriate regulation

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of abutments. I will present to you our clinical experience with abutments as they relate to their safety and effectiveness.

I will then address specifically question number three raised by the panel at the last meeting and will be amplifying on the remarks that I made at my presentation at the November panel meeting.

First, let me say that from the standpoint of a clinician I find that all of these implants work and they work very effectively, the coated and the uncoated. As we will discuss during this presentation, the problems are not of a manufacturing basis but they really are of a clinical nature.

We are comfortable with implants in 1998 and 1997 and before to such an extent that I had this patient here who was going abroad for three years and had a major concern that she was going to lose enough bone here during this period of time that she would be left without adequate bone to place implants, which would present a problem.

And, in fact, that the amount of bone that was being lost incrementally was gradually increasing. She was a patient of mine since 1976 and so, therefore, I had a very strong reason to believe that this would occur. And, in fact, you are looking at the panoramic film of the implants

having been placed and this is three years post-op. And you are looking at the fact that, in fact, that is what happened. Around the natural teeth she lost an extensive amount of bone, around the implants, the implants, in fact, maintained the integrity of bone as fully loaded with their abutments.

We tested the device by placing an implant at 30 degree angle and placing a 30 degree with a universal adapter for this particular implant connected to it. It is machine titanium alloy. And upon this, placed a custom cast post that was fabricated at a 30 degree angle correction, thereby, bringing it back to zero. And placing it within the Instra machine and cycling it through each specimen 5 million cycles apiece for a grand total of 20 million cycles.

What we are looking at here is that in spite of the 20 million cycles or the 5 million per, not one post bent or broke and not even one screw came loose. And this procedure was done many years ago before there were torque drivers.

What we're showing here is why abutments, not implants, are effective. And what we're talking about here is that this is not a mechanical problem. Problems that occur are really more of a clinical nature. These problems

of a clinical nature, with few exceptions, are the reasons that cause implants to fail, whether it's at the surgery or it's at the restoration. There are an awful lot of factors that are involved here, from case planning to the correct seating of an underlying abutment, to the method of temporization, how you go about it, the impression, how accurate it is, the occlusions, the angle corrections, emergence profile, the seating of the overcasting. There are a lot of responsibilities here for the clinicians to make it work. So we're talking about a lot of factors here that are, in fact, clinical that affect the prognosis and the safety and effectiveness.

In fact, when we look at a clinical X-ray and we look at the fact that this abutment is not seated, this abutment is not seated because there's any error in the machining of the abutment or the abutment/implant interface, it is a clinical problem. It is actually a manifestation of how good the osseointegration is because the bone fits so well that it started to go over the implant. And once the bone was contoured, now the abutment is now seated firmly in the patient.

What this slide shows is probably in one composite all the non-natural abutments that you can put in the human mouth. We're talking about an implant abutment. We're

talking about a custom cast post that is going into a natural root. And we're talking about a stainless steel endodontic post that is going into an endodontically treated tooth also.

Now, I will say from the standpoint of a clinician that I have far more comfort with an abutment sitting over this titanium root than I do with this gold post sitting in this natural root, which was obviously placed a while ago, and this stainless steel post that was placed in this root, again, obviously placed a long time ago. The reason why we know is because nobody is using silver points.

The problem that I'm having here is how do we classify abutments. Here we have a Class I device, this custom gold post and this stainless steel post, and yet I as a clinician have a much higher success rate with the implant abutment than I do with the gold abutment or the composite abutment.

As an example, just yesterday, from an anecdotal standpoint, I had a new patient in. We're in the middle of therapy, and, lo and behold, the custom gold post came out. Now in that particular instance, it wasn't the end of the world. All we did was re-cement the post. However, three months ago, I had a patient come in with a custom gold post in their endodontically treated tooth, and the tooth split.

And the patient had to have the tooth extracted and is going through six months' worth of orthodontics in order to either close the space or, alternatively, make a bridge because there was no room even for an implant because of the way the bone was fractured. Yet if it were an implant where the abutment fractured, then, in fact, we would be dealing with just replacement of the abutment.

So now from a personal perspective as a clinician, I would have to say that probably per year I have seen posts come out or roots fracture in maybe five different teeth over a ten-year span, and I've probably seen 50 of them. And yet since 1987 to 1997, I have only had to refix three implant abutments, and this is out of 720 implants. And yet those three abutments were actually manufactured before 1987 and placed before 1987, so I'm not even sure about the statistical analysis. Since 1987 to now, any abutment that we have placed has not had to be redone. But yet out of, say, 500 endodontically treated teeth, we've seen a higher number of replacement.

The service to the patient can be great, obviously. Before we had the osseointegrated implant, this patient, perhaps because there is a very long span here, would not have been amenable from here to here to something of a fixed nature. So we know that the integrated implant

is something that is quite beneficial to the patients.

If we could put the lights up, and we'll put the overhead on.

Turn the lights off. I'm sorry. Next?

Let's address Question 3 as posed by the panel, but somewhat modified on this handout. Number 1, should abutments be classified separately from the implant fixture? And what is needed to provide reasonable assurance of safety and effectiveness for abutments that are sold separately?

Next?

Should abutments be classified separately? Let's take the first part of that issue. The answer is an unqualified yes. And why do I say that? The long history of safe and effective use of abutments provides the strongest argument for their separate classification from the fixture. The abutment, even into the post and core abutment, but certainly for the implant abutment itself, there is a long history of safety and effectiveness, and we'll go into that.

As you saw at the slide presentation just now, the abutment is a stand-alone device. It's very comparable to an endodontically treated tooth with a post and core. And a separate classification of abutments still allows the FDA to provide the appropriate degree of regulation.

Next?

Should abutments be classified separately?

Presently abutments are regulated as accessories to implants. We all know that. That's why we're raising this issue. And unless the abutment is classified separately, that same abutment that is placed on a Class II implant would have radically different testing and regulatory requirements than if it were placed on a Class III implant. And keeping it as an accessory to a Class III implant would impose unnecessary and enormous financial burdens on small manufacturers, in addition to raise costs across the board.

Those who argue against a separate classification for abutments do so out of commercial interest rather than out of a concern for safety and effectiveness. Industry and clinical experience lends support to this statement.

Next?

Between 1987 and 1997, over 3 million implants have been placed and restored with abutments with success rates that we've heard all morning long between 90 and 95 percent in the hands of everyday clinicians. Now, we've even heard numbers higher than 90 to 95 percent, so being conservative, we're talking about that rate.

Abutment results have shown minimal clinical problems caused by design and manufacture. In our

experience, this is confirmed with what our experience is.

The MDRs show that most problems are due to clinical error, not mechanical design. And the materials in abutments that have been used safely and effectively over the last 14 years, we all know what they are. We all know what's acceptable.

Rigorous bench testing, which I showed you in the original slide, which we all know applies stresses that are much greater than those generated in the clinical environment. That alone determines whether an abutment has sufficient strength.

Even though abutment failures are rare, patient safety is not compromised because the repair of an abutment failure is not difficult. The repair is simply either replacement, screw tightening, or prosthesis rework, with, again, no damage to the underlying implant fixtures. Safe and effective for the patient.

This operator has not ever lost an implant due to a defective abutment, and this is out of 720 implants that I have restored. There are precedents for reclassifying accessories by the FDA.

Finally, as demonstrated in the slide presentation, abutments and implants in endodontically treated teeth are very comparable. They both support a

crown or other prosthesis. They both have a long history of safe and effective use. And they both are stand-alone devices from a clinical standpoint.

Now, let's examine this particular question because I'm quite troubled by the wording of the question. It says: What is needed to provide reasonable assurance of safety and effectiveness for abutments that are sold separately? I have a problem with that because we have the same product here. Regardless of who's fabricating the abutment, we have an abutment, and all abutments are the same product as far as safety and effectiveness. Why would we require a more rigorous testing process for one, especially given the safety and effectiveness that we know exists? And this discriminates against the small companies, giving advantage to the large ones, without any benefit whatsoever to the public.

In addition, manufacturers already use rigorous bench testing, accepted materials in fabricating their abutments. And as I have shown in the slide presentation, abutments are stand-alone devices like the post and core. They both support a crown or a prosthesis, and the post and core, as we know, are Class I devices.

What is needed to provide reasonable assurance of safety and effectiveness for abutments that are sold

separately? Coming back to this question and the question of specific controls, which is not on this slide but which was registered in the handout. What specific controls could we add that would be beneficial for implants as well as abutments? Perhaps independent standards organizations would be helpful in developing the appropriate testing criteria.

But more important--and probably this is the biggest key right here--is the allocation of resources for effective education programs, technique manuals, and teaching aids for instruction in the proper restoration techniques for implants. This is very important. This is probably more important than any other factor because of all the factors that I mentioned that are clinical factors that affect implants and abutments versus the machining of abutments.

Next?

We're at a crossroads here. We have an opportunity to protect public safety while at the same time minimizing excessive regulation that will absolutely stifle innovation and pull valuable resources away from educating the clinicians. There is really a lack of need for special controls except in the education area, where we are teaching the restorative dentist to do the job better.

The implant abutments themselves should be classified separately from implant fixtures. They are definitely stand-alone devices. And all implant abutments should be treated equally by whatever standard is applied, whether they are manufactured by Universal or they're manufactured by a manufacturer who's manufacturing an implant also. The standards are there, the specifications are there, in the plans and the drawings and the materials we use, and certainly the safety and effectiveness is there all across the board for abutments. So my conclusion is implant abutments should be classified as Class I or Class II devices due to their clearly demonstrated safety and effectiveness over a long period of time.

Thank you.

DR. GENCO: Thank you very much.

Comments, questions from the panel? Diane?

DR. REKOW: I'm not sure that I follow your logic that a small manufacturer of universal abutments is going to do a better job in educating the clinicians than the manufacturer of the implant who provides their own abutments.

DR. MARLIN: I didn't say that.

DR. REKOW: Okay. I'm sorry.

DR. MARLIN: I'm sorry if you misunderstood me.

What I was saying is that across the board, education is critical. And if you were to pull resources away to be put into testing that is like over-regulation, then how do we teach them?

DR. REKOW: I see. Can I ask one other question? If one company is making the abutment--I guess maybe I need to understand what you count as the abutment. Who owns the attachment and who worries about the mismatch, if any, between the materials types and any potential corrosion kinds of problems you could potentially have by mismatched materials in the oral environment? Whose problem is that?

DR. MARLIN: Okay. In the first place, the question of the mismatched materials I would say would definitely an abutment manufacturer's responsibility. I would take responsibility for that. I have restored both types of implants--I mean, implants both ways. I have used gold posts--out of the 720 implants, I can't give you an exact number, but about 350 were restored with gold posts directly to the implant, and I can tell you that the "galvanic reaction" that we hear about is so minimal that I have seen clinically that I'm not even sure that's as much of a factor--I'm not taking anything away from the couple of articles that were written about that, but does that determine that?

Now, I'm not personally threatened by that because we make machine titanium alloy connected to the implant with the gold post on it, and there's absolutely no way you get a galvanic reaction that far down. So I don't feel threatened by that. But what I will say to you, How do I know this? Because if you have a galvanic reaction between implant and abutment, gold abutment, you get this tarnished abutment. And I almost never saw it. And I have these patients going back to 1985, and so I don't see it as a factor.

But coming back to your question, yes, it is an abutment manufacturer's responsibility. A, as an example, I would not use a 2 percent gold, high palladium content metal, and we tell anybody who's using it, even though we have a buffer of a titanium alloy connector, not to use that kind of a product. So I believe it's the abutment manufacturer's responsibility.

DR. REKOW: And who owns the screws?

DR. MARLIN: I'm sorry.

DR. REKOW: And who owns the screws or whatever other attachment devices you might have for an abutment? Is that part of the abutment or is that--

DR. MARLIN: Oh, the screws and everything that connect--the implant itself is strictly a fixture with an internal thread. From that standpoint, it's a done deal.

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It's a titanium root. Everything else is abutment.

DR. REKOW: Thank you.

DR. GENCO: Further comments, questions?

[No response.]

DR. GENCO: Okay. Thank you very much, Dr.

Marlin.

DR. MARLIN: Thank you.

DR. GENCO: Okay. We'll break now for lunch, and we'll come back at 1 o'clock. I'd ask David Cochran to have had his lunch and be prepared to present at 1 o'clock.

[Whereupon, at 12:22 p.m., the meeting was recessed, to reconvene at 1:00 p.m.]

AFTERNOON SESSION

[1:00 p.m.]

DR. GENCO: Are the people from Strauman USA ready? If so, I'd like to introduce Dr. David Cochran, University of Texas Health Science Center at San Antonio, who represents Strauman USA.

DR. COCHRAN: Thank you, Dr. Genco, and the panel. I appreciate the opportunity to be here with you again today.

As Bob mentioned, I'm professor and chair of the Department of Periodontics in San Antonio, and my expenses have been paid here by the Strauman Company to represent them today, and I'll be the only speaker from this company. I do research and teach and do some consulting work for the Strauman Company, as my disclosure.

I spoke in the November 4th panel meeting, and subsequent to that meeting, the Strauman Company received a letter, as did the other companies, requesting some additional information, and I would like to provide that for you today. The topics that I want to discuss are what was outlined in that letter, and the first one dealt with the safety and effectiveness of the ITI implants in this case, looking at the summary of the coating characteristics, in the case of the ITI implants, TPS.

I was asked by the FDA to look at the clinical results from the life table analysis and failure data. I'm going to provide some information there, compare the success and failure rate to uncoated implants. And I'm just going to mention here today for the sake of time that there is an orthodontic implant, as an implant in another anatomical location, which is made for the palate, a very short implant to help provide orthodontic anchorage, and then just mention a minute special controls.

The ITI dental implant, just to refresh your memory, has been in use since 1974, and there have been over 200 peer-reviewed publications on this system. What these publications document is that the system is a very safe and predictable and effective system for replacement of missing teeth.

Now, the product features of this implant is that it has a single-stage design, as you've heard a little bit about that today. They're both solid and hollow implants. They're made from commercially pure Grade 4 titanium. The portion that goes into the bony part is titanium plasma sprayed. On top of the implant is a machined portion, a transgingival portion, which extends through the connective tissue and epithelium. Inside of the implant, the top of the implant, is a more tapered design to stability the

abutment and the implant. And as mentioned before, there is data both on basic science as well as clinical research that we'll just briefly touch upon today.

When you look at the ITI dental implants, they come as both hollow cylinders as well as solid screw designs, in various lengths, of course, and the cylinders come as both a straight version or what we call a 15-degree angled implant. And the diameter of the solid screws is a standard 4.1 mm thread to thread or 3.3 or 4.8. So there's an option as far as the implants go.

Now, two points about these implants as far as retentive features go. At sort of the gross level or the macro level, on the cylinder implants these are placed with what they call a press fit design; in other words, the implant osteotomy site is slightly less diameter than the cylinder diameter itself. So when you place the implant, you have very tight apposition of the implant into the osteotomy site. You also have two parallel walls there, and then you have these macro retentive holes, is what we call them.

As far as the screw design goes, of course, the threads are there, which provide stabilization as well as increased surface area, as well as force distribution for the implant. So those are sort of the macro retentive

features of the implant.

As far as the more micro retentive elements of the implant, it concerns the surface characteristics of the endosseous portion, which is the titanium plasma sprayed system.

I think it's kind of interesting, too, when we look at the other dental implant companies today. ITI really pioneered the non-submerged approach. So at the time of implant placement, the implant extends beyond the alveolar crest and into the oral cavity. Now several other companies have either made a non-submerged implant, or companies that have traditionally been a submerged company are now placing their implants with an abutment attached at the time of placement. And so the evolution is towards placing implants in a non-submerged approach.

The second feature I'd want to mention is that a roughened implant surface has been used on these implants for over 20 years now, and the reason for that is that there's about 15 years of data to suggest that the roughened implant surface is more osteophilic, if you will. There's more bone-to-implant contact with a roughened surface than there is with a smooth surface. And if you look at the other implant companies on the market today, there's really only one system that doesn't offer their customer a

roughened implant surface.

Now, I want to touch just a minute on the titanium plasma spraying process. We discussed that a little bit earlier, as alluded to, and what happens is that there is an argon gas that's sent through a very intense electric arc, which forms the plasma, hence the name. And the titanium hydride is introduced into this very hot flame of 15,000 to 20,000 degree plasma. Then the particles get accelerated 3,000 meters per second, and this titanium hydride then forms droplets of molten metal. And with the speed that they're accelerated onto the surface of the implant as well as the temperature, the coating is essentially welded to the implant surface.

If you look at the characteristics of the TPS, it's about a 30-micron layer thick by SEM, and what this does is provide a greater surface area than either a polished or machine type implant. Then if you look at some of the measurements using prophylometry, you can see RA and RQ values of 6.6 and 8.5 microns. So it's been a well-characterized surface over the years.

What this does is gives us additional surface area for the attachment of bone. Some of the clinicians feel that you can use shorter implants in these cases. You don't need bicortical stabilization because you've increased the

surface area using the TPS. And this same surface has been used over 20 years, so it's a well-documented surface. It's been in vitro tested in a number of different ways to make sure of the consistency and predictability of that surface.

One of the ways that you can measure what the effect of this is to use either histomorphometrics to look at the amount of bone-to-implant contact, or you can use some sort of functional test. In this study by Wilke, this 1990 study, he took either a machine screw or a TPS screw and put this in sheep tibia bone, and he inserted all these screws with 100 newton centimeters of torque. So they all went into the bone at the same torque. Then they waited 24 weeks, and then they measured the amount of torque removal force required to take the screws out of the bone, and you can see that in the case of the smoother surface, the machine surface, it didn't take any more force to get the implant out of the bone as when put in. But when you looked at the roughened surface, it took a lot more force to get the screws out of the bone than used to put in.

So this shows you one of the functional tests that can evaluate the effect that the TPS surface has on implant removal, a functional test for determining bone implant contact. And there are many others that we don't have time to go into today.

Things you should know about the TPS is that the surface oxide layer has the same chemical composition as the surface oxide layer on uncoated machine titanium. So the TPS process itself doesn't alter the oxide layer, which is, of course, crucial to our bodies, what they look it.

As far as corrosion resistance of the TPS goes, really there are a couple properties. It's a passive oxide layer which is stable and inert under physiologic conditions, and this has really been determined through corrosion testing, and what this corrosion test does is simulate a long-term in vivo exposure. And if you analyze the results of this test, they found that there was no dissolution of the titanium after you simulate 35 years' exposure in the body. So it's a very stable and inert process.

If you look at the adhesion of the TPS to the implant body itself, you can see that--what you see is that strength here to remove that is greater than the bond to the bone itself. So the sheer strength of the TPS coating to the implant interface is greater than that of the implant-bone interface. Take-home--and this is done using the standards that are produced for metallurgy in that the TPS is not going to come off the implant surface.

There are controls, as was talked about a little

bit earlier today in some earlier discussions. There are controls done both on the powder that's used to spray onto the surface as well as tests done on the implant once it's been coated. So looking at the titanium hydride, you see the chemical compositions looked at crystalline and grain morphology. Then once it's been sprayed on the implants, it's inspected under electron microscopy. You look for foreign materials in the coating distribution. So there are controls that can be done to assure that things are done in a consistent manner.

Probably what's most interesting to me, then, is the clinical support for this system, and currently the ITI dental implants that are being used, that we're using today, have been marketed since 1984. There has been no change in thread design on the implant. There's no change in the TPS surface. And the take-home is that the currently marketed ones that we use today have been extensively studied over a long period of time.

If we look at some of the literature, and this is going back to studies from 1984 to 1991, I think it's instructive for us to sort of look at these a little bit more in detail than normal. What we've done--you've seen these last time I presented, but what we've done is gone back--because you asked for information on life table

analysis, we put a little star by the ones that have life table analysis. And Baboosh had 484 patients, you can see here, 1,700 implants. These are solid screw implants. Edentulous mandible, eight-year follow-up. Another country, 146 patients, 500 implants, six-and-a-half-year follow-up. High success rates in each case, 88 to 91 percent.

