

FOOD AND DRUG ADMINISTRATION

DENTAL PRODUCTS ADVISORY PANEL MEETING

RECLASSIFICATION OF OTC FLOW-FORMED

SYNTHETIC TEMPORARY DENTURE SURFACES

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P R O C E E D I N G S

[9:03 a.m.]

Agenda Item: Welcome and Introductory Remarks

MS. SCOTT: I would like to welcome everyone to the Dental Products Panel Meeting. My name is Pamela Scott, and I am the Executive Secretary for the Dental Products Panel.

[Discussion off record.]

[Introductions were made.]

MS. SCOTT: The next item of business are three statements that are to be read into the record. The first statement is a memo that was signed by Dr. Bruce Burlington, the Director for the Center for Devices and Radiological Health. It was signed on January 30th, 1997. I appoint Robert J. Genco, DDS, Ph.D., to act as temporary Chairman for the duration of the Dental Products Panel Meeting on February 12th, 1997. 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.

The second memo is in reference to appointment to

temporary voting status. It was signed by Dr. Bruce Burlington on January 29th, 1997. Pursuant to the authority granted under the Medical Devices Advisory Committee Charter dated October 27, 1990, as amended April 20th, 1995, I appoint the following people as voting members of the Dental Products Panel for this panel meeting on February 12th, 1997. Richard D. Norman, DDS, Richard G. Burton, DDS, Sally Marshall, Ph.D. 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.

This memo was signed by Dr. Burlington on February 7th, 1997. Pursuant to the authority granted under the Medical Devices Advisory Committee Charter, I appoint the following people as voting members of the Dental Products Panel for this panel meeting on February 12th, 1997. Deborah Greenspan, BSD, DSC, and Stanley R. Saxe, DMD. 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.

I would also like to note for the record that the voting members constitute a quorum as required by the Code of Federal Regulations Title 21, Part 14.

The following announcement addresses conflict of interest issues associated with this meeting and is made part of the record to preclude even the appearance of an impropriety. To determine if any conflict existed the Agency reviewed the submitted agenda and all financial interests reported by the Committee participants. The Conflict of Interest Statutes prohibit special government employees from participating in matters that could affect their or their employers financial interest. However, the Agency has determined that participation of certain members and consultants, the need for whose services outweigh the potential conflict of interest involved, is in the best interest of the government.

We would like to note for the record, that the agency took into consideration matters regarding Drs. Richard Norman and Deborah Greenspan. Dr. Norman reported

financial interest in firms at issue but in a related matter that is now concluded, and in a matter unrelated to the agenda items being discussed today.

Dr. Greenspan reported financial interest in a firm at issue, but in a matter unrelated to today's agenda. The agency, therefore, has determined that they may participate fully in today's deliberations. In the event that the discussions involved any other products or firms not already on the agenda for which an FDA participant have a financial interest, the participant should excuse themselves from such involvement, the their exclusion will be noted for the record.

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

[Discussion off record.]

MS. SCOTT: 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.

At this time, I will now turn the meeting over to Dr. Genco.

DR. GENCO: Thank you very much. Welcome everyone, especially fellow panel members and special guests. We are first going to start with Dr. Susan Runner, who is the Acting Branch Chief of the Dental Devices Branch. She will provide us an update on the activities of this branch since the last panel meeting. Dr. Runner.

Agenda Item: Update from the Last Panel Meeting

DR. RUNNER: I just wanted to give a brief update in terms of the activities that the branch has been involved in since the last meeting which was about a year ago.

As you all know, at this time, Dr. Carolyn Tulinda has resigned from the FDA to take a position at the National Center for Toxicological Research. The Division had a final going-away celebration for Dr. Tulinda. Her work with the Dental Products Panel and in facilitating other outreach programs between FDA and the professional community have been invaluable to the agency and we will miss her. We wish

her luck in her new position.

Another change in the branch is that Mr. Louis Havlinka, the former Branch Chief of the Dental Devices Branch, retired after more than 29 years of government service. His regulatory experience was key in developing the dental devices branch. I am now the Acting Branch Chief for the Dental Devices Branch.

The Dental Devices Branch, as you know, is composed of a variety of professional disciplines, including engineers, dentists, dental specialists, sanitarians, biologists. I would like to introduce to you our newest member, who is Dr. Robert Betz, who is sitting over at the side. Dr. Betz is a Board-certified periodontist, and he has spent time both with the Coast Guard as their National Periodontal Consultant and with the Indian Health Service as Periodontal Consultant. We are very happy to have Dr. Betz as a member of our team.

One last issue. Last February you considered the Biora PMA. At that time you recommended conditional approval. The final approval has finally been completed as of September 30th, 1997, with the recommendations that the

panel did make for additional post-marketing studies. So that is basically an update on the branch activities.

DR. GENCO: Thank you very much.

Agenda Item: Issue: Review of Two  
Reclassification Petitions for OTC Denture Cushion and Pad  
Devices

DR. GENCO: We will now go on to the issue of the review of two reclassification petitions for OTC denture cushion and pad devices, sponsored by Brimms, Incorporated, and Mentholatum.

We will today make recommendations to the FDA regarding reclassifications of petitions submitted for these devices and also later today for the temporary mandibular condyl implants for use in tumor resection patients.

The first issue is two reclassification petitions submitted for the OTC denture cushions and pads. We will now begin our open public hearing. Again, Pamela mentioned that anyone who gets up to the mike, we ask you please to speak clearly, of course, because there is a transcriptionist who is going to provide a word-by-word transcript of this proceeding.

Also, we ask anyone who gets up to the microphone to please disclose whether they have financial interest in any medical device company, particularly those companies which might bear upon the issue at-hand. Please state your name, affiliation and the nature of your financial interest if any.

We have one formal request to participate in this open public hearing on the issue of the petitions for OTC denture cushion and pad device. That is Mr. Keith Roberts, who represents the Nuveau Laboratories. Mr. Roberts, we ask you to make your presentation. As you know, we have reserved 10 minutes for you. Clearly, if there are any questions or comments that the audience or the panel would like to address to Mr. Roberts, we ask him to stay at the podium. Mr. Keith Roberts.

[No response.]

DR. GENCO: Okay. Apparently, Mr. Keith Roberts is not here. Does anybody know the whereabouts of Mr. Roberts? Is he out in the hall someplace or predisposed?

[No response.]

DR. GENCO: I guess not.

Okay. Now, formally this is the open part of the discussion. Is there anyone who would like to make a comment at this time?

[No response.]

DR. GENCO: Okay. Let's proceed now to the open committee discussion. We will have presentations by the sponsors of the two reclassification petitions. First of all, Brimms, Incorporated company. Again, whoever is going to present for Brimms, we ask you to make your presentation within 20 minutes. I think this has been described to you. Then you have approximately five to seven minutes for questions.

Could we have the individual who is going to present for Brimms come to the podium? Thank you.

Agenda Item: Sponsor Presentation by Brimms

DR. REITZLER: Good morning, ladies and gentlemen, Chairman Genco, Executive Secretary Scott, and members of the panel. My name is Steve Reitzler, and I am Vice President of Regulatory Affairs for Advanced Bioresearch Associates. My firm has assisted the sponsor, Brimms, Incorporated, in the preparation of today's presentation

supporting reclassification of its Denturite flow-form temporary denture surface pursuant to Section 515(b) of the Federal Food, Drug and Cosmetic Act. In so doing, it is our intention to seek the panel's recommendation for appropriate classification of the subject device and others of its generic type in keeping with the risks to health and benefits identified through valid scientific evidence and the controls available to provide reasonable assurance of the safety and effectiveness of the device.

To begin I would like to introduce the speakers we have assembled here today who, in addition to myself, will take part in our presentation on behalf of Brimms, Incorporated. All of us are paid consultants to Brimms retained for the purpose of this presentation and none hold any financial interest or equity position in the company or any of its products.

[Introductions were made.]

DR. REITZLER: We hope to establish that the flow-form temporary denture surface is reasonably safe and effective as labeled and marketed, that the risks to health associated with its use in accordance with label directions

are well-known and understood, and that these risks can be effectively managed through class I controls and, lastly, that the class III classification proposed by the FDA for OTC denture cushions and pads is unnecessary and inappropriate for the subject device and others of its generic type.

The Federal Food, Drug and Cosmetic Act states that the FDA may, under its own initiative or upon petition by an interested party, change the classification of a class III device to class II if general controls alone would not provide reasonable assurance of safety and effectiveness of a device, but special controls would provide such reasonable assurance, or to class I, if general controls alone would provide reasonable assurance of the safety and effectiveness of the device.

It should be noted here that the subject device has been marketed for over 38 years under the equivalent of class I controls without evidence of unreasonable risk to health.

In supporting our assertion that the subject device is safe and effective and is inappropriately placed

in class III, we will rely upon valid scientific evidence meeting the standards contained in section 860 of the Code of Federal Regulations.

According to these regulations, valid scientific evidence includes evidence from well-controlled investigations, partially-controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device from which it can fairly and reasonable be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use. Regulations also stipulate that the evidence required to establish reasonable assurance of safety and effectiveness may vary according to the characteristics of the device, its labeled conditions of use, including the existence and adequacy of warnings and other restrictions, and, importantly, the extent of experience with its use. We believe that the valid scientific evidence provided to the agency in support of our petition, and which will be summarized here today adequately demonstrate that the

subject device is reasonably safe and effective as labeled and need not be in class III to provide reasonable assurance of safety and effectiveness.

We further believe that the risks to health presented by use of the subject device and others of its generic type are well-known and can be adequately controlled without recourse to the restrictive and costly regulatory burden of class III classification and that the subject device has been marketed successfully and without evidence of unreasonable risks for nearly 40 years under the equivalent of class one general controls. We suggest that reclassification to class I is appropriate.

Should the panel determine that class II is necessary to provide reasonable assurance of safety and effectiveness, however, we believe and will demonstrate today that adequate information exists to establish special controls to provide such reasonable assurance.

At this time I would like to introduce Dr. Brenda Seidman, who will describe the subject device and identify recognized state-of-the-art analytical and biocompatibility methods available to provide reasonable assurance of its

safety and effectiveness.

DR. SEIDMAN: Good morning. My name is Brenda Seidman, and I am a degreed toxicologist. My firm, Seidman Toxicology, provides expert advice and technical support to industry in the areas of toxicology and material biosafety. I am a paid consultant to the sponsor and have no financial interest in Brimms, Incorporated, or its products.

Today, I will be providing a brief overview of the subject device, the materials of which it is comprised, and available methods by which its composition, performance, and safety can be controlled.

Denturite flow-formed temporary denture surface is a soft, synthetic elastomer that flows freely to conform precisely to the contours of gums and dentures. It is created by the consumer mixing a premeasured amount of polymerized polyethyl methacrylate powder and a solution composed of approximately 76 percent plasticizer, 19 percent ethyl alcohol, and five percent polyvinyl acetate as a softener. The polyethyl methacrylate polymer --

DR. GENCO: Excuse me. Ms. Seidman, would you please speak into the microphone? Thank you very much.

DR. SEIDMAN: The polyethyl methacrylate polymer is a homogenous powder of closely controlled particle size and purity containing only trace amounts of FDA-approved colorants. When mixed the plasticizer and alcohol components of the liquid penetrate the polymer particles producing a slurry. As the liquid continues to penetrate the polymer particles the slurry becomes stiffer and, over the course of several minutes, a gel-like elastomer forms. The material is fully set within five to seven minutes. The process is not unlike making a batch of Jello. The setting mechanism is essentially physical in nature. No polymerization occurs in the mouth and no heat is produced. The product performance characteristics are carefully controlled through in-process testing.

The viscous liquid formed by mixing the two device constituents is applied easily to denture surfaces. It is designed to flow freely between the denture and the gums for a period of several minutes under bite pressure until the mixture sets to form an elastomer gel. The flowable nature of the mixed material is designed to fill areas where there is poor fit between gums and denture and flow out of areas

where there is closer apposition.

After the material forms to fit, the denture is removed and any excess material is easily trimmed from the denture edges. The entire device is easily removed from the dentures by soaking them in warm water.

The composition and performance characteristics of the subject device are controlled through rigid specifications by the manufacturer. Methods available for the complete characterization of the device are of three principal types: Chemical tests to evaluate composition, physical tests to assess physical properties, and biosafety assays to evaluate toxicity.

Highly-sensitive analytical methods are available to fully characterize and assess the composition of the device and its constituents. These include recognized state-of-the-art test methods such as NMR, IR, chromatography, such as HPLC, GPC, and GC, mass spectrometry, AA, thermal analyses, specific gravity, and others.

Similarly recognized methods are available to assess and control the physical properties of the device and

its components. These include particle size analyses to evaluate the size and consistency of polymer particles, viscosity determinations to evaluate flow and set rate characteristics of the mixed material, penetrometry analyses to assess the hardness of the finished elastomer, and water absorption tests, among others.

Methods such as these are rigorously employed by the manufacturer to control device properties and production and to ensure consistency and conformance with product specifications.

FDA and ISO recommend specific biocompatibility testing areas for consideration in evaluating the safety of biomaterials for intended uses. Testing areas are therefore dictated by the type of tissue the material contacts and its duration of contact. FDA's testing recommendations are formalized in the Office of Device Evaluation's blue book memorandum number G95-1 and ISO's in its standard 10993-1.

Specific standardized protocols for these tests have been issued by such recognized organizations as ISO, USP, ASTM and AMI.

Brimms subjected extracts of its denture surface

material and its constituents to a number of such tests, employing standard, recognized protocols. They included cytotoxicity testing, single and multiple dosing, oral studies in rats, and intercutaneous studies in the rabbit. Brimms has satisfactorily addressed ISO and FDA recommendations.

Of special significance is the cytotoxicity assay which is a very sensitive predictor for irritation. This study was essentially negative. Furthermore, all such testing was conducted in full compliance with FDA's good laboratory practice regulations. And the results of all tests indicate the device material is safe for its intended use.

To summarize, the subject device is composed of two premeasured constituents, a polymerized polyethyl methacrylate which when mixed by the consumer with an alcohol and plasticizer liquid sets gradually to form a soft elastomeric cushion. The gradual process by which the material sets in the mouth allows it to flow freely such that it fills only areas of imperfect denture fit.

Testing has been conducted which fully

characterizes the device, its components, and its critical properties and such tests are routinely used to control manufacture of the device to assure consistency and appropriateness of performance.

Testing in accordance with recognized standards has shown that the device is not cytotoxic and is otherwise biocompatible.

Lastly, recognized state-of-the-art methods exist whereby such critical characteristics of the device as composition, physical properties, and biocompatibility can be and are evaluated and controlled.

I would now like to introduce Dr. Robert Flinton, who will review clinical issues associated with the use of the device.

DR. FLINTON: Good morning. My name is Robert Flinton, I am Professor of Prosthodontics and Biomaterials at the New Jersey College of Medicine and Dentistry. I am a paid consultant to the sponsor and have no financial interest in Brimms, Incorporated or its products.

I will be providing an overview of the clinical experience associated with the use of the subject device and

will also address issues relating to its clinical use which are key to the decision facing the panel today. While I was not personally involved in any of the clinical research, I have thoroughly reviewed the data.

As was mentioned earlier, the subject device has been marketed as a temporary denture surface for over 38 years. In this four decades of clinical use, it is estimated that approximately 25 million units of the product have been distributed commercially and used in the U.S. In that period of time virtually no evidence of significant or unreasonable risk to health associated with the use of the device has been reported by the manufacturer.

During the period of 1989 through 1996, the sponsor distributed approximately 6.5 million units of the product. Applying the definition of the complaint, as described by FDA's good manufacturing practices and medical device reporting regulation, the sponsor's complaint rate during this period is one per 255,000 units sold. Of these reports, none showed evidence of serious injury. Clearly, these data do not suggest that a significant or unreasonable risk to health is associated with use of the product.

Some years ago, a clinical study of the safety and effectiveness of the subject device was conducted. In this study, which was conducted at the College of Medicine and Dentistry in New Jersey, subjects with poor-fitting dentures were enrolled to evaluate the product with respect to three issues -- product safety, product effectiveness, and the ability of the lay user to properly file the instructions provided with the device.

As an objective trial, without matched controls, this study meets the FDA's definition of valid scientific evidence as contained in the federal regulations presented previously.

In that study evaluating only subjects with poorly-fitting dentures, the study was deliberately biased against the subject device. In the study, a total of 32 patients were enrolled, each had to have at least one full denture judged by a clinical examiner to have a clinically fair or poor fit, scoring for or less on the Kapur Index. All subjects had to be in otherwise good health.

Each subject was examined a total of five times at enrollment following initial application of the device and

at one, two, and three weeks thereafter. Each subject served as his/her own control with comparisons made between pre-study values and those obtained during the course of this study.

At no time during the study were the subjects given any instruction on the application and use of the subject device, but to simulate commercial use by the lay person, were given only the device package insert and asked to use the product according to the instructions.

A variety of safety and effectiveness and consumer use information was gathered at each time period. Such information consisted of both objective data gathered through the testing by the examiners and subjective information solicited from the subjects themselves. A detailed summary of the data is contained in the materials which have been provided to you.

The results of this study indicate that for all effectiveness parameters measured those being overall fit, comfort index, Kapur index, and occlusal contacts. The subject device caused substantial improvement in denture stability and retention. Further, there was no significant

change in freeway space or phonation space caused by the use of the subject device. In only one case was there evidence of denture discoloration.

The first device application lasted an average of approximately 16 days and, in nearly every instance it proved easy to remove.

From the viewpoint of the lay user, the study suggests that the device labeling instructions were easy to understand and follow. This is born out by the fact that all but two applications of the denture surface were graded good to excellent by the clinical examiners and that the majority had no difficulty in removing the device at the completion of the study.

With regard to the slight increase in localized irritation observed during the course of the study, we note that, in no instance was the irritation of a serious nature or sufficient to cause the subject to withdraw from the study. Further, in the majority of the cases, the irritation was so minor as to go unnoticed by the denture wearer. Lastly, no evidence of inflammation or edema was observed in the study.

Of relevance to any discussion of these findings as they pertain to the matter before us today are several key issues: The safety and effectiveness of the device, the risk to the health associated with its use, and the means available to control these risks.

The data just presented from the clinical study clearly established the effectiveness of the device as a temporary denture surface, which is comfortable to the wearer and significantly improves fit, stability, and retention of the denture without affecting freeway space or damaging the denture themselves.

Exclusive of some minor irritation that went largely unnoticed by the wearers themselves, there were no safety issues raised in the study. Further, the published literature and, in my own professional experience, indicate that such minor irritation is a common occurrence associated with denture wearing itself, nonetheless, in any discussion of risks, we must take these data into account.

The FDA has identified several risks potentially associated with the use of the OTC denture cushions and pads. They include improper or increased vertical dimension

of occlusion which may lead to increased biting forces and result in bone loss through resorption and long-term irritation of the oral tissues that may lead to formation of carcinomas.

Please remember that the chemical composition of this device is markedly similar to other materials used by dentists for the stabilization of dentures.

As described earlier, the flowable nature of the material prevents the device from altering the vertical dimension of occlusion because it adapts to proper tissue apposition relative to the various tissue contours which results in varying thicknesses of the material. The net result is zero or a very minimal change in vertical dimension of occlusion or bite characteristics.

The results of the clinical study supports this. As we have explained, the viscosity and set rate of the subject device assure that it will flow freely and not increase the vertical dimension of occlusion.

In contrast, however, the wax-impregnated cotton cushions which the FDA has placed in class I are approximately one millimeter thick, and the thickness always

adds to the vertical dimension. By posing a lesser risk of altering the vertical dimension, then do the wax-impregnated cotton cushions, which the agency has already placed in class I, it is clearly appropriate that this subject device be placed in class I as well.

With regard to the risk of long-term irritation cited by the agency, we note that only one minor localized irritation was seen in a fraction of the clinical study participants. In a study conducted by Leco, et al. comparing tissue response to new dentures, professionally relined dentures, and denture fitted with temporary cushions, comparable, if not higher incidence of local irritation were seen in all three groups.

The fact that local irritation is associated equally with new dentures, professionally relined dentures, and dentures fitted with temporary cushions suggests that it is the use of the dentures rather than any specific material which is the significant contributor.

It must be noted that the continuous wear of hard-surfaced, ill-fitting dentures is significantly more detrimental to the supporting oral tissues, causing rapid

and excessive bone loss, papillary hyperplasia, inflammation, ulcers, epuli and possible tumors.

Proper use is controlled by very strong and direct labeling. These devices are recommended for temporary use and only until the dentist can be seen to re-line or re-make the ill-fitting denture.

Given this limitation on use of the device, the realistic risk of adverse effects are inconsequential when used as directed. Based on the clinical evidence and my experience, I believe this device can safely be used for at least seven to 10 days. Only under circumstances of abuse by the denture-wearer are risks of the types cited by the agency likely to manifest. This is equally a risk with other class I OTC denture retention products such as adhesive and wax cushions.

Labeling for the subject device addresses these risks directly and conforms fully to the FDA's requirements for labeling of such products as delineated in the Federal regulations in that it limits direction for use to temporary refitting and pending unavoidable delay in obtaining professional reconstruction of the denture. It

conspicuously contains the word temporary preceding and modifying each indication for use statement. It includes a conspicuous warning that long-term use of the product may lead to faster bone loss, continuing irritation, sores, and tumors and the device is for use only until the dentist can be seen, and adequately describes the temporary nature of the device, its limitations, and the importance of adhering to the warnings.

Labeling then is a principal means of controlling all risks. It is under such labeling conditions that the subject device has been marketed without unreasonable risk to the health of the patient for nearly 40 years.

As a clinician, I accept that no absolute assurance of safety does or can exist. The subject device is a simple one which when used as directed can avert serious adverse effects such as irreversible bone loss caused by ill-fitting dentures. I believe the risks to the health of using such a product is far less than the risk of not using it.

Adequate labeling is the single most effective means of controlling such risks. It is my understanding

that placing these devices in class III will provide no greater assurance of the adequacy of labeling controls than does class I.

In the interest of avoid the costly and unnecessary regulatory burdens associated with class III and the correspondingly higher cost to consumers, which will inevitably follow, I strongly believe that class I is adequate for this product.

At this time I would like to reintroduce Steve Reitzler, who will summarize our reasons for proposing reclassification of the subject device to class I.

DR. REITZLER: Thank you, Dr. Flinton. Ladies and gentlemen, the device we have described here today is one which has been shown through valid scientific evidence to be safe and effective when used in accordance with its labeling. I remind you here that by regulation any determination of safety and effectiveness for a device must be considered only within the context of its labeled intended use. The device has been distributed widely for over 38 years under the equivalent of class I general controls. During this period, no significant or

unreasonable risk to health has been associated with the device.

The risks known to be associated with its use and which are described by the FDA in its final rule, placing the device in class III are less than the risks known to be associated with wax-impregnated denture cushions the FDA has placed in class I. Further, the risks are well-known to the medical community and are effectively and appropriately managed through labeling which instructs the user in proper use and warns against improper use.

As Dr. Flinton has made clear, the benefits of using the device as indicated outweigh the risks associated with its use. Without such devices the prolonged wear of ill-fitting dentures can cause irreversible bone loss. For these reasons it is our contention that the current class III classification is inappropriate and unnecessary to control the risks presented by the device.

A device is or should be in class III only if insufficient information exists to determine that either general controls alone or general and special controls together would provide reasonable assurance of safety and

effectiveness and if, in addition, the device is life-supporting or life-sustaining, of substantial importance in preventing impairment of human health, or presents a potential unreasonable risk or illness or injury. It is our position that the subject device is not life-supporting nor life-sustaining, is not of substantial importance in preventing impairment of human health, and does not present an unreasonable risk of illness or injury.

As such, it is inappropriate to place this device in class III. We contend that there is adequate information available to demonstrate that general controls alone are sufficient to provide reasonable assurance of safety and effectiveness and that the device should be in class I.

On this slide, a comparison of the three device class clearly demonstrates the differences in control. As you can see, the prodigious general controls apply equally to all three device classes. These general controls include regulations controlling adulteration, misbranding, registration, listing, and premarket notification, banned devices, notification and other remedies, records and reports, and general provisions. The latter includes FDA's

good manufacturing practices regulations by which medical device manufacturing and quality assurance are controlled.

Perhaps a better way to look at this issue is in terms of what reclassification of the device will not change. Reclassification to class I will not change the device materials or the specifications for the device; reclassification will not change the methods by which device materials are characterized and controlled nor the methods by which the device's biosafety is assessed; reclassification will not change the standards and methods by which the device is manufactured, tested or controlled during manufacture; reclassification will not necessarily change the device labeling; and, lastly, reclassification will not necessarily change any other means of regulating the device other than in the mechanism required to reach or remain on the market.

Based upon what we have presented, we believe that the device has been demonstrated to be reasonably safe and effective, that the risks to health associated with the device are well-known and can readily be controlled through labeling and other class I general controls, that no

unreasonable risks to health are presented by the device when used as intended. Accordingly, we believe that class I is the appropriate classification for the device and that class III cannot be sustained.

The appropriateness of class I is supported by the fact that other similar use devices and materials have been placed in class I. These include other OTC denture retention devices such as denture adhesives and wax-impregnated denture cushions.

In considering this reclassification petition, the panel must consider the adequacy of the information we have provided in support of the petition and should prepare a written recommendation for approval. The panel should determine that the information indicates the device is reasonably safe and effective when used as labeled and that the risks to health posed by the use of the device, as indicated are well-known. Finally, the panel should conclude that controls other than those imposed by class III are sufficient to provide reasonable assurance of safety and effectiveness.

This concludes our presentation. We will now be

happy to entertain any questions.

DR. GENCO: Thank you, Mr. Reitzler. Are there any questions for Mr. Reitzler, or Drs. Seidman or Flinton from the panel? Yes, Dr. Norman.

DR. NORMAN: Dr. Seidman, you have given a list of tests that have been run. I notice there was no solubility test. The plasticizers undoubtedly dissolve out during use. Why was that test not done?

DR. SEIDMAN: Well, are you asking the question from the perspective of the biological significance of --

DR. NORMAN: Yes.

DR. SEIDMAN: -- plasticizers? Well, that would be addressed in the extract studies on these tests or even with the cytotox test which, if there was plasticizer that was biologically significant it would bleach out of the material on the auger.

DR. NORMAN: How long were these dissolvable material tests performed?

DR. SEIDMAN: According to USP and ISO, the device is placed on the auger for 24 hours for the auger overlay, which is the most appropriate cytotox method for this device

in my opinion.

DR. NORMAN: However, the materials may be used for a period of time.

DR. SEIDMAN: Right. That is absolutely right. When ISO and USP set up these standard tests --

DR. NORMAN: I am not talking about that.

DR. SEIDMAN: I realize, but it does get at your question. It realized that many of these devices are going to be used for longer periods of time so it set up batteries of tests that it felt were conservative to address the durations of particular tissue contacts. So, for instance, on the cytotox test, even though this device only contacts the cells for 24 hours, that is a very sensitive test. Those cells are unprotected. Then, in addition, you do other tests.

