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PRBDEPARTMENT OF HEALTH AND HUMAN SERVICES  
FOOD AND DRUG ADMINISTRATION  
CENTER FOR DEVICES AND RADIOLOGICAL HEALTH  
OFFICE OF DEVICE EVALUATION

**DENTAL PRODUCTS PANEL**

OPEN SESSION

**Volume II**

Tuesday, January 13, 1998

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Rockville, Maryland

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PANEL MEMBERS PRESENT:

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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

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

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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.