The number of different countries is the point life table analysis, and some of these, whether it be a hollow cylinder implant, hollow screw, or solid screw, all these available, there have been long-term follow-up, and in this case edentulous mandibles, where these implants were first placed, and very high success rates over time. So it's just not one study that you're looking at or one set of patients. You're looking at a number of patients and a number of different implants under various conditions.

If you look at '91 to '94--and I think a point here that needs to be made is that when the Dental Advisory Board made its first recommendation in 1990-1991, they didn't have available all this evidence that we have today. And you guys certainly have a lot more studies at your disposal that you can look at. And this is really when the majority of these papers have been published.

You see, again, large numbers of patients, 156, 84, 126, 33, all the different types of implants that's been

available now since 1984, both fully and partially edentulous, now getting into these implants, various times of follow-up, five years, nine and a half years--again, with high success rates even in ones that are looked at with life table analysis.

If we look at 1995 to 1997, again, a lot of patients have been treated with these implants. A lot of implants have been treated. All the different types that we've seen. So over now probably 20 years we haven't seen problems with the different types of implants. Again, varying times of follow-up, nine-and-a-half years here, two, three years here. But, again, very high success rates, as you've heard earlier today.

Just alone in 1997, more studies, 56 patients here, 12, 109, 1,000 implants here. So it's just not one study that's been looked at. And you look at the follow-up times: seven years, nine years, eight years. There's been not just one study but a number of studies done in different countries, under different indications and different people, with very successful results.

If we look at the one that's--actually not the most recent one just was published by Maritska Stern (ph) on edentulous patients as well, but if we look at the one that's been alluded to a little bit earlier today, here it's

up to eight years. This is done by life table analysis. The analysis is done on three different centers, 1,000 patients, 2,300 implants. Here the number of implants that have been examined in this prospective study--it's a prospective study--up to eight years distribution. And since it has also come up earlier today, at different times of consensus conferences, criteria of success has been analyzed in a number of different articles in the literature. But what was used in this prospective study was what we predominantly use all the time, absence of pain, absence of recurrent infection, mobility, radiolucency, or fracture. So it was very strict criteria that we used to evaluate all these implants at each of the visits.

As the FDA asked about life table analysis, the numbers are presented here for you, and this is the way life table analysis is presented by intervals, of course. And two to three years, after three years you've got 1,219 implants, 98 percent cumulative success rate; four to five years, 500 implants, 96.6 percent implants. And then as these patients get through further time points, they'll be evaluated in this very stringent fashion in a very prospective trial.

So there's plenty of data here, and another thing that was requested was your analysis of your failures. What

we're looking at is we've broken out the data from this one study, and we're looking at the different time intervals here. What you see is in the very first interval, what we call early failures, there was recurrent infection around five implants, eight implants had mobility, for a total of 13 implants out of 2,359 implants that had to be removed.

If you look at the other categories, this is recurrent infections, in other words, infections that were treated and couldn't be resolved, and those implants were taken out. If the implants were mobile, the implants came out. You see that drops off.

Implant fracture, just like it is in all the studies with the ITI implants, there's very few fractures. Progressive bone loss is something we don't see even up to eight years. And even in cases where there's a fair amount of infection, especially as patients lose their plaque control compliance over time, we don't see progressive loss of bone over this time period.

So if you look at these numbers, then, and take all these numbers, you're looking at about 2 percent of the implants that had failures, and the breakdown you can see by category. They're very small percentages in this study.

The way that the infection was looked at at the last examination was when the patients presented for their

last exam, whatever time period that was, if they had any infection around that implant whatsoever, that was considered a failure.

Now, those infections were treated, and some of those implants are going to go on and do very well. But due to the success criteria used, we take the worst-case scenario here with the infection and just say if we add all those up, you're still looking at less than a percent of these implants had any infection around it.

If you look at success by implant type, five-year cumulative success rates, 96 percent; hollow screw was 98 percent; and hollow cylinder was 95 percent. If you look at the data by different parts of the mouth, again, very high success rates. This is the five-year data in the mandible as well as the maxilla.

Also, one of the criteria that are often used for success of implants is that there's less than 1.5 mm of bone loss in the first year of function after loading, and in subsequent it would be less than 0.2 mm of bone loss. This data is not published yet, but from the three different centers it's being analyzed, and you can see that in the first year there's been less than 1.5 mm of bone loss, and in years two to five there have been less than 0.2 average mean bone loss over time.

We were also asked to compare our data to uncoated implants, and if you look at it from the Buser study, which, again, used life table analysis, in the mandible there was about a 97 percent success rate. If you look at Leckholm's (?) data in 1994 in partially edentulous patients, it's 94 percent; in Odell's (?) fully edentulous, it was about 97 percent. So this number compares favorably as well. In the maxilla, about 96 percent; in the Leckholm partially edentulous study, about 92; and Odell fully edentulous, about 87 percent.

What should be pointed out, too, in this comparison is that neither of these studies used life table analysis. And as you know in this room, when you don't use life table analysis, the implants that have been placed in more recently influence the results. And that's why we do life table analysis so you only evaluate the implants at risk during the interval. And so I think when you look at these numbers, these numbers compare very favorably using life table analysis.

So I think what this study does confirm, one of many, as we've shown you, is that the mandibular-maxillary success rates compare favorably with reported Branemark success rates. There are high success rates for hollow and solid implants, and not just from this one study but from

all the different studies I showed you. The ITI implants maintain a high success rate over the long-term follow-up.

As you also know in this room, there are special controls that are available to you if you choose to place these in Class II, as a Class II device. There are a number of special controls that certainly you have available. There are standards for materials. There are standards for lab testing, benchtop testing. There are a number of different guidance documents that the FDA can use for how an implant is evaluated. Good manufacturing practices, the ISO 9001, which the Strauman Company received. And so there are a number of different controls that can be used to make sure that the implants that are sold are reasonably safe in assurance.

So, in conclusion, then, the ITI implant has a consistently high success rate over all anatomical locations. The safe and effective use of the hollow and solid implant plasma sprayed has been confirmed by an extensive body of knowledge. The FDA has sufficient general and special controls to provide reasonable assurance of safety and efficacy. And based upon the clinical and non-clinical results, 200 publications, the ITI system, it is recommended that uncoated and titanium plasma sprayed root form implants be reclassified as Class II devices.

All these numbers are well and good, but I think probably the thing that is most satisfying for me as a clinician is what we do for our patients. And this was a patient that came in, had fractured this tooth off. We extracted the root. We let it heal in, and we came back and placed an ITI dental implant in this area and restored it, and this is a two-year follow-up picture. And I think what you can see is an advantage for this patient in that either of the adjacent teeth were not having to be compromised by being taken down or restored for any sort of reason. And you can have a nice replacement with very pink, healthy tissues.

And in the anterior of the mouth, we have patients that present--this is one of our patients that came and was missing a lateral incisor. This fellow was in his early 20s, had been wearing a partial denture. He got it knocked out in a sporting activity, like a lot of kids do. And we were able to come in here, get rid of the removable partial denture, and provide a restoration that really changes these people's influence.

We have women that come in that will only speak with their hand up at their mouth to hide spaces, and I think when we have the ability to restore these patients, this is really the satisfaction of what we do and hopefully

why we're here today.

Thank you very much.

DR. GENCO: Thank you very much, Dr. Cochran.

Any questions or comments from the panel?

[No response.]

DR. GENCO: Okay. Thank you.

Let's proceed now to the Innova Corporation, Dr. Douglas Deporter and Dr. Robert Pilliar.

MR. KEHOE: My name is Mike Kehoe (ph), and I'm president of Innova Technologies Corporation. I'm just going to mention a few things about the corporation; then I'll turn the meeting over to Dr. Pilliar to speak to the physical characteristics and design of the implant and Dr. Douglas Deporter to speak to the clinical trials.

Innova Technologies is a public corporation headquartered in Toronto, Canada. We have subsidiary offices in San Francisco, California, and Sydney, Australia. We've met the regulatory requirements in Japan, Taiwan, Australia, New Zealand, Canada, and in the U.S. we have both an investigational device exemption and have received 510(k) clearance for sale of the endopore implant in the United States. We also have active research programs in other areas, particularly in oral-maxillofacial surgery, such as a distraction osteogenesis bone plate.

January 1989 was the first human use of the endopore implant at the Faculty of Dentistry, University of Toronto, and in 1992, we received an investigational device exemption from the FDA to conduct clinical trials. In 1994, we received approval from the Health Protection Branch after clinical trials in Canada and the Therapeutic Goods Administration in Australia. In 1995, our 510(k) cleared for the endopore system, but we kept our IDE ongoing with prospective clinical trials. We received approval in Japan in 1996, and as of November 1997, we'd sold about 40,000 implants.

We have continuing clinical trials going on in four countries in six centers, with other 400 patients and approximately 1,100 implants. Right now I think there's 38 publications in peer review journals.

I'd like to turn the meeting over to Dr. Robert Pilliar. He's a professor and director of the Center for Biomaterials, University of Toronto.

DR. PILLIAR: Thank you. I'd like to base my presentation--by the way, for the record, I am a professor at the University of Toronto, Faculty of Dentistry, and the director of the Center for Biomaterials there. I am a co-inventor of this implant system that you will be hearing about, and as such, in accordance with the University of

Toronto policies, I share in some royalties which come back to the University of Toronto for that.

In addition, I also am being paid by Innova for coming down to this meeting today, and also I should state that since this is a public company, I do have some shares in the company. A minor amount.

Now, this is the endopore implant system that I'll be describing to you, and what I wanted to talk about are some of the physical attributes, characteristics of this device, and how they come about through the processing method which is used to make this device.

The rationale for this endopore dental implant is not different from many of the other dental implants that you have heard of today. It's intended to provide reliable implant fixation by bone, in this case ingrowth, into a porous surface region which is formed by a sintering process. And I'd like to just describe that very briefly.

Again, by way of background, I should state that I initially started working on these porous surface implant systems for orthopedic uses back in 1969, and those, in fact, did go into clinical use initially in the late '70s. So there's been along history of these porous surface systems formed by sintering, ones that Dr. Sung has referred to earlier today.

Now, there are many implant systems out there today. Many of them utilize one form or another of mechanical interlock with bone, and I just wanted to note here that what we have here are many designs which contain these macroscopic openings through which bone is intended to grow through, or which have these macroscopic as well as microscopic surface features which are intended to allow for this mechanical interlock of bone and implant. And it's turned out to be a very effective way of stabilizing these devices.

The endopore implant system is made up, as I've mentioned, with this surface region, which is porous, and this is a cross-sectional view of the interface where this coating process--I should emphasize here a coating process is used to create a structure as seen here. What we have, in effect, at that surface region are a number of what I would define a microscopic openings through which bone can grow. So the whole intent, again, is to achieve that type of reliable and mechanical fixation of implant to bone through bone ingrowth in this particular case.

The characteristics of this endopore implant system, it's effectively a cylindrical-type implant system, but with a slight taper angle associated with it. So it's a tapered, truncated cone shape. It's a five-degree taper

angle that you see there.

It's characterized on the surface region by this interconnected porosity which is uniformly distributed through that near surface region. And that I believe is an important and interesting feature of this approach.

The average pore size is around 100 microns or so, and the volume percent porosity which is provided within that surface region is around 35 percent. Most important to recognize is that the result of this sintering operation, after the consolidation of those surface beads or particles which are placed onto the device is a single-piece titanium alloy implant system. In other words, that sintered porous surface region is integrally bonded with the machined, non-porous portion. So after the processing, we have a single-piece implant system. I really think it's important to distinguish that from what I consider a coating, which is one which has an interface which will fail adhesively as opposed to non-adhesively. And I'll mention that very briefly later on.

Some other features of the implant system: It has a smooth, non-porous coronal region, and it comes in a variety of lengths and diameters currently made by Innova Corporation.

Now, the sintering process which is used to form

this porous surface region is a solid state diffusion process. In other words, there's no liquid phase or melting which occurs during that processing. This is the way that we consolidate titanium alloy particles, powder particles, to a bulk form and also to this well-bonded structure to the underlying solid core. And we do that by choosing processing conditions to ensure that we have the required or the desired size, volume percent, and distribution of pores in that surface region. This is done by sintering at 1250 degrees Centigrade in a high vacuum atmosphere furnace, and the end result of that processing is that you have a very strongly bonded surface region where the individual powder particles which are used in the process are well bonded to each other and they're also well bonded to the underlying substrate.

They can be defined and they are characterized by what we define as metallic interatomic bond, so that it's a very strong form of bonding that occurs.

The sinter neck regions, which are the areas of junction between the particles and the particles to the substrate, are substantial; also, the sinter neck zones, when they're examined microscopically, as I'll show you in the next slide, have metallurgical features which are very similar in terms of micro structure. They're the same, in

fact, in terms of micro structure to this neck zone here and the neck zone here. They're very same to the structure that you'd find anywhere in the bulk material. So all this is to say that we do develop this strong metallurgical bond at that junction point after the processing.

So the sintered substrate, surface substrate construct forms a structure with a desirable surface zone network of interconnected pores and channels, and the consolidation of these particles by sintering allows such a structure to be formed, while ensuring the structural integrity of the whole implant component.

Now, this shows you the end result of this type of a structure. This is a histological slide from an early animal study that we undertook to demonstrate how these devices work. And this shows you stained bone tissue which is ingrown into this multi-layered zone here, the surface zone with this interconnected porosity. So we have the ability of the bone to grow into and through these openings, and, in fact, in that manner develop very strong resistance not just to shear forces, which on an irregular or rough surface would develop, but also, interestingly, to tensile forces. We have this three-dimensional interconnection of bone with the porous surface region. This has always been an interesting feature of this approach, of creating these

interconnected surface pores via this process.

Now, the other important aspect of these in terms of characterizing these types of structures is that they have adequate mechanical properties, and we've done that with the implant systems which we form through appropriate interface shear strength tests, appropriate--which, by the way, illustrate that the effective strength of that interface bond, measured in mega-pascals, is in the same range as you would expect for the titanium alloy when you compare shear strengths, for example, and also the fact that the failures which finally do occur when you go to very high loads is a cohesive failure rather than an adhesive failure. So it all, again, speaks to the very strong metallic interatomic bonding which occurs.

Finally, we have also undertaken cyclic testing, interface fatigue testing, again, in shear, and these have been done using a protocol which has ensured that the devices in that surface region will survive loads which are far in excess of those which are expected during in vivo use, up to 5 million cycles, as you see here.

So this is a summary slide, really. What I want to emphasize in terms of these physical characteristics is the fact that this method of processing does result in this single-unit construct with this porous surface region,

which, according to the volume percent, size, and distribution of the pores, is very effective in allowing this type of bony interlock.

Also of interest is the fact that this particular processing method allows us very nice control on those surface zone properties and characteristics and also on the overall thickness of that device. So at this point, Dr. Deporter was going to speak to the clinicals, unless you wanted to have some questions of me.

DR. GENCO: Would you mind, Dr. Pilliar?

DR. PILLIAR: No. That's fine.

DR. GENCO: Does anyone have a question, from the panel?

[No response.]

DR. GENCO: Thank you.

DR. PILLIAR: You're welcome.

DR. GENCO: Dr. Deporter?

DR. DEPORTER: Thank you, Mr. Chairman, members of the panel.

As has been indicated, my name is Deporter. I am a full professor in the Department of Periodontics, University of Toronto. Along with Dr. Pilliar and Dr. Phillip Weston, I'm a co-inventor of what has become the endopore dental implant. There is a patent. It was

assigned to the University of Toronto, and the three of us receive a small percentage of the royalties that are paid to the University of Toronto. Also, since this is a public company, when the company first was formed, I purchased with my own monies a small amount of shares in the company. And, finally, my expenses and a small honorarium are being paid to me for my presentation here today since I'm being taken away from my duties at the University of Toronto.

Now, I am also the first clinician to have used this implant system, and, therefore, I was chosen to present both the data that we've collected at the University of Toronto and also the data that's being presented under the IDE by three American centers.

Now, as you probably know, this implant system was developed with funds from the Medical Research Council of Canada. We began research in 1983, and, of course, we have ongoing clinical trials at the present time. But the first human usage was my and Dr. Watson's investigation, started on a completely edentulous population in 1989, which we treated 52 patients in an identical fashion, in a prospective fashion, each patient receiving three implants in a mandibular over-denture.

At the present time, all of these patients have passed seven years of function, and as you'll see from the

life table analysis, which was requested at the last meeting, I understand, the success rate is somewhere around 93 percent.

We also have ongoing trials in partial edentulism. One set of data is presented on this screen. It's a group of single-tooth patients in the maxilla which I have treated. The majority, if not all, of the patients have passed one year of function. The average functional time at this time is 23 months. The success rate is 100 percent.

Now, the criteria that we've used to assess all implants in all of the trials that we've undertaken, all of the prospective trials we've undertaken, are those published by others, Albrechtson (ph) and others in the literature, so those criteria would be as listed here: lack of clinically detectable mobility of individual unattached implants using manual methods. We've also used the perio test device to detect subclinical mobility or to quantify subclinical mobility, if any. The second criterion is no radiographic evidence of periapical radiolucency. We've gone to the trouble of collecting radiographs as baseline, three months, six months, 12 months, and annual intervals thereafter, using a customized film holder which attaches individually to each implant in order to maximize the opportunity for obtaining the very best possible radiographs. And the

radiographs are then analyzed, examined by a radiologist, Dr. Michael Farrell. So that's the second criterion.

The third criterion would be that after the first year of function, in radiographs there would be less than 0.2 mm of crestal bone loss annually. And the fourth criterion, of course, would be the patient would be in no distress, no signs of recurrent infection or persistent pain or any other symptoms.

Now, in addition to these published criteria, we have also used a series of periodontal parameters, including probing pocket depth, probing attachment level from a fixed reference point, gingival index, plaque index, and sulcular(?) bleeding index upon probing, and we have published this data in 1976 in the Journal of Clinical Perio when all of the patients had passed three years of function. The data presented there shows that they fall within the normal ranges, with teeth in a state of periodontal health, and the data is also very similar to what's been published by other investigators for other implant systems where the implants are in a state of health.

Of course, one never knows how slides will project until the last minute, I guess. This table is perhaps a little bit hard to read, so I'll just lead you through it.

This is a life table analysis for the patients in

over-denture study at the University of Toronto begun in 1989. You see there were 156 implants. That's three implants per patient. Of those 156 implants, five implants failed to integrate--they were all in men--and one implant in a lady. The lady received facial trauma, a direct hit to her implant shortly after re-entry, and that was lost shortly thereafter. So there were six implants lost in the prefunctional period. This is the first time this implant had been used in human beings, and that gave a one-year cumulative success figure of 96 percent.

There were two implants lost from one gentleman slightly after two years of function because of mechanical overload, and another two implants lost slightly after five years in a lady who developed other problems. So this would give a five-year success figure of 94.8 percent, or a cumulative six- or seven-year cumulative success rate of 93 percent. And as I indicated, every one of the patients have passed seven years of function.

So this gives a summary, then, of the results that we've obtained using those criteria that I listed on the earlier slide. We have no clinically detectable mobility, and in fact, a mean perio test value for this group of patients of approximately minus four. Of course, anything below zero is considered to be extremely good. Absent(?)

indicates that there is no sign of periapical radiolucency in any of those standardized, carefully taken films. After the first year of function in which the mean bone loss for the group was basically half a millimeter, 0.45 mm, the overall mean loss of bone annually out to year five was 0.06 mm. So that's about a third of the recommended maximum of 0.2 mm. So certainly we are successful in meeting that criterion. All of the implants are symptom-free, and as you saw with all of the above, there is still a five-year success rate of 93 percent.

At the last meeting, I understand that you were looking for causal factors for implant failure. It's been broken down in this table. There were ten failures, of course, as I indicated. Please focus in on--I think most people are worried about infection with a number of different implant systems. One of the ten implants failed from infection. The others, five were in what has been classified as contraindicated patients because they were heavy smokers, heavy bruxers, and the others basically are one to trauma and the others to mechanical overload.

