FDA Executive Summary

Orthopaedic and Rehabilitation Devices Panel
June 2, 2006

Reclassification Petition for the Non-invasive Bone Growth Stimulator
Docket #: 2005P-0121

Panel Meeting Purpose:

The purpose of the panel meeting is to obtain a recommendation from the advisory panel regarding the proposed reclassification of the generic non-invasive bone growth stimulator device. The FDA has received a petition, submitted by RS Medical, requesting the reclassification of the device into class II. The non-invasive bone growth stimulator is a post-amendments device classified by §513 of the Food, Drug and Cosmetic Act (the Act) as a class III device. The FDA is seeking expert clinical and engineering recommendations regarding the proposed reclassification from class III into class II.

Regulatory History of Non-invasive Bone Growth Stimulator:

The non-invasive bone growth stimulator (FDA product code: LOF) is marketed in the United States as a class III medical device subject to approval of a premarket approval application (PMA).

FDA's regulations for the classification and regulation of medical devices are described in the Act (21 USC 360C), Medical Device Amendments of 1976, and subsequently amended by the Safe Medical Device Act (SMDA) of 1990, the FDA Modernization Act (FDAMA) of 1997, and the Medical Device User Fee and Modernization Act (MDUFMA) of 2002. In accordance with Section 513(e) of the 1976 Amendments, an interested person, manufacturer or importer may submit a petition to reclassify a medical device, including the reclassification of a class III medical device into a lower regulatory class.

The Act established three classes of medical devices, which follow a risk-based model and stratify the regulatory controls needed to provide reasonable assurance of their safety and effectiveness. The three classes are class I (general controls/lowest risk), class II (special controls/moderate risk), and class III (premarket approval/highest risk).

- General controls are sufficient to provide reasonable assurance of the safety and effectiveness of class I devices. General controls include the following: prohibition against adulterated or misbranded devices, premarket notification (510(k)), banned devices, compliance with the Quality System Regulation (QSR) that includes design controls and good manufacturing processes (GMPs), labeling regulations, registration of manufacturing facilities, listing of device types, record keeping, etc.

- Class II devices cannot be classified into class I because general controls by themselves are insufficient to provide reasonable assurance of their safety and effectiveness. Class II devices are regulated using special controls and general controls. Special controls may include guidance documents, performance standards, post-market surveillance, clinical data, tracking requirements, and other appropriate actions the Secretary of the Department of Health and Human Services deems necessary to provide such assurance.

- Class III devices includes devices for which insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of their safety and effectiveness. These devices are life sustaining, life supporting, or substantially important in preventing impairment of human health, or they present unreasonable risk of illness or injury. Class III devices are regulated by using valid scientific evidence to establish the safety and effectiveness of the device. Valid scientific evidence includes well-controlled investigations, partially-controlled studies, uncontrolled studies, well-documented case histories, and reports of significant human experience (21 CFR 860.7 (c)(1)).

Device Description/Principle of Operation:

A non-invasive bone growth stimulator is typically composed of a waveform generator and device accessories which may include electrodes, electrode conductive medium (gel), electrode lead wires and patient cables, coils and positioning accessories, batteries, battery charger, and a physician test meter. Patient contacting surfaces include the treatment coils/electrodes, lead wires, patient cables, and the device outer casing.

The device utilizes an electrical component to produce an output electrical and/or magnetic waveform that is delivered to a treatment site via non-invasively applied coils (i.e., transducers) or electrodes (i.e., capacitor plates). The device also incorporates an internal means to monitor the output waveform and delivery of treatment, and to provide visual and/or audible alarms to alert the user of improper device function. The induced electrical and/or magnetic fields are generated using capacitive coupling (CC), pulsed electromagnetic fields (PEMF), or combined magnetic fields (CMF) (static and pulsed magnetic fields)[1]. The non-invasive nature of device does not necessitate the need for sterile components, however patient contacting surfaces should be capable of being cleaned as needed and biocompatibility must be assured.

The indications for use for this general category of device include:

- Treatment of an established non-union secondary to trauma,
- Treatment of fracture non-unions,
- Treatment of failed fusions,
- As an adjunct to lumbar spinal fusion surgery at 1 or 2 levels
- Treatment of congenital pseudoarthroses (not included within the proposed reclassification), and
- As an adjunct to cervical fusion surgery in patients at high risk for non-fusion (not

[1] The Combined Magnetic Fields (CMF) device is not included within this reclassification petition, but is included within the non-invasive bone growth stimulator FDA product code (LOF).

included within the proposed reclassification).

Reclassification Petition Summary:

RS Medical has submitted a petition (Docket 2005P-0121, dated February 7, 2005) requesting that the agency reclassify the non-invasive bone growth stimulator from class III into class II. The reclassification petition was revised as Amendment 1 (AMD1), dated November 30, 2005.

The FDA has received public comment from bone growth stimulator manufacturers, physicians, and individuals in response to the proposed reclassification. These comments are available on the public docket and are provided on a CD (current as of 4/25/06) within Tab D. (http://www.fda.gov/ohrms/dockets/dockets/05p0121/05p0121.htm)

Reclassification Petition Scope:

The scope of the reclassification petition includes five PMA-approved devices and one device manufactured by the petitioner (as of April 2006, the sponsor has not submitted their device for premarket review and is not legally marketed[2]). The five devices are summarized in Table 1: Proposed Reclassified Devices.

Table 1: Proposed Reclassified Devices

Manufacturer	Trade Name	Application Number/ Date of Approval	Indication for Use	Stimulation Modality
Biolectron	OrthoPak® Bone Growth Stimulator	P850022 02/18/1986	Treatment of an established nonunion secondary to trauma	Capacitive Coupling
Biolectron	SpinalPak® Fusion Stimulator	P850022 / S009 09/24/1999	Adjunct electrical treatment to primary lumbar spinal fusion surgery at one or two levels	Capacitive Coupling
Electro-Biology(EBI), L.P.	EBI Bone Healing System ®	P790002 11/06/1979	Treatment of fracture non-unions, failed fusion and congenital pseudarthroses	PEMF
Orthofix	Physio-Stim® Lite	P850007 02/21/1986	Treatment of established nonunion acquired secondary to trauma	PEMF
Orthofix	Spinal-Stim® Lite	P85007 / S006 02/07/1990	Fusion adjunct to increase the probability of fusion success and as a nonoperative treatment of failed fusion surgery	PEMF
RS Medical[3]	*To be determined*	*To be determined*	*Treatment of established nonunion fractures acquired secondary to trauma and as an adjunct to the treatment of lumbar spinal fusion surgery*	*Capacitive Coupling*

[2] The RS Medical device is subject to PMA approval or 510(k) clearance pending the results of this proposed reclassification.