But are you familiar with the matrix for ISO? You see more and more tests that are recommended for longer contact durations?

DR. NORMAN: I am quite familiar with it.

DR. SEIDMAN: Yes, and then the extracts. You have different extract temperatures and durations. So, for

instance, we could have extracted this material let's say at 70 degrees C for 24 hours and that is still a lot shorter than the devices in contact with the patient. I do not know if that gets at your answer.

DR. NORMAN: No.

DR. SEIDMAN: It does not?

DR. FLINTON: May I offer some response to that also? This material -- the composition of this material is virtually identical to those other materials on the market that are not over-the-counter but are used readily in all dental offices. So it is not that we are introducing a unique material for you.

DR. NORMAN: The plasticizers are not used routinely in other devices.

DR. FLINTON: I believe they are, yes, sir.

DR. NORMAN: Name them.

DR. FLINTON: Botrusol, Cosol, Viscogel all have plasticizers in them of varying degrees.

DR. SEIDMAN: I would also like to comment. I did a literature search on the plasticizer and the peer-review data literature shows that it is not toxic. So I was not

concerned about that plasticizer. The literature supports it is not toxic to further answer your question.

DR. GENCO: Further questions or comments. Yes, Dr. Patters?

DR. PATTERS: Mr. Reitzler, if I understood your last slide, you are not proposing any changes in the labeling as it currently exists on the two representative packages that you provided the panel. Is that correct?

DR. REITZLER: We are not proposing any labeling changes at this point. We do understand that, if it is deemed advisable to tighten or strengthen that labeling, certainly, we are amenable to discussing that with the agency and participating in drafting additions to what are the current labeling requirements in 801.405 I believe.

DR. PATTERS: Could I ask you specifically then what message you would give the consumer on the front of the package when it says it lasts for weeks?

DR. REITZLER: I am sorry. I am not familiar with that statement. That particular statement I believe is a reflection of the clinical study of which you have been provided which did test materials out to three weeks.

Inside the package insert does contain the stronger warnings as to its temporary use, and that it is only to be used until you can see a dentist to have your dentures refit, relined.

DR. GENCO: Further comments or questions? Yes, Deborah.

DR. GREENSPAN: I have two questions. Is the study that has just been cited the only clinical study that has been done of these 32 patients?

DR. REITZLER: It is to my knowledge.

DR. GREENSPAN: The second question is I wonder if one of you could please comment on the toxicity of this product if the powder is ingested, the liquid is ingested, or if the properly-mixed material is ingested?

DR. SEIDMAN: Brimms has done oral ingestion studies of all three and LD50 studies. It is not toxic. You have a package, don't you?

DR. GREENSPAN: I have looked at the package.

DR. SEIDMAN: You do not have one of the recent studies though I guess?

DR. GREENSPAN: I do not have that in front of me.

Essentially my question is what happens if somebody drinks two bottles of this liquid?

DR. SEIDMAN: This is the alcohol? This is an unintended, unlabeled use. I do not know. I am only speculating. You cannot -- first of all, the studies were done in animals. I would have to consider humans. Are you asking for an opinion? I cannot -- I do not have any --

DR. GREENSPAN: Well, I am asking whether you have any data to provide me with some information about what happens if somebody swallows these two bottles of liquid or one bottle of liquid.

DR. SEIDMAN: To really answer that question I would have to get some --

DR. GREENSPAN: -- and whether or not in the packet that has been circulated to us -- because I did not open the packet inside -- there is any information about the ingredients and the specific instructions as to whether they should not be ingested.

DR. SEIDMAN: I cannot answer that; but maybe Mr. Burgesh could answer whether or not there are instructions on the labeling that the --

DR. GREENSPAN: Or warnings. I did not see any in there. I do not see any ingredients. So, if nobody on the panel objects, I am going to actually open the -- Dr. Patters does it say anything on that label about ingredients or instructions not to --

DR. PATTERS: Not that I can see.

DR. GREENSPAN: Thank you.

DR. REITZLER: If I might make two comments. One, the LD50 studies were conducted on the constituents, that being the liquid and the polymer, in addition to the combined product. I believe the LD50s were in excess of five grams per kilogram, which is fairly high.

Additionally, I will not speak to the likelihood of someone swallowing two bottles of this; but, nonetheless, by regulation, the safety of this material has to be considered within the context of its labeled conditions for use and not outrageous abuse.

DR. GREENSPAN: I am absolutely aware of that. But I was curious as to what information was provided to the user. The little bottles are unlabeled. I just wondered what the packet information provided for the consumer.

Thank you.

DR. GENCO: Further comments or questions from the panel? Yes, Dr. Burton.

DR. BURTON: This is for Dr. Flinton. Have you considered the possibility that a patient might have a bridge defect that could be either acquired or congenital that this material because of its flow nature could go into and become trapped and unaware to the patient and then left in the tissue for an extended period of time, obviously easily removed if the patient was aware of it? But, again, because of the fact that it flows in it could become trapped in the defect?

DR. FLINTON: Actually, no because of the nature of the material or the nature of the dentures that we are talking about are not the severity of the well-controlled patients that you are talking about with reconstructive surgery or maxillofacial defects. But I would also suspect that if, in fact, we were to lock in some sort of a defect the result would be some form of a minor irritation that probably would then precipitate a more expeditious return to the dentist.

DR. BURTON: Thank you.

DR. GENCO: Does anybody else have a comment or a question?

[No response.]

DR. GENCO: If not, we would like to thank you very much.

We will now proceed to the sponsor presentation by Mentholatum. Again, the guidelines are a 20-minute presentation and approximately five or seven minutes for discussion after that.

Agenda Item: Sponsor Presentation - Mentholatum

DR. RUBIN: Good morning. My name is Paul Rubin, and I am an attorney from the law firm of Bacon, Gump, Strauss, Howar and Felds. I am here today on behalf of our client, the Mentholatum Company, who markets and manufactures Snug Denture Cushions, which I have a box here -- I know we wanted to hand out a package to everyone. I do not know if we have done that. Great, thank you.

As you know, we are here today to request reclassification of the cushions from class III to class I. I am going to provide some introductory comments and then

Dr. Gettleman will be speaking. First, let me introduce the Mentholatum representatives who are here today who can then be available to respond to any questions the panel members may have.

[Introductions were made.]

DR. RUBIN: One thing I would like to mention first is that we have handed out, in addition to the packet of Snug that is coming around, we have also handed out a proposed labeling for snug cushions. We are willing to retain the current labeling, but we believe that the revised labeling would be more appropriate. So we are going to discuss that. Dr. Gettleman will be discussing that during his presentation.

I would first like to provide some general background information regarding the Mentholatum Company. Mentholatum has been in existence for 108 years. It is a very well-established OTC health product company. The Mentholatum Company is not a particularly large company and has limited resources. Mentholatum has been marketing Snug denture cushions since the late 1960s. Snug was marketed prior to that time by a different company. So Snug's

history goes back to 1939.

We are here today in support of reclassification because we believe that PMA requirements for soft plastic denture cushions would be unjustified. Snug cushions are very simple products composed of a rubbery acrylic. I am going to hold it up. You all should have one in front of you as well. It is very similar to the substance that is used to make dentures. No mixing of ingredients is required for the Snug cushions.

Snug also has an extensive documented positive safety profile. For years, Snug has been marketed subject to FDA's general controls and has a long and established history of safe use. In fact, since 1984, six million Snug cushions have been used and no serious adverse effects have been reported to the Mentholatum Company.

In addition, Dr. Ciancio, in conjunction with Dr. Lociello, conducted an extensive literature search which reviewed literature over the past 40 years. This search also identified no serious adverse effects associated with soft plastic denture cushions. This literature search is part of the package of materials you received from us and is

part of our reclassification petition.

At present, in addition, Mentholatum records indicate that from 1989 to the present time, only 188 customer inquiries or complaints have been received. Of these 188, only four relate to any type of adverse experiences. All four relate to issues involving sore, burning gums, the type of conditions that are by no means extraordinary and may be associated with denture use regardless of whether denture cushions themselves are used.

As part of our reclassification petition, we have provided the panel with data in support of the safety of soft plastic denture cushions. The petition contains two clinical studies, one conducted by Dr. Stallard, and another one conducted by Drs. Lociello and Dr. Anayo. Again, Dr. Gettleman will be addressing those studies in a few moments.

Based upon this information, Mentholatum believes that soft plastic denture cushions do not merit the level of scrutiny associated with more complex devices such as heart valves which have been placed in class III.

With regard to product misuse, we believe that

misuse concerns can be raised for virtually every device and/or consumer product and therefore we believe that misuse concerns are somewhat misplaced.

As you know, FDA-classified wax-impregnated cotton cloth cushions in class I, while all other cushions were classified in class III. This distinction between the two types of cushions was based entirely upon historical reasons and was not based upon any safety or efficacy differences specifically raised by FDA or the panel.

Since Snug has been marketed since 1976 subject to general controls, there is little doubt that general controls provided a reasonable assurance of the safety and efficacy of soft plastic denture cushions such as Snug and this, of course, is the statutory requirement for classification in class I.

At this point, I would like to spend just a few moments and just briefly review the regulatory history of denture cushions in order to establish a framework for Dr. Gettleman's discussion.

Denture cushions, as you know, were initially regulated as drugs prior to the medical device amendments of

1976. After that time, denture cushions were regulated as devices. Historically, the panels that reviewed Snug cushions, that includes both the drug panels, as well as the device panels, only reviewed data on the wax-impregnated cotton cloth cushions.

In 1979, the Mentholatum Company attempted to engage the panel to review safety and efficacy of soft plastic denture cushions, but this data -- because the panel did not have any data before it, it did not review the soft plastic denture cushion issue. This, of course, is the only reason why FDA placed wax-impregnated cotton cloth cushions in class I and soft plastic, as well as all other cushions in class III. Neither FDA nor its advisory panels have ever addressed specifically the safety and efficacy of Snug soft plastic denture cushions.

With regard to the wax-impregnated cotton cloth cushions, the Drug Panel, as well as the Device Panel, reviewed two studies in support of safety and efficacy. One study was a three-year study conducted by Dr. Yurkstiss -- I hope I am pronouncing that correctly -- as well as a six-week study conducted by Dr. Stallard. Both panels, the drug

panel and the device panel, wildly criticized the three-year study conducted by Dr. Yurkstiss due to data inconsistencies. There are comments in the panel discussions that the three-year study is basically irrelevant with regard to the safety and efficacy profile of the wax-impregnated cotton cloth cushions. So, consequently, the classification into class I for the cloth cushions was based virtually entirely on the six-week study conducted by Dr. Stallard.

The panel today has been provided with virtually an identical study conducted by Dr. Stallard on the Snug soft plastic denture cushions. Dr. Stallard has submitted a letter which is part of the reclassification petition which states that the protocols for both studies, as well as the results were virtually identical.

In addition, the panel has before it the three-week study conducted by Drs. Lociello and Dr. Anayo. Consequently, we believe there is much, if not more information in support of the safety and efficacy of soft plastic denture cushions than there was for wax-impregnated cotton cloth cushions.

That is the end of my introductory statement. I would now like to introduce Dr. Gettleman, who will handle the technical and scientific aspects.

DR. GETTLEMAN: I am Lawrence Gettleman. I am Professor of Prosthodontics and Biomaterials at the University of Louisville. I am a paid consultant for Mentholatum, and I have no financial interests in the company or in the product that we are discussing.

My interests are in the biomaterials and prosthodontics and I had NIDR RO1 support for seven years while at Gulf South Research institute in New Orleans to develop a soft liner for dentures that are applied by dentists and dental laboratories and also RO1 support in maxillofacial prosthodontics.

I would like to summarize my comments in six different categories. One is the composition of the material, two is the literature search, three is a description of the clinical trials, four is address the safety issues, five address the efficacy and, six, discuss the labeling.

The composition for Snug material. The final

product has been passed out to you. It is approximately 81 percent poly and butyl methacrylate, which is a similar material to methyl methacrylate which is used to construct the rest of the denture. It has an approximate molecular weight of 200,000. So it is a rubbery acrylic with softer properties than the polyethyl methacrylate used for the rest of the denture. In addition, there is a six percent content of polyethylene glycolmonolurate as a plasticizer. Any residual monomer that was present in the butyl methacrylate is reduced in the processing of the material. Chemical estimates indicate that there is less than half a percent of residual M-butyl methacrylate in the product. The additional 13 percent not accounted for by the plasticizer and the original polymer is made up with fillers and pigments.

The literature on denture cushions is not very extensive. I believe that it has all been sent to you. I might draw your attention, if you had it, to references 74 through 91, which discuss over-the-counter denture cushions. This was done by Dr. Cianco and Loracella. They reviewed the world literature from 1953 to 1996. In part two, in

discussing over-the-counter relined materials, the latest report on this topic in the world literature that we have found was in 1984 which concerned another product.

In the entire dental literature there are no adverse reports on snug soft plastic denture cushions, and very few on other cushions or pad products sold over-the-counter. They found no effect on the oral mucosa or the vertical dimension in these published reports.

Two clinical trials have been conducted over the years, the first one by Heiser and Stollard that was referred to a moment ago that was a six-week clinical trial of complete denture patients, upper and lower complete dentures, average age of 49. There were 33 subjects in the trial. Each subject acted as his/her own control. The quotations from the conclusion of the study by Stollard and Heiser was that the products had significant value to improve fit and stability of denture patients, and that the product was safe and effective. He went on further report no adverse effects on the oral mucosa and that injury was non-existent when the cushions were used for short periods of time. This was the Heiser and Stollard study.

The second study by Lociello and Anayo at Buffalo was a three-week study. The average age of the complete upper and lower denture patients was 58. There were 25 subjects in the study. The only statistically-significant result that was reported was in the improvement and fit -- subjective evaluation of fit of the dentures. In quotations of the conclusions it was noted that the Snug denture cushions improved the fit of dentures particularly from a patient's perspective, and offered temporary relief to the problem of poor-fitting dentures. That is the summary of the clinical trials that have been conducted on this particular product.

Regarding safety. Snug soft plastic denture cushions have an excellent safety record as evidenced in the literature which is non-existent regarding problems clinically. When used according to labeled instructions, they posed virtually no safety risk.

As a practicing prosthodontist, I strongly believe soft plastic denture cushions have a meaningful role to play in treating denture patients to temporarily improve the fit and comfort of dentures. I have encountered patients with

Snug cushions and have recommended them noting no ill effects.

Now, let me point out that, as a prosthodontist, by the time we talk to the patient, are usually in the process of making corrections to the denture. So prosthodontists and practicing dentists do not often advise patients to use these except in temporary or emergency situations.

Denture cushions relieve rather than intensify any oral problems already existing due to the use of ill-fitting dentures. The FDA acknowledged this when it placed wax-impregnated cotton cloth dentures into class I in the early 1980s.

The panel should also keep in mind that the denture cushions are removable from the denture, that is it can be removed from the denture if a problem were to develop. Of course, the dentures are removable from the patient. This is as opposed to other dental devices which are more difficult to remove or certainly most medical devices often placed in class III. Accordingly, any problems arising from the use of cushions or the dentures,

in general, are self-limiting.

Regarding efficacy or effectiveness and benefit to health. The two studies submitted to the panel support the benefit to health of soft plastic denture cushions. Dr. Stollard concluded that soft plastic cushions provide the following benefits: Improved comfort, increased denture stability, improved ability to eat, improved clinical appearance of the oral mucosa.

Dr. Stollard further states that there is little doubt that a significant percentage of the United States population may benefit from over-the-counter availability of soft plastic denture cushions.

Drs. Lociello and Anayo concluded that, in their clinical trial, that soft plastic denture cushions also provide the following benefits: Improved clinical impression of fit and stability by the patient; improved professional evaluation of cushions utility and safety; improved patient impression of comfort and stability, and improved patient impression of the ability to eat.

So, there is evidence based upon the product's composition, clinical trials, and from the world dental

literature that soft plastic denture cushions are safe and effective. There is not evidence to suggest otherwise.

No one disputes the fact that the ideal treatment for ill-fitting dentures is to reconstruct the dentures or modify them in some fashion by the profession. In the real world, unfortunately, many denture wearers are unable to obtain immediate care. Denture cushions therefore, provide these users with a temporary safe and effective option to improve denture fit and improve their quality of life.

Finally, regarding the labeling, Snug soft plastic denture cushions are only intended and labeled for temporary use until the dentist can be seen. How temporary is that? The product that is on the market, the wax-impregnated cotton denture cushions called ISO, or ISO, require daily change, in part, because the cloth may act as a wick that absorbs and releases food products and microorganisms. The Snug soft plastic denture cushions discussed here have been used successfully up to one week, as supported by the clinical study by Stallard.

Replacing the cushions each week for up to six weeks is also supported by the same study. I believe that

soft plastic denture cushions, on the other hand, are better able to resist fowling than wax, cloth-containing, wax-impregnated cloth denture cushions.

Mentholatum currently markets Snug soft plastic denture cushions without providing a specific length of time for which each cushion should be worn, in compliance with current FDA regulations.

The labeling does not address the duration that a single cushion may be worn. In addition, there is no specific guidance or limitation regarding the maximum period for use allowing for change of cushions.

Based upon available information, I believe it appropriate to label Snug denture cushions with instructions that permit use of the single cushion for up to one week, with a maximum overall duration of use of six weeks, unless additional use is recommended by a dentist.

The three-week study conducted on Snug by Drs. Lociello and Anayo, involve the use of a single denture cushion over a three-week period. The investigators found no negative effects from three-week use. Similarly, the protocol for the six-week study conducted by Dr. Stallard

provides that denture cushions may be worn up to six weeks.

Mentholatum, therefore, respectfully submits that each cushion be labeled to be worn for up to one week without being changed. Mentholatum believes that it is being conservative in proposing a one-week time period for the use of each cushion particularly in light of the fact that Snug is composed of a substance that is very similar to the acrylics used to make the dentures themselves.

In addition, Mentholatum is willing to label the denture cushions to be used for a maximum of six weeks, one per week. Thank you.

DR. GENCO: Mr. Rubin, we are about 15-16 minutes into the presentation, just to let you know how much time is left.

DR. GETTLEMAN: We are finished.

DR. GENCO: Oh, you are finished. Oh, well, I see two other gentlemen there. I thought they were going to present. Good. So are there any other comments or questions of Dr. Gettleman or Mr. Rubin?

In the Stallard study, there was about a 16 percent drop-out. There were a couple of reasons. One was

that the patients apparently were -- he speculated were quite pleased and never came back for the recall, which brings up the issue of length of use. You addressed that with the one pad per week per six weeks. What would happen if somebody just left it on for a year and did not replace it? I mean, is there any -- are there any adverse effects reported by dentists or by anybody for that kind of abuse?

DR. CIANCIO: I do not know of any data, Dr. Genco, on that topic. In the study that we conducted, we can only speak from the science we have. The longest any patient did go with a cushion was six weeks. A number of those people did replace them also, but long after six weeks. There Dr. Stallard noted that, at that point, they did not look very nice and the patients would not probably wear them much longer.

As far as the drop-out rate goes in this study, some of the patients dropped out because they insisted they are in an HMO plan. They insisted they have no dentures made after about three weeks.

We found in the Buffalo study that about three weeks was the maximum time that people would like to wear

these cushions.

DR. GENCO: Another reason for the drop-out -- about 11 percent of the patients could not use it. I think there were five women who could not use it. Is this something that you have considered in terms of your instructions -- altering instructions to make it a little clearer for people to use? That would seem to be a fairly high percent of people who just gave up and did not use it - - bought it but did not use it.

DR. GETTLEMAN: It requires a good deal of dexterity on the part of the patient, for the lower and the upper. The lower denture cushion has to be cut out into a horseshoe shape and then applied in some fashion. Part of the study -- the studies involve no instruction, and we let the patients follow the instructions on the package insert to be a true test of what was going on so that they would not be influenced by the personality or whatever of the clinician.

DR. GENCO: Has a change in the instruction been made since the Stallard study? He mentioned in his letter that there was feedback to the company and that changes were

made. I am just wondering if the present-day instructions are more clear than that that may not happen with present-day instructions.

DR. MILLER: I am Joyce Miller. The instructions that we currently have that you see on that package have been implemented since 1984. A Stallard study was done in 1980-1981, but I am not sure that they are that much different.

DR. GENCO: Thank you.

Excuse me. There was a question here?

DR. GREENSPAN: I have two questions. Has anybody looked at the microbial load on the Snug after it has been in the mouth a week? In other words, does the Snug liner support a heavier bacterial or fungal overgrowth at the end of a week? I do not know if you have that data.

My second question is how are patients expected to keep this clean on a daily basis? There was no instruction in the packet as to whether they should not clean them, whether they can use their regular dental cleaning, whether it can be soaked in weak Clorox. I was just wondering what the experience was from the studies about cleaning this.

There are two questions there.

DR. CIANCIO: In the Buffalo study they did look at the debris that was accumulated on the denture when they first saw the patient and they gave a score to that and they then scored it at the end of three weeks, which was quite a long time period to wear one cushion. There they found a slight increase in the overall debris, but nothing significant.

DR. GREENSPAN: So they did not look specifically for candida or for particular bacteria?

DR. CIANCIO: No.

DR. GREENSPAN: They were not plated out or swabbed, stained, or anything of that sort?

DR. CIANCIO: In 1984, the state-of-the-art at that time was not to go into bacterial cultures. But there have been no reports of any fungal overgrowths or any of those clinical problems that we would associate with increased bacteria.

DR. GREENSPAN: You did not see that in your short-term study?

DR. CIANCIO: No.

DR. GREENSPAN: And how did people keep it clean during that study?

DR. CIANCIO: We asked the patients that question, although it does not appear in the report. What they did in cleaning the dentures -- the same was they clean the regular denture. Some of them used things like Efferdent. Others would brush it with toothpaste and a toothbrush. They treated it as though it was their own denture.

DR. GREENSPAN: Thank you.

DR. MILLER: Maybe I can clarify one point too. The package insert does include how to clean it and it does tell you to clean it and wash it under cold water twice daily. It is on the back side of the package insert.

DR. GREENSPAN: Yes, but it only talks about using cold water and leaving it in water overnight. I wondered whether that meant that it should not be used with any other denture-cleaning agents. Is that what that means?

DR. MILLER: That I have no answer for or I am not sure.

DR. GREENSPAN: All right. Thank you.

DR. CIANCIO: I think that point is well-taken. I

know that patients did want to use denture cleansers. They always had. I think we should not have to change the way the patients are used to taking care of their dentures. So I think that should be something that should appear in the labeling.

DR. GENCO: Dr. Saxe.

DR. SAXE: Yes. I have a question that relates to the Stallard Study. That study which is quoted which is number of years ago done approximately 17 years ago or so. In that, as Dr. Gettleman noted, the average age of the subjects was 49 years. As we know, in the last couple of decades, there has been quite a change in the number of individuals who are dentureless, and more and more of our older individuals are retaining teeth.

Right now, we are seeing that, once we reach an age of approximately people in their early 80s, the majority of these people are dentureless and have been 30, 40, 50 years or more. So that my question is related to the age group which was mostly dentureless and are -- would buy this product and are expected to use it according to directions. Dr. Stallard's study -- and I take it, again, the question

has just come up and been answered about the directions, quote from Dr. Stallard: "In regard to utility, a problem did exist with those persons who did not receive professional instruction on the insertion of the cushions. The package insert does not appear adequate." Well that has been changed.

The question, again, is that this older-adult population is -- those who are dentureless are also at risk for chronic illnesses which may impair their and does impair their dexterity -- those who survive a stroke, Parkinson's disease, severe arthritis. So I wonder if relying on this old study is really appropriate for the questions that we are asking today. Can older-adult individuals utilize this material so that indeed it is effective and properly used?

DR. CIANCIO: If I can comment? I think that the Stallard study was 49 years. That was a reflection of that HMO system they were in at that time. The Lociello and Anayo study was 58 years, which was a Veterans' Administration study, which tends to be an older population. There they had people -- I think the oldest was 72 and the youngest was something like 46. But the overall usage of

these people -- they have been wearing dentures in the Lociello study for over 15 years and I think in the other study for over 13 years.

I think that your point is well-taken. But the people you are talking about today tend to have health home care assistants who help them with their home care needs. I think the instructions, as they are now, our study in Buffalo was not instructed -- there was somebody there giving the packet and told to adapt that to the denture. They go into the room, adapt it, put the dentures in and come back and be fitted. So the patients did do that without instructions, just reading the directions. But that was a 58 year-old average population, which is better than the Stollard one.

But I think, you know, again, the point -- we have to consider that people are going to live a lot longer than that in the future. With caregivers, I think that they have dexterity problems. That would be taken care of with instructions as we see them.

DR. GETTLEMAN: That is a good point, Stan as well. We face this problem in removable prosthodontics all

of the time. As people become more elderly and lose the ability to handle this, sometimes they cannot even wear dentures at all or they certainly cannot place them in their own mouths. This limits the type of treatment, if there were various attachments or magnetic -- or that is an advantage of magnetic attachments, for example, over other devices that retain partial dentures. So we face this. This product is not for everybody obviously.

DR. DRUMMOND: Yes. That was actually my question. On the studies they talk about poor and fair-fitting dentures. Are there any cases where you would not recommend this product? How would the person buying this know that they should not be using this product?

DR. GETTLEMAN: Well, this product is only temporary.

DR. DRUMMOND: But my question is you have a definition of ill-fitting, and the patient may or the consumer may have another definition of ill-fitting. Are there any labels anywhere that would recommend not using this product -- I mean, if they have extreme hyperplasia or extremely ill-fitting dentures? Basically, the way I read

this, anybody can use this. Is that what you are saying?

DR. GETTLEMAN: The only one that comes to mind is if the existing dentures have excessive vertical dimension, and the addition of another one millimeter cushion would increase that even more. Indeed, I think that was found in Stollard's study. There were a few patients whose vertical dimension was higher. But that is not the usual situation. Most long-term denture wearers suffer from decreased vertical dimension in most cases and collapse of the face. Therefore, a little opening on a temporary basis is usually not a bad thing.

DR. CIANCIO: I would just add to what Dr. Gettleman just said. In the Buffalo study, they actually measured immediately after a patient placed on themselves both upper and lower, they changed in vertical dimension. I think that the average change was 2.23 millimeters, which is far within the range of people who were all over closed when they have been wearing dentures for a long time period.

DR. GENCO: Further comments or questions? Yes?

DR. BARACH: I would just like to make one quick comment. Some of the very interesting comments about the

utility of denture cushions certainly are apt, however, I think most of them would apply across-the-board to all denture cushions, even those that have already been classified and placed in class I. So, consequently, when you look at the issue of denture cushions as a whole, I think the commonality of issues should be separated from the specific safety and efficacy issues relating to individual cushions. That is all.

DR. GENCO: Thank you. Yes, Dr. Bouwsma, and then Dr. Altman.

