

**SUMMARY MINUTES**

**EAR, NOSE, AND THROAT DEVICES AND DENTAL PRODUCTS  
JOINT ADVISORY PANEL MEETING**

**OPEN SESSION**

**October 6, 2004**

**Gaithersburg Hilton  
Gaithersburg, MD**

**Joint Ear, Nose, and Throat Devices and Dental Products  
Advisory Panel Meeting**

**Attendees**

October 6, 2004

*Chairperson*

A. Julianna Gulya, M.D. (Chair-EN)

*Voting Members*

Herman A. Jenkins, M.D. (EN)  
University of Colorado Health Sciences Center

Jon B. Suzuki, D.D.S., Ph.D. (Chair-DE)  
University of Pittsburgh School of Dental  
Medicine

Domenick T. Zero, D.D.S., M.S. (DE)  
Indiana School of Dentistry

John R. Zuniga, Ph.D., D.M.D. (DE)  
University of North Carolina School of  
Dentistry

*Consultants*

Karen H. Calhoun, M.D., FACS (EN)  
University of Missouri

B. Gail Demko, D.M.D., PC (EN)  
Newton Highlands, MA

Kasey K. Li, M.D., D.D.S. (EN)  
E. Palo Alto, CA

Eric A. Mair, M.D. (EN)  
Wilford Hall USAF Medical Center

Lisa A. Orloff, M.D. (EN)  
University of California, San Diego

David J. Terris, M.D. (EN)  
Medical College of Georgia

Gayle E. Woodson, M.D. (EN)  
Southern Illinois University School of Medicine

*Consumer Representatives*

Elizabeth S. Howe (DE)  
National Foundation for Ectodermal Dysplasias

Carolyn R. Stern, M.D. (EN)  
Rochester, NY

*Industry Representatives*

R. Michael Crompton, J.D., M.P.H. (EN)  
Carl Zeiss Meditec, Inc.

Daniel R. Schechter, Esq. (DE)  
Parkell, Inc.

*FDA Participants*

Sara M. Thornton  
Executive Secretary

A. Ralph Rosenthal, M.D.  
Director, Division of Ophthalmic and Ear, Nose  
and Throat Devices

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Deputy Director, Division of Anesthesiology,  
General Hospital, Infection Control and Dental  
Devices  
Chief, Dental Devices Branch

Eric A. Mann, M.D., Ph.D., CAPT, USPHS  
Chief, Ear, Nose and Throat Devices Branch

Heather S. Rosecrans  
Director, Premarket Notification Staff

Kevin P. Mulry, D.D.S., M.P.H.  
Dental Officer, Dental Devices Branch

EN=Ear, Nose and Throat Devices Panel  
DE=Dental Products Panel

## **CALL TO ORDER**

**Panel Chair A. Julianna Gulya, M.D.**, called the meeting to order at 8:37 a.m. and asked the panel members to introduce themselves. **Panel Executive Secretary Sara M. Thornton** welcomed the attendees and extended a special welcome to new panel consultants Demko, Li, Mair, Orloff, and Terris and the new Ear, Nose and Throat (ENT) Devices Panel Consumer Representative Dr. Stern. She also expressed appreciation for the service of ENT Devices Panel voting members Gulya, Jenkins, and Francis and Industry Representative Crompton, all of whose terms end on October 31, 2004, and welcomed new voting members Mair (new ENT Devices Panel chair), Orloff, and Dr. Kathleen Sie (not in attendance at the meeting).

Ms. Thornton then read the conflict of interest statement. The Agency had no conflicts to report, but it took into consideration certain matters regarding Drs. Demko, Mair, and Terris, who reported interests in firms at issue but in matters not related to the day's agenda. They could participate fully in all discussions.

