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AUG 2 2006

Food and Drug Administration
9200 Corporate Blvd.
Rockville MD 20850**WARNING LETTER**Via Federal Express

Veronica Jordan, Ph.D.
President and CEO
Medelle Corporation
500 West Cummings Park, Suite 2750
Woburn, MA 01801

Dear Dr. Jordan:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your firm from May 10 through May 12, 2006, by an investigator from the FDA New England District Office. The purpose of this inspection was to determine whether activities and procedures related to your participation in the clinical study titled "Protocol No. [REDACTED]" [REDACTED], for the [REDACTED] [REDACTED] complied with applicable federal regulations. The [REDACTED] is a device as that term is defined in section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. 321(h). This letter also requests prompt corrective action to address the violations cited and discusses your written response to the noted violations.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemptions (IDE), Premarket Approval (PMA) applications, and Premarket Notification submissions (510(k)) 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 prepared by the district office revealed serious violations of Title 21, Code of Federal Regulations (21 CFR) Part 812 -- Investigational Device Exemptions and Section 520(g) (21 U.S.C. 360j(g)) of the Act. At the close of the inspection, the FDA investigator presented an inspectional observations form FDA 483 for your review and discussed the observations listed on the form with you. The deviations noted on the FDA 483, your written response, and our subsequent review of the inspection report are discussed below:

1. Failure to allow FDA Investigators to inspect and copy all records relating to an Investigation [21 CFR 812.145 (b)].

You failed to permit inspection and copying of all records by the FDA investigator relating to the investigation for the [REDACTED]. Specifically:

- a.) On the afternoon of the first day of the FDA inspection, the FDA investigator was informed by Kathleen Karloff, Medelle's VP of Operations, that Dr. Claude Ranoux, the Medelle VP of Clinical Affairs, was leaving the next day to monitor the clinical study site in France, known as Site E, and would be taking the entire regulatory file for that site with him. The FDA investigator was not able to review the file completely before it was removed from the firm by Dr. Ranoux.
- b.) On the first day of the FDA inspection, the FDA investigator requested a current copy of the CV for each of the Medelle upper management personnel, and documents to verify the training that was promised in the firm's Corrective Action Plan (CAP) that was submitted to the FDA in April 2005. Specifically, the CAP stated that Ms. Karloff and Dr. Ranoux would be attending the SOCRA meeting in Philadelphia in April 2005 to receive training in FDA Clinical Trial Requirements, Regulations, Compliance, and GCP. Dr. Ranoux provided an old CV from 1995, which was before he began his employment with Medelle. He promised to provide an updated version that would indicate his current position and qualifications, but failed to do so. Dr. Ranoux's training verification was not found in Medelle's training files. He told the investigator that his certificate from the SOCRA conference was at home, and that he would get it. He failed to provide this document also. As noted above, Dr. Ranoux left for France the next day.

2. Failure to maintain accurate, complete, and current records relating to an investigation [21 CFR 812.140(b)].

You failed to maintain accurate, complete, and current records relating to the investigation for the [REDACTED]. This is a repeat violation from the last inspection and it was cited in the previous Warning Letter issued to you on 2/1/05. Examples of this failure include:

- a.) Much of the information on Medelle's master enrollment log does not agree with the source information on the logs faxed to the firm by the study sites. For example:
 - i. For Site A, dates of consent, [REDACTED] are inconsistent for 11 of 21 subjects.
 - ii. For Site C, dates of consent, [REDACTED] are inconsistent for 3 of 11 subjects.
 - iii. For Site D, dates of [REDACTED] are inconsistent for 3 of 6 subjects.
- b.) Site E is the study site in France, and there is no information entered on Medelle's master enrollment log form other than [REDACTED].

- c.) Device accountability records are incomplete and inaccurate:
 - i. For site A, the 4/18/06 monitoring report lists 18 devices received, of which only 17 are accounted for (16 devices [REDACTED] and 1 device on site).
 - ii. The shipping log updated on 5/9/06 notes 18 devices were sent to site A on 11/28/05 and 7 devices were sent to site A on 3/29/06, for a total of 25 devices shipped to that site. As noted above, the 4/18/06 monitoring report notes that only 18 devices were recorded as received at that site, with only 1 device still at the site and 16 [REDACTED]. This leaves a discrepancy of 8 unaccounted devices.
- d.) Adverse event reports were incomplete. Specifically, two Adverse Device Effect (ADE) reports that were found in the study records were initial reports that were missing relevant information. There was no indication that followup information had been requested from the study sites in order to fully evaluate the events, or that evaluations of the events had been performed by Medelle.

