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Food and Drug Administration
9200 Corporate Boulevard
Rockville MD 20850

Michael J. Pappas, Ph.D., P.E.
President
Endotec, Inc.
20 Valley Street, Suite 210
South Orange, New Jersey 07079

Re: Reclassification of Non-Constrained, Mobile-Bearing Ankle Prosthesis
Docket Number 2004P-0457/CCP 1
Dated: October 12, 2004
Amended: September 2, 2005

Dear Dr. Pappas:

The Food and Drug Administration has reviewed the above referenced petition for reclassification pursuant to section 513(e) of the Food Drug and Cosmetic Act (Act). Mobile-bearing ankles are currently Class III (PMA) devices. This petition seeks reclassification of uncemented, non-constrained, mobile-bearing ankle prostheses from Class III (PMA) status to Class II (510(k)) status. The purpose of a reclassification petition is to demonstrate that the risks previously identified for a Class III device, in light of new information, can be adequately addressed/minimized by either general, or general along with special controls, and, therefore, should be reclassified as Class II devices. Based on review of the data submitted in your petition, we believe you have not provided adequate information to provide reasonable assurance of the safety and effectiveness of mobile-bearing ankles. Further, we are not aware of any special controls which allow for the demonstration of the safety or effectiveness of this ankle design or future mobile-bearing ankle replacement devices. Without these special controls, we cannot reclassify uncemented, non-constrained, mobile-bearing ankle prostheses at this time. We will be able to further consider reclassification of these devices once the following concerns have been adequately addressed.

Special Controls – General Concerns

1. Your petition includes proposed special controls that you believe are sufficient to provide reasonable assurance of the safety and effectiveness of the device type you have proposed for reclassification. We do not believe the proposed special controls are sufficient to provide reasonable assurance of safety and effectiveness for this device type. Reclassification of this device type requires standardized, validated means to test and analyze the stand-alone devices preclinically as well as clinical results on enough patients (within a clearly defined patient population) in well-controlled, appropriately designed studies with long enough follow-up using standardized, validated outcomes measures and consistent study methods. In addition, reclassification for this device type requires an identification of the device design features, preclinical test results, patient selection considerations, and labeling/surgical technique considerations that predict successful clinical outcomes in order to define appropriate special controls. Please address the following general concerns regarding the proposed special controls.

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- a. You have developed internal guidelines (or guidances) for testing ankles and have described a very limited amount of testing on the Buechel-Pappas device. In addition, you have attempted to rationalize how hip and knee data apply to the ankle; however, we do not believe you have provided an adequate rationale. Please develop appropriate special controls to mitigate the risks associated with mobile-bearing ankles to demonstrate reasonable assurance of the safety and effectiveness of mobile-bearing ankle designs. In the case of preclinical special controls, such controls should be based on standardized test methods validated specifically for use in testing mobile-bearing ankle devices. The parameters that need to be addressed include device stability and constraint (including long term durability), the polyethylene bearing (including wear and osteolysis), device strength and the risk of dislocation, metal sensitivity, labeling, surgical technique, and appropriate patient selection. These special controls should be developed based on experience with a number of different devices that fall within the proposed Class II device type. Therefore, please describe whether the proposed special controls are applicable to other ankle systems which fall within the proposed device category (i.e., mobile-bearing ankles other than the Buechel-Pappas Ankle).
- b. The proposed indications for mobile-bearing ankle devices are not consistent throughout your reclassification petition. For example, the following intended uses were provided within the petition:
 - i. The CDRH Submission Cover Sheet states the following, “The Buechel-Pappas Total Ankle Replacement System is intended for the reconstruction of painful and/or severely disabled ankle joints resulting from osteoarthritis and rheumatoid arthritis.”
 - ii. The indications included in the package insert states the following: “1. Patients may have a severely painful and/or severely disabled joint resulting from osteoarthritis, posttraumatic arthritis, or rheumatoid arthritis; 2. Patients may have correctable varus or valgus deformity (under 20°); 3. Patients having intact ankle dorsiflexors and plantarflexors; 4. Patients may have a previous failed total ankle arthroplasty provided the medial and lateral malleoli and ligamentous structures are intact; 5. Viable or reconstructable ligamentous and malleoli supports; and 6. Patients may have pseudoarthrosis.”
 - iii. Page 9, Section V.1. (Proposal of a Class II sub-type, Description of the purpose of ankle prosthesis) states that, “A total ankle replacement prosthesis (TAR) is an orthopaedic reconstructive device intended to replace the articulating surfaces of the talar dome and corresponding distal tibial articulation in patients with rheumatoid arthritis, osteoarthritis, post-trauma arthritis and avascular necrosis, provided that viable malleoli and ligaments are present.”

