SUMMARY MINUTES

OF THE

ORTHOPEDIC AND REHABILITATION DEVICES PANEL

MEDICAL DEVICES ADVISORY COMMITTEE

OPEN SESSION

JULY 20, 2000

Gaithersburg Holiday Inn
2 Montgomery Village Avenue
Gaithersburg, MD

ORTHOPEDIC AND REHABILITATION DEVICES PANEL ROSTER
July 20, 2000

Barbara Boyan, Ph.D.
Chair

Albert J. Aboulafia, M.D.
Voting Member

Velia Butcher, J.D.
Consumer Representative

Edward Y. Cheng, M.D.
Voting Member

Maureen Finnegan, M.D.
Deputized Voting Member

Robert Goldman, M.D.
Deputized Voting Member

Kinley Larntz, Ph.D.
Deputized Voting Member

Peter A. Lewin, Ph.D.
Deputized Voting Member

Glenn B. Pfeffer, M.D.
Deputized Voting Member

John A. Robinson, M.D.
Deputized Voting Member

Raymond Silkaitis, Ph.D.
Industry Representative

Douglas G. Wright, M.D.
Deputized Voting Member

Michael J. Yaszemski, M.D., Ph.D.
Voting Member

FDA Personnel
Hany Demian, M.S.
Panel Executive Secretary

Celia Witten, M.D., Ph.D.
Director, Division of General and Restorative Devices

Sankar Basu, Ph.D.
Physicist, Office of Device Evaluation

Gerry Gray, Ph.D.
Division of Biostatistics

Neil R. P. Ogden
Branch Chief, General Surgery Devices Branch

OPEN SESSION

Panel Executive Secretary Hany Demian called the session to order at 9:40 a.m. After reading the deputization of temporary voting member statement, he deputized Doctors Larntz, Lewin, Robinson, Goldmman, Pfeffer, Wright, Finnegan, Li and Lyons. He then read the conflict of interest statement and added that Doctors Cheng, Larntz, Wright and Li could participate fully in the panel proceedings. Additional matters were considered for Doctors Boyan, Yaszinski, Cheng and Li, and they also could participate fully in all discussions. The panel members introduced themselves.

Panel Chair Dr.Barbara Boyan reviewed the agenda for the day and noted there was a quorum of voting members present in this session.

Dr. Celia Witten, Director of General and Restorative Devices presented Dr. Boyan with a plaque for her five year service on the panel. She then gave Dr. Silkaitis a certificate of appreciation for his service from 1997 to 2000. She noted that the new Director of the Office of Device Evaluation is Dr. Bernard Statland.

OPEN PUBLIC HEARING

No one came forward from the audience to address the panel.

Summarizing three letters supporting this device for the treatment of plantar fasciitis, **Panel Executive Secretary**, **Mr. Demian** stated that the OssaTron is an alternative to surgery with little risk of side effects from the procedure.

OPEN COMMITTEE DISCUSSION

Premarket Approval Application P990086: HealthTronics OssaTron Lithotriptor for the Treatment of Heel Pain

Sponsor Presentation

Marie Marlow, Vice President of Clinical and Regulatory Affairs for HealthTronics, introduced the OssaTron, an extracorporeal shock device to be used in the treatment of chronic heel pain syndrome. She added that extracorporeal shock wave devices have been used for many years in the treatment of kidney stones.

Dr. Schultheiss, Director of Sales and Marketing of HealthTronics in Switzerland, reviewed the functional components and technical properties of the device, technical and bench testing, and clinical and non-clinical testing. He emphasized that the power settings are much higher for lithotripsy than for treatment of heel pain syndrome.

Marie Marlow presented the clinical study results. The study was a multi-center, randomized double blind placebo controlled trial that evaluated the safety and effectiveness of this device and the durability of the results of this treatment. The patients were evaluated at twelve weeks, six months and twelve months. Ms. Marlow reviewed the treatment procedure and the evaluation criterion. After identifying the complications from the treatment, she pointed out that pain and mild numbness or tingling were the most commonly reported complications.

George DeMuth, President of StatTech Services, provided the statistical analyses. He reviewed the four criteria for successful treatment and found that the investigator assessment of the heel pain was the most sensitive criterion. The OssaTron was statistically a more effective treatment than the placebo treatment and the effect was sustained.

Marie Marlow concluded that a single treatment was safe and effective. One treatment was sufficient in most patients. When re-treatment was used, approximately

the same success rate occurred as with the first treatment. The complications of the procedure were temporary and resolved spontaneously. She concluded the talk with proposed labeling that included indications, contraindications and precautions.

Panel Chair Dr. Boyan requested that questions be held until after the FDA presentation.

