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April 6, 2004

Re: Medical Device Regulation – A Review of the Sale/Promotion of Devices and Use of Devices Within the Scope of Medical Practice

This letter provides background on the issue of the Food and Drug Administration's ("FDA") regulation of the marketing and/or sale, versus the practitioner use, of powered muscle stimulators for the treatment of dysphagia. This letter is intended to provide an overview of FDA's regulatory authority over medical devices and the use of such devices by medical practitioners, it is not intended, nor should it be construed as a formal legal opinion.

Summary

In short, FDA places restrictions on the labeling, marketing and promotion of all medical devices, including powered muscle stimulators, specifically that medical devices may only be labeled and promoted in accordance with the approved or cleared indications for use. Nevertheless, as described further below, a practitioner may use any approved/cleared powered muscle stimulator for treatment of dysphagia, regardless of the indications for use, when such use is part of the practice of medicine and in the practitioner's judgment is in the best interest of the patient. Furthermore, FDA does not restrict the full exchange of scientific information on treatment uses of devices when unaffiliated with the device manufacturer.

In the United States, FDA regulates the sale of medical devices such as powered muscle stimulators. *See* 21 C.F.R. § 890.5850. Before a medical device can be legally sold in the U.S., the person or company that wants to sell the device must seek approval or clearance from the FDA. To gain an approval, they must present evidence that the device is reasonably safe and effective for a particular use, the "indication," whereas to gain a clearance they must demonstrate it is "substantially equivalent" to an already marketed device. *See generally* 21 U.S.C. §§ 360(k), 360c(i), 360e. Once the FDA has approved or cleared a medical device, a doctor or health care practitioner may decide to use that device for other indications, if the doctor/health care practitioner, in the exercise of their professional judgment, believes it is in the best interest of the patient. The use of an approved/cleared device for other than its FDA-approved/cleared indication is called "off-label use." The FDA does not regulate off-label use or the practice of medicine. Thus, a practitioner may use a cleared device, such as a powered muscle stimulator, for uses either consistent with the approval/clearance, or off-label, when in the practitioner's professional judgment, the practitioner

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determines it is in the best interest of the patient. However, a practitioner is prohibited from promoting the off-label use of any particular medical device.¹ This is not meant to prohibit or restrict the full and free exchange of scientific information, however, such as scientific seminars on types of treatment of a disease or condition. In addition, FDA does also regulate and place limitations on the *manufacturer* of the device, who also may not market or promote the device for off-label uses.

Regulatory Background of Medical Devices

Powered muscle stimulators, such as the MediStim (also known as the "NT2000") for example, are regulated by FDA under the Federal Food, Drug, and Cosmetic Act ("FDCA") as class II medical devices. *See* 21 C.F.R. § 890.5850. Medical devices are classified into one of three classes: Class I, II, and III. The amount of regulatory control over a device increases from Class I to Class III. Therefore, most Class I devices are exempt from pre-market notification (i.e., 510(k) clearance) and may be marketed without seeking FDA clearance or approval. On the other hand, most Class II devices require a 510(k) clearance, while most Class III devices require a Pre-Market Approval ("PMA").

510(k) Clearances

A 510(k) is a premarket submission made to FDA to demonstrate that the device to be marketed is as safe and effective, that is, substantially equivalent ("SE"), to a legally marketed device that is not subject to PMA. Applicants must compare their 510(k) device to one or more similar devices currently on the U.S. market and make and support their substantial equivalency claims. A legally marketed device is a device that was legally marketed prior to May 28, 1976, or a device which has been reclassified from Class III to Class II or I, or a device which has been found to be substantially equivalent to such a device through the 510(k) process. The legally marketed device(s) to which equivalence is drawn is known as the "predicate" device(s). A device is "substantially equivalent" if, in comparison to a predicate device it:

- has the same intended use as the predicate device; *and*
- has the same technological characteristics as the predicate device; *or*
- has different technological characteristics, that do not raise new questions of safety and effectiveness, and the sponsor demonstrates that the device is as safe and effective as the legally marketed device.

See 21 C.F.R. Part 807.100. A 510(k) submission is typically much less onerous, both in terms of time and money, than a PMA submission and normally is reviewed within 90 days of submission.

¹ FDA prohibits a physician or any person acting for or on behalf of a sponsor to promote an off-label use or unapproved investigational device. *See* 21 C.F.R. § 812.7.