Based upon the Agency’s interpretation of the indications for use included within the petition as restated above, it appears that the devices you propose to reclassify are indicated for patients with osteoarthritis, rheumatoid arthritis, post-traumatic arthritis,

and avascular necrosis, provided that viable malleoli and ligaments are present. However, within the petition, you have not presented enough clinical data to provide reasonable assurance of the safety and effectiveness of devices which fall within your proposed Class II device type in treating patients within each of these four distinct diagnostic categories.

In addition, given the poor clinical course of total ankle arthroplasty in patients with avascular necrosis as reported in the literature (References 7, 15 and 45 provided within the petition, and Easley, *et al.*¹ and Clare, *et al.*²), as well as the limited number of patients with this diagnosis reported in the cited clinical studies, we are concerned with your proposal to include avascular necrosis among the appropriate diagnoses for this device category. Please identify appropriate, specific labeling which you believe will ensure reasonable safety and effectiveness of the proposed device category in each of the identified patient populations and may be a special control for the type device. In addition, please ensure that the indications for use are consistent throughout your petition.

- c. Once you believe appropriate special controls have been developed, please demonstrate that the preclinical testing and labeling requirements, which include specific indications for use, are adequate to:
 - i. control the risks to health associated with the use of mobile-bearing ankles, and;
 - ii. provide reasonable assurance of the safety and effectiveness of the devices within your proposed category for reclassification and a means of distinguishing and comparing designs.

The determination of adequacy should be based on a demonstration that the device type, which meets the special controls has achieved successful clinical outcomes. Please be advised that we believe that in order to reclassify your mobile-bearing ankle, adequate clinical data are needed to provide reasonable assurance of the safety and effectiveness of these devices and allow for the identification of all potential risks.

Special Controls – Specific Concerns

2. Appendix E of your submission includes your proposed special controls. In addition to the general concerns regarding these special controls as outlined above, please address the

¹ Easley ME, Vertullo CJ, Urban WC, Nunley JA. Total Ankle Arthroplasty. J Am Acad Orthop Surg. 2002 May-Jun;10(3):157-67.

² Clare MP, Sanders RW. Preoperative considerations in ankle replacement surgery. Foot Ankle Clin. 2002 Dec;7(4):709-20.

following specific concerns. Please keep in mind that special controls which are acceptable to FDA (e.g., consensus standards, guidance documents) are needed to support reclassification of this device type.

- a. Several of the proposed special controls (e.g., fatigue testing, wear testing, mechanical strength of metallic or ceramic components) refer to a demonstration that the device will provide an acceptable life under expected clinical conditions of loading and motion for the number of loading cycles expected during the clinical life of the device. Given that there is very little known about the long-term mechanical and clinical performance of mobile-bearing ankles, the expected clinical conditions of loading and motion and the number of loading cycles expected during the clinical life of the device have not yet been established. Please outline specific special controls which clearly identify validated, standardized testing protocols for mobile-bearing ankle devices including appropriate loading conditions and the number of cycles based on expected clinical conditions.
- b. Your proposed special control for wear testing is based on a test protocol for knees adapted to mobile-bearing ankles. The petition claims that loads and frequency of motion in the ankle are similar to those of the knee with the primary difference that the sliding distances associated with the ankle are about one quarter of those in knees. As a result, you conclude that the procedure of P-001 should produce at least as good an estimate of ankle wear as the knee test protocol for knee wear. In addition, the petition states that based on examination of retrieved ankle bearings, it is recommended that the total wear on both the superior and inferior bearing surfaces should not exceed an average wear of 0.5mm for 10 million loading-motion cycles. We do not agree that the loads and frequencies of motion in the ankle are similar enough to those in the knee to allow for the adaptation of a wear testing protocol designed for the knee to the ankle because of differences in kinematics and anticipated physiologic loads (e.g., an ankle has different anterior/posterior translation, rotational movement, and sliding motion relative to a knee). Please provide a specific special control for wear testing which utilizes a validated, standardized testing protocol for mobile-bearing ankle devices including appropriate loading conditions and times based on expected clinical conditions. In addition, please provide a rationale for the average wear limit and number of loading cycles cited as the limit for the total wear on both the superior and inferior bearing surfaces with clinical data to support the numbers you have chosen as indicative of what would be seen physiologically with typical use. The analysis of explanted devices may help to validate the parameters chosen for your wear testing.
- c. The petition includes a proposed special control that range of motion data on relative motion between the tibial component and the bearing and the bearing relative to the talar component should be provided (including all modes of rotation and translation). In addition, the special control states that it should be shown that the motion provided is sufficient for successful clinical results or substantially equivalent to a predicate. However, these as yet have not been adequately defined. Similarly, the petition