## **BRANCH UPDATE**

**Eric A. Mann, M.D., Ph.D., CAPT, USPHS, Chief, ENT Devices Branch**, provided an update on branch activities since the last meeting, which took place in August 2002. After listing the staff changes in the Branch, he noted that the Agency had approved the PMA for the Karl Storz Autofluorescence System for use in white light and autofluorescence system bronchoscopy to identify and locate abnormal bronchial tissue for biopsy and histological evaluation.

In the area of cochlear implants, Cochlear Americas received approval for design changes to the Nucleus 24 Contour Softip Electrode. It now features an "advance off stylet insertion tool"

and a longer, specialized electrode tip. The MED-EL Corporation received approval for design changes to its Combi 40+ Cochlear Implant System; the contact spacing has been optimized for special cases but still has 12 pairs of electrode contacts. The sponsor also received approval for an MRI compatibility indication for the device. Advanced Bionics Corp received approval for changes to its HiResolution Bionic Ear System to include a repackaged ICS featuring a new silicone-embedded titanium case. The company also received approval for the HiFocus Helix precurved electrode. The device is MRI compatible with magnet removal.

Dr. Mann noted that Advanced Bionics had voluntarily recalled all unimplanted Clarion and HiResolution Bionic Ear systems because of the finding of moisture in the implant case of explanted devices. In some cases, the moisture may result in device malfunction or failure. The company is taking steps to address the problem. FDA has worked with the company to draft notification letters and is not recommending removal and replacement of normally functioning devices.

Finally, FDA is launching a Web site devoted to the topic of cochlear implants at [www.fda.gov/cdrh/cochlear](http://www.fda.gov/cdrh/cochlear).

## **FDA PRESENTATION**

**Heather S. Rosecrans, Director, Premarket Notification Staff**, reviewed the regulations governing over-the-counter (OTC), prescription, and prescription home use labeling and clarified the differences between the three types of labeling. If adequate directions for use for a lay person can be written, then a device does not have to be prescription. Automated external defibrillators, cryotherapy wart removal systems, and pregnancy tests are examples of devices that were changed to OTC labeling via the 510(k) process.

Dr. Mann then presented a history of snoring and obstructive sleep apnea (OSA) devices proposed or approved for OTC use. Several different FDA branches handle the devices, depending on their mechanism of action. Dr. Mann provided device descriptions and information on classification status for nasal dilators, cervical and “snoring” pillows, and mandibular support devices. Nasal dilators for snoring are Class I OTC devices; none have been approved for OSA indications. One cervical pillow for a mild OSA indication has been approved as a prescription device; two others are OTC. Pillows approved for snoring indications are OTC. Four adverse events for nasal dilators and one adverse event for a mandibular support device have been reported to the MAUDE database. No adverse events have been reported for cervical pillows, but minor adverse events are significantly underreported.

**Kevin P. Mulry, D.D.S., M.P.H., Dental Officer**, noted that the scope of dental devices for the panel discussion includes intraoral devices but does not include implantable device, surgical devices, continuous positive airway pressure (CPAP), or diagnostic devices. In 1997, the Dental Panel recommended Class II special controls for intraoral devices for snoring and OSA; the current regulation is at 21 CFR 872.5570. Sponsors must submit a 510(k) for marketing clearance. A Class II special controls guidance published in 2002 specifies the data required in 510(k) submissions, risks to health associated with these devices, and recommended mitigation measures. Various sponsors have requested that the devices be made available OTC. The Agency is asking the panel for its input as to what data sponsors should submit to provide reasonable assurance of safety and effectiveness for OTC use.

The types of dental devices cleared under this regulation are tongue-retaining devices (TRDs), mandibular repositioning devices (MRDs), and palatal lifting devices (PLDs). The

cleared indications are for snoring and mild to moderate OSA, and the devices are available by prescription only.

Dr. Mulry reviewed trends in device design along with the labeling (i.e., contraindications and warnings) for TRDs, MRDs, and PLDs. The devices may cause tooth movement or changes in dental occlusion, gingival or dental soreness, temporomandibular joint (TMJ) pain, obstruction of oral breathing, and excessive salivation. He noted that all submissions for intraoral devices must include a mechanism for oral breathing.