DR. BOUWSMA: From a safety perspective, Dr. Ciancio, I thought you reported on the review of the literature pertaining directly to Snug. What about of the constituents that are used in the manufacture? Has there been a review of those products and so forth and their safety profile?

DR. CIANCIO: Well, I think the best review is in this read submission that was given. There is a Dr. Custiniac, from the Buffalo Toxicology Center and the School of Medicine. He has reviewed the preliminary material that there should be some concern about, which is pure

chloroethylene. In there he points out that, if a patient were to use -- if the maximum amount of pure chloroethylene were to be used from the liner and the patient were to change the liner every single day, he would still come within the range of what is acceptable intake for a person assuming they have intake from air, water, and the denture liner. So, therefore, there would be no safety problem.

DR. GENCO: Dr. Altman.

DR. ALTMAN: My concern is actually one that Dr. Greenspan had on the other product is what is this material made of as far as labeling here. I guess, actually for both products, they seem to have a relatively low number of complaints. But I wonder if that is not because the labeling does not really make it conducive for the consumer to comment. I do not see an 800-number here if you have comments about the product. My concern would be if a grandchild swallowed the liquid or was chewing away at this. You know, it may not be toxic. You may know that, but a grandparent would not know that. We would not even know if you called a poison control center to tell them what the product was made of. So my concern is more information as

far as what the product is in the labeling and consider an 800-number for people to call for complaints or comments.

DR. GENCO: Thank you. Any further comments or questions?

DR. PATTERS: If the company could just clarify the demonstration package that they provided to the panel. It has an insert which is labeled PD-3 in the bottom corner. But a xerox copy of the packaging is labeled PD-4 on the bottom and their appear to be some wording changes. Which of these are the current ones?

DR. MILLER: The labeling that you have is the marketed product that is currently on the market right now. The labeling was changed due to the fact that it will be manufactured in China, not in the United States. There were some modifications that were made to the labeling, but not in context, because we knew we were going to come to the panel and possibly change it again. But we are going to be bringing this product in very shortly.

DR. PATTERS: The PD-4 label is not the one currently in the product?

DR. MILLER: That is the current labeling right

now.

DR. PATTERS: PD-4?

DR. MILLER: But it is not on the market yet.

That is what we consider the current.

DR. BARACH: If I can clarify? Perhaps we were too forward with the panel. We were asked to provide labeling. The PD-3 version is what you would find in the drug stores today in the United States. PD-4 will shortly be introduced. So we wanted to provide complete information to the panel.

DR. MILLER: I would like to make one more statement also that Mentholatum has a satisfaction guarantee. We get a great many customer inquiries, calls all of the time on a regular basis. Much of the complaints in the 188 that we had are returned because either they say that it did not work or they just wanted their money back. We get an awful lot of those. So we do get -- although not by 1-800 number. They can reach us readily and the name Mentholatum is commonly known if they know any of the other products. They know that they can call up at any time. That makes it readily available.

DR. ALTMAN: Does it say money-back guarantee?

DR. MILLER: On this one I am not sure we do. On every other product we say satisfaction guarantee.

DR. GENCO: Okay. Any further questions or comments?

[No response.]

DR. GENCO: I remind you that we are going to have a break soon. After that, Mr. Shipps will give the FDA summary, and then Dr. Norman will give his summary, and then we will go to a discussion and a vote. We have a busy day today. If there are no further comments or questions of the Mentholatum people, I would like to thank them very much.

Let's take a break.

[Recess.]

MS. SCOTT: Mr. Gerald Shipps, of our staff, passed around several of the Snug sample products. I just wanted to clarify that Brimms, Incorporated also had passed out some sample products and material. They had one that, I believe, before the panel meeting. I just wanted to make that clarification that both companies had opportunities to provide sample products and information to the panel.

At this time, also, Mr. Keith Roberts, who wanted to present during the open public hearing is here, and we wanted to give him a couple of minutes to make his statement to the panel. He is from Nouveau Laboratories.

Agenda Item: Open Public Hearing

MR. ROBERTS: Good day. Thank you for the opportunity. My company is a manufacturer of ISO Denture Cushions, which is why I am here. I am a lawyer by training so I do not bring any technical expertise or understanding here. I, therefore wish to make a couple of comments. A number of references were made to the record of the previous hearings which did concern ISO and other denture cushions. I would urge the panel, if the panel wishes to rely on any of these verbal references that we have heard this morning to actually look up the material. Because I attended those hearings and, of course, I read the material very avidly. I do not recall certain things as being true which were stated here. I do not recall that it was true that the study by Dr. Yurkstis was criticized by the panel. There was criticism of earlier studies, but I do not believe it was of Dr. Yurkstis' study. So that is one thing.

The second point is I do not believe that there was any reference by the earlier panel to a wicking action by ISO as the reason for the one-day limitation. I would, therefore, urge the panel that, if it is going to change labeling requirements that there is no evidence, as far as I know, in front of the panel that would justify providing a longer usage period for any other cushion product than is provided for ISO. Of course, that would be a serious competitive disadvantage in the marketplace. Those are my only comments.

DR. GENCO: Thank you, Mr. Roberts. Any comments or questions to Mr. Roberts?

[No response.]

DR. GENCO: Okay. Thank you very much.

According to the Federal Register, at 11:00 we were going to be talking about the mandibular condylar replacement grafts or transplants, or implant. If there is anybody here who would want to discuss that now, although it is a little bit out of order, but we legally must allow you to do that now particularly if you cannot come back this afternoon. Yes, if you cannot come back this afternoon, you

can address those issues now.

PARTICIPANT: I cannot come back this afternoon.  
I am here to discuss the clinical aspects of it.

DR. GENCO: You can? You are able to come back  
this afternoon?

DR. MARX: If your definition of afternoon is  
before 4:30 in the afternoon, yes, I can.

DR. GENCO: Yes, our definition is before 4:30.

[Laughter.]

DR. MARX: As a surgeon, sometimes our definition  
is a little bit different.

DR. GENCO: We can put you on early.

DR. MARX: What time would you care for me to  
present?

DR. GENCO: Probably we are going to take a  
shorter lunch we expect. So we will be back here around  
1:00 or 1:15.

DR. MARX: That would be fine.

DR. GENCO: We could put you on early.

DR. MARX: Thank you. I guess, for the record, my  
name is Dr. Robert E. Marx. I am a DDS, I am an oral and

maxillofacial surgeon, Chief of Oral and Maxillofacial Surgery at the University of Miami School of Medicine.

DR. GENCO: Thank you, Dr. Marx. Yes?

DR. CHRISTIANSON: I would like to speak to that issue too. I will need to leave probably around 2:30.

DR. GENCO: What is your name:

DR. CHRISTIANSON: I am Dr. Christianson.

DR. GENCO: We will get you on the program before then. Thank you.

Okay. Let's proceed now with the discussion of the denture cushions by Dr. Gerald Shipps, who is the Scientific Reviewer from the FDA.

Agenda Item: Open Committee Discussion - FDA Presentation

MR. SHIPPS: My name is Gerald Shipps. I am a Scientific Reviewer for the Office of Device Evaluation, Center for Devices and Radiological Health, the Food and Drug Administration.

Recently, you were asked to review the reclassification petitions for the Denturite and the Snug over-the-counter, (OTC) denture cushions submitted by

Brimms, Incorporated and by Mentholatum, Incorporated. These petitions were submitted as comments in response to the publication in the Federal Register that the FDA is proposing to require the filing of the pre-market approval application or PMA, or a notice of completion of product development protocol, a PDP, for OTC denture cushions or pads, and OTC denture repair kits.

OTC denture cushions are prefabricated or noncustom-made disposal temporary devices that are intended to improve the fit of a loose or uncomfortable denture immediately available for purchase over-the-counter.

The FDA has classified OTC denture cushions, other than those impregnated with cotton cloth into class III because of the concern for, one, safety problems which can result, if patients continue to use ill-fitting dentures in contradiction to product labeling instructions and, two, tissue sensitivity in response to materials used.

There are specific labeling requirements for denture reliners, cushions and pads under 21CFR part 801.403 and part 801.405. Requirements include a warning statement in the labeling, as such devices are for temporary use only

-- that long-term use may lead to faster bone loss, continuing irritation, sores, and tumors. The products are for use only until a dentist can be seen.

The regulations also require that the labeling should contain information advising that the use of these products may temporarily decrease the discomfort. However, their use will not make the denture fit properly.

Special training and tools are needed to repair a denture to fit properly. Dentures that do not fit properly can cause irritation, injury to the gums, and bone loss which is permanent, and may require a completely new denture. Changes to the gums caused by dentures that do not fit properly may require surgery for correction. Continuing irritation and injury may lead to cancer in the mouth. A dentist should be seen as soon as possible.

The American Dental Association, and leading dental authorities have advised the Food and Drug Administration of their concern regarding the safety of denture pads and cushions and other articles marketed and labeled for lay use in the repair and refitting and cushioning of ill-fitting or irritating dentures.

It is the opinion of dental authorities and the Food and Drug Administration that to properly repair and to properly refit dentures, a person must have professional knowledge and specialized technical skill. A layman cannot be expected to maintain the original vertical dimension of occlusion and the centric relation essential in the proper repairing or refitting of dentures. Such products designed for lay use should be limited to emergency or temporary situations pending the services of the licensed dentist.

Reclassification petitions submitted by Brimms, Incorporated, and Mentholatum, Incorporated, request that the Denturite and the Snug OTC Denture Cushions respectively, be reclassified from class three premarket approval to class I general controls.

In the Federal Register dated Tuesday, July 11th, 1995, the FDA proposed to require the filing of a PMA or a notice of completion of a PDP for OTC denture cushions. The FDA intends that, if a final rule based on this proposed rule is issued, PMAs, or notices of completed PDPs will be required to be submitted within 90 days of the effective date of the final rule.

With regard to the proceedings today, the panel will review the scientific evidence and the reclassification petitions for the Denturite and the Snug OTC denture cushions.

Additionally, the panel will recommend as to whether or not the petitions provide sufficient information as to why these devices should not continue to be classified into the present classification of class III or the proposed classification of class I or a classification of class II provide reasonable assurance of safety and effectiveness.

Upon completion of the panel's review of the evidence on the devices referred to it, the panel provides the FDA its formal recommendation. The recommendation includes a summary of the reasons for reclassification, a summary of the data supporting a new assigned class, if any, and identification of the risks to health. The devices recommended for class I, the panel also provides recommendation exemptions from pre-market notification, current good manufacturing practices and records and reports. If the panel agrees with the petitions, then a recommendation is made for these products to be placed into

class I general controls. The filing of a PMA or a notice of completion of a PDP for OTC denture cushions would not be recommended, meaning that it would not be necessary to demonstrate valid scientific evidence for the safety and effectiveness of these products under conditions of actual use before marketing. However, the class I regulatory category of general controls, would regulate the devices by requirements such as those applying to or prohibiting adulteration or as branding, registration of manufacturing and distributing establishments, and device listing, submission of a pre-market notification under section 510(k), unless exempted, notifications of risks and repair, replacement and refund, restrictions of the sale, distribution or use, and compliance with the current good manufacturing practices, records, and reports, and inspections.

If the panel disagrees with the petition, then a recommendation is made for these devices to be placed into class II, special controls, or continued in class III premarket approval. If class II is recommended, and the requirements of class I apply, as special controls that may

include performance standards, specified labeling, post-market surveillance, patient registries, or the development and dissemination of guidelines.

Should continuation of class III be recommended, then the panel is indicating that these devices present a potential and reasonable risk of illness or injury such that the pre-market approval should regulate the products by requiring valid scientific evidence showing reasonable assurance of safety and effectiveness under conditions of use before marketing.

Lastly, we need a recommendation from the panel as to whether the labeling requirements under 21CFR parts 801.403 and 801.405 should be continued, revised or deleted. The word recommendation is emphasized because some may believe that the panel's vote is binding under the agency, but it is not. The panel's review and recommendation to FDA is only one step of the due process afforded to the public during official rulemaking.

After FDA receives the recommendation, it considers the recommendation and the data upon which the recommendation is based and renders its own tentative

decision based upon the public record. The FDA may agree or disagree with the panel.

The FDA will carefully consider the panel's recommendations and the findings will be published in a timely manner in the Federal Registry. It is emphasized that the panel's recommendation is very important to FDA, but it is only one step in the process. The public and the others are assured that all concerns brought to the attention of the agency at any time during the process will be addressed during the course of the reclassification process. Thank you.

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

[No response.]

DR. GENCO: Thank you. You were very clear.

We will now proceed to Dr. Norman, who was a member of the panel, who will give us a presentation on this issue. Dr. Norman.

Agenda Item: Open Committee Discussion -  
Presentation by Dr. Norman

DR. NORMAN: I would like to present some

suppositions to start with. The actual number of dental patients in the unknown, but it is estimated to be between 20 million and 25 million people. Furthermore, it is estimated that just over 30 percent of the adult population over 65 years of age are dentureless.

There are no data to support statistics as to the fit of dentures worn by these patients. But the data that I bring to you is characteristic of the population as a whole. It would be estimated that of that 25 million, maybe 15 million of the denture-wearing population do not have dentures that fit properly. Of this, I would speculate that over seven million of those who are dentureless use dentures that would support or could be used -- could use the type of additives that are before the panel today. This is not good news.

In the past 13 years, in our laboratory, we have conducted product evaluation for several companies concerned with denture additives, but not these two items. If our patient demographics are correct, I think we can draw some conclusions. Most patients have ill-fitting dentures. They adjust to the misfit. The monies for new dentures is not in

the budget and they probably will not get new dentures. Most patients do not use denture aids. The ill-fitting dentures range in age from six months to 45 years.

The second issue I would like to bring before you is the means by which denture fit is regulated or recognized. Of the methods used, the one most respected and most accepted is that of Christian Kapur. He is a prosthodontist who is retired now, but he worked for various universities, and the Veterans' Administration. His evaluation technique to determine the fit of dentures, measures both retention and stability, where retention is determined on a scale from zero to three, and stability from zero to two. By this method, a patient having both a maxillary and mandibular denture would score eight or more for a good fit and less than six for a poor fit.

Most of the patients needing to use either of the two devices before us today, would score less than three by this technique. There are three different types of denture aids, rebases, which are performed by the dentist, the use of adhesives, and cushions. The latter is the subject before us.

There are two major concerns with the latter two types of products, safety and effectiveness. Since the adhesives form very thin layers, it is assumed that they are effective in the less well-fitting dentures. The film thickness is probably in the range of eight microns or maybe a little bit larger, but generally in that range, where we are dealing, in these cases, with millimeters or right at a millimeter at least. So we are looking at very different types of additives.

I believe that we have two problems with the cushions. The first problem is relating to bone loss. There are no adequate studies today which evaluate bone loss in relationship to denture wearers and those who wear various types of denture aids. I do not think there will be a study like this because such a study would involve at least, well, I think a thousand patients, and they would have to be matched sets involving people who do not wear dentures, denture-wearers that have dentures that fit, those that do not fit and use adhesives, and those that use cushions. I do not see anybody sponsoring such a study in the next few years. So we probably will not know the effect

of these materials on bone loss. But the literature cited by the Mentholatum Corporation is quite extensive and contradictory, some saying that dentures that fit poorly cause bone loss and some saying that all dentures cause bone loss, and I think that is true. But there are no good studies that relate to bone loss in relationship to the subject before us. So I think we have to look at other aspects of this, and that is the safety as related to soft tissue.

Nearly all of us have been taught, and I think that it is probably true that most denture irritation is due to inadequate cleaning of the denture. But there is a problem that I think has not been addressed by either corporation and which should be addressed, and that is sensitization of the patient. Because these patients we are talking about are not using these devices for temporary purposes. They are losing them long-term for many, many years. They very seldom see a dentist. I do not think that any warning labels or anything of the nature of the company can persuade these patients to go to a dentist. So we are looking at a problem that is patient orientation more than

it is dental orientation, and they should be protected along this line.

I, personally, believe that we have two products before us and not a similar product. The products differ in their composition and they differ in their mode of application for the patient. I think they should be separated as we discuss one issue versus another.

My own belief is that cushions, whether they be polymer-oriented or cloth-oriented are useful to the dental population and should be encouraged because they supply a need. But I do think that classifying them in class I would be a mistake at least for one of the two products.

If we are going to look at tissue tolerance, I would suggest that a sensitization test be mandated and that it involve at least 50 patients to start with and be run for at least six weeks, and preferably six months.

Agenda Item: Open Committee Discussion and Vote

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

Are there any questions for Dr. Norman or comments? Yes, Sally?

DR. MARSHALL: Dick, are you saying sensitization

to the plasticizer?

DR. NORMAN: Yes.

DR. GENCO: Further comments or questions?

DR. DRUMMOND: I have a question as to is there any, in terms of this rating scale you have below three that somebody with the zero would be allowed to use these products? Do you see any potential problem? Can the clinical condition be so bad that these products can make things worse?

DR. NORMAN: I do not think so.

DR. GENCO: Further comments or questions? Dr. Norman has suggested that we consider these separately rather than both as a generic -- the identity not being generic in your mind. Do the other panel members want to question that or do we all agree with that?

DR. SAXE: Dr. Genco, I think that our vote is really to -- is on the petition, correct, either to accept the petition or not? So it would have to be two separate votes, is that not correct?

DR. GENCO: It is conceivable that, as far as I understand it, we could vote on both at the same time as

well as separately.

DR. MARSHALL: I agree with Dr. Norman, that they are significantly different in their mode of application as well as their composition and we should consider them separately.

DR. GENCO: I see a lot of heads nodding. Any objection to that?

[No response.]

DR. GENCO: Okay. Let me just review some of the questions and considerations to keep in mind. Many of these have been brought up, but let's just go over them. They are in your handout, the green handout in the folder.

We have an overhead here for this. Thank you, Jerry.

So the issue here is reclassification of OTC denture cushion and pad devices questions. First, have the petitions provided sufficient valid scientific evidence to demonstrate how the proposed classification of class I will provide a reasonable assurance of safety and effectiveness in the specific device -- we will consider them separately -- that were the subjects of the petitions and of the broad

spectrum of denture cushion and pad devices? So I think that last issue we have decided would not be a concern. We are not addressing the broad classification, we are just addressing each petition separately. Have I stated that right?

With respect to this one we are looking at safety and effectiveness of each one of the devices. Under this should the OTC denture cushions and pads of different materials be placed in the same classification or different classification? The group has already addressed that. And then we will address whether the OTC denture cushions and pads of different materials placed in different classification groups, which class is appropriate for each group. That is the B under one.

And then, if we feel that the petition does not provide sufficient information to reclassify the device into class I, is there sufficient valid scientific evidence to show that class II will provide a reasonable assurance of the safety and effectiveness of these devices? If so, what special controls are recommended?

Okay. Why don't we take the first one first, the

petition by Brimms. Dr. Norman, do you want to get us started on this one?

DR. NORMAN: I think there is a piece of missing information. There are two problems I think that I see with Brimms' product. One is that it needs to be relabeled to satisfy safety concerns, especially with a warning as to the liquid that is available. It presents a potentially dangerous situation not necessarily to the user, but maybe to the user's family. Since it will be in the home, it should be addressed with a special warning.

Secondly, since the plasticizers, as a group, have not been tested for sensitivity, I think they should be so. In that regard, it probably should be a class II rather than a class III or a class I.

DR. GENCO: Okay. So you are putting on the table a suggestion that we consider the Brimms' product from class III to class II with these special considerations?

DR. NORMAN: Right.

DR. GENCO: One is a further analysis of plasticizer sensitivity and a labeling about ingestion.

DR. NORMAN: Right.

DR. GENCO: Okay.

DR. NORMAN: And I think that similar products that may confront the panel in the future ought to be considered in such light.

DR. GENCO: Okay. Comments or questions?

DR. PATTERS: In the past few minutes, I have taken the liberty of preparing the Brimms product following the directions. I just want to make Dr. Norman aware that the liquid part of the product has a foil seal inside the cap, and the directions are to break the foil seal with the plastic mixing spoon, but I was unable to break the foil seal with the plastic mixing spoon, so I had to use my Swiss Army Knife.

DR. NORMAN: I used a pencil.

[Laughter.]

DR. PATTERS: All I am saying is that it would be hard for somebody to inadvertently consume this product given the seal and how difficult it is to break. However, I do think that the product needs relabeling with regard to both safety --

DR. NORMAN: Well, if children are like my

children, or were, who are now adult, they could have gotten into that bottle easily.

DR. GENCO: Further comments?

DR. GREENSPAN: I am a little concerned that the manufacturer is unable to provide us with information as to the risks if this is swallowed inadvertently. I feel that this product is designed to be used in the mouth and, therefore, people using it will not be as careful as they would be with a bottle of bleach or cleaning fluid and that, although I think that you have to remove the cap and you have to get through the foil, it is possible that this bottle may be left open and part of it may not be all used in the mixing if it is not done properly. But, nevertheless, I think that information needs to be provided with regards to the toxicity of this product. I am not sure whether that can be done with adequate labeling if it goes into class I.

DR. GENCO: So what you are saying is that what we have to address is are we not sure that there is reasonable safety for this product? Therefore, we are asking for it to remain in class III or go to class II.

DR. NORMAN: Safety is a problem.

DR. GENCO: Okay. The special consideration is this issue of -- would be addressed if it was class II by labeling? Deborah, your point was that that would be adequate or would not be adequate?

DR. GREENSPAN: Well, I think that my concern is that not enough is known of the product to adequately label. So what I heard this morning I did not hear information about the toxicity of this product and what the risks are if it is ingested.

DR. GENCO: So you think it is -- it is not reasonably safe?

DR. GREENSPAN: There may be some missing information.

DR. GENCO: Therefore it should remain class III.

DR. GREENSPAN: They could not assure me that it was safe if misused. Not safe is used, but safe if misused. I want to make that clear.

DR. GENCO: Where do you stand, class III or class II, or is it too early for me to ask you that?

DR. GREENSPAN: I think it is too early --

DR. GENCO: Okay.

DR. GREENSPAN: -- to ask that.

DR. GENCO: But you see the issue? If it is class III you do not think it is reasonably safe, therefore, you will want them to come in with a PMA. With class II you think it is reasonably safe and the safety issue can be addressed by labeling. Did I get that right?

DR. GREENSPAN: Yes. But can't the safety issue also be done in class I through labeling, if that is our only consideration for this product?

DR. JEFFRIES: May I answer that?

DR. GREENSPAN: Please.

DR. JEFFRIES: Okay. Labeling is a special control. However, in class I, the labeling is now controlled because there is that restriction 801.405. That restriction was part of the original classification. So, if you are thinking of putting this device in class I but you want that kind of labeling, you would have to state that you want that restriction to continue to exist.

DR. GREENSPAN: May I ask one other question?

DR. GENCO: Sure.

DR. GREENSPAN: Can we request that ingredients be labeled -- be included? Do we have that or not for class I?

DR. JEFFRIES: For devices --

MR. ULATOWSKI: If I might chime in? Tim Ulatowski. Under class I the general controls would consider the current labeling regulations including the restrictive warning for the pads and cushions now in existence. If one wants to further stipulate and define labeling provisions, restrictions that are quite unique and specific to this type of -- this group of devices or, if you subgrouped them in some way, then that may be appropriate for class II, but then you would have to be very specific in terms of exactly where you are heading in terms of those labeling provisions that are now not addressed under current labeling regulations.

DR. JEFFRIES: Yes, I agree. If it is device-specific labeling, it would be a control -- under a special control. So then you are putting it in class II.

MR. ULATOWSKI: If you are talking about ingredient labeling, that is not now a specific provision of the labeling regulations. I would consider that along the

lines of class II labeling provisions.

If I might also add, I am sorry I had to step out for a moment. But, as I caught the drift, realizing that there are risks for a device, if you recognize those risks, understand those risks, or can establish those risks through appropriate measurements and what not that are common within that class, and control those risks then with labeling or through general controls, that is not class III. You understand the device. You understand its parameters, and you can deal with it under other than a premarket scenario. So understand what you have in front of you in terms of the knowledge base and where that then leaves you in terms of the appropriate controls for that particular type of device.

DR. GENCO: So that, if we have concerns about safety either because we did not understand it or because there was some evidence that the safety was not there, then we would be thinking more in terms of class III?

MR. ULATOWSKI: Well, for example, if you had a safety concern with extended use, if patients are harmed with extended use labeling provisions in terms of types of use and how it should be used controls that. It is

difficult, if not impossible, to get a handle on misuse. That covers all device types. It is a question that we are confronted with with all types of devices whether the patient does this or that.

What we are trying to define are appropriate conditions of use, appropriate use, under which that product is safe and effective, with appropriate warnings and precautions about misuse perhaps. But we are trying to define the positive, understand the negative of what might occur and provide directions. But the manufacturer defines the conditions of use of this product, under which parameters it is safe and effective. That is the purpose we have here.

DR. GENCO: I would like to ask Dr. Norman. You brought up two issues, the long-term use, misuse, and the plasticizer sensitivity. With respect to the long-term misuse, the leaving it in for years, you think that is happening. Is there any evidence in the case reports or any report of adverse effects associated with that? Do we have any reason to believe that this theoretical misuse could indeed bring about an adverse effect?

DR. NORMAN: I do not believe that there are adverse effects that are more potentially dangerous with the use of the product against -- versus without use of the product, unless it is the issue of sensitivity. That would occur in a small number of people, but it should be addressed in relationship to the warning for the population as a whole.

DR. GENCO: Okay. Thank you. Sally.

DR. MARSHALL: I wanted to comment on the misuse question. It seems to me that the misuse of the product, in terms of using it too long, that the same questions then would apply to all products, that they can all be misused by using them repeatedly forever if the person is not so inclined to see a dentist again. So I do not really think that that is a problem for this particular material more than it is for any other material.

The question of sensitivity, which Dr. Norman has raised I think is quite possibly valid, I do not know. But then the question is more directed particularly at this material. Because then, if you reuse it, the sensitivity to the plasticizer -- the plasticizer is going to leech out

relatively quickly -- that the more you replace the product, the more frequently you change the product, the more you are going to be exposed to the plasticizer.

DR. GENCO: Further comments or questions? Yes?

DR. BURTON: Dr. Genco, one other concern I have is the fact that, again, when I looked at the package inserts and the packages, there was not a method which you mentioned earlier reporting any adverse reactions or sensitivity issues and, like I said, just a very brief address, no 1-800 number. What goes along with that is that, in the Brimms' brief talked about during the period of 1989 to 1996, the distributed approximately six and a half million units. They had a complaint during this period of one in 255,000. Just knowing what most products would have, that is an exceptionally low number for any product, and I think that is more a problem of reporting that back. I think it would be nice to see some type of method that we may have a better longitudinal and a broader issue. Because, again, the studies are of very limited groups over a limited period of time. I think that a better reporting mechanism or availing the consumer an easy method of

contacting the company and reporting either lack of efficacy or any other problem would be more appropriate. Comments, questions? Yes?