[3] The reclassification petition seeks to reclassify the group of PMA-approved non-invasive bone growth stimulators to class II (subject to 510(k) clearance) and to include the RS Medical device in this group.

Reclassification Petition Exclusions:

The proposed reclassification excludes the following devices, product areas, and indications for use from reclassification:

Devices:

- OrthoLogic™ 1000 Combined Magnetic Fields device, indicated for the treatment of an established nonunion secondary to trauma.
- OrtoLogic SpinaLogic™ Combined Magnetic Fields device, indicated as an adjunct treatment to primary lumbar spinal fusion surgery for one or two levels.

Product Areas:

- Invasive bone growth stimulators, FDA product code LOE.
- Non-invasive bone growth stimulators, FDA product code LPQ – Stimulator, ultrasound and muscle, for use other than applying therapeutic deep heat.

Indications for use:

- Treatment of congenital pseudarthrosis. IFU approved for a commercially available non-invasive bone growth stimulator device (P790002).
- Adjunct to cervical fusion surgery in patients at high risk for non-fusion. IFU approved for a commercially available non-invasive bone growth stimulator device (P030034).

Risks to Health:

The petitioner has identified the following adverse events from the Manufacturer User Facility and Distributor Experience (MAUDE) and the Device Experience Network (MDR) databases[4]. The database search covers the time period from December 13, 1984 (historical extent of database) to the present. The adverse events associated with the non-invasive bone growth stimulator are summarized in Table 2: Petitioner Provided Summary of Adverse Events.

Table 2: Petitioner Provided Summary of Adverse Events

Report Type	**Total** ([#] excluding overlapping events)		**% of Total Reported Events** ([%] excluding overlapping events)
Malfunction or Other (not resulting in adverse event)	10 [8]		21.3% [19%]
Serious Injury or Malfunction (resulting in an adverse event)	Shock	1	2.1% [2.4%]
	Burns	16	34.0% [38.1%]
	Skin Irritation/ Reddened Area	2	4.3% [4.8%]
	No Bone Growth	1	2.1% 2.4%]
	Surgical Intervention	5 [3]	10.6% [7.1%]

[4] Risks to health are identified within Section VI-C: Detailed Description of Risks with Supporting Data (revised as described within the petition amendment).

	Seizure Disorder	1	2.1% [2.4%]
	Increased Blood Glucose	1	2.1% [2.4%]
	Benign Tumor	1	2.1% [2.4%]
	Toe Fracture	1	2.1% [2.4%]
	Hives, Insomnia, Agitation and Anxiety	1	2.1% [2.4%]
Serious Injury (due to improper use of device)	3 [2]		6.4% [4.8%]
Death	1		2.1% [2.4%]
Unknown	3		6.4% [7.1%]
Total	**47 [42]**		**100%**

The petitioner, based on a literature review and the MDRs and MAUDE databases (47 adverse events), has identified the following major risks with the use of the non-invasive bone growth stimulator[5]:

1. **Electric Shock** – A patient or health care professional could be shocked from the use and operation of the device.
    a. Reported Adverse Events – Two MDRs cited an intermittent "electrical shocking" sensation and the shorting of the cable supplying the electrical current from the battery pack.
    b. Cause – AC line voltage exposure during charging, circuitry malfunction, connection/disconnection of electrodes or coils, control circuit failure, damaged channel jacks, defective electrodes/coil delivering inappropriate output, faulty lead wires, inappropriate output, poor connection between electrodes/coils and lead wires, poor solder on circuit board, reposition of electrodes/coils during treatment, and use of AC current source during treatment.
    c. Sequelae of the risk – Pain and discomfort.
    d. Information demonstrating that the stated risk is not a potential hazard of the device, if available – Mitigating activities including device performance testing as outlined within the proposed special controls. (See Pages 16-17)
2. **Thermal Burn** – A patient or health care professional could be burned from the use and operation of the device.
    a. Reported Adverse Events - Sixteen MDRs were identified. Those most notably (7 of 16) included using the device while simultaneously charging and sleeping. The charger became disconnected and subsequently burned the patient.
    b. Cause – AC line voltage exposure during charging, connection/disconnection of the electrodes/coils or control unit while receiving treatment, defective electrodes/coil delivering inappropriate output, incorrect electrode/coil size or alteration, inappropriate output, use of AC current source for treatment, use of control unit and battery charger while sleeping.
    c. Sequelae of the risk – Pain and discomfort, permanent scarring, blisters, and skin

[5] Risks to health are identified within Section VI-C: Detailed Description of Risks with Supporting Data (revised as described within the petition Amendment).

irritation.

   d. Information demonstrating that the stated risk is not a potential hazard of the device, if available. – Labeling change to identify risk of using and recharging device while sleeping. In addition, RS Medical proposes that devices be designed so that the battery cannot be charged while the device is in use and to provide two battery packs with the device. Please note that the FDA could not require a manufacturer to design a device with dual battery packs and FDA could find a new BGS device to be SE without these design features.

3. **Skin Irritation and/or Allergic Reaction** – A patient could experience skin irritation and/or allergic reaction associated with the use and operation of the device.
   a. Reported Adverse Events – Two MDRs for skin irritation/hives. In addition, five reports identified skin irritation and/or allergic reactions as the result of treatment. The reported rates of incidence included 7% (3/43), 7% (3/43), 2.6% (9/337), 2.6% (6/243), and 1.9% (2/107).
   b. Cause – Non-biocompatible device materials, Non-biocompatible electrode gel (capacitive coupling only).
   c. Sequelae of the risk – Discomfort, skin rash.
   d. Information demonstrating that the stated risk is not a potential hazard of the device, if available –Material biocompatibility assessment and testing as outlined within the proposed special controls.
4. **Inconsistent or Ineffective Treatment** – A patient could receive inconsistent or ineffective treatment.
   a. Reported Adverse Events – Fourteen MDRs were for device malfunction and/or lack of bone growth. In addition, seventeen articles were identified as addressing lack of patient compliance, lack of patient follow-up, and device malfunction.
   b. Cause – Batter deterioration, control circuit failure, defective electrode/coils, device damage from dropping or bumping, device short circuits, driver circuit failure, electromagnetic interference (EMI) or radio frequency interference (RFI), failure to follow prescribed use, hardware failure, improper position of electrodes/coil, inappropriate output, incorrect battery/battery charger, ineffective output, low battery voltage, poor interface between electrodes/coil and patient, and switch failure.
   c. Sequelae of the risk – Lack of treatment.
   d. Information demonstrating that the stated risk is not a potential hazard of the device, if available – Device performance testing as outlined within the proposed special controls.
5. **Adverse interaction with Electrical Implants** – A patient with electrical implants (such as cardiac pacemakers, cardiac defibrillators and neuron-stimulators) could experience an adverse interaction with an implanted electrical device.
   a. Reported Adverse Events – No MDRs.
   b. Cause – EMI or RFI.
   c. Sequelae of the risk – Reduced electrical implant performance or failure resulting in patient injury or death.
   d. Information demonstrating that the stated risk is not a potential hazard of the device, if available – Device Labeling (21 CFR §809) to include specific contraindications regarding the use with electric implants, such as cardiac

pacemakers, cardiac defibrillators and neuron-stimulators. Device performance testing as outlined within the proposed special controls.