Clinical testing performance measures for snoring include reduction of snoring based on clinical observation. For OSA, performance measures include baseline and postinsertion polysomnograms (PSGs) measuring apneic events, apnea-hypopnea index (AHI) score, and oxygen saturation.

Dental devices differ from ENT devices in that all dental devices for snoring or OSA are intraoral. They are prescription devices (i.e., none have been cleared as OTC devices), and devices for both indications (OSA and snoring) pose similar risks related to correct selection and fitting of the appliance. Dental devices present different risks from ENT devices; they vary in design and application, and correct selection and fitting is important in preventing injury. Ongoing clinical care by a dentist is critical in monitoring for possible adverse events associated with intraoral devices.

The Dental Devices Branch has received clinical protocols from sponsors to support OTC availability of devices used for treatment of snoring, and it anticipates receiving protocols for treatment of OSA. Issues addressed in the protocols include intervention of a dentist or other competent intermediary to assess the patient's general and oral health status and appropriateness of the device for the patient; lay person self-assessment of snoring versus OSA; and directions

for self-fitting the oral appliance. Questions that have arisen in the course of Agency examination of the devices include whether a lay person can accurately self-diagnose the condition or oral health status and whether a lay person can choose the correct oral appliance and fit it such that the device is safe and effective and does not cause adverse events.

## **OPEN PUBLIC HEARING**

Dr. Gulya read the FDA's statement on transparency of the device approval process and the need for the speaker to put their remarks in context with respect to any financial relationship they might have with an industry that is likely to be impacted by the topic of the meeting.

**Steven Merahn, M.D., Executive Director, Academy of Clinical Sleep Disorders Dentistry (ACSDD)**, urged that oral appliances for OSA and snoring remain prescription devices. Although CPAP involves problems with patient compliance and less costly first-line therapies are needed, the risks of self-diagnosis are too great. ACSDD supports the increased use of oral appliances as first-line treatment for airway-related sleep disorders in a primary care model. The Academy also recommends shifting responsibility of OSA management to an interdisciplinary primary care team of physicians and specially trained dentists to achieve public health objectives but alleviate the risks of self-diagnosis and unmonitored treatment associated with OTC oral appliances.

**Lawrence Epstein M.D., President-Elect, American Academy of Sleep Medicine (AASM)**, stated that the AASM opposes use of OTC dental devices in treatment of snoring and OSA. Oral appliances can be effective therapy for snoring and OSA, but the difficulty in differentiating between OSA and snoring, the need for clinical evaluation and physiologic testing, and the potential for significant complications make it essential that such therapy be

provided under the direction of medical and dental personnel trained in the management of patients with sleep disorders. Approval of OTC dental devices will lead to delayed recognition and treatment of people with OSA and increased adverse events; increased availability will not increase quality of care. Self-diagnosis has many risks, and use of OTC oral appliances may improve the symptom of snoring but leave underlying OSA untreated. It is essential that a dental professional trained in the role of oral appliances in treatment of OSA and snoring, as well as in all aspects of oral health and dental occlusion, be involved in choosing the appropriate device, ensuring appropriate fit, and following up with the patient.

**Kent Moore, D.D.S., M.D., President, Academy of Dental Sleep Medicine (ADSM),** stated that the ADSM is strongly opposed to OTC use of oral appliances and believes that such use would present a significant public health risk. The data do not support safety and effectiveness of oral appliances used in this manner, and unsupervised use of oral appliances will cause significant morbidity to the population involved and have detrimental effects in preventing or delaying the diagnosis and treatment of the underlying sleep-related upper airway disorder. Only a physician can properly diagnose the condition, and only a dentist can properly fit the appliance and monitor its use. The difficulty in differentiating between OSA and snoring, the need for clinical evaluation and physiologic testing, and the potential for significant complications support continued categorization of the devices as prescription only.