FDA Presentation

Dr. Sankar Basu presented the physics of this device. After he described the method of energy generation, he delineated the histopathological change at various energy densities. The energies produced by the OssaTron are below the energy employed in stone breaking lithotriptors. A large amount of experience has been accumulated already with shock wave technology.

Neil R. P. Ogden presented the clinical data for the OssaTron. He reviewed the indications for use, study design, and inclusion and exclusion criteria. The FDA believes that "chronic heel pain syndrome" is equivalent to plantar fasciitis. The trial design and the provided data do not permit analyses of re-treatment results or the durability of the treatment due to insufficient sample size and inadequate follow-up. The variation in complications between treated and placebo groups is not significant. The sponsor did not include plantar fascial tears in their presentation of treatment complications.

Dr. Gerry Gray listed the four success criteria used in the clinical trials: independent assessment of heel pain; self-assessment of heel pain; activity score; and the use of pain medication. When the therapeutic results between OssaTron and the Sham (Placebo) are compared using the above criteria, OssaTron is significantly statistically superior. The difference between these treatment modalities is due to the increased

sensitivity in independent pain evaluation and a higher rate of responders in the OssaTron group. Predictive factors for overall success includes age, baseline heel pain, duration of heel pain and back pain.

Panel Clinical Review

Preclinical Review: Dr. Lewin stated that the study followed the FDA guidelines, and in general the study seemed to be solid.

Clinical Review: Since Dr. Robinson was impressed with the 12 week assessment and with the Sham controls, he found the 12 week data to be convincing; however the remaining data was not convincing to him.

Statistical Review: Dr. Larntz thought that the study focused on the 12 week outcomes and that one cannot make conclusions about patient outcomes after six months in this study. He felt that 12 weeks was not a long enough follow up for these patients. The fact that patients were missing at the 12-week follow up was problematic for him. Another problem in the study was that patients in the repeat treatment were self-selected and therefore the trial followed the patient successes.

Panel Questions

Dr. Richard Alvarez, Dr. John Ogden and Marie Marlow answered most of the questions raised by the panel. When the panel questioned how the device worked, Dr. Ogden stated that no one knew exactly the explanation, however, research was being conducted on the molecular level. In answer to concerns about future training programs, the company representatives stated that similar training would be used as was developed with the 50 nonrandomized patients.

Another concern was that peripheral neuropathy and vascular insufficiency should be more precisely and objectively evaluated on the follow up visits. In addition, more precise patient documentation should be obtained on the patients who did not return.

The panel felt that patients who have osteoporosis should be included in the study. Ms. Marlow revealed that early studies of osteoporotic patients demonstrated increased bone density after treatment with OssaTron at higher energy settings than those used in the application.

The panel also had concerns about the standardization of the injection site for local anesthetic and local blocks. Ms. Marlow verified that no patient included in the study had cortisone injections during the time of the study. Cancer patients will be offered this treatment at some future time. She went on to add that the application of this treatment is with the patient with chronic heel pain , decreased vascularity, increased fibrosis and fluid in the tissues.

Two other questions were raised. Would it be appropriate to use this treatment on patients with failed surgery? What medical personnel should use the machine?

FDA Panel Questions

Mr. Ogden read the FDA questions to the panel.

1. Although different complications were observed with the OssaTron treatments than with the Sham treatments, the panel felt that the side effects were not consequential with this device.
2. From the data presented at this meeting, the consensus was that the use of the Ossa Tron provided clinically significant results.

3. The OssaTron should be used in the treatment of patients with proximal plantar fasciitis.

Ms. Marlow discussed the profile and outcome of the patients who had persistent pain after one OssaTron treatment. She stated that the company made no claims about persistence of pain relief. Most patients with chronic proximal fasciitis recover on their own over a period of five years.

Panel Chair Dr. Boyan adjourned the meeting for a lunch break at 12:30 p.m. The meeting reconvened at 1:10 p.m.

Open Public Session

No one came forward to discuss the device.

Panel Executive Secretary Hany Demian read the voting rules and options. Dr. Robinson made a motion to approve OssaTron with no conditions, and Dr. Yaszinski seconded the motion. The motion passed by a vote of six to four. The voting members stated the reason for their votes.

Panel Chair Dr. Boyan adjourned the meeting at 1:25 p.m.

I certify that I attended the Open Session of the Orthopedic and Rehabilitation Devices Panel Meeting on July 20, 2000, and that this summary accurately reflects what transpired.

____/s/___Hany Demian_____
Hany Demian, M.S.
Executive Secretary

I approve the minutes of the meeting as recorded in this summary.