6. **Internal / External Fixation Devices** – A patient could receive inconsistent or ineffective treatment due to interaction with metallic fixation devices.
    a. Reported Adverse Events – No MDRs. Scientific literature is inconclusive regarding adverse device performance associated with non-magnetic, metallic fixation for either CC or PEMF devices. However, evidence of potential decreased device performance in the presence of magnetic, metallic fixation for PEMF device does exist.
    b. Cause – Interference with treatment field through magnetic field interaction and/or electrical inductance within metallic device.
    c. Sequelae of the risk – Lack of treatment.
    d. Information demonstrating that the stated risk is not a potential hazard of the device, if available – Device Labeling (21 CFR §809) to include a warning or precaution that magnetic fixation devices may interfere with the delivery of an effective treatment signal.
7. **Biological risks: Carcinogenicity, genotoxicity, mutagenicity and teratology[6].** – A patient may experience adverse biologic affects resulting from prolonged exposure to the treatment signal.
    a. Reported Adverse Events – No MDRs. The scientific literature is inconclusive regarding adverse biologic affects.
    b. Cause – Biologic interaction with the treatment signal at a cellular level.
    c. Sequelae of the risk – Patient injury, deformity, and death.
    d. Information demonstrating that the stated risk is not a potential hazard of the device, if available – Device Labeling (21 CFR §809) to include a warning or precaution that the long-term effects of electrical stimulation or magnetic fields have not been studied extensively in humans. The safety and effectiveness in pregnancy has not been studied. Effects of the device on mothers and the developing fetuses are not known. Anyone who is pregnant or intending to become pregnant should be referred to her physician prior to treatment.

In support of this proposed reclassification, the petitioner has provided "new information", as described within §513(e) - "publicly available, valid scientific evidence." Valid scientific evidence may consist of sham-controlled, double-blinded, prospective studies, standard-of-care controlled (non-sham), prospective studies, historic-controlled, retrospective studies, non-controlled studies, and reports of significant human experience with a medical device.

The bibliography is listed in Appendix A of this FDA Executive Summary. The search methodology used to identify these articles is fully described within AMD1 - Attachment II.

[6] In support of the sponsor's biologic risks assessment, the sponsor has supplied summary references to several literature articles. A bibliography of the submitted references is provided in Appendix A.

Summary of Pre-clinical/Clinical Literature:

Reports on Non-unions - The petitioner has submitted 35 articles (5 utilizing capacitive coupling and 30 pulsed electromagnetic fields) involving over 5,600 patients. According to the petitioner, these studies indicate the device's ability to promote osteogenesis in patients with established non-union which may include previously failed surgical attempts to establish union. Treatment variables within these studies included stimulation type, device manufacturer, output waveform parameters, treatment regimen, and time between fracture and stimulation treatment. Successful outcomes were evaluated radiographically (including evidence of trabecular bridging, increased radiographic density, and disappearance of the gap) and/or clinically (including pain relief, lack of movement at the fracture site, and lack of pain at fracture site). In general, the agency has previously accepted studies as evidence of efficacy when both radiographic and clinical success is demonstrated. The radiographic success rate and clinical success rate is presented separately when data was provided in the literature. If radiographic and clinical definitions of union were provided, then overall success rates were considered to include both radiographic and clinical success. If radiographic or clinical definitions of union were not specified, then overall success rates could not be considered to include both radiographic and clinical success. The studies are summarized as follows (additional variables are analyzed and contained within the petition):

Table 3: Capacitive Coupling Use in Established Non-Unions

Author/Year	Type of Study / # of Non-unions	Control Group	Fracture Site, #	Waveform Parameters	Radiographic Success Rate	Clinical Success Rate
Abeed et al., 1998	Prospective / 16	Subject as Own	Radius/Ulna 7, Tibia 6, Femur 3	63 kHz Sine, 6V PTP[7]	68.8% (11/16) – Serial Radiographs	NR
Benazzo et al., 1995	Prospective / 25	Subject as Own	Tibia, Fibula, Navicular, Metatarsal, Talus	60 kHz Sine, 3-6.3 V PTP	Overall: 88.0% (22/25) – Radiographs, Scintigraphy & CT / Lack of pain & return to sports.	
Brighton and Pollack, 1985.	Prospective / 22	Subject as Own	Long bone, Clavicle, Scaphoid	60 kHz Sine, 5V PTP	77.3% (17/22) – Serial Radiographs	NR
Brighton, et al., 1995	Retrospective / 271	Direct Current Bone Graft	Tibia	CC: 60 kHz sine, 5 V PTP DC: 10 μA	Overall 73.1% (198/271) Graft 58.3% (28/48) CC: NR DC: NR - Serial Radiographs	NR
Scott and King, 1994	Prospective / Active 10 / Sham 11	Sham Unit (Randomized & Double-blinded)	Tibia, Femur, Ulna	60 kHz Sine, 5-10 V PTP	Overall: Active: 60.0% (6/10), Sham: 0% (0/11). Serial Radio. / Lack of movement & pain under stress. SD[8]	

[7] PTP – Peak to Peak amplitude.
[8] Statistically significant difference reported in the literature.