**Keith Thornton, D.D.S., Chief Executive Officer, Airway Management, Inc., and inventor of the Thornton Adjustable Positioner,** emphasized the high level of morbidity caused by oral appliances for treatment of OSA and snoring. He has decided to keep his device a custom device; it should not be in the hands of a nondentist. The most critical step to preventing serious jaw position changes is for patients to move the mandible back into position upon

awakening; for that, he provides exercise bite tabs. Because of the potential for so many morbidities, it would be unethical to permit OTC use of oral appliances for treatment of snoring and OSA.

**George Dungan, R.P.S.G.T., Manager of Clinical Research, Respiroics**, stated that Respiroics believes that the OTC availability of OSA screening devices and of snoring treatment devices is necessary to reach a large underserved population. Risks of self-treatment and fit can be mitigated through education and labeling. Labeling for snoring devices should inform users of symptoms beyond snoring that may indicate OSA and direct them to seek medical attention if they currently have symptoms of OSA, if their condition does not improve, or if they experience discomfort or side effects from the use of the device. It is important to develop OTC devices for self-awareness and self-screening for OSA. Such devices must have appropriate sensitivity to detect OSA and deliver unambiguous results. Sponsors of such devices will need to submit clinical data comparing the results of OTC use to the results of a subsequent diagnostic procedure.

## **PANEL PRESENTATION**

**David J. Terris, M.D., Panel Presenter**, listed several issues to consider: the standard of care for OSA diagnosis, correlation of signs and symptoms with OSA (i.e., possibility of self-diagnosis), and correlation of signs and symptoms with objective measures of response to OSA treatment. OSA is a public health problem. It has significant implications for cardiovascular health, neurovascular risk, risk for motor vehicle accidents, and mortality, so correct diagnosis is vital. The Sleep Heart Health Study found a strong correlation of sleep disorders with cardiovascular disease independent of other risk factors. In addition, the increased incidence of

obesity has led to increased prevalence of apnea. The OTC products currently available for snoring have limited efficacy.

Dr. Terris then summarized various means of diagnosing OSA. Attended PSG was first described in 1953 and is the gold standard today. It uses several monitors to record cardiac, brain, and lung activity and assesses snoring sounds, nasal and oral airflow, chest and abdomen movement, and pulse oximetry. Attended PSG involves an overnight hospital stay. Ambulatory PSG equipment measures pulse rate, oximetry, airflow, and chest movement; it is no substitute for attended Level 1 PSG, according to the ASDA position statement. Pulse oximetry has been examined as a screening device, but its sensitivity ranges from 23 to 90 percent, so the method is not reliable. Watch PAT-100, a finger-mounted optic pneumatic sensor, detects episodic vasoconstriction (from sympathetic events) and has shown a promising correlation with PSG. The Sleep Strip, an adhesive, upper-lip device that has flow sensors and oximetry capability, has been shown to have a sensitivity of 70 to 88 percent and specificity of 57 to 94 percent.

PSG is the standard of care for diagnosing OSA; self-diagnosis may not be possible. Risk factors include age, gender, body mass index, and neck circumference. Signs and symptoms include snoring, excessive daytime sleepiness, witnessed apneas, morning headaches, irritability, neurocognitive deficits, impotence, and nocturia. Not all OSA patients snore, and the Epworth Sleepiness Scale (ESS) is not a good predictor of OSA—only about 40 to 60 percent of patients with elevated ESS scores have OSA. Eighty-five to 90 percent of patients have witnessed apneas. Attempts to develop questionnaires and rating scales to assess the presence or absence of OSA have not been successful. The conclusion is that OSA cannot be reliably diagnosed without PSG.