__/s/ Barbara D. Boyan_____
Barbara Boyan, Ph.D.
Chair

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ORTHOPEDIC AND REHABILITATION DEVICES PANEL ROSTER II
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Barbara Boyan, Ph.D.
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Hany Demian, M.S.
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Celia Witten, M.D., Ph.D.
Director, Division of General and Restorative Devices

Peter Allen, M.S.
Engineer, Orthopedic Devices Branch

Harry Bushar, Ph.D.
Statistician, Division of Biostatistics

OPEN SESSION

The meeting was called to order at 1:43 p.m. by **Panel Chair Dr. Barbara Boyan**, who stated that this session of the panel would be considering the premarket approval application (PMA) of Howmedica Osteonics' ABC and Trident Systems. She asked the panel to introduce themselves.

OPEN COMMITTEE DISCUSSION

Premarket Approval Application P000013 Howmedica Osteonics ABC and Trident Systems

Sponsor Presentation

Beth Staub, Vice President of Quality Assurance, Regulatory Affairs and Clinical Research introduced the ABC and the Trident Systems. **Michael Manley, Ph.D., Chief Scientific Officer**, introduced the speakers.

Thomas McCarthy, Hip Project Manager, System III, reviewed the Study Control and next detailed the difference between the ABC (Aluminum Bearing Couple) Systems and the Trident System as a permanently assembled Titanium sleeve around the ceramic cup. He emphasized that only the ceramic inserts are under investigation in these systems.

Michael Bushelow, Assistant Director of Device Evaluation, iterated that the inserts, which are under consideration for this trial, far exceeded FDA standards in all strength testing. Furthermore, the bone stresses generated at the fixation interfaces were acceptable.

James D'Antonia, M.D., Principal Investigator, described the surgical techniques and cited some specific patient cases.

Dr. Manley presented the clinical data noting that in this study the mean age was less than 55 years, the majority of patients were male, and most of the patients carried the diagnosis of osteoarthritis. The patient satisfaction was high both for the ABC Devices and for the Control Device. After Dr. Manley reviewed the changes on the post-operative radiographs, he concluded that the study revealed equivalent performance of hips with the ABC Devices and the Control Device.

He next turned to the Trident results that were equivalent to or better than the ABC results. The operative site adverse event rate was lower with the Trident System than with the ABC Systems or Control System. Furthermore, the Trident System provided multiple revision options.

Dr. D'Antonio addressed the first Panel Question regarding chipping in the ABC inserts. In general, chipping is not of clinical concern, if the liner is not left in a canted position. Beth Staub stated that with proper labeling, training and education this question should not be a persistent problem. Ms. Staub addressed the question of the Trident Systen after seven weeks of clinical trials noting that the ABC and Trident Systems are very similar and that Trident exceeded ABC in almost all tests. Ms. Staub stated that if the Trident System were approved at this time, the ABC and Trident cases would be followed together with the Control Group for an additional two years.

FDA Presentation

Lead Reviewer Peter Allen noted the difference in the ABC Systems was an exterior hydroxyapatite coating on the acetabular shell of System II. The Titanium sleeve

on the Alumina ceramic insert helps prevent chipping in the Trident System. It is the ceramic or ceramic couple that makes these systems investigational.

The FDA found the pre-clinical testing adequate and has no further issues with this portion of the trial. Efficacy studies showed virtually no difference between the two ABC Device scores and the Control Device scores. The major concern with the ABC Systems was chipping, especially during surgery. The secondary end points including patient satisfaction and results of the Health Status Questionnaire show no difference between the three systems.

The Trident System , an updated version of the ABC Systems, shows early, comparable results with the ABC Systems and Control System, without the adverse event of chipping.

Statistical Reviewer Harry Bushar reported that the ABC Clinical Trial was a prospective, controlled, randomized, multi-center study with two study arms. The Trident Clinical Trial has borrowed the Control System from the ABC Study. In regard to safety, the Trident System has had fewer adverse events than the ABC Systems by reducing chipping to zero. The effectiveness or failure rates are comparable between the Control Study and the ABC Study.

Mr. Allen ended the FDA presentation by summarizing the three FDA panel questions.

Panel Clinical Review

Pre-clinical Reviewer Dr. Li started his review by stating that ceramic on ceramic devices had three problems: fracture, loosening of the acetabulum and impingement. He feels that the problem of ceramic fracture has been solved. Over time

there has been a reduction of osteolysis with these devices, however this problem may not be solved. One of the gravest problems is corrosion of Titanium after five to seven years.