- includes a special control that requires that stability analysis of the tibiotalar interface show that the device does not limit tibiotalar anterior/posterior motion or axial rotation under load except for the effect of friction and that the device with viable malleoli and ligaments present provides normal ankle stability or stability substantially equivalent to a predicate. This control also specifies that the device and bearing must be dislocation- and subluxation-resistant and that, under load bearing, it be resistant to medial/lateral and anterior/posterior movement relative to the talar component even under reasonable misalignment of the tibial component relative to the talar component. Given that there are not enough data in the petition or the literature to determine the appropriate balance between motion and stability in the ankle, it is not clear how these proposed special controls can be applied. In addition, the petition does not specifically provide the ranges of motion that can be considered as stable as compared to others that would be considered unstable, with correlation to successful and unsuccessful patient outcomes and adverse events. Please provide adequate preclinical and clinical data to identify the amount and type of ankle motion that is sufficient for successful clinical results. Then, please revise the range of motion special control to more specifically describe the range of motion/constraint requirements based on the data. In doing so, please ensure that adequate device stability, a critical safety consideration, is also addressed. In particular, please describe a validated, standardized protocol which tests whether a device with viable malleoli and ligaments present provides normal ankle stability and tests whether a device is dislocation- and subluxation-resistant even under reasonable malalignment. In addition, we continue to believe that the stability of the device as it stands alone without soft tissue support, which can be considered as the worst case scenario, needs to be evaluated via a preclinical testing special control. Please modify the proposed special controls to address this scenario.
- d. The petition states that increased pain and/or deformity can be reduced by sound surgical technique, adequate fixation and minimal wear. In addition, it states that subsidence and wear reduction are really issues of design and that a good, sound design is in itself a safeguard against subsidence and unacceptable wear. Yet, the petition does not outline the specific aspects of sound surgical technique or the specific design features that address the risks of subsidence, wear and increased pain and/or deformity, nor does it include data to support the stated conclusions. Please outline specific special controls based on standardized, validated preclinical testing for mobile-bearing ankle devices which identify designs with subsidence and wear profiles that provide a reasonable assurance of safety and effectiveness based on adequate clinical data.
- e. The special control for contact area/stress refers to stress limits of 5MPa for walking loads and 10MPa for other, less frequent, activities and states that “These values are within the manufacturers recommendations and are consistent with, or lower than, the stresses seen in the [Buechel-Pappas] B-P ankle which has been shown to be clinically successful with regard to stress and wear.” (p.76) Please provide a detailed explanation outlining how these stress limits were devised. In addition, please

explain how values that are lower than the stresses seen in the B-P ankle are appropriate as special controls.

- f. You describe your proposed Class II device as including a talar component with one or more fixation augments such as fins or pegs to help resist tipping of the talar component under off-center loads; however, you describe your device as using two integrally attached, short fixation fins to eliminate the resorption and associated talar component tilt encountered in an earlier single fin design and to minimize disruption of the central talar blood supply. Please identify appropriate, specific special controls to address the concerns of bone resorption and talar migration.
- g. The petition proposes as a special control that the thickness of the UHMWPE bearing should not be less than 3.0mm based on the thickness used in most of the bearings of the Buechel-Pappas design. Please provide adequate preclinical and clinical data on a number of different devices to support this requirement for bearing thickness.
- h. The petition includes a proposed special control requiring that the degree and nature of bone loss required to implant the device be minimal and not substantially reduce the ability of the bone to support the device thereby increasing the risk of component loosening or subsidence. Please describe a validated, standardized protocol to determine the maximum amount of bone loss which may be present without adversely affecting the ability of the bone to support the device.
- i. As you state in your petition, the rate of meniscal bearing dislocation is increased in cases of subsidence or improper placement. You state that the proposed special control on bone resection and disruption of the blood supply addresses the potential failure modes of component malpositioning due to subsidence or improper placement. We do not believe that this proposed special control adequately addresses these concerns. Therefore, please identify adequate special controls to address the potential risk for component malpositioning due to subsidence or improper placement.
- j. Although you state that the prototype device has an acceptable risk profile, delayed wound healing, infection, talar subsidence, severe bearing wear, malleolar fracture, and tibial component loosening still occur (in some cases at significant rates) as described by the clinical data summarized in the petition. We believe these complication rates signify that the proposed special controls and risk reduction measures do not function adequately to identify clinically successful designs. Please provide evidence that the revised special controls that you submit are adequate to ensure that mobile-bearing ankle designs that are subject to these special controls will have acceptable clinical performance.

