DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Center for Devices and
Radiological Health
2098 Gaither Road
Rockville, MD 20850

5147

Via Federal Express

WARNING LETTER

JAN 25 2001

Jerry I. Jacobson, DDS, DMD
Chair, CEO, and President
Jacobson Resonance Enterprises, Inc.
8200 Jog Road, Suite 100
Boynton Beach, Florida 33437

Dear Dr. Jacobson:

During the period September 11-15, 2000, Mr. Victor Spanioli, an investigator with the Food and Drug Administration (FDA), Florida District Office, and Ms. Barbara A. Crowl, a Consumer Safety Officer from FDA's Center for Devices and Radiological Health (CDRH), conducted an inspection at your facility. The purpose of this inspection was to determine whether your firm's activities as a sponsor/monitor of investigational studies of the [redacted] complied with applicable FDA regulations. This product is a device as defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act.

The inspection was conducted under a program designed, in part, to ensure that data and information contained in [redacted] submissions are scientifically valid and accurate. Another objective of the program is to ensure that human subjects are protected from undue hazard or risk during the course of scientific investigations.

Our review of the inspection report submitted by the district office revealed that there were serious violations of the requirements of Title 21, Code of Federal Regulations (21 CFR), Part 812 - Investigational Device Exemptions and Part 50 - Protection of Human Subjects. Inspectional observations were listed on the Form FDA-483 that was presented to and discussed with you; Frank A. Chaviano, Ph.D., Chief Operating Officer; and Roger S. Gorman, M.D., Research Director/Principal Investigator for your [redacted] clinical trial, at the conclusion of the inspection. The following list of violations is not intended to be an all-inclusive list of deficiencies encountered during our review.

1. **Failure to ensure proper monitoring of the clinical investigation(s) in accordance with 21 CFR 812.40 and 812.46**

For the study, "[redacted]" subject enrollment, informed consent, and data collection/reporting activities were not monitored. Source documents had not been

reviewed/audited to ensure that all inclusion/exclusion criteria and other protocol requirements were met and data discrepancies resolved. There was no documentation that an Institutional Review Board (IRB) reviewed and approved the initial protocol and corresponding informed consent forms used in this study or any subsequent revisions. There was no documentation that advertisements used to recruit subjects were reviewed and approved by an IRB. In fact, there was no documentation that identified the specific protocol(s) used during the study. [redacted] data used for efficacy analysis had not been audited/verified. There were additional unresolved issues with [redacted] of the [redacted] subject [redacted], and treatment of [redacted] subjects with the device following their participation in the study. Treatment of [redacted] subjects was not included in the protocol or consent and the data were not considered for analysis.

Your firm conducted clinical studies during [redacted] in at least [redacted] patients diagnosed with multiple sclerosis, epilepsy, Alzheimer's Disease, muscular dystrophy, cerebral palsy, Parkinson's Disease, microcephaly, brain injury/developmental deficit, hyperactivity/autism, depression, migraine headaches, or chronic pain. These studies failed to conform with Investigational Device Exemption, informed consent, and IRB requirements. For example, there was no documentation that an IRB reviewed specific [redacted] protocols/treatment plans and concurred that the [redacted] device was not a significant risk device when used at various settings on patients diagnosed with the above-listed medical diseases/conditions. The "Hold Harmless Agreement" used for these studies failed to include numerous basic and additional elements of informed consent, and there was no documentation that an IRB reviewed and approved this form. Furthermore, for these [redacted] studies, there was no documentation that the individuals performing the studies were selected based on their training and experience. There was no monitoring of the [redacted] studies and no study monitor was identified. Progress reports were not submitted to the IRB.

In addition, you failed to monitor another clinical study utilizing the [redacted] device at the University of [redacted], which was sponsored by your firm, to ensure compliance with applicable requirements.

2. Failure to comply with prohibitions against promotion and other practices as identified in 21 CFR 812.7

The [redacted] device does not as yet have marketing clearance for any indication in the United States. Misleading and/or inaccurate statements pertaining to the device and related studies were observed in various materials: a brochure; subject-recruiting advertisements; and press releases and other information distributed via the Internet at http://www.jrse.com.