DR. PATTERS: In response to Dr. Burton's comment. I was a little concerned that Mentholatum, in their present package insert, has their full insert, but in the new package insert for their product made in China they have removed their address. It just says Mentholatum, Buffalo, New York. So that would make it even more difficult.

But, on the other hand, I think I would be much more comfortable if the package labeling specified a specific amount of time that one single cushion would be safe for use and effective, as well as specifying a specific amount of time for how long cushions should be worn. Clearly, you cannot control all consumers, but that type of labeling I think would be very helpful. I appreciate the suggestion that I have here in front of me. I believe it is from Mentholatum.

DR. GENCO: Are we tending to love the two now? Are we still -- no? I ask that question. Have you heard anything that would suggest that we should talk about the

two together? No? Okay.

Let's get back to the Brimms' product. Okay. Any further comments or discussion? Are we ready for a vote?

DR. GREENSPAN: May I ask one question? I would like to ask a question of FDA with regard to the misuse of the Brimms' product. The liquid and powder, the ingredients -- and I am not sure if maybe -- either FDA could answer this or whoever can. If this were swallowed and somebody picked up the phone to their local poison center and said my grandchild or I have accidentally swallowed some of this liquid from the Denturite packet, would a poison center have any idea what that was if the ingredients were not on the label?

DR. GENCO: Does anybody want to answer that? We are talking about the Brimms' product.

PARTICIPANT: It is listed at the Poison Control Center.

DR. GREENSPAN: Thank you.

PARTICIPANT: My name is Robert Bernie Seal.

DR. GREENSPAN: Thank you.

DR. GENCO: Okay. Let's -- Jim, did you have

something to say?

MR. ULATOWSKI: No. The only other aspect, in terms of the lumping versus splitting, what was the direction?

DR. GENCO: The direction from Dr. Norman is that we would deal with these separately. In his mind, we should do that.

MR. ULATOWSKI: The concern or the issue is, in terms of the present classification, we have denture pads and cushions with the intended use that Mr. Shipps has identified. They were split, that group was split into the wax impregnated devices and then everything else. So, as you consider, you deliberate this, you have to understand or recognize that you are dealing with a family of products, not just these two products, but a family of products, and you have to accommodate the family within the classification. So we have the wax products, and we have everything else. As you consider subgrouping for reasons of control purposes, if that is a purpose, think about the bins you are creating and what is out there and where they might fall.

Future products need to fall into the bins as well, by necessity, under the 510(k) process. As we review new products, they either have to fall under class I wax products or the other stuff you are creating under this deliberation. So keep that in mind. Be generic in your deliberations and this classification scheme that you are thinking about.

DR. GENCO: With specific labeling for each, which I think we could -- in other words, we could combine them, take a vote, and then have specific labeling for each one of the two products under consideration today. Is that possible?

DR. JEFFRIES: It couldn't be for a specific product. It would be for, you know, if they represent a group of products.

DR. GENCO: For the group, okay.

DR. JEFFRIES: Right. It has to be a group.

DR. GENCO: Okay. Is that an issue?

DR. JEFFRIES: But you can split it. You know, like you could say all things containing a certain chemical should be in class II and have this labeling or something of

that sort.

DR. GENCO: We can?

DR. JEFFRIES: You can.

DR. GENCO: Would that help?

DR. NORMAN: We could classify both of them in class II, but the problem -- and maybe that is appropriate -- the problem lies in the fact that one of them is needed to be mixed and one of them is not, and one of them has considerably more plasticizer than the other, which -- there is a difference in the products.

DR. JEFFRIES: Right. But wouldn't a sensitivity issue apply to both of them? I mean, people who are super-sensitive to chemicals could react to anything.

DR. NORMAN: I think that polyethyl glycol is not a problem that you might see with the combination of three products. It might be more of an issue. I am not willing to defend one over the other at the present time.

DR. JEFFRIES: Okay. Let me take another approach. What other special controls -- what are the special controls that you would apply to the one device that has the less plasticizer? I mean, think about special

controls? Because it would have to --

DR. NORMAN: I am not sure that both of them ought not to be to run sensitization tests.

DR. JEFFRIES: Okay.

DR. NORMAN: And the only way you could do that at the present time is to classify them class II.

DR. JEFFRIES: Right.

DR. GENCO: So is that a reasonable solution in your mind -- that be the special consideration for this group?

DR. NORMAN: It would simplify our proceedings.

DR. GENCO: I think we ought to do what is reasonable and fair.

DR. NORMAN: Well, I see no reason not to run a sensitization test on Mentholatum's product. But it is not as critical an issue I do not think.

DR. GENCO: Thank you.

DR. STEPHENS: We could put them both in class II with controls and have special recommendations.

DR. JEFFRIES: No. I think you would be better off having special controls that apply to both groups. I

mean, it does not hurt for somebody to have a warning. I am trying to think. Whatever you do I think it would be difficult to differentiate between the two types because you have no idea what future products are going to be like. The whole idea is that you are going to have to accommodate different formulations. So, if you are too specific as to the way you would classify them, it is going to be difficult for the FDA to handle different devices down the road.

DR. GENCO: Could a special control be if there is reasonable potential to sensitization that sensitization tests should be carried out? Is that too nonspecific?

DR. JEFFRIES: That is a good question. For exemptions we word them that way. Tim, what do you think?

MR. ULATOWSKI: On its face, it would be for the class of products, if that is your opinion. But, again, think broadly and generically in terms of the class that you are dealing with in your grouping that you have. The requirement does apply to everybody.

DR. JEFFRIES: The thing is that you should also have a level playing field, don't you think, with different corporations?

DR. GENCO: I am sorry. What is the argument, that this would cause problems or not? Would it be reasonable or not? What is your opinion?

DR. JEFFRIES: I think it would be more complicated.

DR. GENCO: It would be more complicated?

DR. JEFFRIES: Yes, if you divided it up. Yes.

DR. GENCO: Dr. Marshall?

DR. JEFFRIES: Because they all have the same intended use.

DR. MARSHALL: It is difficult for me to conceive of a polymer that could be created to serve this function that would not have a plasticizer in it. It is possible that there may be one out there that exists. It seems to me that they are all going to have plasticizers in them. The major difference in the labeling that we are heading towards I think with these two products is that the one product has the liquid that we would like to see something said about do not drink it. But, on the other hand, I do not think it would hurt to say that none of these products should properly be ingested. It is a little easier to conceive of

somebody drinking a bottle of liquid than somebody picking this up and eating it. But I suppose that just because that is not likely does not mean that you cannot label it as such.

DR. ALTMAN: But I can see a kid thinking that is a fruit roll-up, and just chewing on it.

DR. GENCO: Yes. You have permission to speak.

DR. BARACH: Thank you. I appreciate it. I just wanted to point out historically -- I do not know if all of the panel is aware -- the concept of fairness was raised. In fairness, the mentholatum company presented itself to the previous panel meetings which considered the ISO product. The Mentholatum Company attempted to have the panel consider all denture cushions. The panel's response at that time was we have only data on specific cushions before us and consequently will consider that.

Now, after the company has gone to expense and time to address the concerns of the panel about lack of data, the panel is now talking about including other products and future products and things down the road and things that we do not know about. It seems to me that the

fair and appropriate way to do it would be to consider what is before you in terms of data, particularly when you get to sensitization issues. I cannot speak to the Brimms' product, but you have clinical studies which tell you something about potential sensitization and irritation issues. You also have years of clinical experience in the marketplace, notwithstanding the noted problems about lack of reporting, which applies to all OTC products. There is no formal reporting requirement for OTC drugs, devices or everything else. To compare them to the formal requirements for prescription products is I do not think appropriate. Notwithstanding that, if there was a significant sensitization problem with the Mentholatum patch, it would have come out. It would have been apparent. We are a litigious -- I am an attorney -- we are in a litigious society, and these things do come out. We have years of history here. So I would encourage the panel to look at the data before them and be less concerned about the other things that may come down the road that would be consistent with the past activities of the panel.

MS. SCOTT: Could you state your name again?

DR. BARACH: I am sorry, Mija Barach.

DR. GENCO: thank you.

DR. SEIDMAN: May I have permission to address Dr. Norman's concern on the plasticizer and its sensitization?

DR. GENCO: Yes.

DR. SEIDMAN: Okay. I was wondering, first of all, what you are identifying as the plasticizer, the chemical variety that you are identifying as the plasticizer so we are all clear on what that would be.

DR. NORMAN: There is a definition for plasticizer. It would be those which allow the product to be less firm.

DR. SEIDMAN: Generically.

DR. NORMAN: Right.

DR. SEIDMAN: In this case, are you talking about the butyl phthalyl butyl glycolate, or are you talking about the ethyl methacrylate as the plasticizer?

DR. NORMAN: Well, you have not separated them into any classifications. I presume all of them are plasticizers because they do allow you to mix these and it remain soft for a period of time, and they are all

leechable. The three ingredients in the liquid component would have a generic classification as plasticizers. Since you say in your literature that there is no heat created in the formation of the plastic mix, then they have not polymerized or do not polymerize I presume. They would be classified then as plasticizers.

DR. SEIDMAN: I am not a chemist so I cannot respond. But it would be nice if we could agree if you are concerned about the sensitization of the whole product or a particular ingredient in the product.

DR. NORMAN: Just the products in general. I do not think sensitization is a problem, but it has not been addressed. It would not show up in a general -- the people who use this would not recognize the sensitization of the product. They would quit using it because it itched or something like this occurred.

DR. SEIDMAN: Yes. I am not --

DR. NORMAN: So it has not been addressed. It needs to be addressed. It is a minor problem for the population as a whole hopefully. We just do not know.

DR. SEIDMAN: I am not going to say much on this.

My personal feeling when I reviewed this product was that Brimms would have seen from their complaints record. If there was sensitization out there they would have detected it. I do not want to argue it because I am not a clinician.

DR. NORMAN: I do not think you would get that as a complaint. First of all, I am not sure that anybody would recognize it other than when I use this product it is not -- something happens, and they quit using it. We need to know whether it is going to occur or not.

DR. SEIDMAN: For the record, butyl phthalyl butyl glycolate is in the literature as -- there was no reporting of it being a sensitizer. Polyvinyl acetate is not a sensitizer. However, ethyl methacrylate, the monomer, is associated with some sensitization. But, in this product, we have done some chemical analyses and there was no monomer detected.

DR. NORMAN: There ought not to be any -- well, there ought to be a small amount of residual monomer, but it will not be available to the soft tissues.

DR. SEIDMAN: In a chemical analysis we did on the finished product there was none.

DR. NORMAN: Less than a half a percent.

DR. SEIDMAN: Right. There was no detectable monomer. On the cytotox, since the ethyl methacrylate is --

DR. NORMAN: But you are dealing with two things, cytotoxicity or toxicity tests in general are not sensitization tests, and they will not show up -- toxicity tests will not necessarily show up with you run sensitization. They are different from the others.

DR. SEIDMAN: I understand they are different biological phenomena. But there would have to be some chemical presence to cause either one. On the chemical analysis, there was no detectable ethyl methacrylate.

DR. NORMAN: Okay.

DR. GENCO: Thank you. Ms. Jeffries, did you have a comment?

DR. JEFFRIES: I just wanted to re-emphasize the fact that reclassification is thinking of a device in generic terms, what has been on the market and what could be on the market. The purpose of data from devices already on the market is to prove that the device is effective. Obviously, you cannot figure out if a future device is going

to be effective. We just assume that, if current devices are effective, others can be. So you should still be thinking in generic terms.

DR. GENCO: Okay. Let me see if I can summarize where we are. If this were class II, reclassified to class II, then we would have at least one special consideration.

DR. JEFFRIES: One special control.

DR. GENCO: Excuse me, control.

DR. JEFFRIES: Right.

DR. GENCO: And that would be the issue of sensitization to even tiny amounts, small amounts of the monomer, which might reside there. Would that about say --

DR. JEFFRIES: Sensitivity to the materials.

DR. GENCO: Which could be tested. There are well-established tests for that. This is what you are thinking of. Any of these products may contain even the slightest amount which could be sensitizing. It has nothing to do with cytotoxicity. Okay. That is the issue.

DR. JEFFRIES: Right. It is a general risk I gather, sensitivity. But you have to think of a general risk. If there is this general risk --

DR. GENCO: General potential risk for any product, these soft plastic products, any of them will likely contain at least trace amounts of a plasticizer which could be -- or the monomer which could be sensitized. Do I understand that?

DR. JEFFRIES: That is right. And the idea is that it is the potential. It does not have to be a realized risk. It could be a potential risk.

DR. GENCO: Right.

DR. NORMAN: I do not think the residual monomer is a problem. But we do not have any data to show that sensitization is not any problem.

DR. GENCO: With the plasticizer, or residual monomer, or whatever?

DR. NORMAN: Or any combination thereof.

DR. GENCO: Okay.

DR. JEFFRIES: Maybe you should start going through the classification.

DR. GENCO: Yes. Let me just make one other comment. I am hearing that we consider these together as a generic intended use, soft plastic cushions for ill-fitting

dentures, that is the classification. It is not the impregnated wax, it is another home-use soft plastic. I think we are being instructed to look at it that way, not necessarily commanded to do that, but instructed. Is anybody uncomfortable with that before we get into any other issues?

DR. GREENSPAN: I am still slightly.

DR. GENCO: Okay.

DR. GREENSPAN: I am still slightly concerned, although I take the hypersensitivity issue may occur to both of these things. It could also appear with a cotton pad which is already classified in one.

DR. JEFFRIES: That was not requested to be reclassified.

DR. GREENSPAN: Well, I do not think it would be if it is one.

[Laughter.]

DR. GREENSPAN: Sorry about that. How much -- if we are going to put these two products together, how much should the panel be guided by the fact that we already have a product in which is classified in one which also has the

potential to cause hypersensitivity reactions in a very small percentage of individuals?

DR. JEFFRIES: Well, the action before us is consideration of two reclassification petitions for the class III device. So that is the area on which you should vote. It has not been requested that you address the other device.

DR. GREENSPAN: But we have been told about the other device.

DR. JEFFRIES: Right.

DR. GREENSPAN: And we have been told that it has been classified in class I.

DR. JEFFRIES: Right.

DR. GENCO: So the options are class III to class II, which we are discussing or, if that is voted down, then someone could make a suggestion class III to class I. Dr. Greenspan, is this what you are bringing up?

DR. JEFFRIES: I guess if you think that that is -  
- you are right. The class I has already been classified. I honestly do not know if you wanted to put a warning about this wicking action, whether it would apply. But,

certainly, if you are reclassifying the entire generic group and that is going to be part of it, we would take it into consideration. But I think that you should just think about the class III device.

DR. GREENSPAN: May I continue?

DR. JEFFRIES: Because you have not been asked to reclassify the class I.

DR. GREENSPAN: I know. But you told us that we have been instructed that we have to consider these two products as one, that they are a denture cushion and pad device, OTC denture, cushion and pad device, so that everything is going to be under that classification.

DR. JEFFRIES: Right.

DR. GREENSPAN: But now we have an oddball because we have an existing one which is classified as one.

DR. JEFFRIES: Right. But these are class III devices and that is the only thing that is the question today.

MR. ULATOWSKI: If I might address that?

DR. JEFFRIES: Yes.

MR. ULATOWSKI: Certainly, the panel does not have

blindness on. You have information in front of you. I suppose you could take the information on the classification of the class I product in a couple of different lights. One light is that a prior panel consider the data in-hand, the information that they knew about the products at the time, consider the controls that were appropriate and render the decision that class I was appropriate under general controls, that GNP and manufacturing could deal with issues and other general controls. It is within the purview of the panel though to cut a new road if one sees a different direction in terms of the products in front of you at this point in time.

You can use that information that you have in front of you on the class I products as much as you care to in persuading you as to the classification, but it does not restrict you in terms of knowledge of this point in time in dealing with the classification issue in front of you at this point in time.

Does it persuade you to move it to class I? That is for you to decide? Do you think there is something new, new information, information provided by the petitioners

that send you in a different direction? That is your will.  
Whatever you decide.

DR. GENCO: Dr. Marshall.

DR. MARSHALL: I have a question again about the sensitivity issue. Dr. Seidman just told us that the plasticizer is not a sensitizer.

DR. SEIDMAN: We do not have a clear idea what the plasticizer is I do not think.

DR. MARSHALL: Well, I am referring to the plasticizer as the part that is in the liquid. I honestly do not remember the full name of the chemical.

DR. SEIDMAN: Butyl phthalyl butyl glycolate. Yes, the literature indicates combinations -- search of the peer-review literature base.

MS. SCOTT: Dr. Seidman, please go to the microphone.

DR. SEIDMAN: A recent search on agents DB -- this a peer-reviewed bibliographic database managed by the National Library of Medicine indicated that there was no indication of sensitization in that database if you are indicating the plasticizers as the ethyl -- I am sorry, what

is it, the butyl phthalyl butyl glycolate.

DR. MARSHALL: The major component of the liquid, in your case.

DR. SEIDMAN: Yes. The longest name.

DR. MARSHALL: It seems to me that the plasticizer is what is going to leech out. The fact that there is a little tiny bit probably depending on your detection method, there is probably a tiny bit of residual monomer in every polymer out there. If we are concerned about the plasticizer leaching out and not this little fraction of a percent of residual monomer, that we should look at the data on the plasticizer and not worry about the residual monomer. I am rapidly being persuaded that maybe we should not be worrying about sensitization, that it is going to be such a small problem for such a small fraction of the people that the benefits of such a product would far outweigh the risks of a very small number of people becoming sensitized.

DR. GENCO: Thank you. Dr. Cianco.

DR. CIANCIO: Mr. Chairman, I just wanted to point out and answer Dr. Greenspan's comment. The class I category for the Inso Soft Denture Cushion, that study that

that approval was based on was the same study by the same investigator, Dr. Stollard, then conducted for the Mentholatum product for the cushion. That was one of the reasons why we are asking that be given a class I category.

DR. GENCO: Thank you. I have a suggestion. We could proceed with the questions. Maybe out of this will come the decision to consider them separately or together and to take a vote. Is that reasonable? Okay.

First question, is the device life-saving or life-supporting? No.

Is the device for use which is of substantial importance and preventive impairment of human health? No. Any objection to that?

[No response.]

DR. GENCO: No.

Three, does the device present a potential unreasonable risk of injury or illness? That is a key issue. Is there a potential or a realized -- we are talking about the potential unreasonable risk of injury or illness? No? No.

Did you answer yes to any of the above three

questions? No. So, therefore, we go to five.

Is there sufficient information to determine that general controls are sufficient to provide reasonable assurance of safety and effectiveness? These general controls are in class I. No? No.

DR. GREENSPAN: Sorry. Could I have some discussion on that one just to clarify again?

DR. GENCO: Sure.

DR. GREENSPAN: I am sorry to go through this again. How much class I -- how much control we have over labeling if we classify this as class I?

DR. JEFFRIES: You could have some control if you put a restriction as to labeling. But, if you wanted really specific labeling, that would be a special control.

DR. GREENSPAN: If we wanted to put specific things in such as warnings, duration of time per use, per time of use, and then length of time for overall use -- in other words, the product should not be used for more than a week, and then it should be changed and it should not be used for more than six weeks without seeing a dentist -- if we start to get into that type of detail, can we do that in

class I?

I know that one of the manufacturers made some recommendations. But, if this panel wanted to get truly specific along that type of thinking --

DR. JEFFRIES: The more specific you want to be the more likely it should be I think a special control. The other way to do it is to maintain the restriction that is there now. You have to look into that restriction. Do you have that wording?

DR. GREENSPAN: Yes, we have the wording. I think that the panel might want to make some changes. I mean, I do not know. I do not want to speak for the panel. But should the panel want to make changes to the labeling, can we make specific recommendations for the labeling and still leave it under class one?

DR. JEFFRIES: You could if you did it as a restriction.

DR. GENCO: So after the vote we could make specific recommendations for labeling if it is class I?

DR. JEFFRIES: Only if you say it is going to be a restricted device, and that means that a regulation would

have to be promulgated to put in the Federal Register.

DR. GENCO: Okay. Is that --

DR. JEFFRIES: An official restriction.

DR. GENCO: Does that satisfy what you are thinking of?

DR. JEFFRIES: It would not be very flexible. You know, once it is in the Federal Register, that is how it is going to be.

DR. GREENSPAN: So is it better to do it as a class II or as a restricted class I, or you cannot answer that?

DR. JEFFRIES: I cannot answer that.

DR. RUBIN: May I just briefly address the panel please?

DR. GENCO: Sure. I just want to make sure we are clear on this.

DR. GREENSPAN: I am not clear, but I have no more questions to ask.

DR. JEFFRIES: I think usually very specific, device-specific labeling is considered a special control.

DR. GREENSPAN: Thank you.

DR. GENCO: Mr. Rubin, are you addressing this issue?

DR. RUBIN: Yes. The one thing I would like to point out is that the wax-impregnated cotton cloth cushions right now are in class I. There is a restriction on how often the cushions need to be changed. So to the extent that your concerns relate to needing to change the cushion, maximum length of use for one week, that could be an acceptable way of placing it in class I since that is what the current use is for the wax cushions to be discarded after everyday. So, if your limitation is not for detailed specific labeling warnings, but rather relate more to length of use, then I think class I could be appropriate. Thank you.

DR. GENCO: Thank you.

Okay. I will go to question five again. Is there sufficient information to determine the general controls, that is class I, are sufficient to provide reasonable assurance of safety and effectiveness? What is your pleasure?

DR. SAXE: My feeling right now is no because we

were talking about labeling vials of liquid which may be in such products as to ingredients and cautionary statements about their use, as well as the time that a product should be used and changed. So I think there are a number -- if we start looking at the various warnings, labels, restrictions, we are looking I think at special controls and not general controls.

DR. GENCO: Is there a comment, Ms. Jeffries?

DR. JEFFRIES: I agree with him.

DR. GENCO: The rest of the panel? Deborah? Yes, Otis?

DR. BOUWSMA: I think to address his point though, that is a product-specific issue and not a general issue. It depends on what the product looks like as to whether or not it has a bottle that needs to be specially labeled. It may or may not be a part of the product package, as is apparent in the two products that we are looking at today.

MR. ULATOWSKI: The section 801, the labeling regulation, which class I products need to comply with under adequate directions for use provisions is a powerful section and applies to OTC products. The default on devices is that

you are OTC, unless adequate directions for use, for lay use cannot be written, and then you get into a prescription situation. Adequate directions for use under 801 includes, if I might be brief for just a bit here. Directions under which the layman can use the device safely and for the purposes for which it is intended. Directions for use may be inadequate because, among other reasons of omission, in whole or in part, or incorrect specification of statements of all conditions, purposes, or uses for which the device is intended, including conditions, purposes, or uses for which it is prescribed, recommended or suggested in its oral, written, printed or graphic advertising, and conditions, purposes, or uses for which the device is commonly used. If information on quantity, if I can paraphrase, quantity of doses, if it is missing, that is a problem under current regulations under class I. Frequency of administration needs to be stated; duration of administration or application needs to be stated; time of administration or application in relation to meals, time of onset of symptoms or other time factors needs to be stated; route or method of administration or application needs to be stated;

preparation for use needs to be stated. That is under current general control provisions under section 801.

I think that, as one specifies under class II labeling provisions, one is dealing with areas and provisions that are not handled under these specific adequate directions for use provisions under 801. So inasmuch as the company in hearing deliberations can accommodate and adjust to some of the provisions, some of the deliberations stated, the panel may so believe that the manufacturers may comply under Section 801 with those directions of the panel. I would tend to restrict class II labeling provisions to quite unique generic stipulations such as ingredient labeling which is not covered under 801 or other restrictive conditions that are not now handled. The additional labeling provision, which was handled through regulation, but yet under the class I provisions and general controls was the duration of use provision. So that is a very powerful additional aspect to section 801 that currently exists.

So I would not try to attempt to tweak the labeling under class II, but reserve it for a very dramatic

and substantive new directions in terms of labeling provisions that apply to the class of the product.

DR. GENCO: Thank you.

DR. O'NEILL: I have a question. Then under class I, this panel could still make specific recommendations if they felt that the labeling did not comply with those restrictions as listed under class I?

MR. ULATOWSKI: In as much as it is the current state of clinical knowledge as to the usage patterns and whatnot, I think there could be recommendations in terms of the product and labeling improvement that does not take one into a labeling-restrictive situation that would mandate a class II provision.

DR. O'NEILL: That was what I was thinking, labeling improvements.

MR. ULATOWSKI: Labeling improvements you could characterize for their consideration.

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

DR. GREENSPAN: Yes. I have one more question. You talked about manufacturer's recommended times for use.

If it goes into class I, would the manufacturer have to listen to the panel's recommendations for use or would it still be left up to the manufacturer to what they put in the label?

MR. ULATOWSKI: Well, that would be an issue. That would be problematic in their class I. If you have specific directions, provisions, conditions of use that are more restrictive, I think there might be situations where class II specific provisions might have to be the way they go. It depends on how flexible the manufacturing community is to accommodate your suggestions.

DR. GREENSPAN: And if we were to recommend -- because one of the concerns that I think I have heard around the panel is how it has been stipulated (sic). If the panel would like to see ingredients on the box, would that mean it would have to go into class II?

MR. ULATOWSKI: Well, that is currently not a provision of adequate directions for use in 801 as it now stands.

DR. GREENSPAN: So could you do class I with the restriction -- the restriction being that ingredients should

be --

MR. ULATOWSKI: I would see that as a different direction.

DR. JEFFRIES: That is different. That is not a standard restriction.

MR. ULATOWSKI: That is simply stated, but it is very -- as we know from past deliberations, that is kind of a critical area for manufacturers and a contentious area.

DR. GREENSPAN: Yes, I know.

MR. ULATOWSKI: It is not a very simple matter.

DR. BARACH: Excuse me, Mija Barach.

DR. GENCO: Is this on the issue?

DR. BARACH: Yes. It is precisely on it. I have to say first a comment specifically on this. I do not think there is counsel from FDA here. The panel is asking some very specific legal-related issues that carry some ramifications. I do not plan to stand instead of FDA counsel. But I would note that general conditions of use, for example, length of time of use, certainly fall within class I. There is a significant precedent in many classification areas. My colleague, Mr. Rubin, noted one,

which are the wax cushions. The reason you can make those conditions of use part of your reclassification decision is it is based on the data before you which tell you the periods for which you feel it is safe, the conditions of use for which you feel it is safe and effective. Things like labeling for ingredients, however, are very unique and deal with specific situations. Of course, the regulations, in general, by their absence, do not require specific ingredient listings for medical devices. So, if you were to recommend that, I agree, I think that would be something very unique and not normally done for class I.

The other thing I would point out is ultimately the FDA has to make its decision, and that is the binding decision. The panel can make many recommendations to the agency which I think ultimately will be sorted out from the legal standpoint as to how those would find their way into the regulation.

DR. GENCO: Thank you.

Shall we go back to number five? Is there sufficient information to determine that general controls are sufficient to provide reasonable assurance of safety and

effectiveness? What is the panel's view on that?