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Premarket Approval (PMA)

A PMA is the FDA process of scientific and regulatory review of clinical data to evaluate the safety and effectiveness of Class III medical devices. Generally speaking, Class III devices are those that support or sustain human life, are of substantial importance in preventing impairment of human health, or which present a potential, unreasonable risk of illness or injury. Due to the level of risk associated with Class III devices, FDA has determined that general and special controls alone are insufficient to assure the safety and effectiveness of class III devices. Therefore, these devices typically require a PMA application under section 515 of the FDCA in order to obtain marketing approval.

A PMA is the most stringent type of device marketing application required by FDA. The applicant must receive FDA approval of its PMA application prior to marketing the device. PMA approval is based on a determination by FDA that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use(s). Although FDA regulations provide 180 days to review the PMA and make a determination, in reality, the review time is typically longer.

Additional Regulatory Requirements

In addition to the classification procedure, and premarket approval or clearance where necessary, the other basic regulatory requirements that manufacturers of medical devices distributed in the U.S. must comply with are:

- Establishment registration;²
- Medical Device Listing;³
- Quality System ("QS") regulation;⁴
- Labeling requirements;⁵ and

² Establishments involved in the production and distribution of medical devices intended for marketing or leasing (commercial distribution) in the U.S. are required to register with the FDA. *See generally* 21 C.F.R. Part 807.

³ Medical device establishments required to register with FDA must list the devices they have in commercial distribution including devices produced exclusively for export. *See generally* 21 C.F.R. Part 807.

⁴ The current good manufacturing processes ("GMPs") requirements are set forth in the Quality System ("QS") regulation in Part 820 of the C.F.R. They require that domestic or foreign manufacturers have a quality system for the design, manufacture, packaging, labeling, storage, installation, and servicing of finished medical devices intended for commercial distribution in the United States. The regulation requires that various specifications and controls be established for devices; that devices be designed under a quality system to meet these specifications; that devices be manufactured under a quality system; that finished devices meet these specifications; that devices be correctly installed, checked and serviced; that quality data be analyzed to identify and correct quality problems; and that complaints be processed.

⁵ The general labeling requirements for medical devices are contained in 21 C.F.R. Part 801. These include labeling the device to include name and place of business, intended use, and in the case of a prescription device bears

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- Medical Device Reporting (“MDR”).⁶

Powered Muscle Stimulators

Powered muscle stimulators are class II devices. The NT2000 device is a fairly representative device within this category.⁷ According to information available in its 510(k) summary, the NT2000 is a portable two-channel battery operated neuromuscular electric stimulator marketed by Bio-Medical Research Ltd. It is intended for prescription use pursuant to 21 C.F.R. § 801.109. The NT2000 received a 510(k) clearance to market the product based upon a review that the product was “substantially equivalent” (for the indications included in the clearance) to devices already marketed. Based on a finding of substantial equivalence to a predicate device (another powered muscle stimulator), the product was cleared for the following uses:

- Relaxation of muscle spasms
- Prevention or retardation of disuse atrophy
- Increasing local blood circulation
- Muscle re-education
- Immediate post-surgical stimulation of calf muscles to prevent venous thrombosis
- Maintaining or increasing range of motion.

See 510(k) clearance K014019. Use of the NT2000 for treatment for dysphagia is not specifically included in the indications, though it is labeled for “muscle re-education.” Based on this clearance, the NT2000 may be marketed and promoted consistent with the above-indications for use. However, as described below, because the NT2000 is a cleared device, practitioners may use the device for either cleared indications or off-label uses, when in their professional judgment such uses are in the best interest of the patient.

information for use including, indications, effects, routes, methods, and frequency and duration of administration, and any relevant hazards, contraindications, side effects, and precautions under which the device can safely be used.

⁶ Since December 13, 1984, the MDR regulations have required firms who have received complaints of device malfunctions, serious injuries or deaths associated with medical devices to notify FDA of the incident. See generally 21 C.F.R. Part 803.

⁷ Over 100 powered muscle stimulation devices are listed with FDA. See <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRL/listing.cfm>

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Discussion and Analysis**Limitations on Promotion of Off-Label Uses**

As noted above, though FDA does not regulate the "practice of medicine," FDA does regulate the advertising and promotion of devices by the manufacturer. *See* 21 C.F.R. Part 801.⁸ Thus, while the device may be promoted and advertised with claims that are consistent with its approval/clearance, except in certain limited exceptions, a manufacturer may not promote a device for an off-label use.⁹ Therefore for example, the manufacturer of the NT2000 device may not promote the product for indications that have not been cleared by FDA. Promotion of a device outside the scope of its cleared indications could cause the product to be misbranded, a violation of the FDCA. *See* 21 U.S.C. § 331. In addition, a practitioner also may not promote a device for off-label use. *See* 21 C.F.R. § 812.7. However, this restriction is not meant to restrict the scientific exchange of information on particular types of treatments, but rather to prevent the promotion of particular individual devices.

