Healthonics
The Biophysics Health Company™

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm 1061
Rockville, MD 20852

Subject: FDA Docket 2005P-0121
Comments in Support of the Reclassification
of Non-Invasive Bone Growth Stimulator

To whom it may concern:

This letter is written in support of the reclassification of Bone Growth Stimulators (BGS) from Class III to Class II. The following comments are consistent with those delivered by *Healthonics, Inc.* at the Orthopaedic and Rehabilitation Device Panel of the Medical Devices Advisory Committee meeting that was held on June 2, 2006.

1. It was clearly recognized at the June 2 Panel Meeting that attention was diverted from the main issue of the meeting by those speaking in favor of the status quo. The meeting content did not address or reflect its original intent.

   "Is it possible for FDA to define a Class II BGS submission process that will insure that a generic BGS signal that is delivered to the target tissue is equivalent to that delivered in tissue by the approved predicate BGS signal?"

   Since FDA has the waveform characteristics for each of the three types of BGS signals that have been approved (capacitive coupling, pulsed electromagnetic fields, and combined magnetic fields), it is possible for FDA to develop a table of technical parameters that would be necessary for submitters to complete and compare to a predicate as part of the substantial equivalence justification.

   An example of such a *Substantial Equivalence Comparison Table*, which illustrates the key characteristics of each approved type of BGS signal with somewhat widened parameter ranges where these are supported by the scientific literature, is attached. *Healthonics, Inc.* developed this table with

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help from Arthur A. Pilla, one of the inventors and developers of the original BGS devices in the 1970's.

As a suggestion to defining substantial equivalence, it is easy to identify the waveform characteristics of each of the approved BGS devices. Since all original patents have expired, the FDA can identify and mandate the predicate's characteristics to which the 'new' proposed 510(k) device must be shown to be equivalent. For example, since the mechanism of action of sinusoidal and pulse-burst signals has been shown to depend solely upon the electrical gradient waveforms established in tissue and not upon the magnetic component of the signal (if present), *Healthonics, Inc.* suggests this be adopted as the common basis for comparison among these signal types.

Similarly, it is easy to measure the induced electrical gradients from an approved or proposed BGS device either directly in tissues of an experimental animal, or in a saline gel matching the approximate resistivity of actual tissues. *Healthonics, Inc.* suggests the latter approach since it is simultaneously more convenient, more humane, and more easily standardized and reproduced. For further standardization, a uniform gel geometry, such as a rectangular slab of identified dimensions, should be specified.

A suitable gel is prepared by gelling physiological saline (0.9% NaCl in water) with ordinary gelatin or another agent to allow stable placement of probes. Desirably, at least when using gelatin, a preservative is also added. A suitable probe for measuring induced voltage gradients, regardless of whether they are induced by a capacitively or inductively coupled signal, is described in AA Pilla, P Sechaud and BR McLeod, Electrochemical and electrical aspects of low-frequency electromagnetic current induction in biological systems, J. Biol. Physics 11 (1983), pp.51-58.

Using this approach, *Healthonics, Inc.* has measured the characteristics of the presently approved sinusoidal and pulse burst signals in a rectangular, 36 x 52 x 9 cm slab of 0.9% aqueous NaCl plus 2.8% gelatin and 5% isopropanol as a preservative, using the Pilla, Sechaud and McLeod (PSM) probe design, and found the measured waveforms to match published specifications. *Healthonics, Inc.* suggests this combination of saline gel composition and geometry with the PSM probe as a common and easily prepared basis for induced waveform comparison for substantial equivalence.

Each key measured BGS waveform characteristic would be specified to meet an engineering tolerance of ± 10% to each tabulated value, or to lie within each tabulated range, in lieu of submitting clinical study data to demonstrate efficacy.