PARTICIPANT: No.

DR. GENCO: I hear one no. Does anyone disagree with that? Would anyone like to say yes?

[No response.]

DR. GENCO: So that means that it would not be class I. You are comfortable with the alternative? You do not think that class I is sufficient for general controls of use? Yes?

DR. BOUWSMA: Question. The change then that we have to go beyond just general into more special, what is the distinction there? What are the extra things that we are going to ask for to make it class II rather than one?

DR. GENCO: Okay. Dr. Norman, do you want to start that discussion? In other words, if we agree that this should be -- there is a consensus here that this should be -- the answer is no, then it means that it is either class II or class III. So class II would be the special controls. What are those that you might be thinking of?

DR. NORMAN: The majority of comments that I have heard have been on labeling more so than on the issue that I

raised, sensitivity. We have not solved that issue of sensitivity nor have we solved the issue of special labeling. Until we do that I suppose we have to answer this no. If we can agree by vote that those issues are important -- then maybe this is the time to find out whether they are important by vote -- we are going to be in a quandary.

DR. GENCO: Yes. I think these questions do lead us down a path before we vote. Actually we voted before we vote.

DR. NORMAN: I know. But I think until we do that --

DR. GENCO: So let's leave this as --

DR. NORMAN: -- we are still debating as to whether it should be class II.

DR. GENCO: Okay. There is no reason why we have to absolutely answer five before we vote. Let's proceed and leave five as a question mark if you like.

Okay. Where are we now? If we -- is there sufficient information to establish special controls to provide reasonable assurance of safety and effectiveness?

DR. NORMAN: Yes.

DR. GENCO: Okay. One yes on that. Okay. So do we agree to that then? Okay. Any objection to that?

DR. BOUWSMA: Yes, I have the same question. What are the special controls? I mean, it is easy to say yes there are some, but, I mean, what specifics?

DR. GENCO: Well, we have heard labeling and sensitization. We want more specifics about those? Okay. Dr. Greenspan?

DR. GREENSPAN: I think that certainly my concern, and I think it would be good if we could talk about it -- my main concern about this is the labeling. That is one of the reasons why I lean towards class II rather than class I because of the apparent lack of control that exists over what goes into the labeling. So maybe if the panel talks about what it wants to see in the labeling we could get some advice as to whether that could be done under class I or whether it needs to be under class II.

DR. GENCO: Okay. Why don't you give us specific labeling? I think we have had that discussion. Now, let's have a --

DR. GREENSPAN: All right.

DR. GENCO: Would it be for a product or for both, Deborah -- the class or for --

DR. GREENSPAN: Well, we have been asked to judge them together, so we have --

DR. GENCO: No. I think we can do either.

DR. GREENSPAN: We can do them separately? All right. If we start with the one that was presented first then, the Denturite, one of the issues is whether or not the development of hypersensitivity is going to be a problem. One of the representatives, one of our panel members, Dr. Altman, suggested that provision of a good address or a 1-800 number to report problems would increase reporting and, therefore, maybe start to give some information about whether it is a problem or not.

DR. GENCO: All right. Stop there. Is that general controls or does that require class II, an 800 number?

DR. JEFFRIES: I do not think that is anything special. Do you, Tim?

MR. ULATOWSKI: I do not find that particularly unique.

DR. JEFFRIES: Yes, I do not think that is unique.

DR. GREENSPAN: I think the panel's concern is that what we suggest has to be in the labeling. So the other thing that I think we are all concerned about is improper use, particularly because these are products designed to be put in the mouth and, therefore, if somebody sees a child pick up a bit of snug cushion, and I am sorry that I am lumping them together here, and use it as chewing gum, people may be less concerned because they think, oh, that is safe because it is in my mouth anyway. So I think that I would like to see a warning in there saying that these products must not be swallowed. If these products are swallowed, then it must be reported to the poison center. That is all. I mean, it is just that it is not there.

DR. GENCO: Let's deal with that. Is that unique enough to require special control class II or is that general control labeling? That is a consumption -- labeling against consumption, particularly by children it could be worded?

DR. JEFFRIES: It seems kind of specific.

DR. GREENSPAN: It is awfully general. We are

always telling people not to put things in their mouths. I am sure that it is on a bottle of bleach. All I am asking is that it should be in this packet. It may be something that the manufacturers have not thought about. But we sit around here thinking about these things.

DR. ALTMAN: In the general rules, doesn't it say proper use? I mean, couldn't "do not ingest" be considered part of that?

MR. ULATOWSKI: That would be under that provision.

DR. ALTMAN: So that would be a general provision? An 800 number we are hearing could be? The only other issue is product ingredients. Is that considered -- if we want them to label what the product is regardless, put them together. How much product --

DR. GENCO: What is the rationale for requesting product ingredient listing?

DR. ALTMAN: If they do not follow the instructions.

MR. ULATOWSKI: What is the specific risk that you are attempting to control? How do you plan on controlling

it through the labeling that could not otherwise be controlled by the current regulations. What is the specific risk, generic risk of this product class? How are you controlling it? You could probably critique every class I product labeling in the same manner, but that is not quite the direction. The direction is the risk and then the control.

DR. GENCO: Does anybody want to address that? Yes? We are talking about now the specific risk that would require ingredient labeling.

DR. DRUMMOND: When you come back to the issue of people's sensitivity to certain products. If the people do not know what is in it, how are they going to know if they use it whether they will be sensitive to it or not? So that would, from my opinion, suggest that we should have label -- ingredients labeled so that somebody could pick it up and say, well, gee, I may be allergic to this and this and I would rather not lose it so that I know it is here.

So my approach would be then, if you want it for listing the ingredients would be to allow those people who have potential to sensitization to know what is in the

product that they are using.

DR. GENCO: Is there anything in this that is a particularly sensitizing chemical? Like we know that penicillin is.

DR. DRUMMOND: That is the question that Dick has been asking, and the answers are not there. We do not know.

DR. GENCO: Is there anything in the literature or the adverse reports that suggest that this is a particularly highly sensitizing -- these compounds are highly-sensitizing?

DR. NORMAN: Quite the contrary. I think that you would expect them not to be highly sensitive, but you do not know and you do not know how many potentially are involved. If you look at how many people are using these products, and I would have to presume that we are looking at 300,000 to half a million a year, then you are not looking potentially in a very large percentage of the population. But those who sensitive are sensitive.

DR. GENCO: Would these be handled by a label that sensitization potential is there and one should be aware of that? I am trying to work through that.

DR. DRUMMOND: I do not see how a person could know if they are sensitive to a product if they do not know what is in it. I mean, that is --

DR. GENCO: Well, they will be sensitive because they will have a reaction. They will look for --

DR. DRUMMOND: I am not sure they will know they have a reaction. That will be the problem.

DR. JEFFRIES: Can I mention you should be thinking about future products, not just what is on the market.

DR. DRUMMOND: I would assume it would be for all -- any generic product down the road. You can make it with something.

DR. GENCO: All right. So the concern is about present and future product sensitization potential. The question is that would not be covered in general controls, but would require a class II special control.

DR. JEFFRIES: If you are going to label ingredients, yes, because that is not part of the device law --

DR. GENCO: Okay.

DR. JEFFRIES: -- that they are labeled.

DR. GENCO: That is one way to get to the sensitization issue is to label ingredients. That would require class II.

DR. JEFFRIES: I think the labeling for sensitivity could be there -- is covered by our labeling law. If you go to ingredients, that is beyond our labeling law. At least I think that is how it is interpreted.

DR. GENCO: Let me revisit that. The labeling for sensitization could be under general controls class I?

DR. JEFFRIES: I think so.

DR. GENCO: Would that do it, Dr. Drummond, and Dr. Norman, that there is a sensitizing potential?

DR. DRUMMOND: I guess I do not understand. You could put that on any product then.

DR. GENCO: Well, I think the reason you do not is that there are some compounds that are highly immunogenic and induces sensitization and others that do not.

DR. DRUMMOND: Right. But, if you take the opposite viewpoint of a small group of people who are sensitive to breathing basically or anything, I mean, how

much of the population are we trying to protect I guess is the issue we are coming down to.

DR. FLINTON: May I have permission to address the panel?

DR. GENCO: Yes. Is it on this issue?

DR. FLINTON: Yes, exactly.

DR. GENCO: Please identify yourself.

DR. FLINTON: Dr. Robert J. Flinton,  
Prosthodontist from New Jersey.

The issue that we are addressing initially was whether we should -- a product should be a class III or a class I product, not whether this type of material should be used in the mouth. This particular product that I mentioned in my presentation, that there are about five different readily-available to the dental profession materials that contain these plasticites, we do not patch those patients, and we use them with impunity.

So the concern here is, if I have a material that is used by the profession without patch testing and worry and no document of proof over probably 40 years of using these materials to sensitivity, why then is the issue of

sensitivity to the patient using the material himself the issue? Do you understand the difference I am making?

DR. GENCO: Sure.

DR. FLINTON: Not the material itself. We are just saying should he change classification? I think we are putting too much emphasis on probably an extremely remote possibility when the profession and any prosthodontist and probably general dentist in the audience here has used these like materials without ever considering sensitivity as a possibility. Our reactions to date have not even demonstrated that that is a major concern.

DR. GENCO: That it has high sensitization potential. I mean, all things have sensitization potential, but there are some that have high potential and some that have low. I think that that is the issue.

DR. FLINTON: But with a material that has a proven record for numerous repetitive uses.

DR. GENCO: Low -- have a low sensitization potential. I am asking a question.

DR. FLINTON: I am saying that I have never done any sensitivity or patch testing on these materials. I am

just saying that with the documented use of these materials over an extended period of time by the dental profession and, in this case by BRIMMS Marketing, we do not have any documented evidence of such sensitivity. We address the issue of perhaps the leaching out with the repetitive change could augment or accentuate that potential for sensitivity and even on the products we use in the dental office. We change those within a seven to 10-day period on a normal turnover. I just do not think we have any evidence that sensitivity really exists.

DR. GENCO: I just want to make sure that we stay on this issue. We talked about why go to class II. The 800 number, we are told that need not be class II. Improper use, ingestion, we are told that could be class II. Now we are on the issue of ingredient listing and why ingredient listing because of sensitization. We are hearing that there is a low sensitization potential for these materials. I am trying to summarize. If I am wrong, please let me know.

Sally.

DR. MARSHALL: Instead of requiring the ingredient labeling, might it be possible just to say if a rash

develops consult your dentist?

DR. GENCO: Okay. So would that be under class I?  
I guess that was one of the original things we discussed.

DR. MARSHALL: We see that on --

DR. GENCO: Would class I labeling cover that?

DR. MARSHALL: Yes.

DR. GENCO: Okay. Does that satisfy the --

DR. MARSHALL: I think.

DR. GENCO: -- issue of sensitization?

DR. O'NEILL: I think we already answered number three as well -- does the device present a potential unreasonable risk of illness or injury? We said no.

DR. GENCO: Okay. Are we -- I hate to break for lunch now, but that may be prudent. However, let's see if we can resolve that issue. Let's go back to number five.

Do we have sufficient information to determine that general controls are sufficient to provide reasonable assurance of safety and effectiveness after what we have been through? What is your pleasure?

DR. NORMAN: I have not changed my mind.

DR. GENCO: Anybody else want to address that?

DR. GREENSPAN: If we were to ask the manufacturer to provide information of the main product, I know labeling is a very tricky issue. But could that come under class I?

DR. GENCO: Okay. You are saying ingredient listing is under the class I?

DR. GREENSPAN: Well, I am wondering if there is anything that we can do in class I. What I am thinking of is the very small percentage of people who may have a problem with the product. It is a bit like a sunscreen. And then they would like to change to something else. Is there anything that we can request that gives that sort of information to the consumer without us having to put it in class II?

DR. GENCO: That there is X component of this that may cause X problem if you have that change. What is X and what is the problem?

DR. GREENSPAN: Well, if somebody reports getting a sore mouth, it may not be a skin rash. I mean, it could be a skin rash, and it could just be a sore mouth if they are hyper-sensitive to it. I mean, it might help if somebody wants to change products to know what the main

class of ingredient is. Now, if we ask for that in labeling without having to ask for every little thing, could that be done under general controls?

DR. GENCO: That is the component?

DR. GREENSPAN: In other words, whether it is wax-based, or cotton-based, or whether it has got -- and I have forgotten the type of category that the main class decides there is.

DR. JEFFRIES: Wouldn't that amount to ingredient labeling.

DR. GREENSPAN: Without getting into the specifics of ingredient labeling.

DR. GENCO: Dr. Marshall.

DR. MARSHALL: Are you asking just for it to say that it is polymer-based? I do not think that we could make a judgment as to which is likely to be the offending ingredient. Would it be sufficient to say that it is polymer-based?

DR. GREENSPAN: Something along those lines.

DR. GENCO: Okay. So that would be --

DR. GREENSPAN: What do other people think?

DR. GENCO: So, under the class I, can you list that it is polymer-based, and these have a potential to be sensitizing? Therefore, if you get a rash, do not use them? If you get a sore mouth, do not use them? Is this what you are getting to?

DR. GREENSPAN: Something like that. Something that is general enough to still leave it in class I.

DR. GENCO: Is that class I.

DR. JEFFRIES: That sounds device-specific to me.

DR. GENCO: Well, because the soft liners are polymer-based, as compared to the last.

MR. ULATOWSKI: Mr. Chairman, to pull back for just a moment again. There is a different perspective that we are dealing with here in terms of the class II labeling provisions. We are identifying, as I said, the risk and then how you control the risk. If you believe the risk, and it can be a potentially serious risk, it can be controlled through labeling, and so be it. And also the class II labeling is a mandatory sort of directive in that, once finally classified in class II, if that is the outcome eventually, then that labeling directive becomes mandatory

and the products within that class have to change. Whereas, in class I, as you say, wow, you ought to have this, and you ought to have that, there is no real driver that drives the change in the class I products. There are only recommendations and ideas that we are talking about which may or may not be put into place by the manufacturers.

So to get back to what is the significant and major risk-type that you have in front of you, and how is that labeling addressing that risk, do you want to drive it as a panel? Do you want to make it insistent and mandatory? Is it going to overcome that risk? Or do you want to -- do you believe that general controls in the labeling under regulations through some mechanism outside of mandatory and directed provisions are going to take care of things along the path? It is your level of comfort, your level of insistence in regard to these facts.

DR. GENCO: That sounds like a good point to stop for lunch and to think about that and ponder that. In other words, you are saying that we ought to identify the risks that we are concerned about and then determine if the labeling is going to be allowed to happen in the general way

in class I or be very specific and mandatory in the class  
II.

MR. ULATOWSKI: That is right.

DR. GENCO: First identify the risk.

MR. ULATOWSKI: And do you want to drive it or do  
you want some other mechanism under general control to drive  
it?

DR. GENCO: Does the FDA want to drive it or the  
company, yes.

Okay. It is 12:30. We will return here at 1:30.  
The two surgeons who are going to present, we will make sure  
that you present in a timely fashion. We promise you that.  
Thank you.

[Whereupon, at 12:33 p.m. the meeting was recessed  
for lunch, to reconvene at 1:33 p.m. this same day.]

A F T E R N O O N S E S S I O N

DR. GENCO: Welcome back. First, Pamela would like to make an announcement about materials.

MS. SCOTT: If you have any materials that you brought with you that you would like to leave here with the FDA, you can place them on the wall behind me and we will collect those materials.

DR. GENCO: Tim, would you like to make some comment?

Agenda Item: Open Committee Discussion and Vote

MR. ULATOWSKI: Before deliberations resume, just to reset the context. The panel is in the process of identifying the risks, the magnitude, the type, and the benefits and identifying the controls that are appropriate for those risks, to control those risks. With provisions of labeling, as we discussed, class one describes labeling regulations in very general terms. If one has specific labeling provisions that they believe are necessary to control the identified risks, the stated risks, and those need to be mandatory in terms of how you want them to be stated in the labeling, then class two is appropriate and

you can move forward in that manner.

To say class one labeling is to say that there is a general scheme for labeling and provisions for labeling, but it doesn't necessarily dictate the content of labeling. For example, one could not be assured that products already on the market that are class one would change labeling to conform to the wishes of the panel. The class two special controls do driven in a more insistent manner the provisions of labeling.

The other aspect discussed has been materials and biocompatibility. There again, there is nothing specifically in the class one. If that is a specific risk area, and controlling risks through testing or standards or whatever, there's nothing specifically in class one that drives that. You have to make the appropriate decision on whether you need to drive it in terms of the class two special control. So that's generally where we left it and to continue discussion.

DR. GENCO: Thank you. Okay, let's proceed now to does anybody want to make a motion relative to this issue in terms of the recommendations or the appeal before us. Dr.

Patters?

DR. PATTERS: I move that the panel accept the reclassification petition from both Mentholatum and Brimms.

DR. GENCO: So the motion has been made that the panel accept the class three to class one for both products, both Snug and Denturite. Is there a second?

Second by Dr. Stephens. Discussion?

DR. MARSHALL: I have a question, not discussion. Do we later decide on things that we want to require in labeling or is that not part of the --

DR. GENCO: That we would take up separately in any event, whatever the classification. The labeling concerns, as I understand, we take up those separately.

Okay, are you ready for the vote? We're going to give everybody the opportunity to vote, and also the non-voting members to give an opinion.

MR. ULATOWSKI: Mr. Chairman, just for my clarity, by accepting the petitions, you're saying in terms of the question that's in front of you as we left it, that you do believe that general controls are appropriate to control for risks of this product. The labeling provisions would not

then enter into discussion as far as labeling controls. So there would not be any special controls.

DR. GENCO: Okay, so what you're saying is we would not make specific labeling recommendations --

MR. ULATOWSKI: That's correct.

DR. GENCO: -- if this petition was accepted as --

MR. ULATOWSKI: If your recommendation is general controls, then there would be no special control applicable or required. It would be under the general labeling provisions.

DR. GENCO: Okay, I'm sorry. We had that discussion about the general labeling petitions, whether they were adequate or not in each individual's mind. Is that clear?

Okay, let's proceed with the vote, unless there's further discussion, clarification, anybody? Yes.

DR. SAXE: Yes, I think that's the crux of the issue as we just heard that perhaps the thing may be to decide, sort of like identifying the specific risks how we would like to have this labeled, and then it will follow whether it's class one or class two.

DR. GENCO: Well, I think the process could be, we have a motion, it's been seconded, we could vote it up or down and then go from there.

MS. JEFFRIES: I'm not sure that you shouldn't at least look at the supplemental data sheet and come up with a class.

DR. GENCO: Are there any issues here that we haven't discussed previously on the supplemental data sheet? We seem to be going around with these questions.

MS. JEFFRIES: Have the risks been specifically identified?

DR. GENCO: That was a major part of the discussion just before lunch and Deborah listed three or four concerns that were identified as risks, Dr. Norman did. Does anybody want to add to that or have any more comments on that? I think we have clear instructions from Tim that an identified risk, if it needs to be dealt with, has to be dealt with in the, if it's going to be a class two.

MR. ULATOWSKI: No, an identified risk is it of a type and nature that can be controlled under class one.

DR. GENCO: Right. Let me rephrase that, I think

that's what I meant. I think we have identified risks, some panel members have identified risks. The questions that we had were can they be dealt with as a class one in the types of labeling that are allowable or do they need to be dealt with as class two. We had that discussion. Would you like to have further discussion of that issue?

DR. GREENSPAN: Mr. Chairman, would it be helpful if we identified the risks that we think exist and then discuss each one?

MS. JEFFRIES: I'm only suggesting the supplemental data sheet because it's sort of documentation, you would have it all in front of you.

DR. GENCO: Okay, as part of the discussion to this motion, let's go to the supplemental data sheet, I think that's a good suggestion.

MS. SCOTT: I have a question of clarification. Do we need to fill out both the questionnaire and the supplemental data sheet formally?

MS. JEFFRIES: For reclassification, the supplemental data sheet has to be filled out.

DR. GENCO: Okay, with respect to number one,

generic type of device, what is your pleasure? Do you want to consider them separately or both together? Does the motion apply to them together or separately?

DR. PATTERS: Together.

DR. GENCO: And what are you going to call this?

DR. PATTERS: These are denture cushions and pads.

MS. JEFFRIES: OTC, right?

DR. PATTERS: OTCs. I wasn't aware there were any other kind.

DR. GENCO: Okay, so are we agreed that generic type of device is OTC denture cushions and pads and we're considering both?

Advisory panel, I think that's obvious.

Is the device an implant? No.

Four, indications for use prescribed, recommended or suggested in the devices labeling that were considered by the advisory panel. What are those? For ill fitting dentures, what else?

DR. PATTERS: Temporary.

DR. GENCO: Temporary.

DR. NORMAN: They may be used, recommended for temporary, but for a great number of a people who use them, they will use them permanently.

DR. GENCO: The question is indications for use prescribed, recommended or suggested in the labeling. What we're saying is it's temporary for ill fitting dentures, that's what's prescribed, recommended in the labeling.

You're saying that there are other uses that misuse, or beyond labeling use that you're concerned about.

DR. NORMAN: I don't know that it's misuse if they continue to use them. It's no worse than using the denture without a pad.

DR. GENCO: Okay, all right. But I think if you look at number four, it's what actually the manufacturers have listed in the label.

DR. NORMAN: They all recommend that they be used temporarily, but I don't think it's sold that way. The people who buy it buy it for long-term use.

MS. JEFFRIES: We should do whatever intended use in the petitions.

DR. GENCO: Pardon? There was no long-term use in

the petition?

MS. JEFFRIES: No, no, no, whatever the intended use is in the petitions or what's in the CFR now.

DR. GENCO: That's what we put here. Okay, let's go to the next -- I'm sorry.

DR. STEPHENS: I don't think that reclassifying is going to change how people use them.

DR. GENCO: Anybody want to comment to that?

Okay, let's go to five, identification of any risk to health presented by the device, general and then under five there's general and then there's specifics and the characteristics of the device associated. So let's go under general, Mark.

DR. PATTERS: I agree completely with Dr. Norman. There is no more risk and perhaps less risk with this device than wearing the dentures without the device. Therefore, I do not see any specific risk that the device brings about. The risks are greater if you don't wear the device, in my opinion. That's why I'm willing to accept the petition.

DR. GENCO: Further comment? Yes, we're answering number five, general risk to health presented by --

DR. SAXE: Risk to health, now the question is how many people does this affect and to what great extent. But there's a certain segment of the population who have pathology let's say on the palate, whether it's something as serious as carcinoma or not, and that there should be -- this is a risk that if this is a home use product, that a person uses it and doesn't seek professional care. There should be some warning that if there is pain or discomfort that persists perhaps that professional care should be sought and there's a risk that pathology could be self treated thinking that it is denture changes.

DR. GENCO: That's number nine, noted restrictions. Is there a health risk of using it? That's what number five said.

DR. SAXE: If there is existing pathology, there may be a health risk that's not recognized by the person who thinks this is going to provide treatment.

DR. GENCO: Does that come about because of the use or is that because of neglect? They would have the tumor anyway.

DR. SAXE: Something that's caused by the device,

right, it could come up later in this cycle.

DR. GENCO: Do you feel there's any general risk, health risk, presented by use of the device?

DR. GREENSPAN: I think there is the possibility of overuse and extended use and improper time, which --

DR. GENCO: What is health consequence?

DR. GREENSPAN: The health consequence could possibly lead to hypersensitivity because there is no data to say that it doesn't.

DR. GENCO: Okay, so under risks for health presented by the device, we have one opinion. Another opinion that hypersensitivity may come about by prolonged use or by use?

DR. GREENSPAN: That's what was discussed in the panel this morning.

DR. GENCO: Okay, are there any other -- in the panel's mind -- any other health risks?

DR. NORMAN: The only other one would be ingesting it, but that is highly remote.

DR. GENCO: So inadvertent ingestion.

DR. NORMAN: We don't know the consequence of it,

although the toxicology data indicate that it's perfectly safe.

DR. GENCO: So the two health risks then are hypersensitivity and inadvertent ingestion and these are potential and there's no documentation for them, or little documentation either way.

DR. GREENSPAN: And I think we're supposed to be talking about a class, is that right, as well as --

DR. GENCO: Yes, we're talking about the class. We decided that. So under five, risks to health are sensitivity and inadvertent ingestion which are not documented either way and are potential therefore.

DR. NORMAN: Remote, but possible.

DR. GENCO: Okay, any others? These sound like pretty specific. They would be under five, A, B, C, D, specific hazards to health.

Okay, let's go for the first one, sensitivity, what is the characteristic or feature of the device associated with sensitivity? The monomer, the plasticizer, the combination, unknown?

DR. NORMAN: Unknown, but highly unlikely that the

monomer would be involved. Data for polymers in general show that this is not a problem with -- all appear having heat cured polymers, there is I believe less than one percent of the population.

DR. GENCO: How about further comments on the sensitivity, the characteristics of the device which are associated with that particular hazard?

How about the inadvertent ingestion, what is the characteristic or feature of the device that's associated with that hazard?

DR. NORMAN: We don't know.

DR. GENCO: So it's some unknown component of either the liquid or the powder or the gel in the case of the Snug? Okay, any other specific hazard? We're under five, A, B. Now is there a C, a D, an E?

Okay further? Are we ready to go to C, recommended advisory panel classification priority? Essentially that's the motion on the table. That's a variant of the motion, but we can discuss this.

DR. NORMAN: The motion says class one.

DR. GENCO: That's right. Why don't we skip C,

and then we can go to the motion. We have a motion on the floor.

Seven, is the device an implant life sustaining, life supporting? No. Any comments there?

Eight, a summary of information including clinical experience or judgment upon which classification recommendation is based. That's what we heard this morning essentially, depending upon how we decide on the classification. The scientific evidence of safety and efficacy with its limitations, we can summarize that later. Does somebody want to make a comment there that it's inadequate or adequate?

MS. JEFFRIES: You could say the material presented in the petitions and during the presentations, in your clinical judgment.

DR. GENCO: Okay, needed restrictions, number nine, on the use of the device. Anybody want to put a restriction on the use? Yes.

DR. PATTERS: I still believe the labeling should indicate that the device is recommended for use for a certain duration of time for single device and that

accumulated use should not exceed a certain amount.

DR. GENCO: Is there anything more than what you see already on the package insert?

DR. PATTERS: Yes, I would recommend that the device not be used any longer than one week before its changed and that it not be used for a duration greater than six weeks without seeking professional consultation.

DR. GENCO: For both devices?

DR. PATTERS: Yes.

DR. GENCO: Comments, questions on that? It sounds like the recommendation is already on one of the packages and the recommendation from the other company.

DR. PATTERS: Neither are on the package. This supplemental sheet was passed to us. I believe that one of the companies said that they would consider this labeling.

DR. NORMAN: One of the suggestions this morning also included the availability of an 800 number to report complaints.

DR. GENCO: Is that a restriction on use?

DR. NORMAN: It may be eventually, what data is collected. I don't think -- probably not, Bob.