In addition, improvement in the signs and symptoms of OSA do not always correlate with objective measures of response to OSA treatment. Dr. Terris cited several studies in support. In response to a question from a panel member, he noted that OSA only gets worse over time.

**B. Gail Demko, D.M.D.**, presented information on side effects associated with oral appliance therapy for OSA. She noted that she treats fewer than 75 percent of patients referred to her. A study by Fransson published in the *Swedish Dental Journal* found that about 15 percent of patients who reported responding to treatment were false-positive symptom responders; in other words, they felt better, but PSG indicated that they were not.

Most appliances are MRDs, which bring the jaw forward and keep it closed and open the airway. Short-term changes include excess saliva, dry mouth, pain in individual teeth, pain in anterior teeth if the patient is clenching, mobility of anterior teeth, posterior openbite in the morning (probably caused by edema in the joint space), TMJ pain, and allergic reactions (e.g., to latex or to methylmethacrylate). Fibromas and lip irritation are other common short-term changes. Dr. Demko listed various ways of managing the side effects.

Long-term changes include soft- and hard-tissue changes, which need to be addressed in the first 6 months. Hard-tissue changes may be related to incomplete coverage of the dental arch and pressures on the dental arch. Practitioners need to ensure that if there is tooth movement the back molars are not left behind due to incomplete coverage. Anterior tooth movement may cause an anterior interference that can maintain a posterior open bite allowing permanent extrusion of posterior teeth. Once transeptal fibers are activated, they will telegraph the message around the arch and open contacts will occur. Spaces and other long-term tooth movement can be treated with orthodontics. Fluid buildup in the TMJ is a short-term change that can lead to long-term changes.

Dentists disagree as to whether thermal active acrylic appliances move teeth more than hard acrylic MRDs. No published data are definitive. Studies show that 75 percent advancement within a patient's physiologic range is the most effective position; Dr. Demko's patients have been successful between 50 and 125 percent. The jaw must move a minimum of 6 mm, but the more it moves, the more likely unwanted side effects are. Tooth movement can continue past 30 months. One important finding is that many patients who experience changes in occlusion do not report a permanent sense of altered occlusion.

TRDs move the tongue forward and force nasal breathing. They are less effective than MRDs unless the tongue is the only source of obstruction. Side effects include excess salivation, irritation, tongue lengthening, and posterior tooth extrusion. Soft-tissue effects are secondary to irritation from the edge of the device and to tongue bulb suction. Hard-tissue effects are secondary to incomplete coverage of dentition and the vertical dimension of occlusion.

Patient assessment and selection require a complete dental evaluation. Factors to consider in choosing an oral appliance include palate length, oropharyngeal opening, occlusion, excursive movements, midlines, tooth height, wear patterns, TMJ history, hard-tissue topography, and tongue extension. Practitioners should discuss the continuum of sleep-disordered breathing with their patients. Patients who fare best with MRDs generally are retrognathic, thin, young, and female; they have healthy dentition, a protrusive range greater than 7 mm, and moderate anterior overbite. Normal weight, supine worsening of symptoms, macroglossia, and normal soft-palate length are correlated with successful use of TRDs. Obesity, retrognathia, short lingual frenum, and severe OSA are correlated with TRD failure.

Dr. Demko presented brief information on fabrication of MRDs and TRDs, then listed issues involved in patient self-assessment and -treatment. Patients treating themselves will not

have information on factors such as periodontal disease or dentition. Dental parafunctions (e.g., bruxism, clenching), occlusal class, proper fit, and side effects are all important considerations in choosing an appliance. Given that patients often are not aware that they are experiencing permanent changes as a result of appliance wear, self-diagnosis and -treatment may not be appropriate.

All appliances do the same thing: They move teeth or allow them to move. It is not possible to predict who will be successful with oral appliances or who will have unwanted side effects. Patients are not aware of dental changes, and patients with symptom relief may still have serious disease. Few dentists maintain databanks on their patients, so much is unknown.

