

**Proposed Reclassification of Bone Growth Stimulator Devices**  
**Questions for the Orthopaedic and Rehabilitation Devices Panel**

**June 2, 2006**

1. The petitioner defines the bone growth stimulators for reclassification as follows:

*“A Non-invasive Bone Growth Stimulator provides stimulation through electrical and/or magnetic fields to promote osteogenesis to facilitate the healing of nonunion fractures and lumbar spinal fusions. The stimulation may be delivered through capacitive coupling (CC) with electrodes placed directly over the treatment site, or through pulsed electromagnetic fields (PEMF) with treatment coils placed into a brace or over a cast at the treatment site. The device is intended for use for 1) the treatment of established nonunion fractures acquired secondary to trauma (excluding vertebrae and flat bone), and 2) as an adjunct to the treatment of lumbar spinal fusion surgery for one or two levels. The device consists of an output waveform generator, either battery-powered or AC-powered, a user interface with visual and/or audible alarms, and electrodes or coils to deliver the stimulation. Accessories may include additional electrodes or coils, electrode accessories, electrode gel, positioning guides, connectors, batteries, battery chargers, belts and/or belt clips, carrying case, physician test meter, and others.”*

The petitioner does not define the technical specifications for these devices because it believes that *“enough is known about the safety and effectiveness of these devices to make the setting of technical specifications unnecessary.”*

- **Please describe the**
  - **technical specifications, e.g., waveform frequency, amplitude, wavelength, etc.;**
  - **performance parameters, e.g., induced magnetic field, dynamic compensation, orientation, etc.; and**
  - **tolerances****defined by the petitioner for CC and PEMF devices intended to be used for non-unions and/or lumbar spinal fusions.**
  
- **Are these technical specifications, performance parameters, and tolerances adequate to assess whether a new BGS device is safe and consistently reproduces a clinically effective treatment signal for each of the proposed intended uses?**
  - **Please explain the basis for your conclusion.**

2. In order for a device to be reclassified, the petitioner must define a “generic type” of device for reclassification. FDA regulations define a “generic type” of device as “a grouping of devices that do not differ significantly in purpose, design, materials, energy source, function,

or any other feature related to safety and effectiveness, and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness.”

The petitioner proposes reclassification of external bone growth stimulators that work through capacitive coupling (“CC”) and pulsed electromagnetic field (“PEMF”) technology for the treatment of established non-union fractures acquired secondary to trauma (excluding vertebrae and flat bone) and as an adjunct to the treatment of lumbar spinal fusion surgery for one or two levels.

- **Describe how the petitioner has defined the following aspects of the CC bone growth stimulators proposed for reclassification:**
    - **purpose,**
    - **design,**
    - **materials,**
    - **energy source,**
    - **function, and**
    - **any other feature relating to safety and effectiveness.**
  
  - **Describe how the petitioner has defined the following aspects of the PEMF bone growth stimulators proposed for reclassification:**
    - **purpose,**
    - **design,**
    - **materials,**
    - **energy source,**
    - **function, and**
    - **any other feature relating to safety and effectiveness.**
  
  - **Do the descriptions above reflect a “generic type” containing devices that “do not differ significantly” in terms of their purpose, design, function, or other features?**
3. The petitioner may only rely on valid scientific evidence to support a proposed reclassification. Valid scientific evidence is defined as “evidence from well-controlled investigations, partially controlled studies, studies and objective trials without matched controls, well-documented case histories conducted by qualified experts, and reports of significant human experience with a marketed device, from which it can fairly and responsibly be concluded by qualified experts that there is reasonable assurance of the safety and effectiveness of a device under its conditions of use.”

Valid scientific evidence does not include “isolated case reports, random experience, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions.”

- **Identify the studies provided by the petitioner that tested**
  - **CC devices intended to be used for non-unions,**
  - **CC devices intended to be used for lumbar spinal fusions,**
  - **PEMF devices intended to be used for non-unions, and**
  - **PEMF devices intended to be used for lumbar spinal fusions.**
  
- **For the studies identified above, please describe whether they were adequate in the following respects:**
  - **waveform(s) of the device(s) tested,**
  - **sample size of the study,**
  - **inclusion/exclusion criteria,**
  - **treatment regimens,**
  - **durations of use,**
  - **definitions of clinical success,**
  - **definitions of radiological success, and**
  - **safety data.**
  
- **Please state whether any of the studies cited by the petitioner are well-controlled clinical investigations. Specify the device and intended use that each investigation supports.**
  