Special Controls – Labeling

3. The petition includes proposed labeling (e.g., an example package insert and surgical technique manual) as a special control. Please address the following concerns related to the proposed labeling special controls and sample labeling:
 - a. The submitted labeling proposes that your device is indicated for use in patients who have a severely painful and/or severely disabled joint resulting from osteoarthritis, post-traumatic arthritis, or rheumatoid arthritis with correctable varus or valgus deformity (under 20°), intact ankle dorsiflexors and plantarflexors; a previous failed total ankle arthroplasty provided the medial and lateral malleoli and ligamentous structures are intact, viable or reconstructable; or a pseudoarthrosis. The petition does not include enough clinical data to provide reasonable assurance of the safety and effectiveness of devices which fall within the proposed Class II device type in treating patients who fall within each of these anatomic and diagnostic categories. As requested above, based on an adequate amount of clinical data, please identify appropriate, specific patient selection criteria which can serve as special controls and which ensure reasonable safety and effectiveness of the proposed device category in the identified patient populations. Please modify the submitted labeling to reflect these specific indications for use.
 - b. The surgical technique manual may also serve as a special control and should be written to highlight which steps or instruments are meant to control potential risks of device failure. We do not believe that the surgical technique manual you included achieves this function. Please provide an updated surgical technique manual which addresses the following:
 - i. As outlined in the proposed labeling, please describe warnings regarding ankle stability, possible metal sensitivity, proper alignment, infection and malleolar fracture, and describe means of dealing with these potential problems. In addition, the petition states that proper tibial and talar sizing are vital to the success of the device. As was previously requested, please add more detail highlighting the importance of sizing the tibial, talar and bearing components and clearly describe (in detail) how the correct size of each component should be determined to avoid complications such as malalignment or subsidence. Also, as was previously requested, please include a sizing table correlating patient anatomical dimensions with implant component sizing.
 - ii. The petition states that component malalignment is a known cause of device failure. The submitted surgical technique includes warnings regarding malalignment but does not adequately describe preoperative or intraoperative planning instructions to avoid this risk, nor does it adequately describe trouble shooting techniques for when it occurs or when impingement of the trial bearings against the malleoli occurs. As was previously requested, please

include detailed information on preoperative and intraoperative planning strategies to avoid component malalignment and impingement as well as information on how to deal with potential challenges that may arise intraoperatively.

- iii. The surgical technique states that if the talar dome bone stock seems to be insufficient to support the Talar Template, bone grafting or cement can be used to augment the deficient site. Similarly, the package insert states, “Where grafting or cement alone will not provide the adequate base for support because talar erosion is so severe, or there is too much bone loss, the thick talar component should be used.” Please provide an objective measure for determining when the thick talar component should be used (e.g., identify a specific method of evaluating talar erosion and bone loss and the threshold amounts of erosion/ bone loss beyond which the thick talar component should be used). In addition, the statements with regard to the use of bone cement are not consistent with the remainder of the petition which refers to cementless fixation. Please clarify this apparent discrepancy.
- iv. The surgical technique employs the use of a tibial cortical window for device insertion which places a potential stress riser proximal to the window. The patient is to be placed in a cast for 6 weeks, and the technique specifies that at 6 weeks post-op an x-ray should be taken to assure proper implant placement and healing of the cortical window prior to removing the cast and beginning active flexion/extension exercises. The technique does not refer to any radiographs prior to 6 weeks although it specifies that balance weight bearing may begin on the third to fifth postoperative day and may be increased as pain subsides. The surgical technique and petition do not provide a control against the risk of tibia fracture above the prosthesis which is a concern given that weight bearing is allowed prior to the time that bony ingrowth would be expected to occur. Please revise the surgical technique and special controls to adequately address this potential risk.