DR. GENCO: Okay, 10 and 11. Ten really isn't relevant until we take this vote, or may or may not be relevant. Eleven?

MR. JEFFRIES: Is irrelevant.

DR. GENCO: Is irrelevant. Okay, have we done our due diligence with respect to this? Good.

MS. JEFFRIES: Thank you.

DR. GENCO: Okay, yes.

DR. GREENSPAN: I would like to add something to the comment earlier on time to suggest that this is I think a problem for me. I think there needs to be some warning that the product may cause hypersensitivity.

DR. GENCO: So you want it not to be used in atopic individuals? How are you going to put that?

DR. GREENSPAN: No, I think that there should be some warning that --

DR. GENCO: Is that a restriction?

DR. GREENSPAN: I would like to see it in the labeling, and that's what I'm hung up about.

DR. GENCO: Tim has told us if we want it in the labeling, it has to be class two.

DR. GREENSPAN: I know, and I would just like to discuss this a little bit more as to whether we are concerned about the product that it may cause hypersensitivity, in which case the product should not be used any more.

MR. ULATOWSKI: The only point I'm pondering is if that could be done through a recommendation on regulatory change of the provisions under 801. I can't predict the likelihood of that coming about through a regulatory change under 801. But that's a possibility that that could be modified somewhat.

DR. GENCO: Okay, all right, with this in mind, are we ready to take a vote or is there more discussion?

Okay, let's first poll the voting members. Dr. Drummond.

Let me review the -- I'm just going in order here that they're on the list. You happen to be at the top, but the next vote I promise we will start at the bottom. The issue here is to accept -- the motion is to accept the reclassification petition for these soft denture cushions. Yes means accept; no means don't accept.

DR. DRUMMOND: That was a good summary. After listening to numerous hours of discussion here, I guess I'm still concerned as to whether or not a class one classification will answer the questions in terms of duration, total length of duration and sensitivity.

DR. GENCO: Realize that if it's a -- let me paint the scenario, if it's voted down, then we can have another motion to make it whatever.

DR. DRUMMOND: Okay, I would then vote no on the issue because I figure it should be class two at this point on the information we've been presented.

DR. GENCO: Thank you. Dr. Janosky.

DR. JANOSKY: I agree with the motion. I think the general concerns would be sufficient.

DR. PATTERS: I vote yes on the motion. I believe that the device has an extremely low risk.

DR. GREENSPAN: I'm going to vote no on the motion because I am concerned that we cannot ensure enough controls in the labeling. That is my major concern. If I thought that there would be some control over the labeling, so that the products could not in the future be misrepresented, then

I would vote one, but as I can't be assured of that, I will vote against the motion.

DR. GENCO: Thank you. Dr. O'Neill.

DR. O'NEILL: I agree with that, and I think that there are some labeling restrictions that are important and so I will vote against the motion.

DR. STEPHENS: I vote for the motion. I believe that with the information presented, the risks with the device are small.

DR. BURTON: I vote yes. I agree that there's not a large risk to the patient.

DR. NORMAN: I vote no.

DR. MARSHALL: I vote yes, although I have concerns about the labeling and I would like to see stronger labeling, I really don't think there's a significant risk.

DR. SAXE: I vote no because of the labeling. I would like to be able to have fairly strict labeling requirements.

[Laughter.]

MR. ULATOWSKI: What's the count?

DR. GENCO: The count is five to five.

[Laughter.]

One, two, three, four five. One, two, three, four, five. Let's just make sure of that. Let's have a show of hands for yes.

[Laughter.]

Let's have a show of hands for yes.

[Show of hands.]

One, two, three, four, five.

Show of hands for no.

[Show of hands.]

Okay, I understand that there is a possibility the chairman may have to vote. I vote yes. I don't really think there's a -- I haven't been convinced that there's a major general health concern. I understand that the concerns can be addressed in class one type labeling.

Okay, are we finished with this or do we make some recommendations in terms of labeling?

MS. JEFFRIES: Did you want to consider the exemptions. The petition didn't ask for exemptions so I don't know if you want to consider that, if you're just accepting the petition.

MS. SCOTT: Do they still need to answer number 10 on the supplemental data sheet?

MS. JEFFRIES: That's what I was asking about, although the petition did not ask for any of those.

DR. GENCO: What is the panel's judgment here?

PARTICIPANT: No exemptions.

DR. GENCO: No exemptions, okay.

Number 11 is that relevant?

MS. JEFFRIES: No.

DR. GENCO: What about the labeling, again just so I'm clear, we do or do not make recommendations? But the discussions that have been carried out are a part of the record, therefore the FDA would be --

MS. JEFFRIES: Excuse me, you have on here, you identified restrictions.

DR. GENCO: Okay.

MS. JEFFRIES: Which pretty much follows what's already existing. Is that what you --

DR. GENCO: But they would be reiterated by the FDA or somehow in FDA's deliberations --

MS. JEFFRIES: We could get back to the panel.

What they should do probably is write these out and then send it back to the panel.

DR. GENCO: So that discussion will be taken into consideration with respect to the FDA's final decision.

DR. GREENSPAN: Could we just for the record state what those concerns are?

DR. GENCO: I'm sorry, that they're what?

DR. GREENSPAN: That the concerns are things that should be included in the labeling.

DR. GENCO: Yes, I think that's the issue, exactly, that they're not lost because of that vote, they're recorded, they will be on the form and the FDA will take this into consideration in terms of their final.

MR. ULATOWSKI: I suppose within the context of a minority position to state your position.

DR. GREENSPAN: I would like to recommend that included in the labeling are very clearly largely printed maximum duration of time before seeing a dentist.

DR. GENCO: Were you in agreement with Dr. Patters' suggestion of six weeks?

DR. GREENSPAN: Yes, I would.

DR. GENCO: Okay, I mean that's dealt with.

DR. GREENSPAN: And I would also like to see included in the labeling warnings that this product may cause hypersensitivity.

DR. GENCO: That's dealt with I think, that was part of the -- yes, we have that document.

DR. GREENSPAN: All right, fine, thank you.

DR. GENCO: If you want to reiterate it --

DR. GREENSPAN: No, thank you. Not again, that's fine.

DR. GENCO: Okay, we're finished with this topic? Thank you very much everyone for your patience.

Agenda Item: Review of a Reclassification  
Petition for Temporary Mandibular Condyle Implants for Use  
in Tumor Resection Patients -- Open Public Hearing

Okay, now let's open the discussion on the reclassification petition for temporary mandibular condyle implants for use in tumor resection patients. We will now begin the open public hearing and we have a request by Dr. Christianson and Dr. Marx and I've talked to both of them and they would like to go in that order. If anybody else

would like to make a presentation, please let us know now. So Dr. Christianson, again, I think you heard the discussion this morning, but please state your position and any potential conflict of interest and then stay at the podium after your presentation for a discussion.

DR. CHRISTIANSON: Okay, thank you. I'm Dr. Bob Christianson from Denver, Colorado. I'm President of Temporomandibular Joint, TMJ Implants, Incorporated. I practiced oral maxillofacial surgery for about 40 years up to two years ago, and am presently on the Advisory Board of the Department of Biomechanical Engineering at Clemson University. I was previously on the Board of Research and Development at Loma Linda Department of Orthopedic Surgery and I was also an Assistant Clinical Professor of Surgery and Head and Neck Department at the University of California, Irvine.

I brought along a couple of models that kind of tell something about what I want to present, is that all right with you, Mr. Chairman?

DR. GENCO: You have 10 minutes, so whatever you would like to do.

DR. CHRISTIANSON: These are all plastic.

DR. GENCO: Good, I was wondering what you were going to bring out of there.

DR. CHRISTIANSON: I'm going to pass them all the same way if I can. I'm in kind of a funny position here because a few years ago I was talking about making our implants a class two device and I have operated that joint for about 47 years, I started it 47 years ago to operate it, and did so until a few years ago. I still consult with surgeons all across the country.

By the way, I know Howmedica, the company that's sponsoring this reclassification and I have the utmost respect for them as a company. I'm not here to talk about our getting -- my considering getting in to develop a temporary implant for the temporomandibular joint. My first ones put in 37 years ago are still functioning and doing very, very well, so I kind of believe in longevity in these things versus short-term.

The first model I passed around was a skull showing our implants as we make them, a [word lost] fossa implant for the base of the skull. The one that Dr. Burton

has, Captain Burton has right now, is kind of an interesting one that we get lots of models from all across the nation, lots of cases come through our company, but this particular one shows where somebody had been hit on the chin, the normal condyle, right up through the base of the skull into the brain about a half inch a little bit more. These cases have to be operated.

The third model that Captain Burton hasn't seen yet is a tumor, a ameloblastoma on a younger person that is a tumor that is a quasi-malignant type of lesion that requires resection of half a mandible. Well, going back to about 1951 or 1952, I started replacing these jaws at the time I took them out. If I took them out for cancer for one reason or another, I started putting them back in the way they should be.

I have not found in my 47 years or longer of working around this joint reason for a temporary condylar prosthesis. There may be some out there, but I must say I'm having a tough time finding it, because if they have a tumor there and we can replace this, I believe in one surgery. I don't believe in the theory of you do 24 surgeries to repair

a joint or you do 40 surgeries. I've seen many of you in the FDA, and others of you in practice and so forth in universities have seen these cases that have been operated 20, 30, 40 times. I used to look at that and think gosh, I never had to operate on my patients over once or twice and that went on for years. So I'm very much here for getting the job done and be sure that it's done properly if possible that first time.

I'm seeing cases now, and literally hundreds of them, in which we've got an artificial condylar prosthesis going up through the base of the skull into the dura, into the middle cranial fossa and I'm also seeing cases where they put in ribs. I had a case the other day where they put in rib after rib. This thing is so mutilated now that to repair it in this patient is going to take a cardiovascular surgeon, maybe a neurosurgeon and a couple of good oral surgeons to repair it if they don't lose this patient's life. So I'm very strong in the alloplastic reconstruction of that joint. I've seen it operated, or seen, or been aware of literally thousands of patients that have had to have reconstruction of that joint. To put in a condylar

prosthesis without putting in the fossa eminis(?) prosthesis to me was foolishness about 35 years ago. I've seen cases where just the condyle has been put in, but it ended up right straight through the base of the skull. That's not where we want to do it.

The least complicated implant for that joint, as far as I'm concerned, is the fossa eminis implant, the cup you might say for the base of the skull. As I said, I put in hundreds of them. The first ones are still there 36, 37 years ago and they're still functioning like I put them in. The condyle is a little bit more complicated in that it can tend to want to go somewhere. If you don't put a fossa in above it, it has a tendency to, occasionally if you put a prosthetic condyle in, to go back either toward the ear or to continue up into the base of the skull. Neither of those situations are very good.

May I break for just a second to get a glass of water. As I mentioned, in cases of terminal resection, I think it's better to go in and take out the tumor, put in the implant and leave it there. I've done that even as young as 17 month old children or babies. So it isn't a

matter necessarily of age. There are some limiting things that will occur.

I can't perceive of instances where I would put in a temporary and then expect to go back in 30 days later and put in a permanent implant. To me, we've had too much of that sort of thing in which we've put a patient through multiple surgeries or multiple expense to do a job that could have been handled very well the first time. And particularly with some of the technology we have today, as you see in your hands, it's very possible to prepare something that will do the job and get the job done and do it properly.

I would believe that a number of these so-called temporal implants, a little bit like the cushions in the dentures, could turn out to be ongoing permanent implants. I wonder too whether the temporary condylar prosthesis put in there while some other surgeon says wait a minute, we get a fossa eminis and put that in above it and so forth.

I don't think that it makes good sense, and I don't know the lady's name that was sitting over here in the blue with the FDA, but she mentioned about keeping it

generically the same. If you're going to make a condylar prosthesis a class two prosthesis, it's probably more dangerous I think than the fossa is, then you've got to make the whole thing, or you should make the whole thing a class two device. I must say I argued for that a few years ago and there's part of me that still would like to see that happen.

But I think that we need to make everybody sure that's what's being done, both by the surgeon and the manufacturing company, and I happen to have been both, are doing that job properly. So we're trying as a company to not only meet the needs of the implant surgeon, the surgeon doing surgery on this joint, but also meet the need of that patient that they don't have to go through this many, many times.

If they talk about doing this as a generic device, then you've got to put the whole thing in one bundle. But if that's the case, you put TMJ implants past eight or nine years through a lot of hoops in tracking and PMA and everything else to do a good job and then all of a sudden we say it's not necessary. I don't believe that's the case. I

think we should do the job and do it well and be sure that it is doing that job properly. I believe that's about all I have to say, Mr. Chairman.

DR. GENCO: Thank you, Dr. Christianson. Are there any questions from the panel for Dr. Christianson. Yes, Dr. Patters and Dr. Stephens.

DR. PATTERS: Dr. Christianson, do I understand your remarks to say that you believe the panel should reject this petition?

DR. CHRISTIANSON: I do. It's kind of a funny spot for me to be in, but I think that the problem I see with it is that you need the same controls for that condylar prosthesis, which we're doing at this time anyway. But to put that in without the protection of the fossa eminis kept above it is a little bit like putting the head of the femur in and not putting acetabular part in there. You can push this thing right through either the hip bone, the iliac bone, or you can push it right through the base of the skull. And both of those situations are hazardous, but certainly probably nothing is much more hazardous than doing like we see on that one case with the condyle pushed a half

inch through that. That occurred because of trauma, but I've seen that happen numerous times.

DR. PATTERS: You believe the petition as written recommends an unsafe device be reclassified from three to two. Is that correct?

DR. CHRISTIANSON: That's correct.

DR. PATTERS: Thank you.

DR. GENCO: Further comments? Dr. Stephens.

DR. STEPHENS: Dr. Christianson, in the patient with the ameloblastoma here, what type of prosthesis would you use for this? Would this require a custom prosthesis to do this?

DR. CHRISTIANSON: That's what we built, but you could build it any way you want to, the same way of building that thing back in there, but you've got to -- I would not consider building that mandible back and not put a cup above it, not put something there to stop it, because the opportunity for that condylar prosthesis to go back toward the ear is rather great, but it's also rather great to go on up in through the middle cranial fossa.

DR. STEPHENS: Then a similar patient with

malignant disease, would you reconstruct [word lost] as well?

DR. CHRISTIANSON: Can you speak a little louder.

DR. STEPHENS: I'm sorry, a patient with a similar size malignant tumor, would you treat them with primary reconstruction with a custom prosthesis as well?

DR. CHRISTIANSON: I have all the years of my life.

DR. STEPHENS: Have you had situations in which you have had to go back in patients with positive [word lost] in both malignant and benign disease?

DR. CHRISTIANSON: And redo it? Well, I've done it to really young ones and have had to go back and replace it occasionally, but I've also gone back in sometimes to put bone back in with it, but rarely, rarely, we try to get it all done at one time with one procedure.

DR. STEPHENS: But in patients, you've not had a situation where you've had post-surgical positive margins(?).

DR. CHRISTIANSON: Post surgical which?

DR. STEPHENS: Positive margins after your initial

reconstruction?

DR. CHRISTIANSON: Well, really I have, but boy that's been extremely rare, and a patient or two was lost for one reason or another, died for some other reason, but not much because we've tried to keep pretty broad on those things.

DR. GENCO: Further questions, comments of Dr. Christianson? If not, thank you very much.

DR. CHRISTIANSON: Thank you very much.

DR. GENCO: Next I would like to introduce Dr. Robert Marx who is an oral reconstructive surgeon and he's going to present his clinical experience with the use of the temporary mandibular condyle implants, which was presented in the petition submitted by Howmedica. We asked Dr. Marx to please identify himself, his affiliation with the -- or nature of his interest if any in the company, financial. Then when you're finished, would you please stay at the podium and you have 20 minutes. You have 20 minutes, and then when you're finished if you could stay at the podium for questions, we would appreciate it.

Agenda Item: Sponsor Presentations by Howmedica

Leibinger, Inc.

DR. MARX: Certainly. I will try to be brief. My name is Bob Marx. I'm an oral maxillofacial surgeon, board certified for the last 15 years. I'm with the University of Miami School of Medicine and I do tumor reconstructive surgery every day. I'm here at the behest of the Howmedica Leibinger Company, but I'm really here for the benefit of my patients. I receive no financial remuneration from the Howmedica Leibinger Company. I collect no royalties, I have no financial reimbursement from them whatsoever. In an honesty sense, they have contributed in the past to my students who benefit from their educational grants, but neither myself, or any of my other eight faculty have benefited from Howmedica Leibinger. So I speak on behalf really of my patients.

I also probably need to say that I couldn't disagree with Dr. Christianson any more. Some of his statements I hope to address with some of the photos that I will show you.

Now, what we would like to really demonstrate to you is what Dr. Christianson introduced as total TMJ

reconstruction. This is exactly what this proposal is not. This is for temporary condylar replacement for those people who have lost their condyle, as well as a larger portion of their mandibular in benign tumor surgery and cancer tumor surgery.

So you're all familiar with the debacle of our profession that ended up with the Kent Vitech(?) prosthesis and I would like to show you how closely that resembled the models that were brought along to you. This was an economic disaster, it was a patient disaster and this is a typical example of where marketing really overflowed research.

And we saw a lot of people who have these, and in sort of an epidemiologic sense noticed that the fossa is reconstructed and in order to do that you remove a joint and a joint is more than just two bony surfaces. It has synovium, it has blood flow, it has nerve reinnervation to it and most of these were done for patients with arthritides, internal joint derangements, parafunctional habits. That's not what this proposal is about. It is only indicated for patients who have lost segments of mandible inclusive of the condyle due to tumors.

So I think there tends to be a confusion. So bad did this get in our particular profession, that our president of our own organization had to send out a warning about this particular device. Again, I would show you how closely it resembles Dr. Christianson. He talked about his 40 years of experience. Mine, I'm not quite that old, I've only had 20 years of experience, but I will pretty much say that there is no oral maxillofacial surgeon who does more tumor surgery of this nature than I and my unit do because we have a dedicated unit just to that. So of course, there are lawsuits and other things that I won't bore you with.

So many of these had to be taken out for the same reason that the fossa was reconstructed as well, and therefore the synovium was taken out, as well as the temporal bone invaded, and many of the problems were with the fact that this is biomechanically unsound due to leverage arm forces as well as intermediate products from the proplast(?) teflon unitation(?). There's also a difficulty with infections with these simply because the interstices of proplast are around 1.0 to 1.5 microns and most bacteria are a little less than 1.0 micron so they can

reside in the interstices and our macrophages and neutrophils existed about 12 to 15 microns essentially unable to get at these organisms producing chronic infections.

And many of them eroded due to wear. Now, as many discussions as Dr. Christianson may make about the longevity, one thing that these devices do that biologic tissues don't do and that's wear. Biologic tissues readapt and remodel.

Now, here's the application I feel of this type of a device that we're looking to have reclassified from class three just to class two. A young lady who is 15 years of age has an ameloblastoma, a large expansion, a huge expansion, takes the entire condyle. This is the impacted third molar that should be down here. It's brought all the way up to the level of the maxilla in the coronoid process. So this person is not just losing her condyle, but half of a mandible, without any real need to reconstruct this at first because although maybe Dr. Christianson can get away with immediate reconstructions, we cannot.

Well done studies by others have documented if you

reconstruct this person with a biologic bone graft, you're either going to have to settle for a microvascular transfer, the thickness of which is the size of your index finger, or you're going to need to settle for a free cancellous marrow graft which has an incidence of infection of 35 percent in this instance because of the communication to the mouth and the oral flora inherent in the mouth.

So our treatment on this by nature has to be ablative tumor surgery. This is a benign tumor, but is very destructive of bone. So this is half of a mandible being removed. No doubt there's an oral communication. We have to remove the teeth inherent in this to get normal good oncologic control. We have a large tumor specimen.

Radiographically, you can see this is of a larger magnitude than the models that Dr. Christianson has shown you. If he were to use his prosthesis in an immediate sense and expect it to be a longevity procedure, you're going to need to add autogenous bone at the time and risk that 33 percent infection rate published by not only myself but several other individuals.

This is what we're more talking about, something

that doesn't require a 3D CT scan and special models and all the cost expense that goes with this. It takes only the skill of the surgeon, is type four, commercially pure grade titanium, has a condyle apparatus to this. It doesn't need a fossa reduction because in this lady the meniscus, the natural disk is in place, and so was the upper joint space with all of its synovium. There's no reason to remove tissue that is not diseased.

So, this in particular was placed in as a temporary holding device for the express purposes of maintaining the space of the fossa, maintaining continuity, maintaining the occlusion and with it facial form. So here she is post-operatively. She was operated on a Thursday, went back to school on a Monday. So this is very conservative of patients of time away from the work place, time away from the school place. She has not suffered any deformity. One of the great advances in the last two decades in cancer surgery has been the ability to do major ablative surgery without the inheritance(?) of a major deformity within patients and the psychologic distraction that goes along with that. You're able to maintain their

occlusion as well as their form. Then when you can do a bony reconstruction, one is done with a risk of infection that's lowered to three percent. So by a magnitude of 33 down to three percent, you reduce the incidence of infection by two staging this. She has good opening.

Ablative cancer surgery, here's a lady with osteosarcoma. A large tumor resection, you can see the large tumor. This invades even toward the base of the skull. If the meniscus is removed, then we biologically reconstruct the temporal fossa rather than putting a big hunk of foreign body in no matter how theoretically pure this is and no matter how biologically compatible it is. No tissue grows into a foreign body, it encapsulates it at its very best.

So this device was placed in this individual and this is a sternal cleidomastoid, one of many techniques that surgeons have to reconstruct the soft tissue fossa so you do not have a metal articulated against bone. This was placed along with the flap brought up into the temporal fossa. Since you can't get a picture of it since it's up there in a hole so to speak, this only shows the bar in place with the

soft tissue flap.

Now, this is her interestingly enough five years later. She is one of our experience of 70 patients with good follow-up, one of six that did not undergo reconstruction within two years. So when I talk about temporary, I mean really to reconstruct these people biologically within one year and two years at the very most. This person, due to two pregnancies and other happy events after being cured of a malignancy was too busy to have it reconstructed. How well do they do over this period of time? Very well. She's maintained her occlusion, she's maintained her facial form, almost doesn't look like she's had cancer surgery. Is the plate still in there today? Yes, but that is on her recognition of maintaining it and her recognition that it is recommended to be removed and will hopefully some day have one, more of a biologic reconstruction.

This is what you want to prevent by placing these. What if you place a bone graft immediately? I've addressed that. Incidence of infection goes up very high and you may have positive tumor margins and you end up either

chemotherapy or radiating your cancer patients. If you put nothing in there, you end up with patients like this because biologically when the tissue heals the facial nerve prolapses and is contracted into the fossa, so that when a reconstruction is accomplished the facial nerve becomes at risk and you can develop a Bell's palsy like this is and a permanent one at that.

Secondly, the other risk is facial deviation such as this lady who had no real reconstruction here, has her jaw now prolapsed and deviated to the left and has an asymmetry that makes it an inability for her to wear any type of a prosthesis because the ridges just don't match. As she opens, she has a much more prominent deformity and you can see her first molar tooth here aligns with the midline, and of course makes it much more difficult to maintain these teeth as well. So her occlusion is decidedly off if you will.

So the treatment for this is a reconstruction plate with a condyle on it and a biologic reconstruction. Just with the plate, we can restore much of her facial symmetry. Yes, she has soft tissue loss in here, and that

requires other surgeries, but the plate by itself brings her back to midline, restores continuity and in our experience now of 70 with long-term follow-up. That sort of speaks to the epidemiology of this, we're not talking here about every patient. It is an unusual patient both benign and malignant that require the loss of the condyle in the extrapative(?) surgery. So this is not a large patient. We average about 10 per year that deal with the loss of not only a segment of the mandible but one that includes the condyle. Most resections of jaw are able to preserve a condyle, a few are not.

Now, what we hope to get and why we think that the delayed and stage reconstruction is the best is that if Dr. Christianson really did one in a 17 year old, I would ask the question what happened with the growth on this child. You have to grow by the functional matrix today, the soft tissue matrix. Her is a 12 year old, large expansion, another ameloblastoma, resected with the condyle. I'm sorry to go through these fast, I know we're limited on time.

One of the devices that we are talking about for a temporary articulation, if you leave this in, he is going to

over grow on the affected side, he's not going to grow -- this plate will never grow and neither will Dr. Christianson's prosthesis grow. When he finishes growth, he's going to have his chin point over approximating his right commissure and his occlusion is going to go with it. It's going to end up into an horrific malocclusion.

Here too is a person who did not suffer deformity due to his ablative surgery. He too was operated on and returned to the school framework within two to three days. We reconstructed him with something that's biologic. Now, why is a biologic reconstruction more preferred, well just because it is biologic. It will adapt, it will remodel, and in the youth it will grow.

So one of many ways, he talked about rib grafts, they're fine and dandy, but really it's sort of a little bit neanderthal approach. We tend to use a little bit more modern approaches using cancellous marrow, allogeneic condyles to get a condylar morphology. This is it early on. This is, as you can see, a young man now at this point was roughly 14. This is he now at 24, and has shown normal mandibular development and growth. This is all a bone

graft, including his condyle. What we would much rather see in here than a piece of metal and a jaw deviation to the opposite side. So specifically speaking to the youth, I think it is a physiologic detriment to put in something that is not biologically able to adapt. Here he is at 24 and you can see his chin point and midline are on, as well as his facial symmetry.

That was the last slide I had to show you. My summary is I think that with reasonable assurity(?) of safety from a track record that has been very good in our hands and that in other hands, that this for a class two determination probably fits that definition best. Without it, I think patients would suffer facial nerve risk, bleeding risk because the pterygoid plexus of veins prolapses into the fossa, as well as deformity. Thank you.

DR. GENCO: Thank you, Dr. Marx. Are there any questions or comments from the panel of Dr. Marx. Yes, Dr. Heffez.

DR. HEFFEZ: I think Dr. Marx makes very good points about the use of a -- or the need for a temporary

temporomandibular joint replacement following tumor ablative surgery and other ancillary indications. I think it's important to say that these patients cry for this replacement, but the *raison d'etre* for doing this shouldn't be an attack on Dr. Christianson because I think Dr. Christianson's application -- there is no indication for his application for the particular problems that we are talking about. So we should stand alone, not on the attack of Dr. Christianson, but on the indications for actually doing the procedures.

But the points brought up by Dr. Marx are very relevant and as a surgeon, oral and maxillofacial surgeon, many of those sentiments about reconstructing temporarily the mandible and positioning it in the proper position are echoed.

DR. GENCO: Thank you. Dr. Marx, do you want to respond?'

DR. MARX: Well, I was hopefully not attacking Dr. Christianson personally, and if that was perceived I apologize. That was not the intent. I was attacking the concept that he brought out because I think the issue became

confused with his presence here that his prosthesis is really not designed for tumor and reconstructive surgery per se and that I was defending the use as we have defined it, rather than attacking his position. So if that was perceived that way, it may be my fault and I apologize for that.