This represents, just in passing, a group of patients that have received two or more endopore implants in the partially edentulous maxilla. They are part of an ongoing prospective trial for which the average functional

time is 16.5 months. There are 34 patients presented here. The last data was collected December 1, '97. A mean implant length for the whole group was 9 mm, which is significantly less than that generally recommended for the maxilla, 109 implants, and we've lost one. So that gives a 99 percent success at this point.

Now, I don't have a life table analysis for that. I only present that in passing.

The IDE investigations are ongoing in three clinical centers in the United States. There's a mandibular over-denture population in which the identical protocol is used, as we designed for our prospective study at the University of Toronto. There are 92 patients in that study with 275 implants. The average follow-up time is three years. I will show you a life table analysis in a moment. The success rate has been quoted at 94 percent. So basically the same as what we've achieved with our seven-year study in the University of Toronto.

There is also an IDE population of partially edentulous patients, 179 patients, 428 implants, the average functional time two years, and a success rate quoted at 96 percent. Basically the same criteria have been used for assessment of implants as I outlined that we're using in the University of Toronto.

This is a life table analysis for the mandibular over-denture population in the IDE group. You can see again there were 275 implants placed. There were a total of 15 failures. The vast majority of those, 12 of the 15, occurred in the prefunctional period--that is, they did not osseointegrate. After that time, there were only three failures, and they occurred within the first year of function.

Now, as you can see, all of the patients have not passed five years in this group yet, but the mean functional time is three years. The three-year success rate is 94 percent, and basically--well, you can see it doesn't change at all, really, out to the five-year figure. But as I said, fewer patients have passed that point.

This is a life table analysis for the partially edentulous population in the IDE group. Again, I indicated earlier there were 428 implants installed in these patients. As you can see, there were 16 failures, the vast majority of which, nine, failed to osseointegrate. The others, we have a causal table here, I think, as the next slide. Yes.

Now, the causal factors for the losses, these are the causal factors as reported by the three investigators in the three centers in the U.S. that are collecting data for this IDE investigation. You can see, if we're worried about

infection, again, we have one implant that was reported to have failed because of infection of the total number of implants lost. The vast majority were lost for unknown reasons. What that means, I don't know, of course. Those of us who are in implant dentistry realize there are patient-specific factors which sometimes makes it difficult to determine why an implant failed. There are also, of course, operator error issues as well. Unfortunately, seven of those reported were unknown reasons. Then the others basically fall into either--well, one was in a poor location; two were some post-operative pain the patient was complaining about; and the others were for mechanical overloading.

More or less the same result with the partially edentulous data, the causal factors. Five of the 16 implants which failed were reported as unknown reasons, but then the others basically are mechanical overload and two of those 16 failed because of what the operator reported as post-operative infection.

Now, I gather that at the last meeting some questions were asked with regard to if this implant performs equally well in various sites in the jaws, and this is the IDE data which has been broken down into anterior maxilla, posterior maxilla, anterior mandible, posterior mandible in

partially edentulous patients, and you can see that there's basically no difference on site, based on site.

Now, in this cumulative slide--summary slide, rather, of reported cumulative success rates as published in the literature, we've presented some data for the Branemark and for the endopore basically to demonstrate equivalence--the Branemark, of course, being selected because it's the system that's been around the longest, and also because it's the first system to have been proposed for reclassification.

You see the five-year over-denture data reported recently by Jempt (ph) and coworkers for the mandible. It gives a cumulative success figure of 94.5 percent at five years. Our data at five years, which we reported last year in 1997, basically the same, 94.8 percent, or seven years, all of our patients have passed seven years basically unchanged at 93 percent.

So we certainly support, Innova supports and Dr. Pilliar and I as inventors and investigators and experts in this field support the reclassification of endosseous root form dental implants to a type II device. We certainly believe that the endopore qualifies for this reclassification because of the factors listed on this slide. It does have a cylindrical shape. It's made of a

detaining(?) material in size, diameters, and lengths that are typical of the industry, although our lengths are certainly successfully used in much shorter lengths than some other systems.

We use a two-part surgery approach, of course, a screw-fixed hex abutment for prosthetic support. And Mr. Kehoe indicated, there have been more than 40,000 of these implants used worldwide, and certainly the greater than three-year prospective clinical trial studies indicate equivalence with the Branemark system.

Thank you, Mr. Chairman.

DR. GENCO: Thank you, Dr. Deporter.

Are there any questions or comments from the panel? Yes, Leslie?

DR. HEFFEZ: I know that it's critically important to recognize that in the initial year you lose a certain amount of bone around the implant and that thereafter you lose less, but annually you may have a certain loss of bone. One problem I always have is this measurement of 0.2 mm. How does one actually measure 0.2 mm even if the radiographs are taken in a controlled fashion, with no radiographic markers, knowing that the least change will cause a change in your measurement?

DR. DEPORTER: You'll notice that--

DR. GENCO: Excuse me, Dr. Deporter. Could you use the microphone? It's being recorded.

DR. DEPORTER: You'll notice that that is always quoted as a mean value. It's very difficult to measure 0.2 mm on the radiograph. But the criteria that were established by Albrechtson and others was that a mean figure for the group was to be no more than 0.2 mm per year.

DR. HEFFEZ: Right. Which would mean--

DR. DEPORTER: Which would mean that some implants would lose nothing, some would gain, some would lose slight--you know, somewhat more than 0.2 mm. But the mean figure turns out as 0.2 mm. That's the way it's being proposed, so we are simply following the criteria used and established in the literature.

It's difficult to do, off course.

DR. HEFFEZ: I think it probably would be wiser, regardless of who establishes it, to recognize per implant what can be measured and what is significant rather than--

DR. DEPORTER: Well, the significant factor is whether it's progressive. And so you can tell that over a five-year period, for example. There's a recent paper by Ruse (ph) which addresses this I think in a little bit more rationale way, Ruse, and Albrechtson is also on that paper, where they suggest that one way to get around this would be

to produce a cumulative figure over five years. So that if we met the criteria, then any implant surface that you looked at should not have lost more than 1.8 mm of bone. Correct? Not more than 1 mm in the first year, and not more than .2 mm for the remaining four years.

So they've suggested that one should go through every implant in your trial and make sure that no surface, no implant has lost more than that. And I have done that. And there are, in fact, two surfaces that have approaches 1.8, two surfaces of two implants.

DR. HEFFEZ: See, there's the problem. You're taking a mean figure. You're now saying it's applied per implant, that you shouldn't lose 1.8.

DR. DEPORTER: No, no, that's not what I said. All I said was we were meeting the criteria established in the literature that you should have a mean loss of no more than 0.2 mm per year. This is what's generally accepted. But I think that Ruse's proposal that we should look at each individual surface and basically quantify the number of surfaces that haven't or have lost more than 1.8 mm over a five-year period, which, of course, presupposes that every implant is past five years, which isn't always the case in a lot of investigations, as you've seen today. But that's a more rational way to do it, because it is very difficult to

measure 0.2 mm on a per implant basis. But the important thing is that it isn't progressive on a per implant basis.

DR. GENCO: Further questions? John?

DR. BRANSKI: You mentioned a couple times that some implants failed by overload, and I just wondered what is your sort of operational definition of examining a case and determining that the implant did fail by overload. In other words, how do you determine that that is the actual cause?

DR. DEPORTER: Well, it's by deduction, basically, because certainly in the patients that we have at U of T, they're for the most part extremely compliant with things like home care. If you look at our published plaque index data, for example, it's very low. Gingival indices are very low. Mechanical failure is basically an implant which has been successfully functioning, supporting a prosthesis. The home care has been excellent. There's been no sign of infection, and suddenly the implant loosens.

DR. BRANSKI: Well, would you distinguish that from a case where it failed for unknown reasons? Because you mentioned some that failed for unknown reasons.

DR. DEPORTER: Well, basically, I don't know what those investigators classified--why they said it was unknown. My suspicion is that they might have been

mechanical overload, either during the prefunctional period or the post-functional period. So I don't know what--you know, they just said it was unknown reasons, maybe because they didn't think about it long enough or whatever. But I don't have any unknown reasons in my group of patients. Perhaps I'm being presumptive in calling them mechanical overload.

DR. GENCO: Okay. Thank you very much, Dr.

Deporter.

We'll now have Dr. Jack Krauser, who will speak on implant failures.

DR. KRAUSER: Good afternoon. I'm Jack Krauser. I'm a private practice practitioner, and as a matter of conflict of interest, I am the owner of a 510(k) on dental implants and abutments that are at issue for this panel. However, I am not defending or representing my implant systems or premarket notifications in this short presentation.

At the November meeting, I believe it was Dr. Diane Rekow who had actually asked the presenters and the panel, What did implant failure look like? And as a private practice practitioner, I have been gathering this information on my own patients as well as those that have been referred to me. Having a practice in Florida, we have

a lot of patients that move down to our area, so we've been able to not only track our own cases but colleagues' from other areas of the country. So I'd like to present this information.

By the way, my travel expenses were paid for by myself, and yesterday I participated in the Seramed(?) bone graft panel as one of the clinical investigators, and my expenses were not compensated by them.

This first case was done by myself and my teammates approximately three or four years ago, and I showed these X-rays because I'm not quite sure why these implants are at risk or in a failing mode. You see here a failed device, and on the other side, the implants appear to be reasonably stable, although we have some component discrepancy in this area. As we develop the presentation, we'll discuss these aspects.

As a clinician, I've been doing implants since the early 1980s. We started with Nobel Farmer(?) system and Corvent(?) system, which were available at that time. And I have seen a tremendous improvement from the commercial manufacturers. So as a clinician doing the implants, I want to commend our colleagues from the manufacturing arena as they have improved and made consistent design improvements. With regard to the coated companies, there's consistency and

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reproducibility in those devices. I have done some of the Generation 1 coatings and can attest that they are totally different than what is being reproducibly sold on the marketplace today.

I think surface finishes are much greater. At the time we first started doing implants, they were not even delivered to us in a sterile manner. The Striker Company was the first company to actually deliver an implant in a sterile vial, and they are, interestingly, no longer selling dental implants because they're just focusing on their medical devices.

Interface tolerance, several colleagues have discussed this. I think FDA good manufacturing practices and ISO practices for Europe and other countries demand tolerance on all the parts in devices. Dr. Marlin's presentation discussing components for other implants addresses that issue, and I believe the manufacturing integrity is at a great level compared to as it's been in earlier days.

A subtle improvement, such as implant drills, the tolerances are also greater, so we as clinicians who are sizing our cases can use an implant drill to give us a predictable osteotomy site.

This particular slide you will see develop as I

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have presented these topics over time and I have added new material to it. I think it's been clear to the panelists that some of the literature claims that there are excellent results by location, favorable in other areas, and questionable or poor. Some of the data are assuming that there are no differences. You saw two beautiful presentations right before me where their studies are not showing these type of situations. So perhaps bone density might be a critical factor rather than exact location of the mouth.

We must also consider dimensions of implants as they relate to the different shapes of the teeth in the different parts of the mouth, as it may become a problem. This happens to be a cylindrical coated system done in a total edentulous mandible with the ad modum Branemark method of four, five, or six implants in the synthesis with a cantilevered design, bilateral, cross-arch support.

These cases are totally different than partial edentulous unilateral types of cases that we're predictably doing in our practices today with sinus augmentation materials and the partial edentulous non-splinted, cross-arch results. So as clinicians, we are seeing excellent results in these more complex cases as well as the more straightforward mandibular cases.

The density of bone, I believe, is a clinical parameter which is much more important than concepts such as diameter and length, and I believe that the literature has been presented at this meeting that we have seen greater failure in the porous type of bone which tends to be in posterior areas, but not always.

Patient expectations are a clinical concern. We have a dentate skeleton here versus a severely atrophic situation. With a super-imposed tooth, we can see the clinical demand that is put on the practitioners both in the surgical and prosthetic arena to replace the missing parts of tooth structure, soft and hard tissues, and the cases are dramatically different.

We have this caricature from colleagues of one of the implant systems. We must talk to our patients and find out what their requirements are. This particular patient came to me, was unhappy with their situation. Cosmetically, they were unhappy with it. It did have hygiene access. You do see some soft tissue resorption and you do see some radiographic resorption from this cross-arch case. I would agree with them that they are having some complication. Although these implants are not failed, they are in a compromised state.

This particular patient was in an automobile

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accident several years before I saw the patient. You can see some residual scarring. This was done approximately seven or eight years ago by myself. I did not do techniques of isolated bone augmentation as I would today, but we were able to enhance the zone of gingiva, place two successful implants. Here, you can see, is a preangulated component. Now, we can definitely get better aesthetics today. This is the patient's smile, so she is not particularly offended by that, but smile concerns and aesthetic concerns are important, so we must consider the patient expectation.

What are the medical and surgical risks? I believe that endosseous implants are a rather straightforward discipline for surgical therapy and we have the same risk factors as any other oral surgical type of procedure. There are some medical considerations. Uncontrolled diabetics, some of the animal studies are now coming out. Mark Nevans, Ron Nevans' son, has done a very nice study on diabetes. There's work on osteoporosis where it may or may not be a problem. There's definitely some information that age is not particularly a problem, but the information on smoking is that it clearly is a problem.

This particular case I had done about four years before she had represented with this lesion in that particular area. Now, the implants looked to be reasonably

sound radiographically. We disassembled the frame and we saw this particular type of lesion. Now, in my aging population in Florida, I was not adverse to think about squamous cell carcinoma as a particular diagnosis for this particular case since she was a smoker and radiographically did not show any clinical signs of breakdown. And it did turn out that that was, indeed, the clinical diagnosis of her particular case.

As we further developed this etiology slide, we now have two major categories, biomechanics and microbiology. So we've left the patient factors and now we're into certain other aspects. So with etiology, we can look at infectious processes or traumatic or overload factors, or, as we see oftentimes in the dentition, them working together as cofactorial, and then, of course, patients may have some systemic input.

What causes crestal bone loss? We rarely see periapical lesions around implants. We see them breaking down at the crest. If we look at this list of reasons, many of them are operator involved. There are a few implant design which may be from the manufacturer's perspective, but many of these are controllable by the clinician as we are diagnosing and handling the case treatment.

These are two signal tooth molar implants that I

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placed approximately eight years ago, prior to the advent and the popularization of wide-diameter implants. Both of these have some crestal bone loss. They're both still functioning and successful implants. But I think we can do much better for our patients with a wider design in this particular type of clinical indication.

How about two standard size implants rather than one large-diameter implant? I'm sure the manufacturers from a marketing perspective would prefer this treatment plan because they can sell two implants rather than one. Well, we now have a manageable metal fircation which is reasonable to manage. Here is an indication where the implants were closer together and this is actually a non-manageable fircation type of a situation which may break down over time. So the data is now coming in on single-tooth sites and molar areas with a single wide implant or multiple implants.

As you can see on the upper case, implants are being placed predictably into the teragoid area so we don't have to do sinus graft. So as a clinician that's doing a variety of techniques, we are attempting to utilize a variety of methods, both teragoid implants, sinus graft, as I showed earlier, implants below the sinus, and then a total edentulous mandible can predictably, with a cross-arch

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design, give us a cantilevering effect.

What about a unilateral cantilevering effect, and you see over time, this implant and the prosthetic coping has separated from the joint and this whole prosthesis had to be redone with a broken abutment screw on top of the implant.

This is a more dramatic problem related to cantilever. These are two small-diameter microvent-type implants and you see the excessive cantilever that was exerted onto this single implant, two teeth on a 3.25 diameter implant, another dramatic example of an explant of a microvent 3.25 diameter with two teeth for one implant.

Here is a short titanium screw implant, again, in an overloaded situation where you would have a short implant supporting its tooth and an adjacent pontic [ph.] attached to a natural tooth with an attachment mechanism. This is something we find if we carefully review our x-rays. You can see a little bit of crestal loss, but what's interesting about this particular case is the natural tooth splinted to this implant prosthesis had a coping device cemented on the tooth and we see a separation area right here. So we're getting what appears to be an intrusion of the natural teeth. So when we're adding teeth to implants, we sometimes have this intrusion that has taken place and several

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colleagues are investigating the etiologies.

If I could get ten or 13 millimeter long implants in a unilateral design, I would feel comfortable with a cantilever situation for most patients. I would much prefer not to have a cantilever as you see on the x-ray on the right slide.

In a cartoon manner, these show graphically what we are faced with as clinicians with regard to crown implant ratios. If you have a short implant and you're restoring a tremendous amount of former bone and clinical crown, a very simple force can cause what some people like to call overload or a traumatic force. On the other hand, if you have a well-formed ridge, a well-anchored implant, it takes a much dramatic greater force to actually give an overload situation to that design. So while each force might be similar, it could be greater in a site where the implants are shorter in dimension. So as a clinical recommendation, I think the FDA's consideration of length of implants should be within the guidelines that you presently have.

There was an interesting paper from the colleagues about smaller diameter. That may be something that you may want to look at for certain types of indications. Where I could get in four implants, one for each tooth, I believe that's a very predictable situation.

Splinting implants to teeth is not desirable. When done properly, it can work. However, if you look through the literature, Professor Rangert, he has actually talked about "a little bit of play" in the fit over the hex, which helped the situation get a teeter-totter effect, where you're tying a rigid implant to a tooth with a periodontal ligament. I'm not sure that's exactly what we would like to see, but he had mentioned that in his lectures.

The ITI group are much more confident in their concepts of splinting to natural teeth and they actually would recommend a permanent cement. So you see a diversity in what's recommended to the clinicians. I would prefer to do it not with teeth. I'd rather do it just implant-supported.

I've shown this case because it shows beautiful technical laboratory work, probably as lovely as most that you've seen in any of today's presentations. This case was treatment planned to have the natural dentition by itself and the implant restoration by itself. However, when I saw the patient back, what do I see over here? We see a very significant misfit of the case and it is very sad for me as the surgical member of this team to tell my highly qualified restorative colleague and his technician that they basically have to strip this case and do it all over again or you're

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setting this case up for a mechanical problem.

We have looked at breakdown analysis with a lot of factors and prosthetic design comes into play. This is one of the cases that was done by my restorative colleagues in the past. You don't have to be an orthodontist to see that that's a poor prosthetic design. So this is what is contributing to implant complication.

Here is another case with cylindrical implants with a large cantilever and these implants eventually failed and it was also attached to the natural tooth. So this particular prosthetic design was attached to a natural tooth. It had cementation on the natural tooth, a screw design over the implants, a cantilever in a unilateral manner, but I was proud that I enhanced the zone of gingiva, although we wound up losing the implants nevertheless.

Off-angle presentations--I believe that the clinicians today are doing a better job because we have augmentation, grafting, and regeneration to do prior to implantation or in addition to implantation. So I believe that the use of these preangulated components is less than it has been because we, as clinicians, are doing them in a much more precise manner.

This model, I got from one of my local laboratory technicians who asked me what type of components would I

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recommend for these restorations. This is probably not acceptable therapy from a medical-legal perspective in today's environment with what we can do as clinicians in building up and augmenting ridges.

Component fit, I think, is critical, and that comes in the biomechanical arena. A single tooth restoration was placed and at low power, it looks not too bad. Clinical view, we did a new crown here, new restoration of the implant. Everything is looking good. But if you look real carefully right here and right here, there are slight gaps in the prosthesis. This one particularly bothers me because that's a cement zone, cemented crown, and I believe that these types of wiggling and jiggling could cause problems to the ultimate integration of the implant. So this, I would deem in my practice as an at-risk site and we would want this patient to come back at at least a three-month interval for recall.

This is an implant that I had placed in a patient at the time of surgery and I tapped it off access. Implants come in different types of material. This particular system, I believe, was a grade three metal and that is the yield strength numbers. Several of the companies have presented different types of titanium in their systems and they definitely have different types of yield strength. I'm

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not sure that there's any improvement one way or another with integration rates, but there's certainly definite mechanical differences in the different types of materials.