Table 4: PEMF Use in Established Non-Unions

Author/Year	Type of Study / # Non-unions	Control Group	Fracture Site, #	Waveform Parameters	Radiographic Success Rate	Clinical Success Rate
Adams et al., 1992	Retrospective / 54	Subject as Own	Scaphoid 54	NR – EBI, L.P. Device[9]	68.5% (37/54) Radiographs	NR
Barker et al., 1984	Prospective / 17 (9 PEMF/ 7 Sham)	Randomized/ Sham	Tibia 17	1.5 mT peak, 5 msec burst at 15 Hz	PEMF: 77% Sham: 86% Radiographs	NR
Bassett et al., 1982	Prospective / 83	Subject as Own	Tibia 45, Femur 25, Humerus 8, Radius/Ulna 2, Misc 3	5 msec burst of 200 μsec pulses at 15 Hz	90.4% (75/83) – Serial Radiographs.	NR – Lack of motion, pain, & tenderness at stress.
Bassett et al., 1982	Retrospective / 1,078	Subject as Own	Tibia 657, Femur 189, Humerus 52, Radius/Ulna 77, Scapula 19, Misc. 13, Hip 5, Knee 27, Ankle 30, Shoulder 1, Wrist 9.	NR - EBI, L.P. Device	Overall: 77.4% (834/1078) Columbia: 80.9% (178/220) US: 75.7% (473/625) International: 78.5% (183/233) Tibia Overall: 81.9% (538/657) Serial radiographs / Lack of motion, pain, & tenderness at stress.	
Bassett et al., 1977	Prospective / 26	Subject as Own	Tibia 17, Femur 1, Fibula 2, Radius/Ulna 3, Navicular 1, Shoulder 1, Ankle 1	300 μsec pulse at 75 Hz	73.0% (19/26) – Serial Radiographs.	NR
Bassett et al., 1978	Prospective / 220	Subject as Own	Tibia 84, Femur 10, Radius/Ulna 8, Humerus 3, Wrist 1, Ankle 1, Shoulder 1.	5 msec burst of 200 μsec pulses at 10-15 Hz	Overall: 80.6% (87/108). Serial radiographs / Mechanical stability, no tenderness, & function without local splint.	
Bassett, 1981	Prospective / 127	Subject as Own	Tibia 127	NR – EBI, L.P. Device	Overall: 86.6% (110/127). Serial Radiographs/ Clinical NR.	
Caullay and Mann, 1982	Prospective / 6	Subject as Own	Tibia 4, Fibula 2	NR – EBI, L.P. Device	Overall: 100% (4/4). Serial Radiographs.	
Cheng et al., 1985	Prospective / 63	Subject as Own	Tibia 33, Femur 11, Humerus 8, Radius 2, Ulna 3 Knee 2, Radius/Ulna 1.	NR (1.0-1.5 mV/cm)	Overall: 58.7% (37/63) Tibia 78.6% (22/28), Femur 60% (6/10), Humerus 25% (2/8), Radii 50% (1/2), Ulna 0% (0/2) Serial Radiographs / Clinical NR.	
Colson et al., 1988	Prospective / 33	Subject as Own	Tibia 22, Femur 4, Ulna 1, Radius/Ulna 1, Radius 2, Humerus 3.	5 pulses of 300 μsec separated by 1500 μsec at 15 Hz	PEMF: 85.7% (12/14) PEMF/Surgery: 100% (19/19) Serial Radiographs	NR
Delima and Tanna, 1989	Prospective / 29	Subject as Own / Randomized	Humerus 7, Tibia 15, Femur 6, Radius/Ulna 1.	Continuous pulse train at 40 Hz	79.3% (23/29) [10]Serial Radiographs	NR

[9] EBI, L.P. reports an output waveform of 2.5 msec bursts of 250-400 μSec 20 G pulses, repeated at 5-20 Hz.

Dhawan et al., 2004	Prospective / 70	Surgical	Subtalar 64, Talonavicular 42, Calcaneocuboid 41	NR – EBI, L.P. Device	PEMF: 100% (22/22) Control: 89.0% (33/37) Serial Radiographs	NR
Dunn and Rush, 1984	Prospective / 52 (35 PEMF/ 17DC)	Randomized DC Control	37 long bones, carpal navicular, thumb long bones	NR	PEMF 81% DC 82% Radiographs	NR
Fontanesi et al.,1983	Prospective / 35	Subject as Own	Tibia 9, Femur 6, Humerus 4, Radius 3, Ulna 4, Clavicle 2, Carponavicular 2, NR 5	1.3 msec pulse at 75 Hz	Overall: 88.6% (31/35) – Serial Radiographs / Clinical NR.	
Frykman et al., 1986	Retrospective / 44	Subject as Own	Scaphoid 50	NR – EBI, L.P. Device	Radio: 79.5% (35/44) Radiographs. Clinical: Wrist extension 84.1% (37/44), Flexion 92.2% (41/44), Radial deviation 84.1% (37/44), Ulnar deviation 90.9% (40/44), Grip strength 83% (36/44). Referenced to Normal.	
Garland et al., 1991	Prospective / 193	Subject as Own	Long Bones 130, Short Bones 35, Failed Fusion 28	260 µsec 20 G pulse at 15 Hz	PEMF(>3 hrs/day) 80% (108/135) PEMF (<3 hrs/day) 35.7% (5/14) SD Long bones 82.7% (81/98), Tibia 74% (37/50), Short bones 81% (17/21), Scaphoids 76.9% (10/13). Serial radiographs / Lack of motion, tenderness, pain, & cast.	
Gossling et al., 1992	Retrospective / PEMF: 1718 Surgery: 569	Surgical	Tibia 2,287	Varied	Overall: (Radio NR/Clinical NR) PEMF: 81.0% (1392/1718) Surgery: 81.9% (466/569)	
Heckman et al., 1981	Retrospective / 149	Subject as Own	Tibia 94, Femoral Shaft 31, Humerus 9, Ulna 4, Radius/Ulna 4, Radius 2, Carpo-navicular 2, Ischium 1, Femoral neck 1, Metatarsal 1	NR – EBI, L.P. Device	Overall: 64.4% (96/149), Tibia 71.3% (67/94), Femur 51.6% (16/31), Humerus 44% (4/9). Serial Radiographs.	Decreased motion and pain.
Hinsenkamp et al., 1985	Retrospective / 272	Subject as Own	Tibia 148, Femur 55, Humerus 19 Ulna 16, Misc 34	15Hz – EBI, L.P. Device	72.3% (193/267) – Radiographic NR / Clinical NR.	
Holmes et al.,1994	Retrospective / 9	Subject as Own	Proximal Fifth Metatarsal 9	4.5 msec burst of 200 µsec pulses at 15 Hz.	100% (9/9) – Pre/Post treatment radiographs / Pain-free gait, lack of cast.	

[10] Literature reports 82.5% and 82.14% without numerical explanation. Petitioner calculations suggest 79.3% as a correct percentage based upon the reported data.