This trial did extensive mechanical testing under a single condition, and therefore, additional tests should be done under non-optimal conditions. A general issue is mal-alignment or canting of the liner in the shell. Chipping of the liner is an indication of mal-alignment. In some literature, mal-alignment is said to occur in 30% of cases. The current literature regards the metal polyethelene device as standard, however there is little accumulated knowledge about ceramic on ceramic devices.

He questioned whether the study should combine data from liners with and without hydroxyapatite coatings. Further, should the Trident System use data from the ABC tests?

In summary, Dr. Li felt that these devices appear to be safe. The question remains of what criteria should by used in the future to evaluate ceramic on ceramic devices.

Primary Clinical Reviewer Dr. Lyons found ceramic devices clinically attractive due to the smoothness of the surface and inertness of the material. Problems arise with the brittleness of the material, specifically chipping at the periphery of the cup. Training on implantation techniques becomes a primary issue to minimize this problem.

Disclosure to surgeons is needed so that the surgeon understands options with these three devices. For instance, Trident is easier to revise at surgery. Since monitoring is crucial to collecting data on these devices, post market surveillance is an important issue. Retrieval of these devices for additional testing could contribute to better understanding of performance and failure.

Statistical Reviewer Dr. Larntz stated the Howmedica Osteonics made a nice statistical presentation, however nothing is known about the long-term failure rate of the Trident System. If one considered only short term adverse events, one would chose Trident.

A five-minute break was taken at 3:43 p.m.

Panel Questions

The panel had concerns about the difficulty of implantation and removal of the ceramic liner at surgery.

They questioned the importance of canting of the assembly and association with chipping. In the discussion the point was made that Titanium wears faster than ceramic material.

They returned to the difficulty of predicting the future performance of the Trident System.

If chips occur in the post-operative period, are there any untoward biological effects? How would a physician or patient decide which system to use? The underlying question for discussion was, is this product better than what is available on the market?

Dr. Witten clarified for the panel that they would be voting on an entire system and not just the ceramic on ceramic interface.

FDA Questions

Mr. Allen read Question l.

Dr. Lyons felt slipping was not a concern since it could be overcome with training on liner implantation. Ion leaching from Alumina over time could be a clinical problem.

On Question 2, the panel continued to be concerned that the data from the ABC Systems could not predict the future performance of the Trident System.

In answer to Question 3, most panel members felt a five year follow up study was indicated. Dr Li mentioned that ceramic on ceramic devices fail in five years.

Howmedica Osteonics representatives answered the three FDA questions. Dr. D'Antonio noted that the ABC System had an extraction device and that osteolysis was a persistent problem with hip replacement in young patients.

PANEL VOTE

Executive Secretary Hany Demian read the voting instructions to the panel.

Dr.Lyons made a motion for Trident and ABC Systems approval with conditions. Dr. Aboulafia seconded the motion.

The motion passed with a five to two vote. The conditions were discussed and unanimously agreed upon as follows:

1. Warnings to surgeons
2. Disclosures concerning the different systems
3. Education
4. Post market surveillance at the end of 5 years to include retrieval analysis
5. Monitoring of surgeons.

Dr. Witten advised that requesting new clinical data was not equivalent to adding conditions. If the panel was advising a company how to put the product in approvable form , that was not the same as voting for approval with conditions.

Dr. Finnegan made a motion to strike down the current motion and moved to separate the ABC and Trident Systems. The motion was seconded. Dr. Lyons accepted

the motion to strike down his original motion, and he made a new motion to accept the ABC System with conditions. Dr. Aboulafia seconded the motion. Dr. Boyan repeated the conditions for the ABC System and asked for a vote of approval with the above mentioned conditions. The panel voted unanimously to approve this motion.
The panel members iterated reasons for their votes.

Dr. Lyons made a motion to approve the Trident System with conditions, and Dr. Aboulafia seconded it. A discussion followed. The motion was defeated with three for and four against the motion.
Dr. Finnegan made a motion for non-approvability, and Dr. Cheng seconded the motion. The motion passed with a four to three vote. Every panel member discussed their vote and added their suggestion to make the product approvable. Persistent questions remain: corrosion of Titanium, performance in two to five years, additional wear testing, and the performance of the new interface.

Executive Secretary Hany Demian thanked all the participants of the panel and adjourned the meeting at 5:23 p.m.

I certify that I attended the Open Session of the Orthopedic and Rehabilitation Devices Panel Meeting on July 20, 2000, and that this summary accurately reflects what transpired.

____/s/___Hany Demian_____
Hany Demian, M.S.
Executive Secretary

I approve the minutes of the meeting as recorded in this summary.

__/s/ Barbara D. Boyan_____
Barbara Boyan, Ph.D.
Chair

Summary minutes prepared by Lynne Blei
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