This case had the cantilevering effect, because we did not have wide-diameter implants at that time. This is what it appears like radiographically, and when you first look at the x-ray, you don't really see much of what's going on. The patient presented with tenderness, probing, and a swelling in that area. I started disassembling the case and you see the difference between this site and this site is that this has the external hexagon from the top of the implant, whereas this one does not, and there it is.

And at SEM analysis, you see that the abutment screw acted as a fulcrum, and if we go back just to look at the x-ray for a second, when there is bone loss, for whatever the reasons of crestal bone loss, and there were several reasons presented, these mechanical forces of the abutment screw can act as a fulcrum to have fatigue of the implant metal and it could fracture.

Another cantilever design of a fractured implant. This happens to be a fractured cylindrical titanium alloy implant, whereas that's a CP titanium implant.

I believe Dr. Moreland's practice, he claimed that he had not seen in his practice any abutment failure that

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led to implant failure. I'm not sure that's exactly what happened in this case, but this is an abutment failure and the distal implant had become loose from teeter-totter, or maybe it was a coated implant design and had inherent concerns, but I believe it was more of a mechanical consideration.

This particular prosthesis, you can see, has no porcelain in this area. This particular patient had a tremendous and powerful bite. They broke the abutment at this point here and we tapped the case out. We were able to remove the different components, because it was a screw designed case. We placed a healing abutment, referred it back to our restorative colleague, and the case is now able to be redone prosthetically.

Now, this case is interesting because it underscores what happens to our patients if they have a complication or a failure. This is something that's not dramatic. It is able to be redone and replaced, and here are the pieces being broken apart.

This advent of a torque driver has been very helpful to us as clinicians because we're now able to induce the screw tightening to the manufacturer's specifications, which we weren't able to do in the past.

This retrieval study by Andy Bucks on a Sterios

HA-coated screw shows a couple of things, good HA integrity on the surface and excellent integration with a single tooth in load.

A more dramatic explant from the work of Joel Roselick, this implant was also an HA-coated screw in a maxillary sinus augmentation case, and you see intact HA in load. The implant had fractured. You still see some of the osteograph end particles still reabsorbing over time, but you see in function in a compromised bone site the HA material can remain intact.

This was an interesting case clinically because I had had three implants. We had good zones of gingiva and we were seeing this radiographic evidence of breakdown. Prior to opening up the case, I had done some culturing and DNA probe analysis and did not get any positive results to any of the pathogenic flora. We opened up the case and I did not see the pitted HA surfaces we sometimes see when we have problematic infectious sites on the HA-coated implants.

Clinically, there were steep cusps prior to this occlusal grinding that I had performed and we had deemed this case to be more of an occlusal-related problem, and this is that same patient eight years later with no evidence of further breakdown and the patient judiciously uses clohexadine rinse and we have flattened out the occlusal

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scheme in that particular case.

HA definitely has positive and negative effects. This implant case was a three-unit bridge. We see some breakdown. This tissue was biopsied after I had performed the clean-out and I asked the histopathologist, is there any refractile HA material in this granulation mass, and this area right here, all these dark purple areas, are actually particles of hydroxylapatite. Now, if we go back to the clinical design, we see a three-unit bridge on a tooth, and would I do this case the same today? No. I would have a single crown and I would have three implants splinted together. So is this an HA coating problem or is this a Jack Krauser problem?

I was interested in peri-implant infection, and this is just one representative sample from a study that I had done at Ohio State University, one of the graduate periodontists, and we looked at induced peri-implantitis on titanium plasma, HA, and titanium surfaces of exact geometric design screw implants and this was a phagocytotic response to some of the HA that had come off that particular site. We did not see that type of phagocytotic response with the titanium or the titanium plasma. So when Dr. Lore Langer mentioned that implants failed differently, I would concur.

This is what an HA implant looks like when it's in an infectious failing situation. You see the pitted situation on the surface of the implant and you see some bone loss in this area. Today, with augmentation materials, we're able to take this out with a trephine, rebuild the ridge, and redo the case. However, pre-clinically, we have better treatment planning methods and we probably would not run into this because we would not be involved in overloaded situations.

Lore Langer presented a paper that I had done with Thomas Golick that was published in 1991 on consecutively placed HA-coated implants. My contribution was approximately 1,200 implants and Tom Golick's was over 2,000 implants. The study was called a long-term study, but if you really look at the data, it was like some of the other studies where the cases were from one year to seven years.

So taking that criticism properly, I reanalyzed the same data and took only implants that were restored for at least five years and we retrospectively analyzed that information and I did that with a colleague from Sulzer-Calcitek and I did receive a commercial stipend for helping with this project. This data was then presented to the American Dental Association for integral systems ADA provisional and final acceptance as an approved device from

ADA.

So when we looked at the 1,200 originally that were less than the five years, there were actually 325 that were at least five years or more in function. Any failure that had occurred prior to that was included in the failure situation.

Now, if you looked at the results, my area of failure tended to be in the posterior regions greater than the anterior regions, and that tended to be similar to data that was presented by Axel Kirsch at that time, in the early and middle 1990s. He and I would present these data with those types of results. This implant survival by location chart shows really no difference between maxilla and mandible, and in the overall success rate, we had that situation for both arches.

Now, my x-rays were sent to an unknown site and the reviewer was unknown to me at that time, hence the double-blindness, and we had an independent review of the x-rays and it turned out that Marjorie Jeffcoat at Alabama-Birmingham did the analysis of my one to five or greater years post-operative x-rays to determine the bone loss analysis based on, because of her computer program, she could only get a mesial and distal change. Breaking out, because it says all centers, just my data, Krauser's data,

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it shows between 0.2 and a little more than one millimeter of the study that she had seen and it was a progressive situation and it is an average. I think Dr. Hefez asked the previous speaker about how do you determine the bone loss. It's a mean situation of the bone loss. So we did not see tremendous breakdown situations.

These two cases are over 12 years old. They were done in 1985 and these were recalled in '97. You see from the original protocol design, these implants can work nicely in both mandibular and maxillary cases.

I also want to share with you the poor prosthetic concept that was incorporated in both of these cases because the components as given by the manufacturer in 1984 were hardly as good as what we see today.

I just have about three more minutes?

DR. GENCO: About two minutes.

DR. KRAUSER: I'll try to wrap it up. Mambelli was the first to talk about peri-implantitis and microbiological effects and he presented the site-specific nature of breakdown. I believe it goes hand in hand with peri-implantitis or concepts of biologic width when we as clinicians are working with adjacent teeth. So we can handle crown lengthening and sinus augmentation at the same time, and this is a more contemporary way of handling our

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implantations. So we're able to get a better fitting restoration and a better fitting implant restoration with a sinus graft as an isolated area.

I'm doing a small pilot project with Dave Cochran where we're intentionally placing one-stage implants slightly above the crest and we're following them to see if having the microgap above the bone crest makes any difference and we're following a few cases. We have seen microbiological breakdown plaque on these titanium screw implants on titanium as well as HA-coated implants. We believe that the design of implants are risk factors from a microbiological perspective. We talked about roughness earlier today, the hollow and the solid designs, one-stage versus two-stage designs.

This is an interesting case because somebody brought up galvanism. This was a subperiosteal implant in the posterior with root form implants in the anterior and a superstructure of a totally different material and you could see the soft tissue complication and you could assume what the underlying bone complications are.

Those are just showing some problems of patient hygiene. This shows the site specific nature of breakdown. Here, prosthetic design and implant placement became a problem with framework, as it did with this one.

Another situation with a prosthesis over the implant is causing a problem. Sometimes the misfit of the components can cause a fistula, and when it gets severe, you will get an explant device.

Surgical protocol is interesting. Tarnow and Sharf has presented a paper where dental operatory with an aseptic protocol yielded results as good as operating room procedures.

So in summary, there's a great list of biomechanical and force-related factors that go into implant complication and failure. So in conclusion, we, as clinicians, will have patients that are good, the bad, and the ugly, and my final etiology of implant loss slide has added to it the iatrogenic factor, because I believe as a clinician, we are the ones that are causing the complication, not the manufacturers.

So I would like to state that a reclassification for class II will be just fine for a clinician's perspective and education, which we can get because the manufacturers will have more money to spend, would be acceptable.

Thank you for your time.

DR. GENCO: Thank you very much, Dr. Krauser.

We're running a little late. I think what we'll do, unless anybody has a burning question of Dr. Krauser,

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we'll proceed on to Dr. Sendak. I'd like to say that what we're going to do is we're not going to take a break this afternoon. So if any of you have to get up and leave for a minute or two, we'll understand.

DR. SENDAK: Thank you, Dr. Genco. I appreciate coming at the tail end here. I know there's a lot of pressure on time. I'm going to try to be very responsive to that issue and keep my presentation to an absolute minimum.

I had the opportunity before to present on mini-dental implants as temporary or transitional devices. I am the inventory of the Sendak's mini-dental implant. I'm also here as the person involved with regulatory matters, and so I think I'm in a good position to offer some additional commentary that I was not able to present last time at the November meeting. These issues really relate to just a few areas that, interestingly enough, were covered in some respects by quite a few of the other presenters today.

One of the most obvious ones that comes to mind is that, as you know, the mini-dental implant is devised or is conceived as a transitional or temporary implant. It addresses perhaps the most vexing problem facing skilled implant specialists as well as entry-level practitioners and that's the mutual need to smoothly manage awkward transitions from dentate to partial or total edentulous

patient status without resorting to often emotionally devastating removable prostheses at just the wrong moment in the whole process, the reconstructive process.

Also, we have to think about the aging of our population today, the costs of implant dentistry, the time-consuming aspects of it. There are many issues that we are facing today that perhaps mini-implant strategies can begin to address. The temporary transitional use to avoid some of the things that Dr. Krauser was talking about in terms of iatrogenic problems. Dr. Deporter and others were referencing unknown factors in causing a lot of loss of implants for reasons that were somewhat obscure.

Some of these clearly could be suggested to occur because of iatrogenic overload of the devices, the implants, fixtures, while they're integrating because of simply iatrogenic overload from removable prosthodontics, and we're very quick to say how bad a removable prosthesis is, and this is causing all kinds of problems. And we're quick to say, or to suggest, at least, that these are devices that are really creating tremendous problems. They are creating problems, but what other alternatives do we have if we are not going to give a patient a removable to get them through these difficult transitional periods. So that is where, perhaps, the mini-implant has its most immediate and obvious

application.

The device itself is a self-tapping titanium threaded screw indicated for intrabony and intraradicular transitional applications to permit immediate splinting stability and ongoing fixation of new or existing crown and bridge installations of full or partial edentulism and employing minimally invasive surgical intervention. When I say minimally invasive, I mean it. You do not, in most of the applications for this device, have to incise tissue, flap tissue, and ultimately suture tissue, which sounds like pie-in-the-sky time, but, in fact, when applied properly, can be very readily utilized with that particular protocol, as we'll discuss very briefly here today.

While CP titanium may be utilized, the preferred titanium alloy, the titanium 6 aluminum or vanadium formulations are long accepted by a compatible metal, which Dr. Krauser again addressed a moment ago, which has the added benefit of significantly greater tensile strength than CP titanium according to ASTM specifications, the specification being B348, which demonstrates that there's a 62.3 percent greater strength, the tensile strength, than grade four CP titanium, which is the strongest of the commercially pure titaniums.

Now, also, a solid one-piece design for--remember,

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this is a 1.8 millimeter width implant. It's certainly by far the narrowest implant that's come under discussion or observation today and, I'm sure, gives pause when you start to think about whether or not that's acceptable even for a temporary or transitional device.

However, we have been at this for over 20 years plus and we have found that once we made the switch from the CP titanium of the rather crude initial devices, which were essentially modifications of standard titanium root canal posts, manufactured at that time by Dentotis, once we made the switch to the alloy, the problem of fracture was eliminated, and I'll show very quickly just a few bits of data so that you can see, grasp what I'm trying to get at here.

As I said, the solid one-piece design for the combined screw and head portions provides added strength to offset the small diameter, the 1.8 millimeter width dimension of the MDI.

Total device lengths of 14, 17, 19, and 22 millimeters provide a sufficient range to encompass most available ridge heights encountered clinically, increasing the potential indications.

The ability also to deploy multiple MDI elements in the space typically occupied by a conventional width

fixture is an additional useful feature of 1.8 millimeter width MDIs that not only offsets the apparent reduced surface area in contact with bone but also increases the total number of abutment supports placeable for functional stress distribution in any given space.

The soft tissue effectiveness factors that relate to the health of the peri-implant soft tissue environment during the useful life of the mini-implant in situ is quite important, along with the commonly accepted signs of peri-implant health, which include lack of bleeding tendency, lack of pain and tenderness, lack of redness and inflammatory edema, lack of hypertrophic reactivity, and minimal pocket depth with a stable resumed hemidesmosomal hypopolysaccharite attachment at the gingiva cuff level. There is also the still somewhat ambiguous issue of attached peritonized gingiva and its role in peri-implant soft tissue health.

Most contemporary opinion is perhaps best exemplified by the exhaustively documented American Academy of Periodontology view that while attached gingiva is not absolutely essential for peri-implant health, it is considered a useful bulwark against invasive pathogens and peri-implantitis.

The mini-implant occupies a unique position in

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that its ultra-small 1.8 millimeter footprint permits it to be placed directly through small patches of keratinized gingiva, avoiding the areas of unattached tissue, which seem to heal at a slower rate, are associated with reactive edema, and ultimately seem to be less conducive to maintainable peri-implant health.

A retrospective assessment of the 575 mini-implants placed to date have clearly demonstrated the consistent peri-implant health surrounding these small devices and it is the considered opinion of our team that a significant component of this positive health factor may be attributed to the precise ability to target mini-implants into limited areas, keratinized gingiva, without the loss of significant soft tissue substance that often accompanies flap procedures.

Unquestionably, larger, conventionally-sized implants would blunderbuss such small attached tissue patches and end up at least partially in unattached gingiva, potentially, at least, compromising the perceived benefit.

The last issue I want to discuss is to how these are placed and why. They are self-tapping in the real complete sense of that world for a small device. There's an absolute minimal osteotomy or preparation. Minimal drilling is the essential distinguishing feature of all mini-implant

osteotomies. Fine-tapered diamond or carbide drills with copious sterile irrigation are the prime devices for initial penetration through crestal soft tissue and crestal cortical bone and then into the more cancellous medullary bone site.

This minimal osteotomy, usually comprising about one-third of the length of the typical 17, 19, or 22 millimeter length implant, is almost 80 percent of the time--80 percent of the time--sufficient to provide the initial bite for the take of the mini-implant into the bone, just, in effect, like a wood screw. That is truly a self-tapper, if ever there was one. Simple thumb wrench or ratchet wrench drivers are readily effective inserting devices, so then self-tap the mini-implant all the way to the level of the protruding abutment head portion of the implant.

Since the device is a one-piece machine system of unique simplicity, there's diminished potential for insertion complications, and as previously delineated, any misdirected starts may be readily corrected by restarting the insertion process in a different trajectory or contiguous location.

Occasionally, small stubborn areas of dense bone are encountered, not only in the synthesis region but with less frequency throughout the maxilla and mandible. In

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these instances, an internally water-cooled 1.6 millimeter drill is used to lightly and briefly penetrate into these resistant strata but without greatly extending the process to avoid over-instrumenting the bone. Perhaps the most significant cautionary guideline in the entire MDI insertion protocol relates to avoidance of bony over-instrumentation. That's probably true about all implants, but certainly in this case, since there's virtually no real osteotomy going on here to speak of, this is critical in this case.

Osteo-integration can only occur on an immediate basis when maximal self-tapping by the implant is encouraged to happen without the usual fully realized osteotomy associated with conventional dental implant operations.

I would like to also say that we have addressed the issue of strength in a very specific way. We've asked the University of Alabama to do very carefully evaluated testing on yielding strength and on ultimate strength and we've basically shown that at 1.8 millimeters of width, we're getting, literally, with the mini-implants made out of the alloy, just about two times more effective ultimate strength and yielding strength than the CP titanium in this particular application. I am not suggesting that this applies outside of this milieu. This is a particular setting and particular application.

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With this said, I have many other things I would like to address and talk about that I think you would find interesting and compelling, but I know the time is really very pressured right now.

So I'd just like to conclude by suggesting, with respect, that the FDA could perform a very useful function in leaving what is essentially or permitting what is essentially a very simple traditional implant device with considerable strength, one-piece casting ability, and easy insertion and reconstructive protocol to be placed into a class II category. I think it would then have its greatest application and usefulness in this field and we do need a device of this sort. After 22 years of applying it, I think I can speak with some satisfaction and assurance on this subject. Thank you.

DR. GENCO: Thank you, Dr. Sendak.

Are there any comments or questions from the panel?

DR. STEPHENS: Yes, I just have one.

DR. GENCO: Yes, Willie?

DR. STEPHENS: What would you consider the upper limits of the length of time that this implant ought to stay in, and is it different for multiple units than one unit, single units?

DR. SENDAK: Well, these, when they're placed, according to standards that we've just been suggesting, are free-standing and can support themselves. They are not sort of depending, they're not sort of leaning on anything else. They can be self-supporting and they get immediate integration. If you use the classic Branemark way of looking at it, you get a close--by self-tapping, you're getting an immediate integration. That should be self-tapping, or that should be integrated, rather, and that can be used in any one single application or multiple application. I've used them in all manner and variety of application.

I'm not sure I totally answered your question, though.

DR. STEPHENS: How long is temporary?

DR. SENDAK: Well, temporary, we like to use the term--I mean, for FDA purposes, we're using the term temporary strictly. I prefer the term transitional because one man's or woman's temporary is someone else's transitional, which could be for an extended period of time. It depends really on what the application is. What are you trying to do, in other words?

I think these can sustain themselves for as long--if they're placed according to the protocol, they can

sustain themselves for as long as necessary. They can be backed out easily when they're placed in for short-term periods because it's just a question of reversing the procedure. The 1.8 millimeter width permits a back-out without, even though they're a close approximation of bone, they're not integrated in the sense that a large implant cannot be really rotated back out. Yes?

DR. STEPHENS: Six months or five years?

DR. SENDAK: Well, as I say, I've had some inadvertently where patients--we've placed these in patients--my first case, about 23 years ago, was for a voice teacher who did not want to have any transition with removable. So we put a simple removable denture on top of a whole flock of these in the mandible where there was no room for anything except these, and I don't know whether I should be happy, apologize, or congratulate myself, but the patient is still wearing the same system.

Now, I am not standing here before the FDA and suggesting that that's the way anyone here should look at. But I think looked upon as a transitional device, I think it has enormous application in that respect.

Did I properly answer you?

DR. STEPHENS: Not really.

DR. SENDAK: Not really? Can I amplify on it?

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How long have I had them in? Well, as I say, some have been in many, many years, sometimes because the patient wouldn't permit anything else.

DR. STEPHENS: We have to distinguish between temporary, or temporary but you can leave it for a long time.

DR. SENDAK: Well, temporary, if you're waiting simply for other implants to integrate, conventional implants, which is the sort of baseline application here. You have a series of implants. You don't want iatrogenic damage to those implants, classic implants, whatever type you choose to use. Any of those that were discussed today could be the kind of implant.

If you want to support a fixed temporary prosthesis or transitional prosthesis or whatever you want to call it during that period, these devices consistently have been shown to do that, and we received our 510K the end of last year, I'm pleased to say, because I think we were able to demonstrate that this, in fact, was the case. We also received--again, that doesn't perhaps have too much bearing on the whole situation, but we did receive a patent allowance for the whole device and reconstructive protocol, suggesting at least that this is an innovative approach to a classic problem.

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DR. GENCO: Comments, questions, further?

[No response.]

DR. GENCO: Okay. Thank you very much, Dr.

Sendak.

DR. SENDAK: Thank you.

OPEN COMMITTEE DISCUSSION AND VOTE

DR. GENCO: We will now proceed to the open committee discussion and vote. We have been presented with questions and considerations by the FDA and I'd like to have you look at those and let's discuss them.