After you believe special controls that are able to mitigate the risks associated with mobile-bearing ankles are established, be sure to address the following additional concerns which were noted during the course of our review of your petition.

Device Characterization and Associated Risks

4. You propose a new generic classification for ankle joint replacements in 21 CFR 888.3120 named, “Ankle joint metal/polymer/metal anatomically semi-constrained, congruent, mobile-bearing, porous-coated, uncemented prosthesis.” The device is indicated for the replacement of the superior articulating surface of the talus and the mating distal surface of the tibia. You describe this device type as having the following properties:

- three-part partial ankle joint (i.e., metal tibial and talar components with an intermediate polymer bearing);
- articulating surfaces are metal/polymer/metal;
- anatomically semiconstrained;
- uncemented fixation;
- metal articular surfaces are polished;
- bone contacting surfaces of metal components have a sintered bead porous coating, falling within the porous coating specifications listed in 21 CFR 888.3358 and ASTM F1147;
- the bearing allows the following range of motion:
 - under compressive loading bearing limits only rotation in the frontal plane between the talar and tibial components;
 - bearing provides only rotation in the lateral plane between the bearing and the talar component by their respective articulating surfaces; and
- anterior-posterior and medial-lateral translation and axial rotation limitations of the tibia relative to the talus are provided by the natural malleolar articulations and the ankle ligaments and not by the prosthetic elements.

For a device category to be reclassified, you must clearly identify the category, in this case mobile-bearing ankles, based on common characteristics; identify the risks associated with devices that fall within that category through preclinical, animal and/or clinical testing; and for a class II type device, identify adequate special controls to mitigate the risks and thus provide reasonable assurance of the safety and effectiveness of the device type. We have a number of concerns about the adequacy of the identified risks and the ways to mitigate them that are identified in your reclassification petition. Please address the following:

- a. While the petition describes the device category you propose for reclassification based on common characteristics (although, as noted above, clarifications to the proposed indications for use are needed), it does not discuss the devices described in the literature which fall within the proposed Class II device type. Often reclassifications are based on experience (both preclinical and clinical) with a number of different devices including those that have been approved through the premarket approval (PMA) process signifying significant clinical experience with the device category. Currently, in the case of mobile-bearing ankles, there are no devices which fall within the device category proposed for reclassification that have been approved through the PMA process, and your petition appears to be limited in scope to two

mobile-bearing ankle designs with primary emphasis on the Buechel-Pappas (B-P) Ankle. Please provide a clear description of all of the mobile-bearing ankles being studied and/or marketed as described in the literature, and please clearly outline which of those devices fall within your proposed Class II design and which you believe should remain in Class III. In addition, please clearly compare the characteristics of each device discussed with the characteristics proposed for the Class II device.

- b. Section X of your submission identifies an extensive list of risks and risk reduction measures associated with your mobile-bearing ankle design; however, to support a reclassification of a device category, the risks for the entire device category of mobile-bearing ankle designs need to be identified based on preclinical, animal and clinical testing, along with the special controls to mitigate those risks. Considering all of the devices discussed in the item 4.a and the clinical outcomes reported in the literature for those devices, please identify a complete list of potential risks that encompasses all of the mobile-bearing ankle designs which fall within your proposed Class II design.

Clinical Summary

5. Section XII of your petition includes a summary of clinical findings including the following summary tables: short term follow-up: cemented total ankle arthroplasty; and longer term follow-up: cemented total ankle arthroplasty; the Agility Total Ankle System manufactured by DePuy Orthopaedics; the Scandinavian Total Ankle Replacement System (S.T.A.R. Ankle) manufactured by Link Orthopaedics; the predecessor: B-P Total Ankle System (Shallow Sulcus) manufactured by Endotec; and the B-P Total Ankle System (Deep Sulcus) manufactured by Endotec. Please address the following concerns related to the clinical summary provided:
 - a. The summary tables include only a selection of the available literature references on mobile-bearing ankle devices, and Section XII does not clearly describe how the referenced articles were selected. To provide a balanced review of the available information, we believe that you should prospectively identify a comprehensive literature review method and include summary tables which more accurately depict the range of available literature. In doing so, please include outcomes that are supportive of this petition as well as outcomes that may not be supportive of this petition.
 - b. The clinical summary of the B-P Total Ankle System (Deep Sulcus) includes data on 74 patients reported by Buechel, 74 patients reported by Doets, 19 patients reported by Su and 23 patients reported by Keblish. Similarly, the clinical summary of the S.T.A.R. Total Ankle System includes data on 65 patients reported by Valderrabano, 131 patients reported by Schernburg, 25 patients reported by Kofoed, and another 76 patients reported by Kofoed. In general, the cited studies do not represent controlled clinical studies and the data were collected retrospectively. In addition, the sample