- **Are the studies' treatment parameters similar or comparable so that the petitioner may draw conclusions based on a pooling of the studies' results?**
  - **Do the cited studies involving PEMF external bone growth stimulators support the down-classification of CC external bone growth stimulators?**
  
  - **Do the cited studies involving non-union uses support the down-classification of external bone growth stimulator devices intended to be used for spinal fusions?**
  
  - **For the petitioners purposes, is it appropriate to combine: a) sham-controlled, double-blinded, prospective studies (Level I), b) standard-of-care controlled (non-sham), prospective studies (Level II), c) historic-controlled, retrospective studies (Level III), and d) non-controlled, case series (Level IV) in order to draw safety and effectiveness conclusions?**

- **In combining studies with various designs (i.e., Levels of evidence), how do confounding variables, differing definitions of success, different patient populations, and the different study designs affect the strength of the petitioner’s conclusions?**
  
- **Overall, has the petitioner presented sufficient valid scientific evidence to support the down-classification of**
  - **CC devices intended to be used for non-unions,**
  - **CC devices intended to be used for spinal fusions,**
  - **PEMF devices intended to be used for non-unions, and**
  - **PEMF devices intended to be used for spinal fusions?**
  
- 4. The following table lists several risks to health FDA believes are associated with the use of external bone growth stimulators and the petitioner’s proposed controls for addressing these risks.

<b>Risk to Health</b>	<b>Proposed Special Control</b>
Electrical Shock	<ul style="list-style-type: none"> <li>● Preclinical Analysis and Testing</li> <li>● Electrical Equipment Safety</li> <li>● Software Life Cycle and Risk Management</li> <li>● Labeling</li> </ul>
Burn	<ul style="list-style-type: none"> <li>● Preclinical Analysis and Testing</li> <li>● Electrical Equipment Safety</li> <li>● Software Life Cycle and Risk Management</li> <li>● Labeling</li> </ul>
Skin irritation and/or allergic reaction	<ul style="list-style-type: none"> <li>● Biocompatibility analysis and testing</li> <li>● Labeling</li> </ul>
Inconsistent or ineffective treatment	<ul style="list-style-type: none"> <li>● Preclinical Analysis and Testing</li> <li>● Electrical Equipment Safety</li> <li>● Electromagnetic Compatibility</li> <li>● Software Life Cycle and Risk Management</li> <li>● Animal Studies</li> <li>● Clinical Studies</li> <li>● Labeling</li> </ul>

Risk to Health	Proposed Special Control
Ineffective treatment due to magnetic fixation device	<ul style="list-style-type: none"> <li>• Labeling</li> </ul>
Damage to electrical implant	<ul style="list-style-type: none"> <li>• Labeling</li> </ul>
Biological effects of stimulation	<ul style="list-style-type: none"> <li>• Labeling</li> </ul>

- **For the health risks identified in the table above, please state whether the special controls proposed by the petitioner would adequately address each risk.**
  - **For the proposed special controls that you conclude are adequate, please specify the valid scientific evidence that supports the adequacy of each special control.**
  
- **One of the proposed special controls to mitigate the risk of an ineffective or unsafe device is a clinical study. What types of differences among bone growth stimulator devices or changes to an existing device would necessitate a clinical study?**
  - **Please describe the elements and design of a clinical trial that would adequately evaluate the safety and effectiveness of external bone growth stimulator devices.**
  
- **Does this table identify all of the potential health risks associated with CC and PEMF external bone growth stimulators intended for the treatment of non-unions and/or lumbar fusion?**
  - **If not, what additional health risks should be considered?**
  - **What special controls would adequately address these additional health risks?**
  
- **Are the health risks associated with the treatment of established non-union fractures and the adjunctive treatment of lumbar spinal fusion “similar” enough that the petitioner’s proposed special controls for CC and PEMF devices constitute a “similar” set of regulatory controls that would assure the safety and effectiveness of new external bone growth stimulator devices? As discussed in question #2, the regulations require the petitioner to identify a “generic type” of bone growth stimulator device “for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness.”**

5. **Has the petitioner demonstrated that the current PMA review—requiring clinical studies demonstrating safety and effectiveness, and FDA’s premarketing assessment of manufacturing—are unnecessary to reasonably assure the safety and effectiveness of new CC and PEMF external bone growth stimulators?**
  - **Please specify the valid scientific evidence that supports your conclusion.**