The first is, as we know, all endosseous dental implants of all types are presently class II medical devices--class III medical devices. Given the information that we have received and heard regarding each subgroup of dental implants, do you think there's sufficient data to establish appropriate special controls to adequately control the level of risks and to provide a reasonable assurance that the device can be used effectively, and that really leads to the second question if class II is recommended.

Does anybody want to begin this discussion? Yes, Mark?

DR. PATTERS: Certainly for the root form implants, I would say there are very few things in dentistry that we have this much data and this much data which is

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overwhelmingly positive in showing safety and effectiveness. So my answer for the root form implants would be unequivocally yes.

DR. GENCO: Okay. You're thinking, then, of class II recommendation with controls?

DR. PATTERS: I am, indeed.

DR. GENCO: Any further discussion of that for the root form? John?

DR. BRUNSKI: I was just going to ask just for a clarification, perhaps, from the FDA. I was reading through some of the documents on special controls and I understand that the use of a guidance document is a perfectly fine means of establishing a kind of a special control, and in that guidance document, a number of things can be often specified, correct? Am I correct in thinking that way?

DR. GENCO: Yes. What I've heard is, I think today and last November, we heard at least three types of special controls, one technical, standards for materials, standards for benchtop testing, standards for manufacturing, either GMP or ISO 901.

And then we heard another type of control, which was that as appropriate clinical investigation may be required, even though it's a 510K, it's a modified 510K, and please, people from FDA, correct me if I'm wrong on this, so

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that those guidances with respect to the clinical protocols, number of studies, number of subjects, conditions of studies, outcome variables, et cetera, could be established, have been established, may be modified.

And then the third type that Dr. Marlin discussed and that is educational special controls. So I think those, if the decision was to reclassify it as class II, then those three types of special controls, any combination of which could be applied to these implants.

Okay. Let me ask, we heard root forms and I think we heard also about some unique root form implants. For example, we heard about the Sargon type. We heard and read about the teragoid implants. Now, when we mean root form, are we to include those two or the traditional screw, hollow screw, basket-type, solid core with one or another coating? I'd like to get you to think along those lines. What do we mean by--how are we going to define root form endosseous implants? What's included? Mark?

DR. PATTERS: I'd be willing to interpret that as broadly as possible. It will be the manufacturer's responsibility to show that their product is essentially equivalent. So I'd look at it broadly.

DR. GENCO: Okay. So let's go to the example of the teragoid. So what you're saying is that if the implant

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was designed for the teragoid, if it's a root form type, that maybe the FDA might require clinical studies, as appropriate?

DR. PATTERS: Exactly.

DR. GENCO: Okay. How about the Sargon type? That is, you could interpret that as having a special retention device. Let's look at that in particular. Is that one with a retention device that's so unique as to remain in class III or what are your feelings? Would that be a class II, with in mind that one could require clinical studies, as necessary. Leslie?

DR. HEFFEZ: My impression of that implant, it's more--with an internal device, that it should be considered as a class II device and it would simply be a modification of an existing. That's my impression.

DR. GENCO: Okay. Are there any root forms that we've heard about today or read about since November that would not be in this definition of root forms? We saw pictures of those with fins, various types of designs. Any limitation in terms of diameter?

DR. HEFFEZ: My impression is that if the implant, the means of retention is primarily through the use of the screw-type device or cylindrical type device, that its principal means of retention is through that means an

alteration of its surface and it should be considered a root form implant. Any other modifications other than I've just--I mean, if the principal means of fixation is the cylindrical or the screw-type form, that it should be considered--

DR. GENCO: So you would include the bicortical screw, the Oratronics?

DR. HEFFEZ: Yes.

DR. GENCO: How about the last one that we heard, the Sendak mini-implant?

DR. HEFFEZ: The way I try and perceive this is that they should be almost grouped in the pattern of their failure. If they're going to fail in the sense that a majority of these fail and then simply remove the implant, it may be encased by fibrous connective tissue, I think that they should be lumped together. So I think the pattern of failure is the same and I would consider them all together.

DR. GENCO: Okay. Any further comments, then? I think what I'm hearing is that the mini-implants, the Sendak, the Oratronics, the Sargon, and the teragoid, plus the traditional screw, hollow--

DR. PATTERS: The bicortical screw.

DR. GENCO: The bicortical screw is the Oratronics. Yes?

MR. LARSON: Well, in the U.S., Oratronics refers to a blade implant. That's why Tronics Oral is--

DR. GENCO: Oh, Tronics Oral. So we can be very clear, Tronics Oral, the bicortical screw, the two-and-a-quarter diameter bite, the 26 and 36 millimeter length. Okay. John?

DR. BRUNSKI: And by the way, when you're saying teragoid, are you referring to the Onplant or the Zygomatic or--

DR. GENCO: No. No. Zygomatic is--

DR. BRUNSKI: Okay.

DR. GENCO: I purposely didn't bring in the Onplant. I mean, we could discuss that, but it doesn't seem that that is root form or is--not traditionally endosseous, although it could have an endosseous component. Now, if you want to include that, this is the time to do it. Jim?

DR. DRUMMOND: I guess I have a question as to a lot of these implants have much stronger clinical studies than other implants.

DR. GENCO: Okay.

DR. DRUMMOND: If we group them all together, do we then go back and ask for some of these newer products to substantiate or do we classify them as something else? I'm getting confused.

DR. GENCO: Sure. No, I think the special controls could include clinical studies, as appropriate. Now, the "as appropriate" is decided, I think, by the FDA staff. Tim, is that correct? In other words, we're dealing with five or six today, but you may get number seven tomorrow.

MR. ULATOWSKI: Right. You're dealing with what you have in hand--

DR. GENCO: Exactly.

MR. ULATOWSKI: --and if you're going to lump, you have to deal with the data in hand. Anything that comes down the pike, should you, for example, recommend class II, we'd deal with in a 510K with clinical data or whatever else you would suggest in determining, yes, it's in the same bin or it's not.

DR. GENCO: Right. So you could get the seventh next week with a new kind of fin or what have you, a little different, maybe significantly different, but still within the endosseous root form concept that you could make the judgment to ask for special--excuse me--special controls could include clinical studies.

MR. ULATOWSKI: Right, and also the class II and the 510K process allows for progression of technology over time as new designs come forward and data is assembled.

DR. GENCO: John, is that clear? In other words--

DR. BRUNSKI: Yes.

DR. GENCO: It may very well be that those that we've heard about today don't have sufficient data. I'm not saying they don't, but they may not. Excuse me, Jim, I guess you asked the question. I'm sorry. So that the FDA could ask for even some of those that we heard today for the data, even though they're class II, to approve the 510K. In other words, it would be a modified 510K with data. And then the other special controls are the technical aspects and education, if we think that's appropriate.

DR. BRUNSKI: Just the other clarification is, in November, we had that grid where we were also considering the indication at the same time. How is that figuring into the decision making?

DR. GENCO: Okay. One of the considerations that I heard then and heard today was the anatomic location. Is this what you're talking about?

DR. BRUNSKI: Well, also issues like for, let's say, immediate loading as opposed to delayed loading. You know, if a device is, let's say, class II or we decide it's a class II recommendation that something that's done in a delayed loading situation, we have to separately consider whether to specify something for immediately loading.

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DR. GENCO: Susan, do you want to address that?

DR. RUNNER: From my review of the transcript last time, no one mentioned last time any special concerns about location, immediate loading, extraction sites, those types of issues. If you do have issues about them, you should let us know now. But the way I had interpreted from the last meeting, you just basically split it into those four groups, root form, blade, special retention, and temporary. You did not mention anything with coating or with any locations or other indications as being significant in terms of classification.

DR. GENCO: Do you feel differently now? Does anybody feel differently with respect to that particular question of indications, either anatomically, anatomic indication, or load, immediate load, extraction socket, immediate or late, and any of those considerations of concern for anybody with respect to classification or special controls.

DR. BRUNSKI: Probably because I left early, I didn't come in, or didn't hear the end of that meeting in November, but my only concern would be that it seems to me we're leaving a fair amount to the FDA to decide, because just personally speaking, it isn't necessarily obvious to me that every single root form implant is equally well

substantiated in these various kinds of indications. You know, that's just my feeling about it. I don't have any objection in proceeding to group them the way we're grouping them, but the indication issue is something that I guess the FDA will have to handle in some respect if we're not.

DR. GENCO: Would you like to give--I mean, you could talk about a special control for--what would you like, implant in extraction sockets to be evaluated separately from healed ridges? Is that the kind of--

DR. BRUNSKI: Well, here's a question maybe for the FDA. I mean, if somebody came out with an implant and wrote down specifically, this has an indication for immediate loading, would the FDA be likely to want to see something in a guidance document form to substantiate that?

DR. RUNNER: Well, typically, in the past, we've approached those different indications with requesting clinical data. But as time went on, it was pointed out to us that many of these indications, like using a fresh extraction socket or immediate loading, were actually pre-amendments claims and, therefore, were allowed to be included in the claims for various 510K implant systems that are on the market. So that's how they came to be. If we felt it was something that was not pre-amendments, we would have asked for clinical data. But people kept finding more

examples of implants that were pre-'76 that were used in fresh extraction sockets or immediately loaded or were of a particular diameter.

DR. GENCO: But would there be--

DR. BRUNSKI: Even if it's pre-amendments, if the product comes along, you still may request data to substantiate its equivalent performance.

DR. GENCO: Does the panel--is there sufficient concern of that to articulate this in special controls? In other words, studies to be required as appropriate, for example, preloading, immediately loading versus delayed loading, fresh extraction socket versus ridge. John, do you feel comfortable? We can, I think, word that special control in such a manner to spell out some of these conditions that we're aware of now that you have concern about.

DR. BRUNSKI: I don't know if I'm arguing for that so much as I'm just making sure that there are existing mechanisms in a special controlled fashion that could ultimately be brought to bear should somebody at some point think that this is relevant. I mean, there's so many different indications and so many different kinds of implants that I think it'd be difficult for us to look at each one and start to craft language on that.

DR. GENCO: Okay. Would something like this, clinical investigation, as appropriate, would be required for unique applications, indications, design? Is that sufficient? I mean, that could be a special control, I think, Jim?

MR. ULATOWSKI: We would retranslate that probably as far as the special--well, in the sense that the special control is a guidance document, and in the body of the guidance document, we would accommodate those concerns.

DR. GENCO: Okay. With some specifics?

MR. ULATOWSKI: Right.

DR. GENCO: Okay. Yes, Dr. Jordan?

DR. JORDAN: In these special controls, will you be asking the manufacturer to do the studies or would you be asking them to contract with someone to do it independently?

DR. GENCO: I think that's up to the manufacturer. As long as they're good studies, whether they did them in house or contracted with universities or what have you, I don't think that's--

DR. JORDAN: Well, sitting here in the consumer's seat, I don't share the opinion that we've heard lots of good studies here today. We've heard a lot of studies. I find it difficult to form some out. I don't know what success means. In some studies, there's a whole variation.

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You have a ten-year study and five people have been in the study for ten years. That's not a ten-year study to me.

So I think somewhere, if we're going to start requiring this to happen--I mean, intuitively, class II doesn't bother me, because intuitively, and I'm being intuitive, too, I haven't seen many people running around complaining about their dentures or their prostheses not working well.

But in terms of an objective study, I think if one is going to rely on it, there needs to be better controls than I've seen today in terms of the quality of research that's going to document it and I would not want to just say, let the manufacturer, who has an obvious interest, who's both the dentist sometimes and the manufacturer, too, be the one to also provide me with the data. I'm going to guess what the data's going to be in some of the cases.

DR. GENCO: Dr. Runner, do you want to address that?

DR. RUNNER: Unfortunately, that's the way the agency works, in that we give the responsibility for the studies to the companies and we assume that the data that is provided to us is valid. If we have any questions about the validity or the truthfulness of the data, we have methods for investigating that. But we go by the assumption that

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all data provided to us is valid and above board.

MS. SCOTT: If I can add to that, the panel can outline clinical study recommendations or clinical protocol that the panel would like to see in a guidance document that FDA produces in terms of what type of study protocol is recommended for these clinical studies in order to provide the type of data that's necessary to evaluate the devices. So that may help, too.

DR. RUNNER: And the guidance documents that we already have have specific testing requested, so that there are parameters as to the type of testing we would request for bench testing, coating characterization, et cetera.

DR. JORDAN: I may misquote, and I apologize if I do, but I do recall in some studies, some of the major presenters, the majority of the data were done in private doctors' offices. I'm a private physician as well as working at a medical school and I do data also from my office as well as the medical school. There is no question that what I can do in my office is much easier than what I would have to do if I go through an IRB in a medical school. I think if you're going to put this responsibility back on the manufacturer, then I think there should be some university, some independent IRB regulating this and not just my company saying, I've done this data.

DR. GENCO: I'm familiar with some of these guidance documents, having been involved in their drafting, and I know that, as Susan said, there are suggestions or requirements that they be independent, at least two independent, and they be multi-center. Of course, I think every one of them goes through the IRB. Even though they're done in an office, there are independent IRBs that if you're not associated with the university, you can hire an IRB to approve them. So I think they would all be done according to the Geneva Convention.

I mean, obviously, we would want that in the guidance document. I can tell you it's probably in the guidance document, but we can reiterate that. We can reconfirm that. So are there any other recommendations you'd make? Independent means there's PI who's not a member, not part of the company. He or she may get a grant from the company to do the study, but that PI is an independent operator and they're multi-center and some of the--

DR. JORDAN: Well, multi-center, and three different private doctors' offices is multi-center. I think a university should be involved somewhere with that.

DR. GENCO: Okay. So you would like to add multi-center, including at least one of the centers, a

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university center?

DR. JORDAN: Yes.

DR. GENCO: I think we can add that to the guidance.

MR. LARSON: A comment, though.

DR. GENCO: Yes.

MR. LARSON: I think that does fly in the face of even the regulations in terms of the definitions of valid scientific evidence. FDA has a lot of mechanisms to monitor, to audit studies. They have a whole bioresearch monitoring unit, biometrics and surveillance. So they have the opportunity to review. If a company sponsors a study, the company in the regulations has very specific responsibilities. Now, I realize the regulations that I'm referring to are IDE regulations, but FDA can certainly apply those standards to any study that they're looking at. So I think that the idea that a priori a study sponsored by a company is suspect, I think is inappropriate.

DR. JORDAN: I didn't say a study sponsored by a company is suspect, but some can be. I will certainly say on the record, I could pick the data apart from some I've heard today and yesterday, and I think if we're going to now allow this to be a class II, there should be more controls than we've had and I see nothing wrong with any study having

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at least one university-associated study being involved with it.

MR. LARSON: But I think it would be the first ever FDA regulation or guidance that would specify that.

MR. ULATOWSKI: I would agree with your comment, that such a restriction would be unique, unless--only if there was some particular aspect of these particular devices that demanded some clinical study requirements in order to assemble valid scientific evidence. But otherwise, sponsor manufactured and conducted studies are a fact of life in devices and in drugs and in biologics and there's adequate safeguards with regards to bioethics and the conduct of research that are in place.

MR. LARSON: Just one more comment on that.

DR. GENCO: Sure.

MR. LARSON: I think a lot of what we've seen today, some of the studies are studies that were done in preparation for the possible call for a PMA and were done to those standards. Others are not. I don't think we should fault the companies for presenting whatever data they have because they were asked to come with whatever data they have, and some of it is better quality than others. But if a company is asked specifically by FDA to present in a submission clinical data, FDA has a lot to say about how

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they present that, what kind of data they gather.

DR. JORDAN: Remember yesterday?

DR. GENCO: Okay. Shall we proceed? I think we can revisit this issue when we talk about special controls if we decide to reclassify.

Willie?

DR. STEPHENS: I have one recommendation. I think that this application ought to refer specifically to implants that are done as two-stage and implants that are going to be--that immediate loading of implants ought to be a separate application because I think that's a fundamental difference and what we're looking at is with endosseous implants at this point. So I think that this ought to apply specifically to implants that are not loaded immediately.

DR. GENCO: So you're saying that--

DR. STEPHENS: There should be a special control, I guess--

DR. GENCO: Oh, all right.

DR. STEPHENS: --but we ought to be specific about that.

DR. GENCO: So that you're reiterating John's point, in a sense--

DR. STEPHENS: Yes.

DR. GENCO: --that the special control for

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clinical studies should spell out that those for immediate loading be specifically tested under those conditions.

DR. STEPHENS: Yes.

DR. GENCO: Diane?

DR. REKOW: I have a little bit of a concern for non-growing patients, and I don't know that I've seen any data about that, so I'd like something someplace said about that and I'll let you wrestle with where that goes.

DR. GENCO: I think that could come in the clinical guidelines, that special consideration be given to adolescents and young patients who are growing in these studies, or you would like to limit them to non-growing patients?

DR. REKOW: I'd like to hear what the rest of the panel has to say.

DR. GENCO: Okay.

DR. REKOW: I mean, maybe they're close to the end of their growth. Maybe they're--

DR. GENCO: We are writing these special controls. Are we agreed to reclassify? Does anybody disagree? That is, the root form the way we've defined it, which is fairly all inclusive? Does anybody feel uncomfortable with that?

[No response.]

DR. GENCO: Okay. Then I would--does anybody want

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to make a motion? Yes, Mark?

DR. PATTERS: I move to grant the petition and reclassify root form implants as class II.

DR. GENCO: Does anyone second that?

DR. RUNNER: I'm sorry.

DR. GENCO: Sure.

DR. RUNNER: Just for a point of order, we're not actually considering a petition. It's just reclassifying. Although there was a petition, this isn't specifically considering the petition.

DR. GENCO: So the motion is to reclassify root form implants in this all-inclusive definition as class II medical devices.

DR. HEFFEZ: I second it.

DR. GENCO: Willie?

DR. STEPHENS: No, I almost wonder if we ought not say that it is for adults, in adults, or--we can do that?

DR. GENCO: I think we're all agreed, also, there will be controls. So the logic to me would seem to be to vote to reclassify and then get into the controls in some depth, the three levels of controls, if we wish to recommend those three levels.

Tim?

MR. ULATOWSKI: I have a comment, or there was a

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question about if a product has a 510K. Right now, it's been cleared under a 510K and the panel agrees hypothetically to move products to class II of this type that we're discussing right now. If there's a paucity of data on a particular type of implant that was nevertheless cleared under 510K, can we go back and get that data?

Well, I think you've got to consider the totality of the group that you're considering and understand from your experience and knowledge and background exactly everything that falls in that group. It may not necessarily be required to go back and get data, depending on your experience as clinicians, but it'd be unlikely that we'd see, for regulatory purposes, to see additional data if you put them all in the same bin.

DR. GENCO: Okay. Thank you for that clarification. So we're ready now for discussion on the motion, which has been seconded, to reclassify the--recommended reclassification of the endosseous root form implants in this most generic, general description, including all that we've heard today, as medical device class II. Discussion?

DR. REKOW: Can I ask a question?

DR. GENCO: Yes.

DR. REKOW: In light of what Tim has just said,

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does that mean that we could still request some more data from some of the groups that haven't really provided a lot of data, or does that mean that, across the board, some people get lucky?

DR. GENCO: Tim, do you want to answer that?

MR. ULATOWSKI: Well, if you've got some residual concerns, I think you've got to deal with that as far as whether you want to lump or split, leaving an open concern for the industry for some additional follow-up studies for consideration. But I think as you recommend for reclassification, you are--everything that's in that bin is going to move to wherever you want to put it, and so you've either got to decide to lump or split, I think, at this point in time.

DR. REKOW: But if the controls include some performance data--

MR. ULATOWSKI: Well, that's primarily for new products coming down the pike.

DR. REKOW: That wouldn't apply to anything that--

MR. ULATOWSKI: That's not to say that they won't be studied, but it would be for regulatory purposes for new products coming down, to see whether or not they would be substantially equivalent to what you're lumping into that bin.

DR. GENCO: Jim?

DR. DRUMMOND: I think my interpretation of this is that if something's new enough that we're not heavy with clinical data, if we group them all together and pass them, we can't get the data. Is that what you're saying?