For example, it is claimed in the brochure that through studies performed at several clinical facilities and institutions in the USA and Europe, in a majority of cases the [redacted] had been able to help alleviate a wide variety of illnesses: neuro-degenerative diseases like Alzheimer's, multiple sclerosis, and Parkinson's; cerebral palsy, autism, and epilepsy; and migraine headaches. It is also claimed that FDA has determined that there is no significant risk in working with these treatment devices. As you are aware, FDA's determination of nonsignificant risk in regard to the use of the [redacted] device applied only to the treatment of [redacted].

Advertisements used to recruit subjects state that the "treatment is safe" and include a reference to "FDA (IRB) Approved Study." You may not claim that a device under investigation is either safe or effective, and the implication that FDA approved the study is objectionable.

Information on your firm's website included numerous inaccurate or misleading statements. For example, in an "investment survey" report it was claimed that FDA had ruled that use of the company's [redacted] entails non-significant risk. As discussed above, the FDA non-significant risk determination applied only to the treatment of [redacted]. Also included in this report was the statement "since safety is not an issue." Furthermore, reference was made to the conduct (with FDA's blessing) of various Institutional Review Board (IRB) studies. FDA had not "blessed" nor reviewed any of these studies, but recommended that your firm rely on the reviewing IRB's risk determination for these studies.

In various news and press releases found at your website, reference was made to ongoing animal and human research and product commercialization activities based on the [redacted]. In one such release [redacted] completion and execution of multiple manufacturing and distribution agreements covering the newly developed and patented [redacted] was announced. Furthermore, marketing, sales and manufacturing of the [redacted] were to commence on or before the end of [redacted]. Although it was stated during the inspection that arrangements had not yet been concluded for product commercialization as discussed in the releases, some of the information contained therein was misleading as to the actual status of these activities.

A press release [redacted] references a [redacted] and goes on to describe to the planned "marketing, manufacturing and distribution of these non-medical devices." Your reference to these products as being "non-medical devices" is incorrect. This device would require FDA approval prior to marketing for the medical indications cited.

You should be aware that a sponsor or investigator, or any person acting on their behalf, is prohibited from promoting or test marketing an investigational device until after FDA has approved the device for commercial distribution. No claims can be made, either explicitly or implicitly, that the device is either safe or effective for the purposes for which it is being investigated. Press releases may not be used as promotional tools or as an attempt to commercialize a product prior to approval or clearance.

In [redacted] you submitted data from the [redacted] study to FDA in support of a [redacted]. As discussed above, significant deficiencies relating to that study were observed during the inspection and included, but were not limited to, your failure to monitor subject enrollment, informed consent, and data collection/reporting activities. There were issues with IRB review and approval. Source documents had not been audited/ reviewed to ensure that protocol requirements had been met and that the data were accurate. Deficiencies were also recognized during CDRH's Office of Device Evaluation review of your [redacted] submission.

We acknowledge receipt of Dr. Chaviano's letter, dated December 28, 2000, requesting that the referenced [redacted] be withdrawn. We understand that this was due to your need for additional time to respond to FDA open questions and that it is your intent to submit [redacted] during [redacted].

Even though the [redacted] was recently withdrawn, there are still several outstanding issues. During the inspection Dr. Chaviano was asked to provide a listing of all [redacted], including the [redacted] models, and provide their current location. This information was not available at the close of the inspection. Also, you were advised to review, for accuracy, all documents posted on your website and make corrections as necessary. As of the date of this letter, a response to these issues has not been received.

Within 15 working days of receipt of this letter, please provide this office with the requested information on the numbers/ locations of all [redacted]. Identify those sites conducting clinical and non-clinical trials with the [redacted] device. Also, confirm that information on your website has been reviewed for accuracy and corrected. Your response should be directed to the Food and Drug Administration, Center for Devices and Radiological Health, Office of Compliance, Division of Bioresearch Monitoring, 2098 Gaither Road, Rockville, Maryland 20850, Attention: Barbara A. Crowl. A copy of this letter has been sent to the Food and Drug Administration's Florida District Office, 555 Winderley Place, Suite 200, Maitland, Florida 32751. We request that a copy of your response also be sent to that office.

Please direct all questions concerning this matter to Ms. Crowl at (301) 594-4720, ext. 168.

Sincerely yours,

Charmaine Moore, RPh

for Larry D. Spears
Acting Director
Office of Compliance
Center for Devices and
Radiological Health