DR. STEPHENS: I would like to agree with Dr. Hefez's comments and would like to ask Dr. Marx a question. We have not done as many as you have, probably half as many, but I was wondering have you had any problems that you think are specific to the condyle piece of this prosthesis? We have not seen a specific condyle related problem except perhaps in patients who have been irradiated. I was wondering if you've seen problems that you think are specific to the condyle portion of the prosthesis.

DR. MARX: No, we have seen almost none. Again, that almost sounds too good to be true. We have, of our experience now with 70, one patient who has pain in the area, but he has had both radiotherapy and additional surgery there. It's difficult to determine what the source of his pain is. But the benefits of maintaining his jaw,

this man lost his mandible bilaterally and only has a floating chin segment and due to his health risk is not a candidate for reconstruction at this time. So he has some pain there, but he is one out of 70 which is an incidence of 1.6 percent. So no, we haven't observed specific problems related to the articulation of that metal joint.

DR. STEPHENS: One other question. In a patient who had an intracranial continuity(?) tumor, where the middle cranial fossa was resected, how would you reconstruct it?

DR. MARX: That's a good question. First of all, those patients are extremely rare to have a tumor, even squamous cell carcinoma, even rarely involved condyle and if it's at the cranial base, generally speaking that's usually a terminal sign. Many of those people are not even operated, they're radiated or right now they're usually given what's called gammaknife(?) radiosurgery, which is a focused type of radiosurgery. So it comes up very infrequently. I can only think of one patient that I've had to do that and we have reconstructed their temporal bone with a bone graft at the time, as well as a tissue flap for

cover and a reconstruction plate with an articulation device.

DR. STEPHENS: One other question. In a patient whom you might have positive margins after the resection, would you remove the entire plate and replace it after second resection or have you not had this problem?

DR. MARX: If you have a patient who you place one of these in and has positive margins or --

DR. STEPHENS: Positive bone margin.

DR. MARX: Positive bone margin, yes, and you therefore require radiotherapy is I guess your answer, or chemotherapy?

DR. STEPHENS: Either.

DR. MARX: Yes, we have a number of patients on that, even if the margins aren't positive, there are various criteria for post-operative radiotherapy such as an N3 neck, such as a depth of invasion greater than four millimeters. There's a variety of criteria that are called oncologic safety. We still radiate those patients with that plate in place, and the reason is you do get some scatter back off of titanium and some back shielding, but with proper radiation

angulation, neither produces a risk of diminishing the radiation result, nor have we observed high incidence of osteoradionecrosis from that. So in spite of the placement, they have stood up well to both chemotherapy and radiation therapy postoperatively.

DR. GENCO: Are there any further questions? Yes.

DR. GREENSPAN: Thank you for your presentation. You described a wide variety of patients, different types of tumor, different ages. Could you comment on whether the group, there was any similarity at all between any of your patients or were they all very distinct with regards to age, tumor type, location, radiation therapy, chemotherapy, failure rates, or are they all very individual cases?

DR. MARX: No, you're very right. All of these tumors have a different biologic potential and have different enzyme capabilities. Every individual is an individual and comes to us with anything from alcoholism to diabetes, to other things we have to work around. If there's a commonality, it is a patient who has a squamous cell carcinoma, a smoking history, has really a fair amount of alcoholism in their history or are not really "a good

wound healer" and yet these plates have stood the test of time simply because of the soft tissue around them is either preserved due to again some of the advances in head and neck cancer surgery or reconstructed at the time. Many of these have tissue flaps brought up as that one patient I showed you had a local tissue flap, but it's hard to genericize them and put them all in the same category. They span a spectrum of benign to malignant tumors and in the malignant tumor population, a certain percentage chemotherapy and radiation. So I can't categorize them into a lump.

DR. GREENSPAN: May I ask another one? You said you did not see a high incidence of osteoradionecrosis. Did you see any?

DR. MARX: Yes and no. I don't want to be nebulous about that, yes we did, but not at the condylar segment. We see that at the distal segment of bone and it's of no higher incidence than our incidence in the plates that we use that have a proximal end of bone and distal end of bone. It is very low. It has improved over time. When we as a profession began using the plates, they were made out of stainless steel. The science of the plate biology was not

as well known, so in the era of 1980 to 1985 there was an incidence of about 12 percent in our hands, there is an incidence of two percent since then.

DR. GREENSPAN: And how many patients would that be? I'm trying to get a handle on how many we're looking at.

DR. MARX: If we're talking about what pertains to this document, this classification, those with a condylar head on them, as I said, in a major tumor center, we do this quite a bit. We average 10 patients a year.

DR. GREENSPAN: With squamous cell carcinoma?

DR. MARX: That would be the lion's share of them.

DR. GREENSPAN: And radiation therapy?

DR. MARX: No, about 40 percent are benign tumors like the young lady with the ameloblastoma that happened to be large. About 60 percent would be -- about another 10 percent would be osteosarcoma, 50 percent would roughly be squamous cell sarcoma. Of those 50 percent, half of them would receive radiotherapy.

DR. GREENSPAN: And of that percentage who receive radiation therapy, what percent would develop an osteo?

DR. MARX: Osteoradionecrosis?

DR. GREENSPAN: Yes.

DR. MARX: Of that segment or of any part in the jaw?

DR. GREENSPAN: No, no, of that segment. In fact, answer both questions, that's interesting.

DR. MARX: In that segment we have had none. On the distal margin where you really have a smaller tissue envelope, why don't you get osteoradionecrosis up in the condyle, you had the masseter muscle and you had the blood supply plus the temporalis muscle that really add an element of protection from it. Distally, where you're at the mentalfarmin(?) area perhaps when radiation to the floor of the mouth goes on there, it's usually interstitial radiation, much more damaging to tissue and a thinner tissue envelope.

DR. GREENSPAN: Now you've raised another question. So may I ask another question, please? So if you -- the site where you see the most osteo, do you think that's related to greater dose, and if so what dose? I was thinking that if you're dealing with squamous cell

carcinoma, you're probably going to get a slightly higher dose to traditional sites such as floor of mouth or eventual lateral tongue. You're going to, with field sparing, you're going to get a higher dose to that region anyway than you are the condylar region probably. Now you've added the additional comment that many of them also get interstitial radiation. What I'm trying to get at is do you think that where you see the osteoradionecrosis it's actually related to the amount of rads that are delivered that site?

DR. MARX: Well, yes.

DR. GREENSPAN: As opposed to your implant?

DR. MARX: Exactly, you asked me the question we've done the most research on and what we're most noted for and that is osteoradionecrosis. No doubt it's more of a site specific and a radiation dosage phenomenon, that is the existence of the plate, we see mostly osteoradionecrosis in that area due to the anatomy and the fact that interstitial radiation is much more damaging to mandible than is external beam cobalt radiation for the simple reason that interstitial radiation is closer from target to source and you don't have fractionations. So protection against

radiation is distance and it is healing interval called fractionations with time. So if you put implants into the floor of the mouth, the greatest blood supply to the mandible is through the lingual periosteum, about 70 percent, so an implant to the floor of the mouth with radiation therapy is going to damage that lingual periosteum much more.

DR. GREENSPAN: Do you think then you see the same percentage of osteoradionecrosis in those who have this implant than those who don't?

DR. MARX: Oh, yes, it's the same, roughly the same.

DR. GREENSPAN: It's roughly the same, and what percentage would that be?

DR. MARX: It depends on what institution you're talking about.

DR. GREENSPAN: No, in your experience. I'm trying to get at some sort of control group, which is so hard in the use of this type of procedure.

DR. MARX: The incidence of osteoradionecrosis in all comers in our institution is low because we specifically

try to prevent that with good dental care and other features and it's around two percent.

DR. GREENSPAN: Whether they have the implant or not.

DR. MARX: Whether they have the implant or not.

DR. GREENSPAN: Thank you very much, Dr. Marx.

DR. GENCO: Yes, Dr. Heffez.

DR. HEFFEZ: I think one of the largest concerns is not so much the osteoradionecrosis, one of the most concerns of the surgeons are the soft tissue concerns. Even though there's adequate soft tissue brought to the site following radiation treatment, many times that soft tissue will atrophy. But it's in the literature and my personal experience that one of the concerns is not so much the osteoradionecrosis, but the soft tissue exposure of the plate afterwards.

However, please comment afterwards, I think that the important thing to realize is this is a complication related to the horizontal part of the plate, if you like, not anything to do with the condylar segment, and that many times we do resect the mandible and place a plate to hold a

proximal and distal segment without concern for the condyle because the condyle is preserved. We still have those concerns in those cases. So what is really at issue is whether the condyle segment, addition of the condyle segment adds any further morbidity to the patient. The answer would be no and in your experience if you could help us out.

DR. MARX: Yes, our experience would confirm that, that the addition of the condyle to the plate does not add any greater risk for osteoradionecrosis. You're right, the problem is mainly soft tissue radiation necrosis and the thinning of soft tissue in that area. Some of the modern day flaps, the free vascular transfers, and particularly the pectoralis major which we have published on, maintains the nerve segment of that muscle so that the muscle does not atrophy. So some of the modern myocutaneous(?) flaps like the trapezius and the pectoralis major are able to bring up the parent nerves with it so that the muscle doesn't change. In fact, we have made a case for putting the muscle back down where it came from and you redevelop the muscular forces that that once created. It's a nice additive thing for some of our cancer patients.

DR. GENCO: Further comments, questions from the panel? Dr. Christianson.

DR. CHRISTIANSON: I just wanted to make a statement or two. I appreciate Dr. Marx's comments, most of them, but the comparison of the proplast teflon fossa eminis implant has nothing to do with our metal implant. The same metal is used in our condylar prosthesis and mandible is the same one used in the implant. So there's no biocompatible problem. The use of that versus the use of temporal muscle flap or the muscle in there, it's as different as night and day. That tissue or temporal flap brought down or ear cartilage put in there has a great deal(?) for failure. We've seen probably 12,000 of these implants put in with a high degree, 90 something percent success. I've almost never seen that fossa come out, but I have seen muscle flaps adhere and ankylosis occur. I've seen grafted bone, which has been put in there by the tons, fuse up the base of the skull. I've seen many, literally hundreds of perforations, he talked about one, hundreds of perforations of the base of the skull, and it comes from putting in a metal against a fossa whether it's got temporal flap against it or just has

bone against it.

So I would say this sounds good for 70 and I would walk right with him and replace some ameloblastomas and sarcomas and this sort of stuff. I've been replacing those since 1952, and in young kids, 17 month old, not 17 year olds, I've done 14, 17 months. But I would never go in there and not put that fossa above that. If I'm going to put a joint in there, I would make that thing a total joint, the same thing they do in the hip joint. I think to do less than that, you're going to have to go longer than he shows and with more cases than we're talking about here and really study it before I would ever put my word on it. I'm not against Dr. Marx or Howmedica, he's done a fine job in his presentation, but there's a great difference between that teflon implant which is 26(?) of them failed and what we put in which haven't been failing.

DR. GENCO: Thank you, further comments or questions from Dr. Marx?

Thank you very much, Dr. Marx.

We will now proceed to a sponsor presentation by Howmedica Leibinger.

I'm sorry, that was the presentation Dr. Marx gave on behalf of the company. Okay, now we will precede to the FDA presentation and Dr. Susan Runner will give that.

Agenda Item: FDA Presentation

DR. RUNNER: Okay. Howmedica Leibinger has requested reclassification of the temporary mandibular condyle implant from class three to class two. The population that is intended to be treated with this temporary condylar implant is described as being terminal cancer patients needing resection of the natural condyle and prosthetic replacement to improve the quality of life, as well as the benign tumor population that was just described.

As the sponsor has documented in their petition, benign and malignant tumors involving the condyle are rare, but do require aggressive treatment and possible eventual reconstruction. The sponsor has based their reclassification request on factors related to the intended population. It is important to bring this up, and I'm sure you're all very much aware of this, that the intended population is fundamentally different from the broader category of temporal mandibular dysfunction patients. I

think that's very important to realize.

Temporomandibular joint disorders that were recently defined by an NIH Technology Assessment Conference refers to a collection of medical and dental conditions affecting the TMJ and/or the muscles of mastication, as well as the contiguous tissue components. The conference further stated that although specific etiologies are sometimes apparent, such as degenerative arthritis, oftentimes the group of patients has no common etiology and there's no biological explanation of this group of disorders.

The severity of the presentation of that particular disease may range from noticeable but clinically insignificant to a debilitating pain condition or dysfunction. And as you all are aware of the past history, that given the variation among the problems that are labeled TMD, it is not surprising that controversy has emerged over time. Practitioners have tried a variety of different treatments and different specialties have treated these patients. In some cases, patients have improved and in other cases the results have been disastrous.

The NIH Conference specifically stated that

surgical indications in this patient population are very limited, so that's the TMD patient population. Again, the patient population that would be considered for the temporary mandibular condyle replacement is different and requires a different set of standards for evaluating the indications for surgery and the type of implant to be placed and the safety and effectiveness of the implant.

The types of concerns that FDA has about TMJ implants are enumerated in our guidance document. Now granted, that guidance document is intended more for the implants that were intended for the TMD patient population, but many of the concerns in the guidance document relate to mechanical testing of these types of implants and material considerations for these implants. They would be applicable to these temporary implants as well.

As you've heard several times today, the agency relies on valid scientific information to determine the classification of a device. A wide range of information may be considered, including well controlled studies, partially controlled studies, documented case histories from experts and significant human experience. The sponsor has provided

references from peer reviewed literature to support the reclassification petition as well as Dr. Marx's presentation today.

The charge then to the panel is to determine how the proposed classification will provide reasonable assurance of the safety and effectiveness of the device. In determining the safety and effectiveness, the panel will consider among other relevant factors the persons for whom the device is represented and intended, the conditions of use of the device, including conditions of use prescribed, recommended or suggested in the labeling or advertising of the device, and the probable benefit to the health from the use of the device weighed against any possible injury or illness from such use.

If you agree with the reclassification petition, you agree that there is enough information to state that yes, the device may have risks, but these risks may be handled with special controls and a class two designation. If you disagree with the petition, you agree that the class three premarket approval is required, and a device is class three as you've heard if insufficient information exists to

determine that general controls and/or special controls are sufficient to provide reasonable assurance of safety and effectiveness.

I think after Dr. Stephen's presentation, I have the questions on overheads for you.

DR. GENCO: Thank you, Dr. Runner. Any questions from the panel or comments of Dr. Runner?

Okay, I think that it's almost an hour and a half that we've been functioning here. I think our physiologic demands suggest that we maybe take a five minute break and then we will come back with Dr. Stephen's presentation.

[Brief recess.]

DR. GENCO: We're going to have a presentation now by Dr. Willie Stephens and after that we will have a question and answer period and then go to the supplemental questions. Dr. Stephens.

Agenda Item: Presentation by Panel Member -- Dr. Willie Stephens

DR. STEPHENS: My presentation is I think relatively short because I think there's been a lot of information presented already and I don't think that I need

to repeat it. Howmedica has submitted a reclassification petition for the temporary use of their mandibular condyle implants to be used with their reconstruction plate in patients undergoing ablative surgery. The device is intended to be used and left in place until permanent autogenous reconstruction can be undertaken.

The sponsor has submitted this request for the use of this procedure for a very narrow indication and that is for the temporary use in patients undergoing ablative surgery to remove benign and malignant tumors that involve the mandible and condyle. The condyle implant, this is essentially a marriage of a class two and a class three device, because I believe the mandibular bone plates are classified class two and the mandibular condyle will be or has been placed into class three. I think that it's the condyle portion that we're primarily interested in.

There is probably some confusion which I will speak to briefly about the reconstruction for total temporomandibular joint reconstruction and the use of the condyle prosthesis and bone plate for tumor reconstruction. In patients who are undergoing temporomandibular joint

reconstruction for temporomandibular joint disorders, only the condylar head basically has been removed. So these patients have an intact muscle system, most of the bone is intact, and it's usually in a system that is in fact dysfunctional and causing increased loading(?) of the temporomandibular joint. These are patients who have had a significant amount of their not only bone structure, but usually muscle structure that has been removed as well, and the soft tissue structures are not in direct biologic continuity with the bone plates. So these patients actually don't have the capacity to load these devices to nearly the extent that patients load total temporomandibular reconstructions where only the condylar head has been removed.

The devices are fabricated from, there are a number of materials that are used for the devices that are presently on the market, titanium alloy is used, stainless steel is used, chrome cobalt materials such as vitalium(?) is also used.

Patients who are undergoing extensive ablative surgery, there are basically three types of reconstruction.

They're either immediately reconstructed with autogenous bone or they delay reconstruction without any type of temporary or intermediate device or they have delayed reconstruction with a temporary device. In this case, it's a bone plate with a condylar head.

The reasons for delayed reconstruction, which I won't go into in detail as Dr. Marx has, but are quite compelling. Immediate reconstruction in patients, particularly those who have intraoral communications, have a very high infection rate. The possibility of the need for additional surgery if there are positive margins is there. There is often the need for tissue recovery or for the treatment with radiation therapy, chemotherapy and by delaying the surgery you reduce the risk of losing a bone graft if it becomes infected or you have to go back. Also if that happens, you have a wasted bone graft and a wasted donor site.

In addition, surgery time at the time of surgery is also important because these patients are often high risk surgery patients and increasing their surgery time at the time of their initial reconstruction is sometimes

counterproductive. The reasons for using a temporary prosthesis is again it prevents soft tissue collapse, it makes the secondary reconstruction much easier potentially sparing vital structures such as the facial nerve, lingual nerve, vascular structures, prevents deviation of the mandible to the opposite side. And I think also it's particularly important for these patients, particularly with tumor surgery, it allows them to have much better mastication and speech during a healing period and their self image is better and risk of depression and these types of contributions to healing complications is greatly reduced.

I think that the application has been well presented and I don't think there's anything else I have to add.

Agenda Item: Open Committee Discussion and Vote

DR. GENCO: Okay, thank you very much, Dr. Stephens. Any comments, questions of Dr. Stephens?

DR. DRUMMOND: Can I just ask a general question? How many people per year are we talking about?

DR. STEPHENS: I would say it's probably between

100 and 200 I would think.

DR. MARX: [Off mike.] If you include all the centers in the United States, I think it's somewhere between 400 and 500.

DR. DRUMMOND: They all would want to use this implant then. Are we talking a device or are we talking surgical technique or discussion?

DR. MARX: I'm not sure I understand your question.

DR. DRUMMOND: If there's a population base of 400 or 500 people who might be available to use this type of device, would all surgeons use this or are we talking surgeons training to use it?

DR. MARX: You're never going to get all surgeons to use anything.

DR. DRUMMOND: I already know that.

DR. MARX: I would estimate and speculate to you that the majority of surgeons would use this type of a reconstruction because there's nothing else that is comparable in an acceptable fashion. There are few alternatives to this. DR. DRUMMOND: But is there a large

group of surgeons who believe not to do anything?

DR. MARX: Not any more if I could use that term. The reason is I've been in this business for 20 years. When I first started as a young buck, the cancer surgeons that day had the attitude of "cut them and leave them". Due to patient's demands and knowledge of better biologic reconstructions and hopefully results that I've shown you, patients' demands and modern day trained surgeons really don't leave patients with deformities as much as they used to. There are still a few people who will not reconstruct yes.

DR. STEPHENS: I think the number of patients who might choose another type of reconstruction is higher than - -the number of surgeons who might choose another reconstructive method is higher than the number who wouldn't reconstruct at all.

DR. DRUMMOND: But we're still talking two operations ideally.

DR. MARX: Two operations ideally, yes.

DR. BURTON: I would just like to comment. I would agree with Dr. Marx that is has decreased radically

but it certainly is institutionally driven, training driven and geographic, however you want to describe it. But there are still a number of people out there who ascribe to what would be older schools of thought who do not reconstruct these at the time initially. So again, you've got a pool, but the number who potentially could receive this is below that number.

DR. HEFFEZ: When we talk about two operations, you have to realize just for clarification purposes the first operation is to extrapate(?) the tumor and you're placing the implant at that time, so it's not as if there is a tremendous additional time involved in reconstructing the mandible at the time of the primary surgery. So the second surgery is what we're talking about reconstructing the patient long-term with an autogenous bone graft.

DR. MARX: Two operations are many times better than one. If you do a long cancer operation some of the nicer studies have shown that the greater the blood loss the higher the recurrence rate is for squamous cell carcinoma due to a lot of theories. But one operation that's lengthy in time and has greater anesthetic risks and more blood loss

is more detrimental to that patient than two well planned staged surgeries that have a more definitive outcome. That may be philosophical, but it has been ours, and I think that the results have tended to be much better with a two controlled stage procedure.

DR. GENCO: Dr. Greenspan.

DR. GREENSPAN: Yes, could I have some clarification whether we're talking about reclassification of all mandibular condyle implants for this special population or are we just talking about this particular titanium implant?

MR. ULATOWSKI: It's all particular implants within that classification group for that particular intended use.

DR. GREENSPAN: And Dr. Marx, could you just remind me, you were talking about one specific one, weren't you?

DR. MARX: I was talking about one specific one, but I have experience in the others as well. They are within a classification that there is not a great deal of difference to them in biologic product. I think it would be

appropriate to put them together.

Now, I was surprised to see Dr. Christianson here and his prosthesis because they're designed differently. That would be an outlier. That would be a different design and one that I'm not particularly in favor of or have really thought well to use.

DR. GREENSPAN: If I could just ask another question, you talked about titanium having advantages over stainless steel when it came to scatter during radiation therapy. Is that correct, did I hear that correctly?

DR. MARX: I don't think I said that, but there is a slight advantage. Stainless steel still does very well clinically, but there is less scatter of radiation with titanium than there is with vitalium or stainless steel.

DR. GREENSPAN: Thank you very much.

DR. MARX: All three of which are within an acceptable framework. There is scatter, there is back shielding so to speak, but the degree of affect on the final outcome has been within acceptable limits.

DR. GENCO: I seem to recall we were given a paper by a Japanese group and they did 34 cases. They did

stainless steel and titanium. I think the statement was made that the titanium was not lasting as long, or more prone to fracture. Has this been your experience? Is that a potential problem with the titanium, the lack of -- increased fracture.

DR. MARX: Titanium will fracture sooner and more often than will either stainless steel or vitalium, but that's why with this particular product and most of the other companies, a grade four titanium is used which is more fracture resistant. Most of the fractures in the early titanium products came out of the AO Synthes(?) group, if I could use that name, and they had some design errors. Those have been improved with time.

DR. GENCO: Another question along those lines. Another issue that was brought up in that particular paper was that if you did subsequent radiologic investigation of tumor recurrence that titanium could be used because it didn't scatter in the CT scan, whereas stainless steel or cobalt did. Is that something --

DR. MARX: That's quite true. If there is any detriment to non-titanium alloys is that both stainless

steel and vitalium will scatter MRI, in fact you can't use MRI in stainless steel because of the magnetic fields. In vitalium it's a little bit iffy so to speak. Some MRI specialists will and will not. It will scatter CT scans.

DR. GENCO: Whereas the titanium much less.

DR. MARX: Much less, and it's not been a detriment to pick up recurrences and for post-operative evaluations.

DR. GENCO: Along the lines of now looking at this as a generic group, are the others that are out there on the market also titanium?

DR. MARX: Yes, to my knowledge, all of the corporations who manufacture plates are using titanium. There is no more vitalium or stainless steel.

DR. GENCO: Grade four titanium?

DR. MARX: I can't be sure of that. Grade four I know is what the Howmedica Leibinger Company uses. I think the lowest they're using is grade three for any other company.

DR. GENCO: Thank you.

DR. HEFFEZ: There are different systems to

reconstruct the condyle, but what's important to mention and I need maybe Dr. Marx to comment is that some systems use standard screws to hold the horizontal piece into the mandible. Others use special type of screws which are designed not as traditional screws, for example, the Thorpe(?) System. I think it's important that if we consider labeling the product because we're approaching this from a generic point of view, is that there has not been really a testing of those type of screws and that we should be cautioned to use standard screws in securing the device.

DR. BURTON: Isn't that addressed I think in the warnings though, at least in their application, because it says that temporomandibular condyle implants from one manufacturer must only be secured using associated bone plate screws and drills supplied by the same manufacturer. I think the comment that Dr. Greenspan made earlier is the fact that the plating systems themselves are already the two(?) and what we're really at is the condylar extension of that, as really the three component that we're looking at, is that correct?

DR. GENCO: It sounds like we're ready to go to

this supplemental data sheet which gets to some specifics in an orderly fashion. If you would like, we could do that soon.

DR. DRUMMOND: I'm trying to learn something here today. If you did not have these "temporary implants" and could not repair the jaw with bone, what would you do?

DR. MARX: You wouldn't have too many other choices. You would let the mandible, as the term goes, swing free and you would have jaw deviation and scar tissue that would form. That was one of the points I was making.

DR. DRUMMOND: There are no other titanium or any implants that you can use to replace the condyle?

DR. MARX: You can put a plate in without the condylar apparatus, but then you would have still a deviation because it wouldn't sit in the proper position. It wouldn't be able to maintain the continuity. So the only other alternatives are to literally wire somebody's jaws together until enough scar tissue forms to hold it, which is roughly three months, which is difficult for patients to endure and still their jaw will collapse to the affected side. The other alternative is to put on external skeletal

pins called the Joe Homora(?) System or its variations where you have maybe two pins sticking in the cheek bone, the zygoma, two in the midline of the symphysis and you have an external plastic bar, somewhat unsightly. It holds the jaw in the correct position, but leaves you with pin sites, potential for infection because of a percutaneous pin through the skin. So that's what I mean, those alternatives have been not very acceptable.

DR. DRUMMOND: So this classification is any metal implant that replaces the condyle?

DR. MARX: I don't know if it's any metal implant. It is a -- I would recommend a 2.4 or 2.7 metal plate because smaller plates will tend to fracture.

DR. DRUMMOND: Okay, but basically it's an implant that's made out of an implant material, usually metal, to replace the condyle temporarily.

DR. MARX: Right, correct, yes temporarily. The proper term should be stabilization bone plate with a temporary condylar articulation head to it.

DR. STEPHENS: I would just like to make one comment and I think that it's important because a lot of

this revolves around the old temporomandibular joint reconstructions and the problems that have been seen with this device have to my knowledge, and certainly in our practice, not been related to the condyle itself but primarily to the plate, plate fractures. I don't know if Dr. Marx has had any problems with the condyle, but we have two or three patients who have had some problems with mobility that require physical therapy and the therapy after radiation therapy. But I think that's an important part of the thing for us to consider in going forward.

DR. ALTMAN: My question is really what is temporary. I don't have a problem with this product, but somebody may come along later and say instead of doing a class three, we're going to call it a temporary replacement so they don't have to do the PMAs. Does FDA have a definition of temporary as less than five years or can anybody just call it a temporary and say well nothing is forever? Are we opening up the door when we're classifying just temporaries?