It should be noted that while signal timing is easily defined and measured and can reasonably be required to meet ± 10% tolerances, electromagnetically induced gradients are highly nonuniform and cannot be expected to do the same. For example, in a cylindrical slab geometry with magnetic induction and for a given magnetic field strength, the induced voltage gradient is proportional to the radius as explained in the Pilla, Sechaud and McLeod paper cited above. As a result, it is unreasonable to expect any inductive BGS device, <u>including those already approved</u>, to give ± 10% uniform intensity over the treatment volume.

Healthonics, Inc. suggests instead that a range between upper and lower limits be defined as shown in the table, and that for each new proposed device regardless of the coupling mechanism a set of at least ten individual measurements, distributed throughout a typical treated volume or its equivalent in a gel slab, be shown to lie within this range.

2. The FDA states in FDA FR Doc E7-476, section VIII, dated January 17, 2007, *Panel Recommendations; FDA's Findings*,

   "...there was not adequate evidence in the petition to establish that the petition's proposed special controls could be used to adequately mitigate the risk of inconsistent or ineffective treatment."

   Since FDA has taken no action to rescind or cancel currently approved BGS-device PMA applications, based on Panel Meeting presentations, it must be assumed that the approved devices all deliver consistent and effective treatment. Therefore, devices that are engineered to be equivalent/generic copies of the existing BGS waveform devices with respect to the identified characteristics in a standardized tissue model (gel and probe combination) would be presumed to deliver consistent and effective treatment as well.

   In Section VII (c) of FDA FR Doc E7-476, it is important to note that the FDA agrees that special controls were sufficient to control for a variety of potential risks posed by patient use. Publication by the FDA of a *Substantial Equivalence Comparison Table* as discussed in (1) above would provide a basis for consistent and effective BGS treatment devices as currently defined under Class II requirements.

3. The implications of a decision by FDA not to downclassify BGS as requested by RS Medical's petition are:

   a. Innovation of BGS technology will be stifled, as the approved devices represent the same signals that were sold 25 years ago – none of the companies who distribute approved devices have significantly modified or improved their characteristics.

b. No competition in the BGS market will be developed.

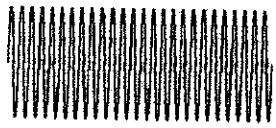
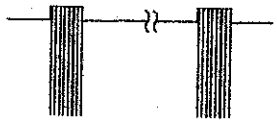
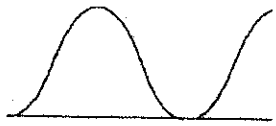
c. Millions of patients who could benefit from BGS treatment will be denied access due to the excessive retail cost of these devices.

Healthonics, Inc's Management strongly recommends and supports the down-classification of BGS from Class III to Class II.

Sincerely,

Jim Naftel
President

Comparison of General and Technical Noninvasive Bone Stimulator Signal Characteristics

Signal Characteristic	Sinusoidal signal	Pulse burst signal	Combined Magnetic Field signal
Pulse shape	Sine	Rectangular	Sine superimposed on constant level
Mono- or biphasic	Biphasic	Biphasic	Monophasic with respect to magnetic field
Pulse frequency (within bursts if present)	60 KHz	4350 Hz	76.6 Hz
Pulse duration, nominally shorter phase if not equal	8.3 μsec	28 μsec.	6.53 msec
Pulse duration, nominally longer phase if not equal	Same, both phases are equal length.	200 μsec	Same, both phases are equal length.
Continuous or intermittent (pulse burst)?	Continuous	Intermittent	Continuous
Burst repetition rate, if present	N/A	15 Hz	N/A
Burst length or duty cycle, if present	N/A	5 msec	N/A
Principal energy affecting tissues	Electric*	Electric*	Magnetic*
Intensity: electric or magnetic field induced in tissue	1-10 millivolts per centimeter, peak to peak**	1-10 millivolts per centimeter, peak to peak**	40 uT peak-to-peak sine wave plus 20 uT steady field**
Net charge	Zero	Zero	Zero
Sketch of waveform (not to scale)			

* Per Arthur A. Pilla's letter to Janet L. Scudiero, CDRH, dated May 17, 2006.
** Measured in tissue or in saline liquid or gel with equal electrical resistivity.