Ito and Shirai, 2001	Prospective / 30	Subject as Own	Tibia 30	5 msec square wave at 15 Hz	83.3% (25/30) Serial Radiographs.	NR – Lack of motion and pain at stress.
Madronero et al., 1988	Prospective / 11	Subject as Own	Radius 11.	NR	60.0% (6/10) – Callus presence.	NR
Marcer et al.,1984	Retrospective / 147	Subject as Own	Tibia 102, Femur 32, Humerus 13	5 msec burst of 200 μsec pulses at 15 Hz	72.8% (107/147) – Radiographic NR / Clinical NR.	
Meskens et al., 1990	Retrospective / 34	Subject as Own	Tibia 15, Femur 9, Humerus 5, Ulna 2, Radius 2, Fibula 1	NR	67.6% (23/34) – Serial radiographs / Lack of motion on stress & pain on percussion.	
Meskens et al., 1988	Retrospective / 57	Subject as Own	Tibia 57	NR – EBI, L.P. Device	75.4% (43/57). Serial radiographs / Mechanical stability & lack of tenderness.	
O'Conner et al., 1985	Prospective / 54	Subject as Own	Tibia 30, Humerus 7, Femoral Shaft 7, Radius 6, Femoral Neck 2, Ulna 1, Tibial Non-union 1	5 msec burst of 20-22, 200 μsec pulses at 15 Hz	83.3% (25/30). Serial radiographs (bony bridging) / Clinically stable.	
Satter-Syed et al., 1999	19 (13 completed)	Subject as Own	19 long bones	NR	84.6% (11/13). Serial Radiographs / Clinical immobility, absence of pain, and ability to lift leg	
Sedel et al., 1982	Prospective / 39	Subject as Own	Tibia 20, Femur 11, Humerus 4, Radius/Ulna 2, Ulna 1, Clavicle 1	NR (1-1.5 mV/cm)	83.7% (31/37). Radiographic NR / Clinical NR.	
Sharrard, 1990	Prospective / 45	Sham	Tibial Shaft, 45	20 pulses repeated at 15 Hz	Stim[11]: SD 45% (9/20) OS 50% (10/20) RD Sham: 12% (3/25) OS 8% (2/25) RD Radiographs	Stim: Motion - 7/20 Pain – 0.9±1.2 Tenderness – 1.6±2.4 SD Sham: Motion - 13/25 Pain – 1.5±2.1 Tenderness – 2.7±3.1
Sharrard et al., 1982	Prospective / 53	Subject as Own	Tibia 30, Femur 7, Ulna 6, Radius 4, Knee 2, Ankle 2, Humerus 1, Capitellum 1	5 msec train of pulses at 15 Hz	Overall 71.7% (38/53), Tibia 86.7% (26/30), Femur 57.1% (4/7), Ulna 50% (3/6), Radius 75% (3/4), Humerus 0% (0/1), Capitellum 0% (0/1), Knee 50% (1/2), Ankle 50% (1/2). Serial radiographs / Lack of motion, tenderness, & pain under stress.	
Simonis et al., 1984	Prospective / 15	Subject as Own	Tibia 11, Radius/Ulna 2, Ulna 1, Knee 1.	3 msec burst of 236 μsec pulses 25Hz	86.7% (13/15) Serial Radiographs.	NR

[11] OS – Orthopedic surgeon, RD – Radiologist.

Reports on Adjunctive Lumbar Spinal Fusion - The petitioner has submitted eight articles (utilizing one capacitive coupling and seven pulsed electromagnetic fields devices) involving over 1,100 patients. According to the petitioner, these studies indicate the device's ability to promote osteogenesis in patients as an adjunct to the treatment of lumbar spinal fusion for one or two levels. In six studies, concomitant treatments were performed (i.e., lumbar fusion surgery), with stimulation administered postoperatively. In two studies, stimulation was used at least nine months post surgery in a non-operative attempt to salvage failed fusion. Treatment variables include stimulation type, output waveform parameters, and treatment regimens. Effectiveness outcomes were assessed radiologically and clinically. Radiographs were assessed for evidence of the formation of bridging, bony masses and assimilation. Clinically, subjects were evaluated for evidence of pain, use of pain medication, physical activity levels, and occupational status. The studies are summarized as follows (additional variables are analyzed and contained within the petition):

Table 5: Adjunct to Treatment of Lumbar Spinal Fusion

Author/Year	Type of Study / # Fusions	Control Group	Treatment Plan[12]	Waveform Parameters	Radiographic Success Rate	Clinical Success Rate
Bose, 2001	Retrospective / 48	Subject as Own	PLF and PEMF	NR – Orthofix Device[13]	97.9% (47/48) - Radiographic fusion (two point bridging, no radiolucency, intact hardware.)	4.2% (2/48) Excellent 79.2% (38/48) Good 16.7% (8/48) Fair 0% (0/0) Poor Pain, physical activity level, work status.
DiSilvestre and Savini, 1992	Prospective / 31 Active, 22 Control	Historical	PLF and PEMF	1.3 msec at 75 Hz	A4: 35.3% (11/31) A3: 61.3% (19/31) A2: 3.2% (1/31) A0-A4[14]	Active: 64.5% (20/31) at 2 months, 96.8% (30/31) at 4 months. Control: 36.4% (8/22) Pain regression.
Goodwin et al., 1999	Prospective (Randomized & Double blinded) / 85 Active, 94 Sham	Concurrent	PLF, ALIF, or PLIF and CC	60 kHz 5V peak to peak	Active: 90.6% (77/85) Sham: 81.9% (77/94) Radiographic bilateral bony masses	Active (SD): 88.2% (75/85) Sham: 75.5% (77/94) Pain, physical activity level, work status.
					Overall (SD): Active 84.7% (72/85), Sham 64.9% (61/94).	
Jenis et al., 2000	Prospective / 22 PEMF, 17 DC, 22 Control	Concurrent	PLF and PEMF or DC	PEMF: NR – Orthofix DC: EBI – implantable	Grade 3: Control 81%, PEMF 65%, DC 61%. Grade[15] Bone Mass	Control: Excellent 43%, Good 43%, Fair 14%. PEMF: Excellent

[12] PLF-Posterolateral Lumbar Fusion, PEMF-Pulsed Electromagnetic Fields, CC-Capacitive Coupling, DC-Direct Current, CMF-Combined Magnetic Field, ALIF-Anterior Lumbar Interbody Fusion, PLIF-Posterior Lumbar Interbody Fusion.

[13] Orthofix reports an output waveform parameter of 260 µsec 20G pulses repeated at 15 Hz.

[14] A0 bilatera1 non-union; Al uniiateral non-union; A2 insufficient fusion on one side; A3 continuous fusion without hypertrophy; A4 fusion with hypertrophy of fusion mass.