MR. ULATOWSKI: Let me defer to Susan on that. I'm not sure we have a firm definition, but it might be a

clinical situation.

DR. RUNNER: I don't think we have a firm definition. I think we would be looking to you for some guidance in terms of what would be temporary, but you have to realize that these temporary prostheses are fundamentally different in structure than the total joint replacement devices that are on the market. These devices have a long bone plate extension and they just totally -- you couldn't use in these types of patients, you couldn't use the typical TMJ total joint replacement type of device. I suppose you could envision the scenario where somebody would take one of those old devices and add a long extension and call it temporary, but I don't think that would fly. It would not be --

DR. GENCO: Would it be reasonable to say that temporary or not temporary is an independent consideration from the classification? I can envision a classification of a temporary that could be class one, two or three.

DR. ALTMAN: I think if we're asking somebody to do labeling, is that not a time when we would say that temporary, that it would say this is not recommended for

more than one year's time, I mean require that for temporary or two years -- DR. GENCO: That would be part of the class two special controls, yes.

DR. ALTMAN: We're just looking at what was recommended and that wasn't recommended.

DR. GENCO: Well, are we ready to look at the questions and then maybe go through the supplemental data sheet because I think --

DR. MARX: Can I give the panel just some input, our definition of temporary which may be useful to you, our definition of temporary marries the biomechanics of these devices along with the biology of the different tumors. Generally when we want to reconstruct a cancer patient, 70 percent of people who will fail a cancer surgery and develop recurrence do so within the first year, 90 do so within the first year. So if I would have to put a number on this, it would be two years -- temporary means two years or less. I know there are going to be outliers in this obviously like the one patient I showed you that didn't want it removed and keeps it in for years, but we recommend two years or less it be replaced.

DR. ALTMAN: What I'm asking a manufacturer to put on the label that this is not recommended for more than two years.

DR. MARX: I think two years would be a very reasonable number to pick.

DR. GENCO: Thank you. Okay, Susan, would you put the questions up for us just to refresh our memories about what we should be considering. Perhaps you could go over these and rephrase them and make the emphasis where you think we should be concerned, Susan.

DR. RUNNER: The first question for you to consider in your deliberations is are the benefits and risks associated with the temporary use of these devices in tumor resection patients established? If so, identify the benefits and risks of this device for the temporary use in tumor resection patients. I think your discussion has generally addressed those questions unless you have any further additions.

DR. GENCO: Anybody have any further comments here? Just to go over the risks, Deborah brought up the possible intrinsic radiation necrosis, and you're convinced

that that's not an increased risk from the data quoted by Dr. Marx.

DR. GREENSPAN: I would very much appreciate the comment from our other oral surgeons as to whether his comments, his experience is obviously very wide, that's one of the risks I would be concerned about and maybe can be addressed under special considerations of collecting information.

DR. STEPHENS: I have not see it as a problem, particularly for the condylar portion. The problem with radionecrosis or a proximal stump(?) of this, but I've not seen a problem related to the condyle.

DR. GREENSPAN: But nevertheless, the success of the reconstruction depends on its weakest points and that's why I asked Dr. Marx, and he is probably gone(?), to just elaborate on that.

DR. GENCO: Any other risks that have come up, aside from the obvious surgical risks and risk of recurrence, but not related to the device?

PARTICIPANT: Fracture.

DR. GENCO: Risk of fracture, Dr. Marx talked

about the type four titanium as being less prone to fracture with data.

DR. HEFFEZ: I think you still have to mention the risk of fracture, because as the piece is work hardened, you will increase the risk of fracture. You have to mention

that. DR. GENCO: So that is the consideration Dr. Marx gave us with respect to the biomechanical as well as the biologic considerations. You shouldn't leave them in more than two years because they do risk fracture after that, is this what you're saying essentially?

DR. HEFFEZ: In my experience, the risk in leaving it longer is more soft tissue perforation rather than the fracture of the plate.

DR. GENCO: Okay, so there's a third risk, soft tissue perforation for --

DR. HEFFEZ: That's related to the radiation of the soft tissues and the functioning of the soft tissue matrix moving over the plate.

DR. GENCO: And it's a late event.

DR. HEFFEZ: In my experience, it's a late event.

Another consideration, a biomechanical

consideration, is if you notice the condylar head is screwed to a plate, so it's not one continuous piece. Therefore, one has to consider the loosening of screws related to attaching the condyle segment to the other piece that's attached to the mandible proper. That's again a mechanical --

DR. GENCO: Is this theoretical or has that been -

-

DR. HEFFEZ: I have not seen it, but it's something to consider.

PARTICIPANT: I haven't seen it either.

DR. GENCO: Okay, so have we covered the risks then? I think the benefits are clear. We've gone over those three or four times. Thank you.

DR. RUNNER: The next question was is it accurate to name or label this device as temporary based on its use in clinical practice.

DR. GENCO: Are we clear on that? Anybody want further discussion? Okay.

DR. RUNNER: Number three is, is it necessary to define temporary use of the device. If so, how would one

define the temporary use of the device?

DR. GENCO: We have a suggestion of two years. Anybody disagree with that or have a modification of that?

DR. HEFFEZ: I think two years is a good amount of time, but you have to qualify it indicating that in some circumstances depending on the medical condition of the patient, or the state of the disease, a more prolonged period of time may be necessary.

DR. GENCO: So if we state it as no more than two years, that wouldn't allow the flexibility. Somebody would be in jeopardy if they went three years, but they may have good biologic reasons to do that.

DR. HEFFEZ: Right, exactly, I think you need to leave some qualifier.

DR. GENCO: Dr. Marx, is that reasonable?

DR. MARX: I agree.

DR. RUNNER: The fourth question is given the potential that the device could remain in the patient for an extended period of time or in effect remain as a permanent implant, what additional risks are involved? Would this be an impediment to the reclassification of this device into

class two for temporary use? If so, what additional information or data would be necessary to reclassify this device for temporary use?

DR. GENCO: Is the increased risk of fracture after two plus years?

DR. HEFFEZ: In my experience, no.

DR. GENCO: No. Okay, what is the answer to the question in your minds then? Is there anything that would, with extended use, that would suggest this should not be class two, that extended use should indeed be tested as a class three for PMA. I think that's another way of putting this. Anything you would like to see tested as a PMA relative to extended use?

DR. HEFFEZ: I personally believe that with extended use, there's a greater risk for soft tissue necrosis or dehiscence, however that is not related to the condyle segment and is related to the horizontal portion which is used traditionally in ablative surgery to hold the segments.

DR. GENCO: So we're arguing that a class three PMA would not answer that question.

DR. HEFFEZ: That's correct.

DR. GENCO: The chances are the answer would be it's not the condyle, it's the plate.

DR. HEFFEZ: Exactly.

DR. STEPHENS: And that's a small risk relative to the benefit.

DR. BURTON: I would concur with that, but like I said it's the horizontal component of the plate that you always have problems with. The condylar segment, because again it has more soft tissue that has [word lost] and a sufficient blood supply that that does not show the soft tissue necrosis.

DR. HEFFEZ: Thank you. We should say also that if you lose the horizontal component you lose the condyle component. I mean we shouldn't be ignorant of that fact.

DR. DRUMMOND: Can I ask a question then? If you're worried about fracture, do you want to evaluate fatigue of this material, because the longer it goes the more fatigue there's going to be, the more susceptible it will be to fracture?

DR. HEFFEZ: I think that has been studied because

that material has been used for bone plating for other purposes.

DR. DRUMMOND: Of this size though? This looks to be rather long and narrow.

DR. RUNNER: If I can comment, bone plating applications typically request some sort of mechanical bench testing.

Fifth, are there sufficient data to establish appropriate special controls to adequately control the level of risks and to provide a reasonable assurance that the device can be used effectively?

DR. GENCO: I think we've heard several of those, temporary, used in conditions where there optimally would be a second surgery. Others?

DR. HEFFEZ: The statement made by Howmedica Leibinger dated February 5, 1997 lists several labeling suggestions on its second to last page. I suppose these are indications, techniques and indications that should be followed in order to minimize the risks and I think they should be included.

DR. RUNNER: I think there's also the guidance

document, which is a very typical special control, which has information that we would like to know about any implant, and that already exists and can be modified.

DR. PATTERS: [Off mike.] I would recommend patient registries [words lost] patients involved here and the need to track the overall performance of this implant.

DR. GENCO: Further comments about that, special controls? Okay.

DR. RUNNER: I think you've basically answered this question already. Is it of sufficient valid scientific evidence to show that the temporary mandibular condyle implants for use in tumor resection patients can be used with a reasonable assurance of safety and effectiveness within class two under special controls?

DR. GENCO: Any comments? It seems that there are at least two independent studies, fairly big series, that substantiate this, neither of which is associated with the company, neither is company studies as I read them.

Okay, it looks like we've come a way then to understand what's being requested. We could either go to the supplemental data sheet, fill this out, and then come to

a motion or entertain a motion now and then we can go to the supplemental data sheet. Yes.

DR. PATTERS: I will move acceptance of the petition.

[The motion was duly seconded.]

MS. JEFFRIES: I would like to hear something definite. Have you really identified the special controls? Have you stated them for documentation purposes?

DR. GENCO: Okay, I think maybe we can do the same as we did before, as part of the discussion of this motion we can go with the supplemental data sheet and get the specificity, would that help?

MS. JEFFRIES: Right, we need documentation though.

DR. GENCO: Okay, good. Any general questions? Then I would suggest we go to the supplemental data sheet before we take the vote. Okay, all right let's proceed.

So, the generic type of device is a temporary mandibular condyle implant, does that describe it? That's how Howmedica Leibinger described it, but I heard Dr. Marx use other terminology. Is there a better terminology?

DR. HEFFEZ: Can you repeat the terminology?

DR. GENCO: Temporary mandibular condylar -- or condyle implant, temporary mandibular condyle implant.

DR. HEFFEZ: I need a clarification. You're saying the indications aren't tagged to that.

DR. GENCO: Well, number four would be indications for use. We're just talking about the generic type of device. The idea here is that it should cover all those out there on the market and future devices for the same purpose.

MS. JEFFRIES: I know it's contained(?) -- the identification would include the name of the device and the indications for use, that's what you're used to seeing.

DR. HEFFEZ: Right, because I would be concerned that with just the title, that it would be utilized for general temporomandibular joint reconstruction.

DR. GENCO: Oh, I see what you mean. You would like to see in the description of the device the use, to be absolutely sure that it's clear, the use. I see where you're coming from.

DR. HEFFEZ: Or at least say for specific indications.

MS. JEFFRIES: That is covered by number four. If you answer four, the description of the device becomes one and four together. It's always a device for an intended use.

DR. HEFFEZ: Okay. You cannot therefore advertise the device as being a temporary condyle device without mentioning the indications?

MS. JEFFRIES: That's correct.

DR. HEFFEZ: Okay.

DR. GENCO: I think two and three are obvious. Let's go to four then, indications for use prescribed, recommended or suggested in the device label that were considered by the advisory panel. Does somebody want to start listing those?

MS. JEFFRIES: Well, the petition says temporary use in tumor resection patients, period.

DR. GENCO: Okay, that's it. Any other?

DR. HEFFEZ: One could make an argument in a severe traumatic case such as a gunshot wound an evulsive(?) wound that one could make an argument for.

DR. STEPHENS: I would leave it with tumors. I

think once you open the temporomandibular joint you can get into trouble. I would leave it there for now.

DR. GENCO: What do the panelists feel? Dr. Stephens makes a point.

DR. BURTON: I agree with Dr. Stephens. I think that I would rather leave it at just the tumor at this point. When you start, as soon as you put an extra descriptor in there, you're going to open the door and that's what I've been afraid of on this one from the beginning.

DR. STEPHENS: I think there are other reconstructive options often times in those cases anyway, because that's a different subset than what we're talking about here.

DR. BURTON: A whole different classification of patient.

DR. GENCO: Okay, all right. Identification -- any risks to health presented by the device? First general, are there any general toxicity, any general concern about health adverse effects?

DR. HEFFEZ: The material has been used

extensively for facial fractures and other reasons, so I would say no.

DR. GENCO: So general, none.

Now, specific hazards to health? These are now the special controls. Okay, so I made a list -- we were discussing risk of fracture and I'm not sure how you felt about that. Is that a problem or not, risk of fracture?

DR. HEFFEZ: In my experience, it's a low risk, but it exists.

DR. GENCO: What is the characteristic or feature of the device that's associated with that? Maybe this is the place to make some statement about the type of alloy.

DR. RUNNER: I think the answer to that would be covered in the guidance document where we request certain mechanical testing and documentation of materials.

DR. GENCO: Okay, so it would be the characteristics of the material, the biomechanical characteristics of the material.

DR. RUNNER: Right, and the size.

DR. GENCO: Okay. Happy with that?

Soft tissue perforation.

DR. HEFFEZ: Dehiscence.

DR. GENCO: Dehiscence? And the particular property of the device that's associated with that?

DR. HEFFEZ: I don't know if it's particular to the device, it's more so the nature of the tissue bed that - - specifically post-radiation. You're more likely to see it following radiation patients. So it's not innate to the material.

DR. GENCO: So there's no feature of the device per se. Is it the horizontal bar that impedes blood flow to the flap or --

DR. HEFFEZ: It's essentially the soft tissues moving or stretching progressively over a long period of time over a rigid bar that causes the dehiscence.

DR. GENCO: Okay, so that's the characteristic of the device, the rigidity.

DR. HEFFEZ: All right, well, yes, I guess so, yes.

DR. GENCO: We're trying to answer these questions. I also heard loosening of the condylar component from the rest of the bar, the screws?

DR. HEFFEZ: I think you have to mention loosening of any screws related to this device because it would lead to failure of the device, whether it was on the horizontal component or the attachment of the condyle to them.

DR. GENCO: So the component would be the screw and its design and length, et cetera.

DR. HEFFEZ: Okay.

DR. GENCO: And that's probably dealt with in the guidance as well.

Any others?

DR. HEFFEZ: I would consider, and I welcome other opinions, the problem with CT scanning and MRI related to these. In my experience, the term is signal noise when it refers to magnetic resonance imaging. When you refer to CT scanning, you refer to scatter artifact. The metal, although titanium is significantly better than all other metals, it can interfere with the interpretation of the film if that specific section is evaluated.

DR. GENCO: And the particular characteristic is the?

DR. HEFFEZ: It makes the film less readable.

DR. GENCO: The device has either scatter or the noise characteristic --

DR. HEFFEZ: On the CT scan would cause scatter artifact or on a magnetic resonance image cause signal noise which would interfere with the interpretation of the images.

DR. GENCO: And this is inherent in the property of the metal?

DR. HEFFEZ: Yes, and different metals create different degrees of noise or scatter artifact.

DR. GENCO: Any others?

MS. SCOTT: I have a question. There were I believe some risks identified in the petition and I was wondering if the panel felt as though those risks should be listed or addressed.

DR. HEFFEZ: One of the risks is that they do -- it is preferable that some soft tissue be placed at the level of the glenoid fossa so that the interface is not metal to bone, that there is some tissue lying there. It could be the natural disk or some transplanted tissue. Failure to do this it's possible that you could have

resorption of the glenoid fossa or migration of the condylar segment into the bone. I personally have not observed it.

DR. GENCO: Any others?

DR. HEFFEZ: The incorrect placement of the device can lead to contralateral joint problems due to adaptations that are occurring in the contralateral joint to make up for inadequate function on the side that was -- let's put it in better words or words -- contralateral joint dysfunction related to the reconstruction procedure.

DR. GENCO: Is there something inherent in the material or the device that leads to that?

DR. HEFFEZ: No, it's the technique or the nature of the disease.

DR. GENCO: I mean if somebody made the horizontal extension too narrow, too short?

DR. HEFFEZ: If he made it too short, it would result in a deviation of the jaw, which would therefore stress the contralateral side, so it would be inappropriate technique as opposed to inherent to the material.

DR. GENCO: Okay, so the device used with an inappropriate technique could lead to that.

DR. HEFFEZ: That is correct.

DR. BURTON: I think what you're addressing, as I said, is both that they listed in the petitioner's document about changes in contralateral joint and malocclusion. Those are not inherent to the device. That is really more of a technique problem with the surgery to produce that, so it's not device driven, it's actually technique driven.

DR. GENCO: So the device doesn't actually shrink causing that --

DR. BURTON: The device does not actually cause that.

DR. GENCO: Okay, further controls?

DR. HEFFEZ: One other control I would put in is that it should not be resterilized. I don't know if that would be part of standard procedure, but if it was fitted into the -- and found to be not an accurate fit and another one was selected, that that material should not be resterilized.

DR. GENCO: Is it because of the porosity that we heard about before? I know that was another material, but is there something intrinsic about this titanium that it

can't be sterilized?

DR. HEFFEZ: No, it can be resterilized, however, the problem is if the material gets scratched in some way, there can be some embedding of tissue in it or bacteria and if improperly cleansed afterwards the protein would just remain on the metal and be implanted in the next patient.

DR. GENCO: Okay, so the characteristic is the surface is easily scratched, which means that it might be more difficult to clean and sterilize and that's a unique feature of titanium.

DR. HEFFEZ: I would say yes, titanium is a soft metal in general.

DR. BURTON: Is it possible just to specify that it's a single use, single patient item probably would be --

MS. JEFFRIES: Not to be reused.

DR. BURTON: Yes, not to be reused.

DR. JEFFRIES: That could be a labeling.

DR. BURTON: Yes, it could just be labeling issue and that would eliminate that problem.

DR. STEPHENS: I think we need to specifically say that this is not to be used to treat TMD as well.

DR. HEFFEZ: I think that would be a wise thing.

DR. GENCO: What is the problem? I know there's a problem, but put it into terms. In other words, what is the hazard?

DR. STEPHENS: This device is not to be used for the treatment of temporomandibular joint --

DR. GENCO: What's the hazard of using it for TMD?

DR. STEPHENS: It's specified specifically for temporary use for tumors.

DR. GENCO: I would just say here's a specific hazard to health, what's the hazard to health of using it for TMD? It doesn't correct the problem, makes it worse?

DR. HEFFEZ: Most of the people with TMD have normal masticatory forces. When you look at this subset of population, many of them have lost their -- they're unable to generate the same degree of masticatory forces as a temporomandibular joint patient traditionally does. Therefore, they are more likely to cause loosening of components or resorption or embedding of the condyle into the glenoid fossa.

DR. STEPHENS: And the condyle head portion should

not be used alone.

DR. GENCO: Okay, are we getting on to item nine? So any other hazards? We've got risk of fracture, soft tissue dehiscence post-radiation, loosening of screws with subsequent failure, interference with CT scan and MRI. I can't read my writing here -- oh, metal to bone contact to be avoided in the fossa, and contralateral joint dysfunction. And then we've listed --

DR. BURTON: And probably malocclusion, probably changes -- probably contralateral joint problems and malocclusion we probably actually fit into one because probably one causes --

DR. GENCO: Okay. Then the surface characteristic reuse, sterilization potential for transmission of infection, and then the use in the normal masticatory patient where the loosening or resorption can occur, the TMJ use.

Okay, any other hazards?

Okay, let's go to now the recommended advisory panel classification priority. Okay, classification, that's the motion. The motion is to accept Howmedica Leibinger's

recommendation for transfer from class three to class two.

Are we ready to vote on that?

MS. JEFFRIES: Can I interrupt? You haven't established your special controls. I think you should go back, the general questionnaire has a section seven in which you choose special controls. Maybe you should specify that before people vote so they know what they're voting on, to state the special controls.

DR. GENCO: Okay, were they more than the control of those eight --

MS. JEFFRIES: I think you need to say labeling guidance document, those are basically the two. Identify them for the record.

DR. GENCO: Okay, so labeling and guidance document that addresses the specific hazards listed above or something like that.

DR. PATTERS: I still suggest a patient registry.

DR. BURTON: I would agree with that. I think you're talking about a small enough group here. Again, nobody even really knows how many of these would be used or could be used or would be used looking down the road. The

registry would give you that kind of documentation later on.

DR. GENCO: Okay, thank you, Ms. Jeffries. So to address these specific hazards, appropriate labeling --

MS. JEFFRIES: You're identifying as special controls --

DR. GENCO: -- labeling considerations, guidance documents that are already in existence and in addition to that a patient registry.

MS. JEFFRIES: Okay, great. I just wanted everyone to know what they're talking about.

MS. SCOTT: The panel may identify anything that they think would be appropriate as a special control for this device.

DR. GENCO: Okay, any others?

Okay, let's proceed then to -- I suppose we could go through seven, eight, nine, 10 and 11 and then go to the vote. Number seven, it's an implant, is it life sustaining or life supporting, it has been classified other than class three what are the reasons. So I guess we have to take the vote first because it's a class three. Yes, okay.

Are you ready to vote? Any further discussion

then on the motion to accept the reclassification?

Okay, let's go around the table again. Let's start with -- okay, we ended up with Dr. Saxe, let's start with him.

DR. SAXE: I accept the motion.

DR. GENCO: Okay, Dr. Marshall?

PARTICIPANT: She's gone.

DR. GENCO: Dr. Norman?

DR. NORMAN: Accept the motion.

DR. GENCO: Dr. Burton?

DR. BURTON: Accept the motion.

DR. GENCO: Dr. Stephens?

DR. STEPHENS: Accept the motion.

DR. GENCO: Dr. O'Neill?

DR. O'NEILL: Accept the motion.

DR. GENCO: Dr. Greenspan is gone. Dr. Patters?

DR. PATTERS: Accept the motion.

DR. GENCO: Dr. Janosky?

DR. JANOSKY: Accept the motion.

DR. GENCO: And Dr. Drummond?

DR. DRUMMOND: Accept the motion.

DR. GENCO: Dr. O'Neill, oh, you voted, right.

Let's see, Dr. Greer is not here, Dr. Wu-Yuan is not here, Greenspan, and Marshall are not here.

Okay, it sounds unanimous.

Now, let's proceed to number seven. If it is not class three, why are we allowing a lower classification and what is the supporting documentation and data? Is that the Howmedica presentation?

MS. JEFFRIES: It's the special controls and the petition.

DR. GENCO: Special controls as we --

MS. JEFFRIES: Will provide a reasonable assurance of safety.

DR. GENCO: Okay. Number eight is the summary of information including clinical experience or judgment which the classification is based upon. That's the presentation of the company plus the presentations we've heard and the discussion from the experts.

Okay, restrictions on use of the device. We had quite a few of those.

DR. PATTERS: Not for treatment of TMD.

DR. GENCO: Okay, so not for treatment of TMD.

DR. HEFFEZ: I was just going to say that TMD has a wide definition and some people would include neoplasia of the condyle as a TMD diagnosis.

DR. PATTERS: Is there a bit more specific term?

DR. HEFFEZ: This is restrictions.

DR. GENCO: Unfortunately, this says restrictions so we would have to --

PARTICIPANT: That is a restriction.

DR. PATTERS: The restriction would be permanent use.

DR. GENCO: Okay, so put it that way, restricted to use in patients undergoing ablative surgery for tumor.

DR. PATTERS: Restricted to rather than restricted from.

DR. HEFFEZ: Don't we want temporary use?

DR. GENCO: And temporary use.

DR. HEFFEZ: Do we have to say as defined temporary here in this section or no? What temporary is defined as or no?

DR. GENCO: Temporary use, two years? Two years

with qualification.

Okay, any other restrictions?

Are we helpful here with the way we're wording these restrictions?

MS. JEFFRIES: The single use or the non-reuse, I heard someone mention that.

DR. GENCO: I'm sorry, I didn't hear that.

MS. JEFFRIES: Single use.

DR. GENCO: Single use. Further?

Okay, number 10, we don't have to deal with that. Number 11?

Now, do we deal with more specificity on the controls or is there sufficient --

MS. JEFFRIES: No, as long as you -- I think the FDA will probably get back to you when more specific measures -- the guidance document will probably be revised and it will be given back to you for a review. I suspect they will also have you review the labeling. The patient registry gets set up by another section of FDA.

DR. GENCO: And as you understand, this would be done by mail or at another meeting?

MS. JEFFRIES: I suspect -- well, Susan, it's up to you.

DR. RUNNER: I suspect we would present it at a subsequent meeting.

DR. GENCO: Okay. That brings up -- are we finished now with this issue? That brings up the question of subsequent meetings. Pamela, every ready with organization here would like us to get our calendars out.

Susan, there are items that now you know the panel should be addressing shortly is that why we're doing this?

DR. RUNNER: No, but we need to have the dates preset in case some issues do present themselves in the next year.

DR. GENCO: So does that mean we should do several for next year or just the next one?

DR. RUNNER: I think Pam will do four.

MS. SCOTT: I believe the first or the next tentative date we have set was May 21 through 23.

DR. GENCO: Okay, is that a bad day for anybody else but me? That's all right with me, I'm sorry.

MS. SCOTT: It was also in the, unfortunately I

don't have my notebook where I wrote it down, but it was in the cover letter that we sent to everybody, May 21 through the 23. That seemed to be okay with everyone's calendar, particularly the voting members.

The next date I believe was in July, the 7 through 9 -- you have 14 through 16? Okay, July 14 through 16. We have a conflict. And November 3 through 5. Okay? So we have May 21 through 23 as a tentative date, July 14 through 16 tentatively, and November 3 through 5.

These are tentative dates set by FDA for panel meetings. We do this for the purposes of the public. If we decide to have a panel meeting, we will announce it in the Federal Register, if there are issues that need to be brought to the panel and if not, then we will not schedule a panel meeting for those dates.

DR. ALTMAN: Pamela, how soon in advance will we know if we're not meeting like in May?

MS. SCOTT: We usually make a decision about two months -- we try to make a decision two months before the scheduled date as to whether or not we are going to have the meeting.

DR. GENCO: Okay, any other business?

MS. SCOTT: I would just like to remind the panel members to hand in the memo regarding the disposition of the materials that were sent to you. That memo was sent to you in the last mail-out. To make sure that you hand that in to me, or if you're going to be sending your materials back to FDA, to make sure that you mail that memo back to us.

DR. PATTERS: Excuse me, Pam, in returning materials to FDA, reprints that are in those materials, they don't need to be returned? They're not considered confidential? Reprints of scientific articles.

MS. SCOTT: No, I don't believe so.

DR. PATTERS: We can keep those or dispose of those?

MS. SCOTT: Yes.

DR. GENCO: Are we finished?

MS. SCOTT: Yes.

DR. GENCO: I would like to thank everybody, especially Dr. Hefez and Dr. Burton our special consultants. Pam, you did a wonderful job and I thank you very much for your help. If it wasn't apparent, this was my

first time on reclassification two and I would like to thank Susan and Tim and Ms. Jeffries for your patience. Thank you.

MS. SCOTT: I would like to thank all the panel members for coming out and assisting us in handling these two issues here. I would also like to thank Dr. Genco for taking on this task. I think Dr. Genco did a very nice job in handling the meeting. Also, I would like to thank all the FDA staff who were involved in preparing this meeting.

[Whereupon at 4:10 p.m., the meeting was adjourned.]