DR. RUNNER: Tim, are you saying that--what we're saying is that the things that are already cleared for 510K, if you classify them into class II, they're going to remain in class II and cleared and no additional data will be required. However, when something new comes down the pike, when somebody comes in with a new application, we will then be able to apply the special controls. The ones that are already cleared are going to stay cleared as class II.

MR. ULATOWSKI: Of course, those that are put into class II, the special controls that we define, may include also something like labeling or--and then all those products move to class II under the reclassification, would have to comply with the labeling special control, for example.

DR. GENCO: Could you give us an idea of what you've required for 510Ks for implants, endosseous implants? Maybe that would help. For example, do you require that they be tested in adults, not in children?

DR. RUNNER: Most of the 510Ks that have been cleared do not have clinical data associated with them

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because they were pre-amendments class III devices, and therefore the companies were pulling together that clinical data. We do require complete chemical composition, complete characterization of the coating as described before, mechanical bench testing of the implant and the abutments. If we find that there's something that is unusual in terms of its design, we have required clinical data. But by far, the majority do not have clinical data.

DR. GENCO: Mark?

DR. PATTERS: I don't think we should lose sight of the fact that we're classifying a generic device. Now, some particular devices in this generic classification are very well studied. Some are not that well studied. But it really doesn't matter. It's a generic device of an endosseous implant, not a particular company's endosseous implant.

MR. ULATOWSKI: That's absolutely correct. And again, once you reclassify, there's products that are legally marketed right now and you're going to reclassify them class II. They're still legally marketed. They don't have to come back again to us. They don't need another 510K. So they're out there, they have to comply with the special controls. The data business would not apply, I would estimate.

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DR. GENCO: So you have approved by 510K those devices that have demonstrated to your satisfaction that they were substantially equivalent to the PMA, or to the pre-amendments, excuse me, devices?

MR. ULATOWSKI: Right. And by saying originally class III, the panel was originally saying, well, we don't know enough and so we want to have a PMA and get the clinical data. But now if you move to class II, you're saying what we've heard today and what's been submitted to us by companies gives us enough confidence that this bin we have defined, there's enough data supporting it. It's the alternative method.

DR. GENCO: So let's go back, then, to our definition of what these root form endosseous implants are. Do you still want to include all of those in that definition, given this new information?

DR. DRUMMOND: I'll go back to my original question. Do all the implants we discussed today have clinical data that follows "normal" standards for clinical data that some of them do have? I think I've already answered that.

DR. GENCO: Tim?

MR. ULATOWSKI: It was a good comment from a

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staffer that there were some discussed today that were still pending clearance, so they're not okay. They're not--

DR. GENCO: What happens to them, if they're pending clearance? If it was--

MR. ULATOWSKI: Well, if they're still pending, if we reclassify, they'd still be subject to evaluation and decide whether they're equivalent or non-equivalent.

MR. LARSON: And the special controls--

MR. ULATOWSKI: If they're equivalent and you should so reclassify them, they'd be subject to the special controls.

DR. GENCO: Okay. So we recommend reclassification. You make the decision. So if something's pending, you're going to hold off until you make that decision?

MR. ULATOWSKI: No.

DR. GENCO: So something could get in between--

MR. ULATOWSKI: Wherever we're at at that point in time, whatever the standing requirement is. So the 510K, be it PMA, be it whatever--

DR. GENCO: Okay. That's only fair. All right. So it could very well be that some of these that are in now would get approved under the old condition and not--because the decision for a class II may not take place immediately.

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Yes?

MR. LARSON: Just for perspective, though we recognize that the quality of clinical data varies rather widely and there may be some that don't have clinical data, I think we need to think as to the whole bin that we're putting these into. Have there been disasters? I think those who are in the clinical and research community can better judge that than I. But are there disasters lurking out there or is there a reasonable level of confidence that the bin is okay?

DR. GENCO: Yes. One of the questions we have to answer is, does the device present a potential unreasonable risk of illness or injury. Does anybody want to address that? I mean, if that's an important issue. Does anybody think that there is unreasonable risk of injury? Then you think there isn't, so we've answered no to that.

Do you think we have sufficient information that we can establish special controls for all new devices in this category to provide reasonable assurance of safety and effectiveness? I mean, that's another issue. If you do, then you would vote for class II.

[No response.]

DR. GENCO: Okay. Further discussion? Are you ready for the vote?

DR. BRUNSKI: Maybe as a suggestion, I mean, actually, you started to look at this questionnaire. Isn't the process of arriving at the classification requiring going through this questionnaire, rather than just voting?

DR. GENCO: Well, let's do that as part of the discussion, then. Is the device life-sustaining or life-supporting?

DR. PATTERS: No.

DR. GENCO: No? Is the device for a use which is of a substantial importance in preventing impairment of human health? Is it of substantial importance in preventing impairments of human health? In other words, is it of substantial benefit to the patient? That's the way I interpret that.

DR. PATTERS: Yes.

DR. GENCO: Yes. Does anybody disagree?

Does the device present a potential reasonable risk of injury or illness? We answered no to that.

Is there sufficient information to determine that general controls are sufficient to provide reasonable assurance of safety and effectiveness? Remember, if you answer yes to that, you go to class I.

DR. PATTERS: No.

DR. GENCO: Okay. Is there sufficient information

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to establish special controls?

DR. PATTERS: Yes.

DR. GENCO: Okay. Therefore, we are at class II, which is, is there sufficient information to establish special controls to provide reasonable assurance of safety and effectiveness. If it's yes, then we would be recommending classification in class II. Is the answer yes? Does anybody disagree with yes?

[No response.]

DR. GENCO: Okay.

DR. RUNNER: Can I ask one question?

DR. GENCO: Yes.

DR. RUNNER: Can I clarify that you are including all root forms, all implants that are root form with special retention features and root forms that are temporary in this grouping?

DR. GENCO: Yes. I mean, I've asked that question, I think, three or four times. Let's ask it again to make sure everybody's comfortable with that. Remember, some of those don't have the data that others do.

DR. DRUMMOND: I guess I'm not comfortable until we get the data, and what I'm hearing is if we don't get the data, they'll still get improved anyway because we're reclassifying all of them.

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DR. GENCO: Because they're in the process or have already been classified?

DR. DRUMMOND: Yes.

DR. GENCO: Mark?

DR. PATTERS: You really can't separate those unless you believe that they are for a different intended use. If you do, then you can separate them. But if they're for the same intended use, the data is not the issue. It's a generic device we're classifying. Some have good data, some do not.

DR. DRUMMOND: That's not my interpretation. My interpretation is some of them don't simply have the clinical data and it's more testimonial than clinical. That's what bothers me.

DR. PATTERS: But that's not the issue. It's a generic device and the question is, is there enough data about this generic device to feel that the device is safe and effective? That's the only question, in its intended use. Now, if you believe the device has a different intended use, you could look at that device differently. Correct me if I'm wrong here.

MR. ULATOWSKI: Mr. Chairman?

DR. GENCO: Yes?

MR. ULATOWSKI: There's a number of

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classifications that are in the regulations that are split, same device, different characteristics or uses. It depends where the panels have felt this particular size of device or particular use of a device or whatever should be a different class than another size or use. So intended use alone is not the only factor that may be considered in the classification. There can be other factors.

DR. GENCO: So the issue is, of these unique ones that we heard today, and maybe unique is not the term, but let's be specific. For the Sendak mini-temporary, for the Tronics Oral bicortical screw, and for the Sargon, are they sufficiently different than the other implants which we're reasonably comfortable with, endosseous implants, to require special studies or special classification? Leslie?

DR. HEFFEZ: I think the one currently classified as a special retention device, that's the Sargon, should be--is misclassified. I believe it should be placed in a root form. That's my impression.

DR. GENCO: So you would want to keep it in with what we're talking about as root form--

DR. HEFFEZ: Yes.

DR. GENCO: --and what we're going to vote on?

DR. HEFFEZ: Right, and I would say that we have not considered an implant as a special retention device.

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That's my impression.

DR. GENCO: Okay.

DR. MORGAN: Can I ask one question?

DR. GENCO: Yes.

DR. MORGAN: If we classify everything as class II, can the things in the bin have different special considerations or does that get applied across the board? Like do we ask for special considerations that were unique to different types of implants that were all generically root form implants?

DR. GENCO: Yes. I would imagine for a temporary one you could ask the question Willie asked. Well, how long is temporary? The studies should be under temporary use.

DR. MORGAN: So would that kind of answer James' question that some people have good clinical data that support being class II where others did not? Would that satisfy that?

DR. GENCO: Yes, but remember, some of these already are approved or are in the bin.

DR. MORGAN: So once it goes in the bin, it's just--

MR. ULATOWSKI: Mr. Chairman?

DR. GENCO: Tim?

MR. ULATOWSKI: Yes. Reading from the

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regulations, 860.3(i), generic type of device means a grouping of devices that do not differ significantly in purpose, design, materials, energy source, function, or any other feature related to safety and effectiveness and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness. So there's a number of qualifications.

DR. GENCO: So that the answer to Andrea's question is no, you really--they should all be amenable to the same set of standards, special controls.

MR. ULATOWSKI: Whatever you place in the bin should have the same--

DR. GENCO: Okay. That's a very important distinction, then.

MR. ULATOWSKI: --finding.

DR. GENCO: Right. In other words, you should feel comfortable that each one of these we've defined as endosseous will be subject to the same set of special controls. Okay. I'll ask again. Are there any of those that you want to remove from this definition? John?

DR. BRUNSKI: Well, yes, I think I would, but just one other clarification. In other words, if ones are in the hopper now awaiting 510Ks or already have one and we reclassify the IIIs to the IIs and they're in that bin, does

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that mean that existing guidance document that exists right now can't be changed with respect to any of those? I'm wrong about that, right?

DR. RUNNER: The ones that have already been cleared have been cleared according to the guidance document and other recommendations. The ones that are in the bin would be cleared according to the guidance document. The guidance document can always be changed at some point through appropriate methods, if it's felt necessary.

DR. BRUNSKI: So all the ones we've heard about today have basically been cleared, I guess, with--

DR. RUNNER: There are a couple of them that we heard about today that have not been cleared.

DR. BRUNSKI: Well, for example, the Sargon, I mean, to me, in my mind, I mean, mechanistically, it's a very different active device. It's a device that actively is turned. It presses on the bone, et cetera. I mean, I agree with Dr. Hefez that in terms of some of the risks, some of them are the same, but others may not even be really well known yet.

DR. RUNNER: And that device has been cleared and it was cleared with clinical data.

DR. BRUNSKI: It was?

DR. STEPHENS: If we were to put the Sargon in a

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category of special retention, we could do that because we wanted additional different information, but it could still be a class II device, is that correct?

DR. GENCO: So are you suggesting that?

DR. STEPHENS: I would be more comfortable with that, yes. I think that I would be comfortable with the Sargon being--I wouldn't have any problem with it being a class II, but I would like it in a classification as an implant with special retention features.

DR. GENCO: So endosseous root form with special retention, that's a different class II?

DR. STEPHENS: A different class II.

DR. GENCO: Okay. What do we do with that? Do we come up with special controls for that class II? So you have some special controls unique from the special controls for the others in that category?

DR. STEPHENS: I think that we would want studies to--we could request additional studies for it.

MR. ULATOWSKI: There's possibilities for post-approval, post-clearance investigations or follow-ups. The panel may recommend in that area. I'm just saying that the product's going to be out there if you put it into class II.

DR. GENCO: So, let's see. Let's play that

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scenario. Let's not just talk about Sargon. Let's say a device with special retention is already on the market, has 510K approval. We put it as a class II device into another category with specific special controls. What happens now? Will that device be now subjected, required to come up with these--

MR. ULATOWSKI: It has to meet the special controls. It's on the market.

DR. GENCO: Even though it's on the market?

MR. ULATOWSKI: It's on the market.

DR. GENCO: So this post-market application of special controls based upon this decision?

MR. ULATOWSKI: There is an element of that in the special controls described. You can identify something there for study.

DR. GENCO: Okay. I think before we do something like that, we ought to have some very good idea of what the issues are. Willie, do you want--

DR. PATTERS: That's true for all devices, though, not just those with special retention features. They still have to meet the special controls--

MR. ULATOWSKI: If you're class II, you'd still have to meet the special controls, but the special controls can vary.

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DR. GENCO: Even though they've been on the market for a number of years?

DR. PATTERS: That's correct.

MR. ULATOWSKI: Right.

DR. GENCO: So if the special control is a unique study, let's say some study in--a unique study--

MR. ULATOWSKI: Knowing it's a follow-up. It's not a pre-approved study.

DR. GENCO: Are you comfortable with that, then? Okay. Good. So I hear that we're lumpers and not dividers at this point.

George, you had something to say?

DR. McCARTHY: I just wanted to throw in my two cents worth on the Sargon implant. It's an implant that has moving parts. It basically, by the developer's own words, it is capable of doubling its diameter. So that, to me, makes it a really unique implant.

DR. GENCO: Would you be comfortable with special controls for that sort of implant but keep it in the same group of endosseous root form--

DR. McCARTHY: Yes.

DR. GENCO: Okay. It looks like we're closer to a vote. Does anybody want to discuss this further? Jim? We're going to vote now to recommend classification in class

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II for the whole lot of what we've heard and some that we may not have heard about.

MR. ULATOWSKI: So are you collapsing the four categories?

DR. GENCO: No. Oh, excuse me. We're only talking about the endosseous root form. We're not talking about the blade or--

MR. ULATOWSKI: Okay.

DR. GENCO: What was the other one? Excuse me. In a way, we're collapsing the special retention that we heard about and the temporary into the root form and leaving the blade out. Is that clear? Both Mark and Leslie, who have made and seconded, you're clear? Okay. That's clear.

MR. ULATOWSKI: Good.

DR. GENCO: Okay. Are we ready for the vote, then? Thank you, Tim, for pointing that out.

I'm not exactly clear of the voting members here. I think I've got them all down, but maybe, Pam, you can help me here. Let's start, then. I've got them in a list here. Let's start at the back end of the list. Dr. Rekow, what is your vote?

DR. REKOW: I approve.

DR. GENCO: Dr. Morgan?

DR. MORGAN: I agree.

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DR. GENCO: Dr. Heffez?

DR. HEFFEZ: I agree.

DR. GENCO: Dr. Brunski?

DR. BRUNSKI: Agree.

DR. GENCO: Dr. Patters?

DR. PATTERS: Agree.

DR. GENCO: Dr. Stephens?

DR. STEPHENS: I agree.

DR. GENCO: And Dr. Janosky?

DR. JANOSKY: Agree.

DR. GENCO: Okay. Thank you very much.

The next step is to discuss special controls.

Now, I just put out a suggestion that, from what I heard today and previous experience, there are at least three types of controls. One is these technical controls, like standards for materials, standards for benchtop testing, and then manufacturing standards.

Is that well established? Do we have to do much with that? Is there a committee--Floyd, help us here--that has already discussed this? Is that in progress? Is it done? Where are we with those technical aspects?

MR. LARSON: I wish I could say that it's all done. There are aspects of it that are being dealt with, but, for example, on x-ray diffraction analysis of HA

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coatings, there is a task group that is trying yet to develop a standard even for the method. It's a little more specific and probably closer with regard to fatigue testing of dental implant assemblies, and that is encouraging in that there is an ISO working group that is well along in the process of developing a standard for that. But I cannot say that that standard exists.

DR. GENCO: So one option would be that we would recommend voluntary standards, such as the ASTM and the ISO standard.

MR. LARSON: Yes. Now, for the materials, the voluntary standards are well in place.

DR. GENCO: Okay.

MR. LARSON: I mean, for titanium, for example, for the titanium alloy.

DR. GENCO: Right.

MR. LARSON: So we're quite accustomed to using those standards in our communication with FDA on 510Ks.

DR. GENCO: Okay. Let's deal with that. Does anybody have any problem with that, voluntary standards for the materials using the ASTM and ISO standards recommendations? Yes?

DR. REKOW: What happens when I want to introduce a magic polymer as my blade implant? Sorry.

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DR. GENCO: No. That's a good question.

DR. REKOW: I mean, on root form.

DR. GENCO: Yes, root form. I think what we're talking about here, and we probably should be specific, are titanium and coated titanium, hydroxyapatite coated titanium. We haven't really heard of any other--

MR. LARSON: And titanium coating.

DR. GENCO: Yes. Titanium, titanium coated, and hydroxyapatite coated titanium. Have we heard of any others? I think we can say that, I think, specifically. Those are the materials that we're talking about with respect to this form, and as a matter of fact, we can add that to the definition. The definition of root form includes those made of titanium with either titanium or hydroxyapatite coating. So if somebody came with a new material, glass or whatever it is, that would be a very different situation. Mark?

DR. PATTERS: Would it be incumbent upon them to show that their material was substantially equivalent, and that's the FDA makes that interpretation.

DR. GENCO: Okay.

MR. ULATOWSKI: You want to retain flexibility in product development. A corollary to this standards discussion is at FDA, there is a new law FDA is working

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under and part of that new law deals with the recognition of standards and the use of standards by the industry and that will be picked up, I think, pretty quickly by our staff in recognizing certain standards. But the element of that use is the voluntary nature of the use of those standards.

DR. GENCO: Okay.

MR. ULATOWSKI: Using them speeds the process, but you may choose not to use those standards and do something else.

DR. GENCO: Okay. Is everybody comfortable with that, then, to use those voluntary standards that are already pretty much in place--

DR. REKOW: For those materials.

DR. GENCO: For those materials. What about the benchtop? Floyd, what is the status there? These are in progress to be developed?

MR. LARSON: Some of them are in progress. I can't say that it's comprehensive even with regard to being in progress. I'd say that the one that I think is the most relevant to this right now is the ISO fatigue testing standard and you've just put a fire under me to help move that along.

DR. GENCO: Is there any specific recommendations in terms of the benchtop testing that we should address?

DR. PATTERS: Doesn't the guidance document address that?

MR. ULATOWSKI: Yes.

DR. PATTERS: The existing guidance document.

DR. GENCO: It does?

MS. SCOTT: Yes. There are recommendations in the existing guidance documents. However, if the panel believes that there are certain specific recommendations that may not be included in the guidance documents or that they want to reiterate, you should state that today.

DR. GENCO: Yes?

MR. LARSON: Floyd Larson. I haven't been saying my name. Sorry. One of the problems with the kinds of standards that are developed in the voluntary arena is that the first stage is to get a standard that specifies a method in common. It's sometimes quite a long process beyond that to get a performance standard.

For example, when I say we're developing a standard for fatigue testing, we're not saying what's good and what's bad. So the combination of that voluntary standard on the method with FDA's requirements on the values to be obtained or their good engineering judgment on a case-by-case basis is what we've been going on and I think that is appropriate for this.

DR. GENCO: And this panel really can't add much to that. So we'll go with what is in the guidance documents and--yes?

DR. BRUNSKI: Well, when it comes to fatigue, I was just going to ask that I would like to see some flexibility in the guidance document to anticipate various types of active retention mechanisms, like we've been confronted with now. In other words, the fatigue standard that I presume you're working on is largely concerned with testing abutments and axial loading, bending loading. It doesn't really necessarily deal specifically with some sort of development which is maybe coming out into the bone and may also be, at least as a thought question, being concerned with fatigue of those parts.

So the current guidance document doesn't specifically break that out, but yet, I mean, I would just like to suggest that that's an area where we might want to think about other kinds of fatigue tests that might be relevant for certain other kinds of implants than we see right now.

DR. GENCO: Yes, Dr. Larson?

MR. LARSON: For the panel, I think that's particularly difficult because I don't think even you and I could anticipate or even for an existing implant figure out

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how to do that kind of fatigue testing. With the testing that we've done so far, just managing to somehow test an implant, not the structure on top of it, is difficult.

DR. BRUNSKI: But by analogy, I mean, before we had HA coatings, we weren't worrying about measuring bond strength of coatings to surfaces.

MR. LARSON: Yes.