					Density: Control 106%, PEMF 125%, DC 126%.	35%, Good 50%, Fair 10%, Poor 5%. DC: Excellent 32%, Good 37%, Fair 31%. Pain, activity level, work status.
Marks, 2000	Retrospective / 42 PEMF, 19 Control	Concurrent	PLF and PEMF	NR – Orthofix Device	Active: 97.6% (41/42) Control: 52.6% (10/19) SD Serial radiographs	Active: Excellent 16.7%, Good 57.1%, Fair 21.4%, Poor 4.8%. Control: Excellent 0%, Good 57.9%, Fair 26.3%, Poor 15.9%. Pain, activity level, work status.
					Overall: Active 97.6% (41/42), Control 52.6% (10/19) SD.	
Mooney, 1990	Prospective (Randomized & Double blinded) / 98 PEMF, 97 Control	Concurrent	ALIF or PLIF and PEMF	NR – Orthofix Device	Active: 92.2% (90/98) Control: 68% (66/97). SD. Serial radiographs.	Active: Excellent 51%, Good 35.8%, Fair 8.2%, Poor 5%. Control: Excellent 36.1%, Good 50.5%, Fair 13.4%. Pain, activity level, work status.
					Overall: Active 91.8% (90/98), Control 68% (66/97). SD.	
Simmons, 1985	Prospective / 13	Subject as Own	PEMF	50 msec burst of 250 μsec pulse at 2 Hz	Increase in bone 85% (11/13), Solid fusion 77% (10/13). Serial radiographs.	NR
Simmons et al., 2004	Prospective / 100	Subject as Own	PEMF	5.85 G, 26 msec pulse	67% (67/100). Serial radiographs.	Excellent/Good 42% (42/100). Pain, activity level, work status.

Reports on Preclinical Findings - The petitioner has cited 21 articles in the petition amendment reporting on 21 studies in animal models. In addition, articles are presented which report on 14 studies in cell culture systems in examination of the mechanism(s) of action of various electrical stimuli in bone. The sponsor has acknowledged that submitted summary of the literature is not comprehensive.

Studies conducted within animal models are intended to evaluate new signals, dose/ response relationships, and the potential pathways of bone repair processes. Reports of preclinical effectiveness studies in animal models were reviewed and are described. The results of these

[15] Grade 1 - obvious pseudoarthrosis with clefts within the fusion mass and discontinuity between the transverse processes. Grade 2 - possible pseudoarthrosis with lucencies within the fusion mass. Grade 3 - solid arthrodesis with trabecular bridging bone.

studies range from generally positive affects including recovery of strength and load bearing capability, increases in synthesis of extra-cellular matrix, and formation of bridging bone, and more advanced healing (Bassett et al., 1982; Brighton et al., 1985; Guizzardi et al., 1994; Darendeliler et al., 1996; Fredericks et al., 2000; Inoue et al., 2002.) to generally negative affects (no improvement).

Table 6: Animal Studies Exhibiting Positive Effect

Author/Year	Animal Model	Stimulation / Parameters	Generalized Results
Bassett et al., 1982	Rat - radial osteotomy	PEMF (EBI) (≥20 pulses, 200-250μsec, burst width 5-50msec)	Significant increase in load (5msec burst width, 250 μsec, square pulse, 5 Hz)
Brighton et al., 1983	Rabbit -tibia1 growth plate	Capacitive coupled (60KHz at 2.5, 5, 10, & 20V peak to peak)	Accelerated growth (5 V exhibiting maximum growth)
Brighton et al., 1985	Rabbit -fibula osteotomy	Capacitive coupled – Dose/Response study.	Improvement assessed by radiograph, stiffness, and histology (220mV, 250pA, 60KHz (0.33V/cm) most effective)
Kold et al., 1987	Horse - graft incorporation	PEMF (EBI) (30 ms burst at 15 Hz, (+24mV 250 μsec and 14 μsec of -130mV))	Increase in graft incorporation.
lannacone et al., 1988	Rat - costochondral junction in vitro	PEMF (200 msec burst at 4.3KHz, burst of 20 pulses 5ms wide, repeated at 15Hz)	Stimulates growth (Macrophotographically). Thermal effects observed. Effective range 0.5 - l.l5 mV/cm and 6.11 mV/cm.
Aaron et al., 1989	Rat - Decalcified bone matrix	PEMF (4.5 msec burst at 15 Hz, 20 pulse burst 200 μsec wide)	Stimulation of cartilage synthesis
Guizzardi et al., 1990	Rat - arthrodeses lumbar spine	PEMF (Not provided)	Evidence of bony fusion callus (4 weeks) Evidence of cartilaginous fusion callus with inner calcification (8 weeks)
Wilmot et al., 1993	Rat - condyle growth	PEMF magnetic PEMF electrical (control)	PEMF-E & M significant negative effect on articular zone.
Suizzardi et al., 1994	Rat	PEMF - 18 hr/day	Acceleration of bony callus formation (4 weeks). Decreased effect over time.
Matsunaga et al., 1996	Rabbit	PEMF – (Varied)	Significant alkaline phosphatase activity and osteogenesis.
Yonemori et al., 1996	Rabbit - bone marrow	PEMF - 2G, 10Hz, 25 psec pulse with /without trauma compared to Direct Current.	lntramedullary bone formation and alkaline phosphatase activity increased more with DC then PEMF with trauma.
Darendeliler et al., 1997	Guinea pig - mandible	PEMF, Static magnetic field (SMF), and control	Accelerated bone repair in PEMF and SMF.
Glazer et al., 1997	Rabbit - spinal fusion	PEMF (Orthofix)	Radiographic fusion not stat. sign. Increased stiffness per tensile testing stat. sign. Histology - bony growth for PEMF.
Grace et al., 1998	Rat – patello-femoral groove	PEMF (380 psec square wave at 2 hr/day)	Increased vascular reaction, early chondrogenesis, and bone formation.
Fredericks et al., 2000	Rabbit – tibial osteotomy	PEMF (EBI)	Increased torsional strength, accelerated fracture callus (radiograph), and increased bone relative to cartilage (histology).
Fini et al., 2002	Rabbit – Hydroxyapatite implants	PEMF (75 Hz, 1.6mT for 3 weeks)	PEMF micro hardness increased and HA integration increased.
Inoue et al., 2002	Cannine – tibial osteotomy gap	PEMF (EBI) 1 hr/day for 4 weeks to 8 weeks (post op)	Increased load bearing recovery, bone formation, mechanical strength, and periosteal callus (radiograph).