In response to a panel question about the seriousness of the dental changes, Dr. Demko noted that as soon as she sees detrimental changes, she tries to get the patient to go back on CPAP. Patients with dental changes usually do not complain about anything but cosmetic problems and do fine functionally. Permanent changes occur between 6 and 12 months.

**PANEL DELIBERATIONS**

The panel did not vote, and it was not asked to achieve consensus on the members’ answers to the FDA’s questions. The goal of the deliberations was to help the Agency formulate an approach to evaluating future device applications intended for OTC availability.

**Question 1: As noted in FDA’s presentation , the following types of devices may be considered for or have already been cleared for OTC status for the indications of snoring and/or OSA:**

Device	Snoring	Mild OSA	Moderate OSA	Severe OSA
Tongue Retaining Device	Rx			
Mandibular Repositioning Device	Rx	Rx	Rx	
Palatal Lifting Device	Rx			
Nasal Dilators	OTC			
Cervical Pillows	OTC	OTC		
Mandibular Support Devices				

**Please discuss the risks and benefits of allowing devices to be marketed over the counter for the treatment of (a) snoring, (b) mild OSA, (c) moderate OSA, (d) severe OSA. In particular, please discuss the overall risk/benefit ratio assessment as it relates to level of disease severity and discuss the potential risks related to delay in professional diagnosis and treatment resulting from OTC availability and use of these devices.**

The panel discussed each device in turn and generally concurred that OTC marketing is not appropriate for the dental devices but could potentially be appropriate for certain ENT devices. Some panel members thought that MSDs or some subset of the currently available devices had the potential to be marketed OTC. The distinction between mild, moderate, and severe OSA needs to be better defined. This topic will need to be revisited once a reliable way to distinguish between snorers and those who have OSA is developed.

**TRDs.** The panel was unenthusiastic about OTC use of TRDs for OSA. The access to care issue is counterbalanced by the need for appropriate diagnosis and monitoring. Risks include venous congestion, airway blockage, and edema. Real-world use of the devices needs to be studied, in part because its efficacy for snoring treatment is not entirely clear. Labeling should discuss the potential for changes in dentition. The risks outweigh the benefits for OTC use for OSA. Moreover, if TRDs were approved for OTC marketing, too many patients would inappropriately select the device because it would be the only device available.

**MRDs.** Panel members concurred that MRDs should not be approved for OTC marketing for either snoring or OSA. The risk of eliminating snoring but leaving OSA untreated is too great. Unlike inappropriate use of OTC reading glasses or even hearing aids, the problems associated with improper MRD use are such that the risks of OTC distribution far outweigh the benefits. Properly fitting and adjusting MRDs requires a health care professional. The data on adverse events are from prescription devices, not “boil-and-bite” devices; one has to assume that the latter are associated with worse adverse events.

**PLDs.** The panel again concurred that the risks of OTC use exceeded any potential benefits. A review of the literature yields little information on PLD efficacy and adverse events. As with the other devices, ensuring appropriate fit is an issue that arises with potential OTC use.

**Nasal Dilators.** Nasal dilators may be effective for snoring treatment, but they are not effective for OSA treatment. Moreover, postmarketing studies on devices such as Breathe Right strips found no difference between snorers who wore the strips and those who did not. Complications included skin irritation and discomfort. Again, missed OSA diagnosis is of concern. There is no reason to change the OTC status of nasal strips, but sponsors would need to provide data for an OSA claim.

**Cervical Pillows.** Cervical pillows have already been labeled OTC for treatment of snoring, and two pillows are available OTC for mild OSA. Data do not demonstrate an effect for snoring.