DR. BRUNSKI: But then when they came on the market, that's now a test that's in the guidance document. So similarly, although maybe we don't have a lot of them right now, we might have a lot of implants sometime that have a lot of active internal gizmos.

MR. LARSON: And by no means am I suggesting that we shouldn't be concerned about that. I'm just saying that for the panel to make very specific recommendations would be impossible, I think. One of the issues, though, is FDA can, as they see these things coming, start asking for additional testing, I mean, but they have to do it when they see them.

DR. GENCO: So are we comfortable, then, with the recommendations for these benchtop standards as they are in the guidance documents and as they're evolving? Okay.

I think the manufacturing, that's pretty much up to the FDA and we're reasonably comfortable with that, the GMP and ISO standards.

Any other specific controls with respect to the technical aspects? Anything unique?

[No response.]

DR. GENCO: Okay. Let's go, then, to the clinical investigation guidances. As I recall, there's a long history of those guidances going all the way back to the early '90s and they're reasonably mature. They have had another iteration, at least with the American Academy of Perio and the FDA and several other organizations. Is there anything specific that this panel might want to add to those?

I can tell you, overview, that the guidances are for two fairly large, 50-patient studies, independent, multi-center, outcomes being survival, using the criteria that we've heard today of freedom from pain, freedom from infection, freedom from radiographic change, and freedom from mobility.

I heard something about in non-growing individuals. Do we want to make sure that's in the guidances for these special--for the studies?

DR. REKOW: I'd feel a lot more comfortable if that were the case.

DR. GENCO: Has this come up as an issue? How about in the studies of ectodermal hyperplasia? What was

the situation there? George, had those kids stopped growing or were they--

DR. McCARTHY: No. Actually, we probably at NIDR probably placed more implants in kids than anybody in the world. I think we've placed about 700 in adolescents and children and it really is site-specific. Of course, these are unique individuals, too. We sought patients who had--the fewer teeth they had, the better. We actually published, the youngest case in the English speaking, or actually in the world literature is three years and 11 months with a five-year follow-up that was published in the Journal of Pediatric Dentistry, I think, in May.

It really is very, very site-specific. The anterior mandible is a very safe place to place implants in kids four, five, and six years. In fact, SIU is continuing on with that with the Foundation for Ectodermal Dysplasia, placing implants.

However, in that same child that I just mentioned--these implants, by the way, in the youngest child, the implants were actually surgically placed in another place and he was referred to us for follow-up treatment. We did the second-stage surgery to uncover the implants and reconstructed them. The maxillary implants were, at age ten, were--we decided to put them to sleep and

not do anything with them because they weren't prosthetically useful. They were in the fore of the nose at the age of ten, so you can definitely get into trouble with placing them in very young kids. So it really tends to be very, very site specific and it just depends.

DR. REKOW: I would be comfortable if there's just some way that that has to be said, so the assumption is not that anybody can use them anyplace, any time, for any--

DR. GENCO: Is that a labeling concern?

DR. REKOW: Probably.

DR. GENCO: Okay. Maybe we can address it there.

DR. STEPHENS: Are you referring to a child without a syndrome who's missing teeth or more to these type kids?

DR. REKOW: No. I'm thinking--the thing that brought it to mind is, for instance, the missing laterals, an orthodontist that wants to put the prosthesis in early and get the kids all gorgeous and those sorts of things.

DR. MCCARTHY: I think there's a party line on that, too. The maxilla, the anterior maxilla is a place where you can get into trouble because of the way the face grows.

DR. REKOW: So that was what prompted my thinking about it, and I haven't even thought about your--

DR. GENCO: Would a labeling caveat, such as for use in non-growing individuals, particularly not to be used in maxillary anterior--

DR. McCARTHY: That certainly would--the trouble you're going to run into is what determines non-growing. It even varies by sex. I think the recommendation is that you can get away with maxillary interior implants, for example, lateral incisor in females at about 17 or 16 and when the boys, you should wait a little longer.

DR. GENCO: Yes, but aren't there ways of doing that? I mean, they may not be--

DR. McCARTHY: Yes. That would be a warning label, essentially.

DR. GENCO: Yes. I mean, if you use the term non-growing, that puts the onus on the clinician to determine that they're non-growing. I mean, I think there are ways of doing that that are reasonable. They may not be precise.

DR. REKOW: Yes. I'm real comfortable with that.

DR. GENCO: Okay. Good. So that would be labeling, then.

Let's go back to the clinical studies. From what I've just said about the clinical studies, is this fairly accurate, Susan, Tim, Pam, the overview that they're--

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MR. ULATOWSKI: We understand where you're coming from.

DR. GENCO: Two 50-patient studies, independent, multi-center, outcomes being success, and we've heard over and over again that life table analysis for success be determined, to determine the proportional success every year or at every interval, fairly straightforward. We heard many of those studies today.

Anything else that you'd like to see? Cause of failure, I think we emphasized that, a table of cause of failure, fracture versus infection versus occlusal overload. Consideration of patient selection, risk factors, inclusion, exclusion criteria. Yes?

MR. LARSON: Floyd Larson. I want to go back to the criteria for success that you mentioned. You mentioned four criteria, one of them being mobility. While that's very well established since the earliest studies as maybe the principal criterion, we ought to give some thought to the increasing use of cemented restorations and the appropriateness of mobility determination on individual implants.

DR. GENCO: Yes. I think somebody dealt with that, one of the last presentations this afternoon. I apologize I don't remember exactly who it is to give you

credit. But the consideration was that it would be a mobile implant with the abutment off.

MR. LARSON: Right, but the point is that if you are dealing with the real world situation of cemented multi-unit restorations, there are going to be a lot of prostheses which are not amenable to that mode of examination and there are certainly, and again, I'm obviously not a clinician, but clinicians who deal with those kinds of cases have other ways of assessing whether or not the implant is successful.

DR. GENCO: That's right. I think the other three criteria often will be seen, and the fourth one we discussed, and the fifth was the alveolar crestal height loss, one millimeter in the first year, 0.8 cumulatively over the next four years. So any one of those--

MR. LARSON: As a mean for the system.

DR. GENCO: Well, no, per tooth.

MR. LARSON: No.

DR. GENCO: That is, an implant failure is defined as one that has above those thresholds of interproximal bone loss. I think--we can argue about that, but I think we might leave the clinicians who've designed the studies to tell us what their measuring.

MR. LARSON: Okay, except that half the Branemark

implants would have been failures.

DR. GENCO: Well, as I say, I don't want to second guess those guidances. The committee spent many, many months talking about those things. But there is a radiographic criteria. There's a mobility criteria. There's a pain criteria. There's an alveolar crestal criteria. There's an infection criteria. Some of the infection criteria require suppuration. Some don't. And then there's a whole set of periodontal criteria that could be applied, also.

Okay. Are you comfortable, then, with those guidances the way I've stated them--I hope I've been reasonably accurate--as the clinical trial guidances?

[No response.]

DR. GENCO: Okay. Let's go to--we're not considering patient registries or device tracking, are we? Is there any necessity for that?

[No response.]

DR. GENCO: Let's go to labeling. We've heard one consideration for labeling and that is the recommendation they not be used in non-growing individuals, particularly in maxillary anterior. Any other labeling considerations?

DR. HEFFEZ: Leslie Heffez. The immediate implant loading versus non-immediate loading, have we or are we

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going to consider that? I do think that that's distinctly a different hat. Most of these, we're considering a delayed fashion.

DR. GENCO: Okay. Do you want to add that as part of the guidance, that if the indication is going to be for immediate loading, that they be tested in these clinical studies under those conditions, otherwise the claim can't be made? Is everybody comfortable with that? Does that make sense from the point of view of the FDA?

[No response.]

DR. GENCO: Okay. So if somebody's going to make that claim, our implant is super-duper for immediate loading, that the clinical studies support that. Okay.

Any other special controls? Yes?

DR. MORGAN: You mentioned education as part of it.

DR. GENCO: Yes.

DR. MORGAN: I was thinking, for some of the implants that--like the Zygomatics implant where it's very technique sensitive, that that might be a special control for that specific implant.

DR. GENCO: Okay. Willie?

DR. STEPHENS: The manufacturers already have that built in. They require their own training course before you

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can purchase and use the implant already.

DR. GENCO: Okay. Any other special educational controls that you think should be applied? Tim?

MR. ULATOWSKI: I just want to clear up my own mind on one aspect, and that is you mentioned the clinical study aspect and the two study, 50-patient aspects, and your consideration was in regard to that for new products coming down the line, prospective studies, so on and so forth. I just wanted to see if there was a residual concern about the database on any existing products that you have in your bin and was there still a mind to get some data on any of those products in some way, shape, or form?

DR. GENCO: Another way of asking that might be, of any of the products that we've heard about or know about, would you lessen that standard for clinical study, the temporary--

MR. ULATOWSKI: No. I'm saying, would you increase--

DR. GENCO: Oh, increase that?

MR. ULATOWSKI: Add a class to expectation for certain types of devices.

DR. GENCO: The one we've heard--

MR. ULATOWSKI: But that's difficult because you're kind of defining in this bin, in one bin for

classification.

DR. GENCO: The one we've heard was for the claim of immediate loading to be tested under those conditions, but it could be that same protocol, that same two, 50-patient multi-center study. That's what I'm hearing. Leslie?

DR. HEFFEZ: What are the ones that are in the bin? Are those only the presentations that we received, or are there others that are in the bin that we haven't heard about?

MR. ULATOWSKI: Everything that's in the bin right now is what's been pre-amendments or substantially equivalent within the root form devices you've characterized.

DR. RUNNER: That original grid that you collapsed was everything that we had pretty much--

DR. GENCO: Any feelings, then, about additional studies for any of those, the "special retention" and the temporary? Tim is asking, do you think there need to be more studies of those than the guidances that I outlined?

DR. HEFFEZ: I think to place an implant in the category of special retention device, I think the manufacturer should indicate or should prove that the special retention device is the primary reason for

classifying it that way. In other words, that you have another implant that is retaining, that it's just an auxiliary portion of the implant as opposed to the primary part of that implant.

DR. GENCO: What we've done is collapsed it, so I guess it's not special retention anymore.

DR. HEFFEZ: Yes.

DR. GENCO: But you're saying if one makes the claim, they should prove it?

DR. HEFFEZ: Yes.

MR. ULATOWSKI: If you're not differentiating any special controls, then we're going to be collapsing these things there.

DR. GENCO: But the point is, if somebody makes that claim, we've collapsed. But somebody wants to differentiate themselves and say, well, we have endosseous root form class II but we have special retention, don't you require that that be justified, that claim, clinically justified?

MR. ULATOWSKI: There'd be some additional aspects to the study.

DR. GENCO: Okay. So that's really a labeling and a claim justification, then, and that's covered. We've got that covered. Just like the immediate loading claim

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labeling? Okay. Yes?

DR. REKOW: Did we or did we not take the moving parts implants out of this?

DR. GENCO: No.

DR. REKOW: I thought that we had done that before we voted.

DR. GENCO: No. It was in. I'm sorry if you didn't understand that. I thought we discussed it several times and people were comfortable that it was in. But I think the point of moving parts was made. The point of if the claim was going to be special retention is made, that it be justified by a study.

MS. SCOTT: Dr. Genco, could I just ask Mr. Ulatowski to clarify. Were you referring to additional studies for implants that are already cleared or additional studies for those coming down the pike?

MR. ULATOWSKI: Well, it's this bin question again. It's additional studies for those that are already marketed. I thought I heard a concern about some devices, but if that's gone by the wayside during the discussion, so be it.

DR. GENCO: Okay. Let's proceed. Any other special controls, now? Let me just reiterate. Performance standards are voluntary, both for materials and for bench

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measures. We don't think that patient registries or device tracking is reasonable. Testing guidelines, that's the bench testing, I take it. Then the others is the clinical studies, and we talked about those. Those studies should be relevant to the claims made, and the labeling, the one labeling concern was to use in non-growing persons especially in maxillary anterior region. And then the last one was the education special control, particularly for the--well, for the teragoid implants. Any others? I guess not, just for the teragoids.

Yes?

MS. SCOTT: Dr. Genco, can you clarify for the clinical study special control that for all types of implants in this bin that come down the pike in the future or certain implants within the bin that the panel would recommend clinical studies for, only be as appropriate at this time.

DR. GENCO: I think we started off by saying as appropriate and I think we outlined a lot of the concerns. The concerns, let me go over those again, were immediate loading, the concerns for if a device had special retention claims that then there be specific studies required to substantiate those.

MR. ULATOWSKI: Pam is trying to get at under the

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510K process, you can analyze a product by its descriptive features alone--

DR. GENCO: Right.

MR. ULATOWSKI: --and possibly render a decision if it's so similar without the need for additional clinical--for clinical data.

DR. GENCO: So what we're saying is if there's either something in the bin or something that comes down the pike that is a clone of something that's already been studied ad nauseam that there need not be further studies. Does everybody understand that?

[No response.]

DR. GENCO: Okay. I think that we're clear on that.

We have a series of questions to answer. If a regulatory performance standard is needed to provide reasonable assurance of the safety and effectiveness of the class II device, what is the priority for establishing such a standard? Now, this regulatory performance standard, define that for me. Have we defined anything like that?

MR. ULATOWSKI: No. None of the standard we are talking about are regulatory standards.

DR. GENCO: Okay. So that's not applicable.

For a device recommended for reclassification in

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class II, should the recommended regulatory performance standard be in place before the reclassification? That's not applicable.

For a device recommended for class III, that's not applicable.

Now, number four, because of any potentiality for harmful effect or the collateral measures necessary for the device's use, can there otherwise be reasonable assurance of its safety and effectiveness without restriction on its sale, distribution, or use? Where are we with that one? That's no, isn't it? No restrictions.

Okay. Now, the supplemental data sheet--oh, it's yes.

MR. ULATOWSKI: There are some prescription use--

MS. SCOTT: Prescription use only type restrictions, things of that sort.

DR. GENCO: Okay.

MR. ULATOWSKI: Sometimes there are some other limitations on types of professionals that can use it, but--

DR. GENCO: So these can't be put in by non-professionals. It's prescription use, then. Okay.

Now, the supplemental data sheet, indications for use prescribed, recommended, or suggested in the device labeling that were considered by the advisory panel. I

think we did consider those. Any specific use, like immediate loading or specific retention or use in children would have to be considered either in the testing or in the labeling.

MS. SCOTT: Dr. Genco, if you could just formulate a statement as to the general intended use or indications for use for this type of device and the stated name for this device for the record so that when we go back to write the regulation, it will be stated.

DR. GENCO: These are endosseous dental implants and the use of these endosseous dental implants--let me try it and then the panel can help--is to replace missing teeth, to restore function, aesthetics, and phonetics.

MR. LARSON: Dr. Genco, jumping off from the existing regs might be a way to go. Obviously, we're narrower than that, but 872.3640, do you want that--

DR. GENCO: All right, please.

MR. LARSON: This is the existing endosseous implant description in the regs. "An endosseous implant is a device made of a material such as titanium intended to be surgically placed in the bone of the upper or lower jaw arches to provide support for prosthetic devices, such as artificial teeth, and to restore the patient's chewing function." So that's what we--

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DR. GENCO: Okay. So we can get that into the--

MR. LARSON: Right, but that's not necessarily--we're narrower than that because we've said root form.

DR. GENCO: Right.

MR. LARSON: And we've also specified the material more precisely than "such as titanium". But it's a jumping-off place.

DR. GENCO: Okay. The generic device's endosseous root form implant made of titanium, titanium alloy, coated with titanium or hydroxyapatite. Is that--

MR. LARSON: Or not coated. Uncoated or coated with--

DR. GENCO: Uncoated or coated. Right.

MR. LARSON: And then you go into the "intended to be".

MR. ULATOWSKI: It depends on how you come out with the other ones.

DR. GENCO: Pardon?

MR. ULATOWSKI: It depends how you come out with the other ones, what the ultimate final regulation would look like, but it's right to start this way--

MR. LARSON: We don't have to actually write these words.

MR. ULATOWSKI: You can concentrate on the subcategory for now. What you've just said is an overlay, the introduction, if you will, to the classification.

DR. GENCO: Okay. Are there any risks to general health presented by the device? Does anybody know of any risks to general health? No?

[No response.]

DR. GENCO: How about specific hazards to health? In failures, you get resorption of alveolar bone. Dr. Krauser showed some examples. Is that a specific hazard? Infection?

DR. HEFFEZ: Leslie Heffez. I think it's dependent upon the patient's systemic condition. If the patient had a history of bacterial endocarditis, they're more at risk for developing bacterial endocarditis and the use of an implant might be, maybe not a contraindication, but a precaution that if it fails or shows evidence of failure, it may increase the risk of recurrent bacterial endocarditis. So I would say something to the effect that it's really contingent upon a patient's general medical condition but there's nothing specific to the implant that presents a hazard to the patient's health.

DR. GENCO: Okay. Any other specific hazards to health?

DR. REKOW: You might say, in addition to being the systemic condition, the general oral health of the patient, too. I think that that's--

DR. GENCO: So local infection related to general oral status?

DR. REKOW: I think so. But again, not the implant.

MS. SCOTT: Dr. Genco, I don't know if the panel wants to address this, but in the initial classification of endosseous implants, there were a number of risks that the panel, that the original classification panel identified that was published in the Federal Register notice, and I don't know if I can remember all of them off the top of my head.

DR. GENCO: Yes. I think we could look at this now again, five years later, seven years later.

MS. SCOTT: Right.

DR. GENCO: Are there any others? We're talking about infections such as subacute bacterial endocarditis, associated to the general patient condition which may increase, the risk may be increased, and local infection around the implant may be increased by local oral conditions. Is there anything else?

DR. BRUNSKI: This is John Brunski. See, I'm not

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sure exactly how you're defining health, but I view this as these are specific risks associated with using an implant.

DR. GENCO: Right.

DR. BRUNSKI: Yes, you can lose some bone because of, well, as we've heard, inflammation due to bacteria, maybe overloading. The implant could fracture. You could hit some nerves. I mean, I'm not sure. Are we trying to specify risks that are associated specifically with putting an implant in?

DR. GENCO: Sure.

DR. BRUNSKI: I mean, those are some that come to mind.

DR. GENCO: Okay. So we've dealt with three types, then, infections such as SBE, local infection that results in bone loss and other tissue loss, and then nerve paresthesia, or nerve damage. How about sinus perforation?

DR. HEFFEZ: I would say sinus inflammation/infection of the sinus, perinasal sinuses.

DR. GENCO: Any others?

DR. MORGAN: Would you consider mandibular fractures in severely atrophic mandibles that were trying to be restored with root forms?

DR. HEFFEZ: I would agree.

DR. GENCO: Now we get into--some of these are

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probably related to any or all surgery you do. I mean, you could break a person's jaw. You could have an air embolism not related to implants particularly. Are there any others, then?

[No response.]

DR. GENCO: Okay. The recommended panel classification is class II. What is the priority? Now, what does that mean, the priority for FDA making this final decision?

MS. SCOTT: Yes. That's the--

DR. GENCO: Okay. What is the panel's feeling about the priority? What are the options here? What does high priority mean, something within weeks, months? I know this has been going on for a couple of months, anyway.

MR. ULATOWSKI: It's been going on for years. In the general scheme of things, considering current, it would probably be within this year, fiscal year.

DR. GENCO: So not high but moderate?

MR. ULATOWSKI: High would be this fiscal year.

[Laughter.]

DR. GENCO: Well, I'm glad to hear that, because I was on the panel in 1991.

Okay. If the device is an implant or is life-sustaining or life-supporting and has been classified

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in a category other than the class III, explain fully reasons for the lower classification with supporting documentation. I think we'll defer on that because that's really what we've been doing for about four days. These forms are really brutal, but bear with me.

Summary of information, including clinical experience or judgment upon which a classification is based. We can do that later.

Identification of any needed restrictions on the use of the device. I think we should do that now, restrictions on the use of the device. In non-growing--

DR. REKOW: Didn't se just do that?