Table 7: Animal Models Exhibiting Negative Effect

Author/Year	Animal Model	Stimulation / Parameters	Generalized Results
Armstrong and Brighton, 1986.	Rabbit – Tibial growth plate	Capacitive Coupling (continuous, 5V peak to peak, 60kHz sine wave for six weeks)	No significant difference in tibial lengths. Failure to thrive compared to normal animal.
Muhsin et al., 1991	Rat – Tibia non-union	PEMF (2-4 weeks)	No significant difference in healing rate.
Kahanovitz, et al., 1994	Dog – Spinal Fusion	PEMF (1.5Hz, 30 msec pulse, 260μsec burst, 1G) 0.5-1 hr/day	No statistical difference. (radiograph/histology)
Leisner et al., 2002	Rat – ulnar fracture	PEMF (PAP IMI®, Biopulse) – (1μs pulse, 15Hz, high output) 2x 5min/week for 7 weeks	Delayed callus formation and increased fibrous bone formation.

Studies conducted at the cellular level are intended to investigate the sequence of events which occur as a result of electrical stimulation; the interaction of the fields at the level of the cell membrane with regard to ion channels and receptor interaction; signal transduction, and cell types that do/ do not respond. The regulation and concentrations of calcium at the cellular level are also studied. Subsequent effects on DNA and RNA synthesis in gene expression for and of growth factors also appear to be involved. These actions can increase proliferation and/or differentiation, depending upon cell type, and ultimately result in increased matrix synthesis. The 14 studies are summarized as follows (additional variables are analyzed and contained within the petition):

Table 8: Literature Related to Mechanism of Action Studies

Author/Year	General Cell Type	Electric Stimulation / Parameters	Generalized Results
Fini et al., 2005	Articular cartilage	PEMF	Increase proliferation and matrix synthesis
Aaron et al., 2004	Not Specified	Capacitive coupling Inductive coupling	- Increase proliferation: Increase TGFb mRNA, BMP-2,-4 mRNA - Increase proliferation: Increase TGFb mRNA and protein
Torricelli et al., 2003	Human Osteoblast-like cells	PEMF - 75 Hz, 2.3mT, 1.3ms pulse (12 hr/day for 3 days)	Improved proliferation with exposure to PMMA.
Yamamoto et al., 2003	Rat calvarial osteoblasts	Static magnetic field 160mT	No increase in Cell proliferation
Diniz et al., 2002	Osteoblasts	PEMF, 1.5 Hz pulse burst, 7mT peak	Proliferation phase: Increased proliferation, differentiation, and mineralization. Differentiation stage: Increased differentiation and mineralization. Mineralization phase: Decrease bone-like tissue
Spadaro and Bergstrom, 2002	Rat calvarial cells	PEMF	Parathyroid hormone refractory effects, Increasing Ca uptake in bone, Decrease osteoclast absorption effects.
Guerkov et al., 2001	Human Hyper-trophic and Atrophic non-union cells	4.5 ms bursts of 20 pulses repeating at 15 Hz, 8 hr/day for 1,2, or 4 days (EBI)	Time dependent increase in TGFβl (Day 2 & 4 atrophic). No increase in cell proliferation, thymidine incorporation, ALP, collagen, PGE2, osteocalcin.

Lohmann et al., 2000	Human Osteoblast-like	15 HZ (EBI devices) 8 hr/day for 4 days	Decrease in proliferation, Enhanced differentiation, Stimulate TGFβ1.
Hartig et al., 2000	Osteoblast-like (bovine origin)	Capacitive coupled saw-tooth pulses of 100 V and 16 Hz frequency (6kV/m across membrane)	Sub-confluent: increase cell numbers & ALP activity. Confluent cultures: matrix maturation.
Bodamyali et al., 1998	Rat osteoblasts	PEMF (EBI bone healing system) 1 day	Increase bone nodule number and size Increase in mRNA for bone morphogenic proteins
Brighton et al., 1992	Rat calvarial cells	Capacitive coupled 60 kHz, 0.0001-20 mV/cm, burst patterns constant to 5 msec.	Increase proliferation - 0.1, 1, and 20 mV/cm continuously for 6 hours or 20 mV/cm pulsed.
Fitzsimmons et al., 1992	Human Osteosarcoma	Capacitive coupled, 10 - 16 Hz	14 Hz optimum increase in cell proliferation, IGF-II levels, and IGF-II mRNA
Goodman et al., 1983	Salivary gland cells	PEMF Biosteogen (EBI) 5 - 90 min, 1.5 mV/cm, 200psec pulse	Induced cell transcription
Hinsenkamp et al., 1978	Adult Frog red blood cells	(EBI) 4 -5 mV/cm for 0.35 sec.	Chromatin modifications - induction of transcription.

Petitioner's Proposed Reclassification:

The petition proposes to reclassify the generic device, non-invasive bone growth stimulator, from class III (PMA approval) into class II (special controls) to include CC and PEMF devices. Devices of this generic type have been regulated by CDRH since 1979. The petitioner is not proposing the reclassification of CMF devices, other product groups, or certain indications for use as described previously. The petitioner believes that a sufficiently large body of clinical and preclinical evidence has become available during this time to indicate that this generic device, when used in accordance with its approved labeling, demonstrates adequate safety and effectiveness. The potential risks associated with the use of this generic device have been identified from information provided within the published literature and MDR database. The petitioner believes that these potential risks may be addressed via special controls as proposed in the CFR listing.

Petitioner's Proposed Special Controls

The special controls listed below were proposed by the petitioner as being adequate to ensure the safe and effective use of the non-invasive bone growth stimulator as a class II device.

Sponsor-Proposed Draft Guidance Document (submitted for FDA review)

1. Guidance document, "Class II Special Controls Guidance Document: Contents of Pre-market Notifications [510(k)s] for Non-invasive Bone Growth Stimulators". Please note that this guidance document was prepared by RS Medical. If the reclassification petition is approved and the identified devices are reclassified, a Special Controls guidance document will be prepared by FDA.

FDA-Recognized Performance Standards

2. 21 CFR Part 898 Performance Standards for Electrode Lead Wires and Patient Cables.
3. ISO 10993: Biological Evaluation of Medical Devices: Part1: Evaluation and Testing
4. IEC 60601-1: Medical Electrical Equipment, Part 1: General Requirements for Safety
5. IEC 60601-1-2: Electromagnetic Compatibility for Medical Equipment: Requirements and Tests.

Existing FDA Guidance Documents

6. "Guidance for the Content of Pre-market Submissions for Software Contained in Medical Devices." http://www.fda.gov/cdrh/ode/guidance/337.pdf

Petitioner Proposed CFR Listing

As the petitioner is not proposing the reclassification of CMF devices and certain indications for use that are currently described within product code LOF, the proposed CFR listing would need to be modified to address these devices and indications for use as remaining in class III.