**MSDs.** Insufficient data are available to support an OTC recommendation.

**Question 2: If, after your discussion of Question 1, you believe that certain devices would be appropriate for OTC treatment of OSA, please discuss the following:**

- ?? **How adequate product labeling can be written to assist the user in self-diagnosing and differentiating the severity of OSA he or she is experiencing to ensure proper use**
- ?? **Any other general or specific labeling restrictions which you believe would be appropriate for OTC devices to treat snoring and/or OSA**

Although panel members determined that none of the devices under discussion were appropriate for OTC treatment of OSA, they discussed issues involved in labeling devices for treatment of snoring and OSA. Labeling should mention that snoring can be a sign of OSA; list risk factors, signs, and symptoms of OSA; and provide referrals to helpful organizations.

Labeling is an opportunity for raising public awareness of OSA.

In response to a question from Dr. Rosenthal about which signs and symptoms should be written into labeling for snoring devices, Dr. Mair referred to an article in *Sleep* summarizing

AASM task force recommendations as to the cardinal features of OSA: choking or gasping during sleep, recurring awakening during sleep, unrefreshing sleep, daytime fatigue, and impaired concentration. It was suggested that labeling should note that even snoring without those symptoms could indicate OSA, so the user should consult with a physician. Risk factors such as hypertension and obesity should be listed. Labeling should state that adverse effects related to the device can take place without the user being aware of it and urge users to consult with their doctor and have regular dental evaluations. Adverse events such as jaw movement and dentition problems should be listed.

Again, panel members noted that mild OSA has not been well defined and that it thus does not make sense to distinguish between mild, moderate, and severe OSA in labeling. Most patients do not know their AHI or what category they fall in. Panel members suggested including wording such as “this product should not be used as the sole component as management of mild OSA—use only as part of a therapeutic regimen.”

**Question 3: Please discuss the following aspects of the clinical data that may be appropriate to be included in marketing submissions for snoring and/or OSA:**

**3a: Clinical study design, including control group, if needed**

Panel members discussed various study designs. It was divided as to whether patients could serve as their own controls or whether a control group would be necessary. It was noted that if changes in anatomy occur, the patient is not truly serving as a control. Other issues included variability in PSG results (both for readers and patients); controlling for regression to the mean; controlling for bias by having someone other than the investigator conduct the sleep study; the “first-night” effect, benefits of home (ambulatory) versus laboratory sleep studies; need for subjective patient data, such as what the patient ate and drank before the sleep study; and expense associated with multiple sleep studies. Many panel members felt that it was best to

use the gold standard of an attended sleep study and supported the idea of a randomized crossover design. Using patients as their own controls has been done in past, but most studies are unimpressive.

**3b: Endpoints that would be acceptable for the assessment of the effectiveness of treatment**

Panel members suggested the following endpoints: dental arch alignment; pre- and postexamination of occlusion; soft-tissue exam; measurement with questionnaire and/or spouse or bedmate; TMJ evaluation; and any appropriate electronic evaluations, such as myography. Other suggestions for primary endpoints included change in respiratory disturbance index, O<sub>2</sub> saturation, and snoring loudness. Mandibular devices should have primary endpoints defined according to the indication (snoring or OSA). Secondary endpoints include snoring, duration of treatment effect, headaches, cognition, and hypertension. Studies should assess patient compliance.

Results for appliances take 3 months for patients who are self-titrating. The slower and further they go, the better the outcome, but the greater the side effects. Patients should be followed for 6 months for efficacy and 1.5 years for adverse events if a manufacturer wants to advertise that its device leads to fewer problems than others on market.

**3c: Degree of improvement for each of the endpoints that would be clinically meaningful, assuming an acceptable adverse event profile.**

For OTC devices, device sponsors would have to demonstrate that consumers could achieve proper fit and provide information showing that the labeling and warnings are educating consumers about snoring versus OSA. The results would have to be validated at the clinical level. The standard definition of success should be subjective improvement (visual analog scale 1–10). Measuring decibels is harder and requires the subject to wear an oronasal microphone. Another measure is AHI <5. Standard measures of success are 50 percent or greater reduction in AHI and respiratory disturbance index scores of <20. Measures of oxygen saturation may be

necessary, depending on the study. Clinically meaningful secondary endpoints might include time to onset of effect and duration of effect, protruding mandible, and sleepiness score.