DR. GENCO: Well, yes, but bear with these forms. One day, you and I will sit down and we'll redo the forms for the FDA.

DR. REKOW: No.

[Laughter.]

DR. GENCO: Restrictions on the use of the device. In non-growing--I mean, in growing adults, in growing individuals.

MR. ULATOWSKI: It depends how you want to consider that. That sort of thing, you can look at two different ways. One way is in labeling people, may say, depending on the data, there's no data that show the safety

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and effectiveness in this group of patients so you have to be cautious. The other way is, we found out that if you do it, these are the problems.

DR. GENCO: I think that's the case.

MR. ULATOWSKI: So you're not limiting a dental professional from moving forward based on his or her experience and knowledge necessarily. You're informing, but allowing, as well. By restricting, you're saying, no.

DR. HEFFEZ: So is that a contraindication versus a precaution?

MR. ULATOWSKI: Yes.

DR. HEFFEZ: So our label is for precautions and not contraindications?

DR. GENCO: Okay. Precautions--

MR. ULATOWSKI: Unless that's your decision.

DR. GENCO: No. I think, obviously, there are uses in growing individuals that the NIDR has worked out very nicely, in ectodermal hyperplasia, or dysplasia. But I think the precaution--how does that sound--precautions in growing individuals, precautionary use in growing individuals.

Any other? I mean, there are obvious surgical and risk factor precautions. Do we get into that or is that something that's well known, shouldn't be used in

uncontrolled diabetics--

MR. ULATOWSKI: Well, those are things we probably--well, you can recommend those things, although we would pick those up in the normal course of business.

DR. GENCO: All right. And they're not all that well studied anyway. I think we'd be a little uncomfortable with that.

I think we're finished with this form.

MR. ULATOWSKI: On the data, what basis of data--

MS. SCOTT: Right, number eight.

MR. ULATOWSKI: All you need to say is--I suggest that all you need to say is, based on the presentations and data submitted by the applicants and other speakers and the basis of our own experience utilizing these products and so on and so forth.

DR. GENCO: All right. Now, we've got another question to deal with. The Dental Products Panel recommended that abutments be classified separately from the implant fixture. What is your feeling, panel? Should the abutments be classified separately from the implant fixture, and if so, what classification? Does anybody want to start the discussion?

DR. HEFFEZ: Leslie Heffez. I feel that this should be classified differently and it should be classified

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as class II.

DR. GENCO: Okay. Process, now. Pam, do we go through the same process for the abutments?

MS. SCOTT: Yes.

DR. GENCO: Okay.

MS. SCOTT: If you're recommending classification into a different class, then we would need you to fill out the questionnaire, take the vote, and the supplemental data sheet.

DR. GENCO: Yes?

MR. LARSON: Point of clarification. We're talking about abutments, using the term abutments. In the ISO task group, we recognized that we had a real terminology problem when we were talking about testing things and I'm not sure what to suggest, but the word "abutment" is a real difficult thing to explain in a generic sense. So I wonder if we can come up with a more generic term?

DR. GENCO: I think that we heard the definition of an abutment was everything but the implant--

MR. LARSON: Yes.

DR. GENCO: --and the implant has within it a place for the screw. So it's everything but the root portion of the implant.

MR. LARSON: Okay. Rather than using the term

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"abutment", could we use the term prosthetic components?

DR. GENCO: Okay. All prosthetic components normally used with implants? Maybe we could have a suggestion for the term here. Yes, please, Dr. Marlin?

DR. MARLIN: If you go into all prosthetic components, then you're getting into crowns and over-denture prosthesis and I think that that would be kind of like awfully hard to regulate. If I might suggest that all prosthetic components that are directly connected to the implant would serve as the abutment.

MR. LARSON: And maybe manufactured could be in there, too?

DR. MARLIN: Yes. Let's rephrase that. All manufactured prosthetic components that are directly connected to the implant would serve as the abutment, or that serves as--to receive another prosthesis of some form. In other words--

MR. LARSON: Okay, but could we use the terminology, actually, manufactured prosthetic components? We don't want to get into the temporary things that could be class I or--

DR. MARLIN: Right.

DR. GENCO: Premanufactured means not fabricated by the dentist.

DR. MARLIN: Right.

DR. GENCO: Is that what you mean?

DR. MARLIN: But you could have, for instance, as an example, a castable pattern that's premanufactured. A premanufactured directly connected component or to be used as a castable piece that's been--in other words, using the word "premanufactured", I think, pretty much covers it, that's directly connected to the--

DR. GENCO: So those are the two essential components, premanufactured, directly coupled.

DR. MARLIN: Correct.

DR. GENCO: Thank you.

MR. LARSON: But what will be the actual words that are used as the title? Are you still thinking abutment?

DR. MARLIN: I think in the clinician's side, they look at an abutment as that. But if you determine that it has premanufactured or premachined, using the terminology we just did, you can use the term abutment because you've defined it more narrowly. Is that helpful?

MR. LARSON: Okay. It's just we found in Bangkok as we were talking about this that we had no idea when we finished what we really meant by abutment.

DR. MARLIN: Yes.

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DR. GENCO: What if we say something like this, implant abutments. I mean, that's the common term.

DR. MARLIN: Right. Shall be defined as--

DR. GENCO: Yes, to include--

DR. MARLIN: To include.

DR. GENCO: --all premanufactured prosthetic components directly connected to implants.

DR. MARLIN: Right.

DR. GENCO: Okay. Are these life-sustaining or life-supporting? No.

Is the device for a use which is of substantial importance in human health? Yes.

Is there potential unreasonable risk of illness or injury? No.

Number four, did you answer yes to any of the above three questions? Yes.

Number five--

MS. SCOTT: Then you to go seven.

MR. ULATOWSKI: Then go to seven.

DR. GENCO: Seven, is there sufficient information to establish special controls to provide reasonable assurance of safety and effectiveness? I heard yes. That means that they should be in class II and so if that's the case, it looks like we are probably ready for a motion.

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DR. HEFFEZ: I move that the so-called abutments be classified as class II devices.

DR. GENCO: Does anyone second that?

DR. MORGAN: I second the motion.

DR. GENCO: Seconded, Andrea. Any discussion? Anybody uncomfortable with that?

[No response.]

DR. GENCO: Okay. Are we ready for the vote? Any discussion? Any comments?

[No response.]

DR. GENCO: Let's start at the top of the list here. Janine?

DR. JANOSKY: I agree.

DR. GENCO: Willie?

DR. STEPHENS: I agree.

DR. GENCO: Mark?

DR. PATTERS: Agree.

DR. GENCO: Dr. Brunski?

DR. BRUNSKI: Agree.

DR. GENCO: Dr. Heffez?

DR. HEFFEZ: Agree.

DR. GENCO: Dr. Morgan?

DR. MORGAN: Agree.

DR. GENCO: Dr. Rekow?

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DR. REKOW: Agree.

DR. GENCO: Thank you. Now, what are the special controls? Do we have voluntary performance standards here, Floyd?

MR. LARSON: Yes.

DR. GENCO: Are we satisfied with those? Do we want to make any comment to them?

MR. LARSON: I think the combination of voluntary standards and testing guidelines would provide very good control of these.

DR. GENCO: And those are fairly well in hand, fairly well established, or are in the process of being established by reputable groups?

[Laughter.]

MR. LARSON: Reputable or not. No, really, they're the same ones that we were talking about before.

DR. GENCO: Okay. Does anybody want to make any further recommendations for special controls?

[No response.]

DR. GENCO: Are we comfortable, then with class II with special controls? The special controls are well in hand in terms of performance and testing standards.

[No response.]

DR. GENCO: There's no regulatory performance

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standard needed for this, is that true? So question two is not applicable, also. Also, question three is not applicable.

Is there anything that we should be concerned about the restricted sale, distribution, or use because of any potential harmful effect? No? It's prescription use. So that's yes, then.

Supplemental data, generic device, we'll reword that, advisory panel. Is the device an implant? No.

Indications for prescribed use, recommended use--do you have some words, Floyd, for the indications for use?

MR. LARSON: I'm sorry.

DR. GENCO: Well, if you do, we can put that in, indications for use of these abutments. Is this to replace--

MR. LARSON: Well, there's nothing in the regs right now, so we have to come up with it.

DR. GENCO: Okay. Does somebody want to make some suggestions? These abutments are, what, to--

DR. RUNNER: How about as an aid for prosthetic rehabilitation?

DR. GENCO: That sounds good. Okay.

Any risk to general health? Any risk

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specifically, specific hazards with their use? No?

DR. REKOW: Well, I don't think we can be quite that--

DR. GENCO: Okay.

DR. REKOW: There's a potential, again, it's related to clinician practice, but you could potentially have parts that get dropped. I mean, there's all those little nonsense things. If you have a second surgery, you've got all this stuff that's related to the second surgery to uncover them and all those related things.

DR. GENCO: You mean the surgical complications associated with second surgery?

DR. REKOW: Yes. I mean, it's certainly a lot easier surgery than the first one, but there's still an open wound that you're creating to do the transcutaneous portion of it.

DR. GENCO: Okay. Any other specific hazards?

MS. SCOTT: Originally, the panel identified also, and the panel may want to discuss this, as to whether or not this is still appropriate, abutment fractures, screw fractures.

DR. REKOW: Excuse me, Pam. What did you say?

MS. SCOTT: Originally, I believe, if I'm not wrong, the classification panel originally identified

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abutment fractures as one of the risks.

DR. GENCO: And screw fractures. Any others?

DR. HEFFEZ: If it does fracture, it could also lead to loss of the implant. I don't know if that has to be mentioned. It could render the implant not useful.

DR. GENCO: Okay. Any others?

[No response.]

DR. GENCO: All right. We're recommended class II. The priority here, high again, since this has been under discussion for a long time. Is that the panel's recommendation, high priority?

[No response.]

DR. GENCO: Okay.

DR. HEFFEZ: Can I go back to hazards of health? Also, I would think if the fracture of the abutment goes unnoticed and it's a two-unit component, it could affect the health of the adjacent dentition or adjacent implants.

DR. GENCO: Okay. Now, if the device is an implant or is life-sustaining or life-supporting, has been classified in a category other than class III, what are our reasons for the lower classification? Is this that generic statement, the reasons that we've heard?

DR. HEFFEZ: It's not an implant, though.

DR. GENCO: Oh, it's not an implant, so that's not

applicable.

So the summary of information is based upon what has been presented to the FDA. Okay.

Any needed restrictions on the use of the device other than the prescription?

[No response.]

DR. GENCO: Okay. Are there existing standards applicable to the device? There are, these testing standards and these materials standards.

MR. LARSON: Certainly the materials standards.

DR. BRUNSKI: Perhaps we should just say, see the relevant sections of the guidance document.

DR. GENCO: Okay. I think we've answered those three questions. Is there anything else that you want us to deal with?

DR. RUNNER: You haven't made a recommendation on the blade implants.

DR. GENCO: Okay. So we collapsed everything except the blade implants. What is your feeling?

DR. HEFFEZ: Also, the Onplant. We did not discuss that.

DR. GENCO: We did not discuss the Onplant. What are your feelings with respect to the blade implant? One possibility is to leave it in class III. Another

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possibility is to reclassify it class II. Does anybody want to start the discussion? Dr. McCarthy, you've been quiet.

DR. McCARTHY: I'd like to stay that way.

[Laughter.]

DR. GENCO: I didn't mean to put you on the spot.

DR. McCARTHY: I think the blade is really--I have no clinical experience whatsoever with the blade implant. To me, it's a unique piece of equipment. I think it is--while it resides in the bone, in that respect, it's endosseous, I think the study that got quoted to this panel, it's not good to have an institutional memory, but in '91, it was the Kapur study and the Kapur studies really have raised more question about it than they answered, I think. So, I mean, I would favor leaving it as a class III device.

DR. GENCO: Now, since then, there are some monkey studies, the Fritz studies. Is anybody aware of any other human studies that would make us think any differently? Yes?

DR. SCHNEIDER: Yes. In Europe, there are--

DR. GENCO: Do you want to identify yourself and come to the microphone?

DR. SCHNEIDER: I'm Dr. Raymond Schneider. In Europe, the blade implant is more highly received. I want to first point out that one of our pre-amendment device, a

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Ramus implant, was started. Just a little history on blade implants. They are extremely effective. It depends where. It's also site-specific.

For example, I'll give you the Ramus implant is a one-stage site-specific implant in the posterior. It is made by Pacific Implant Company and they only really basically make that one implant, Ralph Roberts. When that was a pre-amended device, and I have several of that type in patients and of all of them that I've done, only one has been removed by mistake. So anything I've had is just the prejudice of other practitioners thinking that they're poor implants.

If a blade can be put on good solid bone, it is going to be just as effective as any other implant. So what I'm saying is those studies, yes, in Europe there are some very fine, excellent studies that show its usage. But again, it's site-specific. When it's used in the proper indication, they have very good statistics on those implants.

DR. GENCO: I don't think we have been presented with them. In contrast to the other data, and I was on the panel in '91, I mean, there's been a tremendous amount of data presented since '91 on the others and I'm just--

DR. SCHNEIDER: I would ask the panel to ask for

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data and I'm sure that it can be brought forward, some very fine testimony. I didn't hear that today, but I didn't hear anybody asking for that data.

DR. GENCO: We had a presentation at the last meeting in November which was really the core data. Again, as I recall, no new data to my mind, except for the Fritz studies in the monkey where they're taking a very different approach.

DR. SCHNEIDER: What I found was the problem is a lot of the practitioners weren't bringing data forward because of hearing that it was a pre-amendment device, that no longer--they were grandfathered in, and grandfathered in to them means forever. They don't have to bring information forward. I know that's not true, but I'm saying for the professionals. Now, that is not true in Europe. In Europe, they really have to continue on their studies and they had that. So I think in the United States, maybe some of those studies have not been backed up, but they are available and I would not like to see for the American public all those blades put into a class III.

DR. GENCO: I think ample opportunity was there for those studies to come in. Susan?

DR. RUNNER: They already are class III. It's a matter of whether you want to reclassify them as class II.

DR. GENCO: Right.

DR. SCHNEIDER: So in other words, my understanding is implants that are already approved will not be disapproved just from this statement.

DR. RUNNER: No, but if they remain in class III, then PMAs would be called for for blade implants.

DR. MCCARTHY: What I think it amounts to is that we've not seen any data from the manufacturer or manufacturers. At least, I haven't seen anything compelling or convincing to make me want to think that these should be class II. They may very well be. Like I said, I don't have any clinical experience whatsoever.

DR. GENCO: I think the panel was quite open to data and reclassifying a whole series of endosseous implants, quite different from what we heard in '91. But we haven't heard that same data for the blade implants, and I think if we had and it was reasonable--

DR. SCHNEIDER: As a member of the American Academy of Implant Dentistry and International Congress of Implant Dentistry, in as far as being represented in the world community and seeing what's going on, I was over in Germany in the DGZI. I'm really surprised that you do not have that information. I find that--I'm very concerned for the public.

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DR. GENCO: You heard it today. We got a lot of data from Europe today on other implants, so I don't understand, either, if it's there. At any rate, thank you very much for bringing this up.

I ask the panel, then, is there reason to reclassify blade implants into class II or do something else with them or leave them in class III for the time being? Yes?

DR. HEFFEZ: My suggestion is we don't have enough data to change the classification. We can table it and leave it as a class III.

DR. GENCO: What is the process? Is the process to leave it, to ask for more data, to ignore it? How do we go about it? Do we have to make a positive decision?

MR. ULATOWSKI: Well, the--

DR. GENCO: Or recommendation?

MR. ULATOWSKI: Come the time to submit a PMA, the applicant can always petition for reclassification, even now, but I'm not sure we'd bring it back until we saw some effort there.

DR. GENCO: Okay. Fine. So the feeling of the panel is to not reclassify it, to leave it as is, is that right? Does somebody want to make that as a motion? Floyd?

MR. LARSON: I can't move, but--

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DR. GENCO: No. Do you have something to say?

MR. LARSON: I did have a question. Procedurally, then, do the regs get written with blade implants described using the existing class III endosseous implant definition and with root form removed from that definition?

MR. ULATOWSKI: Yes. We'd have to modify that.

MR. LARSON: Okay. But you do that. We don't have to do that.

DR. STEPHENS: Is this blade implants only or are we including Ramus implants in that group of implants with these?

DR. GENCO: I think we had some data on blade implants, the Kapur study, but nothing on Ramus or others that I was aware of, either '91 or November or now.

DR. RUNNER: I believe the subperiosteals are a different classification, correct, the subperiosteals?

MR. LARSON: The subperiosteals are custom.

DR. RUNNER: They're in a different class.

DR. GENCO: And the Ramus ream is not custom. That's premanufactured, so that could conceivably be placed in the same category as blade, is that what you're saying?

DR. STEPHENS: That's what the question is.

DR. GENCO: The question is. Has anyone--

DR. BRUNSKI: I know I did, in the packet of all

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the stuff we've received, I know I have seen something about the Ramus ream from Dr. Roberts. I know it's in our packet. Now, whether that implies that it was--I mean, I have seen something in our packet.

DR. GENCO: Is there enough data to deal with that, either as a part of the blade definition or separate?

DR. HEFFEZ: I think if we were to define blade implant, then generically, I would think the Ramus ream would fall into that category since it is essentially a slot made in the bone and an implant banged into it.

DR. STEPHENS: Then I would make the motion that we leave the Ramus ream and the blade implants in class III for the time being.

DR. GENCO: Second to that?

DR. REKOW: I'll second it.

DR. HEFFEZ: I second it.

DR. GENCO: Okay. Further discussion? Comments?

[No response.]

DR. GENCO: Let's take the vote, then. Diane?

DR. REKOW: I approve of the--yes.

DR. GENCO: Dr. Morgan?

DR. MORGAN: I agree.

DR. GENCO: Dr. Heffez?

DR. HEFFEZ: Agree.

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DR. GENCO: Dr. Brunski?

DR. BRUNSKI: I agree.

DR. GENCO: Dr. Stephens?

DR. STEPHENS: I agree.

DR. GENCO: Dr. Janosky?

DR. JANOSKY: I agree.

DR. GENCO: Okay. Thank you.

Now, the Onplant. Is there an action to be taken or is their 510K approved or what's the status and what can we do to help?

MR. ULATOWSKI: Let us talk for just a moment here.

DR. GENCO: Surely.

[Pause.]

MR. ULATOWSKI: Our recommendation would be to not consider it at this time as within the bins that have been discussed today.

DR. GENCO: Okay. Fine. Thank you. So it's neither endosseous, it's neither blade endosseous or any of the other categories.

MR. ULATOWSKI: Its status is pending.

DR. GENCO: Okay. Fine. Thank you very much.

MR. LARSON: Mr. Chairman?

DR. GENCO: Before we leave the class III, we have

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to give Pam or the FDA our reasons for leaving blades and Ramus in class III. Can I paraphrase some of that discussion as that we didn't see any data that would justify putting either one of those into class II, in contrast to some of the other implant data, the root forms, which there was a remarkable amount of information obtained between '91 and present which would justify reclassification. Any other comments as to the reason for leaving those two in class III?

[No response.]

DR. GENCO: Okay. Any further comments?

MR. LARSON: I just had a question about other indications within the root form area. How far are we extending the root form area in terms of, for example, it was mentioned briefly that there are orthodontic indications for a root form type of implant in addition to the Onplant. Is that covered here, or how are we handling that?

DR. GENCO: Good question. What is your feeling?

DR. RUNNER: The way we've dealt with those indications is that we've found them substantially equivalent to endosseous implants for other indications because they're placed--

MR. LARSON: On the basis of clinical data?

DR. RUNNER: Yes.

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DR. GENCO: Anything else that you'd like us to discuss, Susan, Tim, Pam?

[No response.]

DR. GENCO: Okay. Fine. I'd like to thank the panel for this marathon session and I'd like to thank those from industry. It was a very productive session. And thank you, staff, for treating us so well. We will see you in the summer.

[Whereupon, at 4:47 p.m., the meeting was adjourned.]

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