§ 8xx.xxx Non-invasive bone growth stimulator.

(a) Identification. 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 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.

(b) Classification. Class II (Special Controls). Non-invasive bone growth stimulators must comply with the following special controls:

i. FDA guidance document "Class II Special Controls Guidance Document: Contents of Pre-market Notifications [510(k)s] for Non-invasive Bone Growth Stimulators";
ii. 21 CFR Part 898 Performance Standards for Electrode Lead Wires and Patient Cables;
iii. ISO 10993: Biological Evaluation of Medical Devices: Part1: Evaluation and Testing;
iv. IEC 60601-1: Medical Electrical Equipment, Part 1: General Requirements for Safety;
v. IEC 60601-1-2: Electromagnetic Compatibility for Medical Equipment: Requirements and Tests; and
vi. FDA guidance document, "Guidance for the Content of Pre-market Submissions for Software Contained in Medical Devices."

FDA Comments

The following FDA comments are intended to provide clarification regarding the proposed reclassification.

1. The safety and effectiveness of the FDA approved devices listed within this proposed reclassification has been established through published literature regarding devices approved through the PMA process. The proposed reclassification includes the following devices:
    - OrthoPak® Bone Growth Stimulator (P850022 - 02/18/1986) (CC). Indicated for the treatment of an established nonunion secondary to trauma.
    - SpinalPak® Fusion Stimulator (P850022/S009 - 09/24/1999) (CC). Indicated as an adjunct electrical treatment to primary lumbar spinal fusion surgery at one or two levels.
    - EBI Bone Healing System® (P790002 - 11/06/1979) (PEMF). Indicated for the treatment of fracture non-unions, failed fusion and congenital pseudarthroses.
    - Physio-Stim® Lite (P850007 - 02/21/1986) (PEMF). Indicated for the treatment of established nonunion acquired secondary to trauma.
    - Spinal-Stim® Lite (P85007/S006 - 02/07/1990) (PEMF). Indicated as a fusion adjunct to increase the probability of fusion success and as a nonoperative treatment of failed fusion surgery.

    The proposed reclassification excludes the following devices, product areas, and indications for use from reclassification:

    Devices:
    - OrthoLogic™ 1000 Combined Magnetic Fields device, indicated for the treatment of an established nonunion secondary to trauma.
    - OrtoLogic SpinaLogic™ Combined Magnetic Fields device, indicated as an adjunct treatment to primary lumbar spinal fusion surgery for one or two levels.

    Product Areas:
    - Invasive bone growth stimulators, FDA product code LOE.
    - Non-invasive bone growth stimulators, FDA product code LPQ – Stimulator, ultrasound and muscle, for use other than applying therapeutic deep heat.

    Indications for Use:
    - Treatment of congenital pseudarthrosis. IFU approved for a commercially available non-invasive bone growth stimulator device (P790002).
    - Adjunct to cervical fusion surgery in patients at high risk for non-fusion. IFU approved for a commercially available non-invasive bone growth stimulator device (P030034).

2. The cited scientific literature indicates that small differences made to the general device type can be shown to be either unsafe and/or ineffective. These differences may include the alteration of the treatment signal and associated treatment field. Although some treatment signal/field modifications can affect the device's safety and effectiveness, the scientific literature indicates that most modifications within a given range do not result in unsafe or ineffective treatment.

3. The issue raised by the proposed reclassification is whether sufficient scientific knowledge exists to adequately define the risks to health associated with the proposed generic device type and if the proposed special controls are sufficient to control these risks to health. In assessing the risk profile for any device it is not possible to prove that a particular adverse event will not occur, i.e., the absence of the event is not proof that it could not occur. Therefore, the proposed special controls should be evaluated to determine if they can control, not eliminate, such risks to health.

FDA Questions for the Panel

Questions regarding the Reclassification Petition submitted by RS Medical:

The petitioner (RS Medical) has submitted a reclassification petition for a general non-invasive bone growth stimulator (BGS) device. The petition seeks reclassification from class III (premarket approval) to class II (special controls) for both Capacitive Coupling and Pulsed Electromagnetic Fields devices. The petition excludes invasive BGS, Combined Magnetic Field (CMF) BGS, and non-invasive ultrasound BGS.

1. In regards to the following devices which are proposed for reclassification, do you believe that the device description adequately describes and characterizes the devices? If not, what changes in the definitions or characterizations do you recommend?
    a. Capacitive Coupling
    b. Pulsed Electromagnetic Fields

2. In regards to the following devices which are proposed for reclassification, do you believe that the risks to health are adequately described? If not, what additional risks do you believe should be included?
    a. Capacitive Coupling
    b. Pulsed Electromagnetic Fields

3. Special controls have been proposed to address the risks to health identified for each of the above device configurations. Do you believe appropriate special controls have been identified to adequately address these risks? If not, what additional controls, if any, do you recommend to address these risks?

4. Device labeling has been cited as a control with which to address risks to health. The proposed labeling requirements are consistent with those generally found in current non-invasive BGS package labeling. This labeling generally includes device description, type of materials, indications for use, contraindications, adverse events, precautions, warnings, a listing of compatible components, and sterility information. What additional labeling, if any, do you recommend for Capacitive Coupling and Pulsed Electromagnetic Fields devices?

5. Do you believe the data presented in this petition supports the reclassification of:
    a. All non-invasive Capacitive Coupling BGS devices identified in this petition? If not, which types of non-invasive BGS devices do you believe are inappropriate for reclassification, and why (e.g., they have insufficient information and/or special controls)?
    b. All non-invasive Pulsed Electromagnetic Fields BGS devices identified in this petition? If not, which types of BGS devices do you believe are inappropriate for reclassification, and why (e.g., they have insufficient information and/or special controls)?

General Questions:

1. A general device type does not necessary restrict the included devices to an identical or a single technology. Several devices, product areas, and indications for use have been excluded from this petition.
    a. The proposed reclassification excludes the Combined Magnetic Fields (CMF) device. Please discuss if the risks associated with this device type are significantly different than those risks associated with the proposed general device type.
    b. The proposed reclassification excludes the invasive bone growth stimulators (FDA product code LOE) and the non-invasive ultrasound bone growth stimulators (FDA product code LPQ). Please discuss if the risks associated with these product types are significantly different than those risks associated with the proposed general device type.
    c. The proposed reclassification excludes indications for the treatment of congenital pseudarthrosis and as an adjunct to cervical fusion surgery in patients at high risk for non-fusion. Please discuss if the risks associated with these indications for use are significantly different than those risks associated with the proposed general device indications for use.

Appendix A
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