sizes and follow-up times are not adequate to form the basis for any conclusions regarding safety and effectiveness and it is not clear whether each of the referenced articles represents a unique dataset. Based on the comprehensive literature review that you perform, please provide thorough clinical summary tables which outline all the clinical outcomes of your device as well as all of the other devices which fall within the proposed Class II device type. In order to write adequate special controls to allow reclassification of this device type, clinical results on a sufficient number of patients (within a clearly defined patient population) in well-controlled, appropriately designed studies in the general orthopedic community with longer-term follow-up using standardized, validated outcomes measures and consistent study methods are needed.

- c. We have encountered several instances where the data outlined in the summary tables do not match the data presented in the referenced articles. In other cases, you only present the abstract rather than the complete article. For each reference, please either provide a copy of the article or confirm that no article is available. In addition, please review the referenced articles and ensure that the summary tables accurately reflect the data presented in the complete references.
- d. The summary tables include information on survival rates; however, it does not appear that a consistent method was used to calculate survivorship. To allow for appropriate comparison, please revise your summary tables to clearly outline any differences in the methods used to calculate survivorship. In doing so, please ensure that data on all secondary interventions (rather than only device removals) are presented to provide a complete picture of the safety profile of each device.

Surgeon Training

6. We request that you provide a more-detailed description of the proposed training program to assure adequate surgeon training and experience. In your revised description of the proposed training program, please address the following concerns:
 - a. describe whether you plan to include surgical technique practice using cadaver training; and
 - b. while the exact topics that will be covered are not clear from the brief outline provided, we are concerned you may be proposing topics that have not been adequately studied or described in the reclassification petition such as sub-talar fusions combined with ankle arthroplasty and revision procedures. Please justify the inclusion of any surgical techniques in the training program.

General Concerns

7. The petition includes several references to the knee joint which we suspect are inadvertent errors. For example, page 196 states that “In the literature, titanium alloy (Ti-6Al-4V) articulating surfaces have been shown to produce metallic particles resulting in an adverse tissue response and high third-body wear. Therefore, it is recommended that the titanium femoral components have a treated surface (e.g., nitrogen ion or TiN coating).” Similarly, page 189 of the petition states that “The following is a specific discussion of how you should apply this Class II Special Controls Guidance Document to a premarket notification for the knee joint patellofemoral and femoral metal/polymer porous-coated uncemented prostheses.” Please clarify these apparent typographical errors and remove any unintended references to the knee joint from your petition.

We would like to stress that we do not believe your petition includes special controls sufficient to mitigate the risks and thus provide reasonable assurance of the safety and effectiveness of the device category proposed for reclassification. These special controls should be developed prior to resubmission of this petition. The deficiencies identified above represent the issues that we believe need to be resolved before our review of your reclassification petition can be completed. In developing the deficiencies, we carefully considered the burden that may be incurred in your attempt to respond to the deficiencies. We believe that we have considered the least burdensome approach to resolving these issues. If, however, you believe that information is being requested that is not relevant to the regulatory decision or that there is a less burdensome way to resolve the issues, you should follow the procedures outlined in the “A Suggested Approach to Resolving Least Burdensome Issues” document. It is available on our Center webpage at: <http://www.fda.gov/cdrh/modact/leastburdensome.html>.

If you submit information addressing these deficiencies, we will reevaluate your reclassification petition. Please provide five (5) copies of your response to this letter. The information should reference the above docket number (2004P-0457/CCP 1) and be submitted to:

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane
Room 1061
Rockville, MD 20852

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If you have any questions related to reclassification, please contact Ms. Marjorie Shulman at (301) 594-1190, extension 132. For scientific and technical assistance, please contact Mr. Hany W. Demian by email (hany.demian@fda.hhs.gov) or by phone at (301) 594-2036, extension 184.

Sincerely yours,

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Director
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