Practice Of Medicine

Since the initial passage of the FDCA in 1938, Congress was concerned that FDA's regulation of drugs and devices not impinge on a physician's ability treat and "practice" medicine. (The FDCA was "not intended as a medical practices act and [did] not interfere with the practice of the healing art." S. Rep. No. 361, 74th Cong., 1st Sess. 3 (1935)). In 1997, with the passage of the Food and Drug Administration Modernization Act ("FDAMA") this concern was made explicit in the statute. FDAMA added section 906 to the FDCA. It states:

Nothing in this Act shall be construed to limit or interfere with the authority of a health care practitioner to prescribe or administer any legally marketed device to a patient for any condition or disease within a legitimate health care practitioner-patient relationship. ...

See 21 U.S.C. § 396. Thus the first and primary inquiry is whether a practitioner is using a device that has any approved or cleared indications. Once the device has been cleared or approved for any use, a practitioner, in the course of exercising professional judgment, may use that approved/cleared device for any other use (assuming the device itself is not modified).

⁸ Both the Federal Trade Commission ("FTC") and FDA regulate the advertising of medical devices. Although FDA's regulation of advertising and promotion is technically limited only to "restricted" devices, *see* 21 U.S.C. § 352(q) & (r), generally speaking, almost all advertising and promotional materials for a device will be considered to be "labeling" by FDA, and thus within the scope of FDA's authority. *See* 21 U.S.C. § 331.

⁹ FDA's off-label information dissemination policy has been challenged in court based on First Amendment commercial speech grounds. *See Washington Legal Foundation v. Henney*, 202 F.3d 331 (D.C. Cir. 2000). However, this is beyond the scope of this letter.

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Use of Powered Muscle Stimulators for Treatment of Dysphagia

Dysphagia is defined as difficulty in swallowing. One type of treatment for dysphagia is the use of a powered muscle stimulator to "re-educate" the throat muscles necessary for pharyngeal contraction. Another type of treatment would be to re-educate the suprahyoid muscles necessary for laryngeal elevation. Although it appears that there is only one powered muscle stimulator device that is specifically cleared for the treatment of dysphagia, *see* Freed Bioelectric: Dysphagia Treatment Device (K002410), (now marketed as the VitalStim), other powered muscle stimulator devices intended for electrical nerve stimulation may also be used by practitioners for the treatment of dysphagia when in the practitioner's professional judgment it is in the best interest of the patient. Because of the practice of medicine exception explained above, this would be the case even if powered muscle stimulators did not contain specific labeled indications for muscle re-education.

However, as noted above, the NT2000, for example, is indicated for "muscle re-education." Thus, even though the device is not specifically indicated for dysphagia, a practitioner, in the course of exercising professional judgment, may use the device for the treatment of dysphagia. In fact, since the device is indicated for "muscle re-education," treatment for dysphagia would not even be considered an off-label use, since "muscle re-education" is a general indication, the scope of which can include dysphagia. Thus, the primary difference between the NT2000 and the Freed device is simply that the Freed device may be *labeled, advertised and promoted* for the treatment of dysphagia, while the NT2000 may not be labeled or promoted for treatment of dysphagia. Nevertheless, both devices may be used by practitioners for the treatment of dysphagia where, in the professional judgment of the practitioner, such treatment is in the best interest of the patient. Furthermore, the teaching or training of practitioners in the use of a powered muscular stimulator for the treatment of dysphagia would not be considered promotion of an off-label use, where the devices are cleared for "muscle re-education." However, such training should be structured so as not to promote any specific brand of device for dysphagia which has not received FDA approval/clearance for dysphagia treatment.

Conclusion

In conclusion, FDA places restrictions on the labeling, marketing and promotion of powered muscle stimulators, such that they may only be labeled and promoted in accordance with the approved or cleared indications for use. Nevertheless, a practitioner may use any approved/cleared powered muscle stimulator for treatment of dysphagia, regardless of the indications for use, when such use is part of the practice of medicine and in the practitioner's judgment is in the best interest of the patient. Moreover, FDA does not restrict the dissemination of scientific information on the use of powered muscle stimulator devices in the treatment dysphagia, so long as promotion of a particular device is not occurring.