**3d: The specific adverse events, if any, that should be carefully assessed by FDA from the clinical trial**

Panel members suggested looking for a worsening of dental effects such as, changes in occlusion, TMJ problems, soft tissue, arch alignment, behavioral changes (e.g., worsening snoring or sleep patterns), fibrosis, and changes in dentition. For the TMJ, adverse events include onset of pain, limited opening, and joint sounds. It was noted that mandibular devices can have ameliorating effects on TMJ. Events can be categorized as appearance related or pain related, transitory or permanent. Some changes may not be important to patients. Some changes are not clinically important to start but may cross a line into serious adverse events that affect health; where that line lies cannot be predicted. Some patients are willing to put up with massive changes in bite and other elements to feel better. Oral mucosal changes, particularly in smokers, may not be device related. Worsening apnea may be an adverse event.

**3e: Would any of the responses to 3a-d be different based on severity of snoring or OSA?**

Panel members were not entirely in agreement. Some said that their responses would be no different. Other members suggested that endpoints would be different; for sleep apnea, it would be improvement in respiratory disturbance and AHI <5 whether the patient had mild, moderate, or severe OSA. Snoring outcomes are more subjective and may depend on what the patient's sleep partner says. For that reason, a control group probably does make sense.

One panel member noted that four snoring parameters—percentage of snoring originating in soft palate, average loudness, average loudness of total snoring, and average palatal flutter frequency—have been examined in multiple studies. One could look for statistically significant changes in the palatal flutter frequency, which would increase; the other three parameters would decrease.

In response to a question from Dr. Mann as to how to compensate for PSG variability and first-night effect in study design, a panel member responded that despite its flaws, PSG is the gold standard. Subjects need to spend two nights in a sleep lab; if results are wildly discrepant, the data are not sufficient.

**3f: Any specific considerations in trial design for OTC considerations**

Panel members emphasized that they did not want to be viewed as endorsing the devices for an OTC application for either sleep apnea or for snoring. They emphasized that the baseline exam is important and that anything that is marketed must be truly efficacious. Devices marketed for snoring would not need sleep study data.

**3g: Any specific device types or indications that would not require clinical data**

Panel members asked questions to clarify the 510(k) process. Panel members expressed concern that within the category of nasal dilators, nasal strips are grouped with devices that could get lost in the nose. Efficacy data should be required for substantially equivalent strips. Panel members noted that FDA provides an abundance of guidance that helps sponsors select devices that are substantially equivalent. Many applications are based on design controls, bench testing, and so forth.

**OPEN PUBLIC HEARING**

**Edward F. Grandi, Executive Director, American Sleep Apnea Association,** described the organization's mission. Taking a more cautious approach regarding currently prescribed devices is the prudent thing to do and encouraged requiring strict clinical data for new devices. Screening devices, whether questionnaires or other tools, must be developed for people who have snoring or other sleep problems. Another issue is access to sleep studies. By raising

awareness of OSA, we are increasing the need for access to diagnosis and affordable treatment. This should not be done at the expense of a population already suffering a great deal.

Sally Thornton noted that two people, Barry Krakow and Alan Barnes, had registered to speak but could not attend. Their comments were made available to the panel and to the transcriber for the record.

## **ADJOURNMENT**

Dr. Gulya thanked the panel and participants and adjourned the meeting at 3:46 p.m.

I certify that I attended this open session of the Joint Ear, Nose, and Throat Devices and Dental Products Advisory Panel on October 6, 2004, and that these minutes accurately reflect what transpired.

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Sara M. Thornton  
Executive Secretary

I approve the minutes of the October 6, 2004, meeting as recorded in this summary.

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A. Julianna Gulya, M.D.  
Chairperson

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