3. Failure to immediately conduct an evaluation of all unexpected adverse device effects [21 CFR 812.46(b)].

You failed to immediately conduct an evaluation of unexpected adverse device effects that were reported to you by clinical investigators. Specifically, your records indicate that Medelle has received two ADE reports since the study started in January 2006. The two reports present at Medelle were incomplete initial reports from the study sites. There was no documentation in the Medelle files to verify: (1) that any investigation was conducted on these events to obtain the followup information or (2) that Medelle evaluated relationship of the events to the study device. The two ADEs were as follows:

- a.) A subject at Site A was hospitalized for respiratory difficulties on 4/14/06, 3 days after [REDACTED]. No other information was recorded on the form, and the report was unsigned and undated. There was no evidence that Medelle attempted to obtain the followup information, or that any evaluation of the event was made to determine relationship of the event to the device.

In your written response to this observation, dated May 23, 2006, you included followup information that was received from the CI, and noted that the ADE was closed by the CI on 5/15/06. The CI said the subject was first diagnosed with [REDACTED] which can cause respiratory problems. The diagnosis was later changed to pneumonia, and the CI assessed the relationship of the device to the event as “not suspected.”

Medelle’s response included a commitment to follow up on all ADEs in the future, and the monitoring SOP was modified to clarify handling of ADEs. This response is inadequate. There is still no documentation of any evaluation of the event by someone at Medelle who would be qualified to perform that task. The changes to the SOP also do not address the means by which Medelle will evaluate an adverse event (AE) to determine if it meets the 10-day reporting criteria as an unexpected ADE, if the event is related to the device or study procedure, or if the event presents an unreasonable risk to study subjects which would require

termination of the study.

- b.) A subject at Site D was hospitalized on 4/1/06, the same day the device [REDACTED]. The report form was signed by the clinical investigator and dated 4/5/06, but the fax date on the form read 5/10/06. The form noted that the subject experienced abdominal pain, nausea, diaphoresis, and near syncope following [REDACTED], and was hospitalized overnight. The CI assessed the relationship of the device to the event as “not suspected.” There was no evidence that Medelle attempted to obtain followup information, or that any evaluation of the event was made to determine relationship of the event to the device.

In your written response to this observation, you included a telephone contact form from Dr. Ranoux that was dated as completed on 4/2/06, but that was not included in the sponsor records at the time of the FDA inspection. The form noted that the event was thought to be a result of [REDACTED]. Her condition stabilized after administration of fluids, and the subject was released from the hospital the next day. Medelle’s response again included a commitment to ensure that all documentation is filed in the study records, and to revise the SOP. This response is not adequate as noted above in item 3-a.

In addition, you failed to adhere to your SOP QMS-005 – “Clinical Monitoring Procedure” which states that “Any Serious Adverse Device Event must be recorded by the Investigator on the Adverse Event Form and must be reported to Medelle immediately and must be followed up by a fax to Medelle within 24 hours of learning of the event. Medelle must report this event to all other Investigators in the study.” There is no documentation present in Medelle’s files that these two events were reported to the other study sites.

4. Failure to secure the investigators’ compliance with the investigational plan and applicable FDA regulations [21 CFR 812.46(a)].

You failed to ensure that all clinical investigators participating in the study adhered to the investigational plan and FDA regulations. An example of this failure includes:

- a.) An ADE report was submitted to Medelle outside the timeframe required by your SOP QMS-005 – “Clinical Monitoring Procedure.” Specifically, the procedure requires that “Any Serious Adverse Device Event must be recorded by the Investigator on the Adverse Event Form and must be reported to Medelle immediately and must be followed up by a fax to Medelle within 24 hours of learning of the event.” The report present in Medelle’s files indicates that the ADE that occurred at Site D on 4/1/06 was not faxed to Medelle until 5/10/06. There is no documentation in the study files to indicate any action taken by Medelle to correct this non-compliance issue.

The violations described above are not intended to be an all inclusive list of problems that may exist with your clinical study. It is your responsibility as a study sponsor to ensure compliance with the Act and applicable regulations.

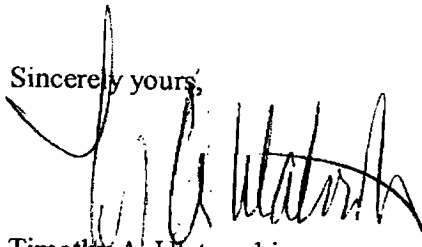
Within fifteen (15) working days of receiving this letter, please provide written documentation of the additional actions you have taken or will take to correct these violations and prevent the recurrence of similar violations in current or future studies for which you are the study sponsor. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to you. Please send your response to:

Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance, Division of Bioresearch Monitoring, HFZ-311
9200 Corporate Boulevard, Rockville, Maryland 20850
Attention: Ms. Doreen Kezer, Chief, Special Investigations Branch.

A copy of this letter has been sent to FDA's New England District Office, One Montvale Ave., 4th Floor, Stoneham, MA 02180. We request that a copy of your response also be sent to that office.

If you have any questions, please contact Ms. Doreen Kezer at 240-276-0125 or at Doreen.Kezer@fda.hhs.gov.

Sincerely yours,



Timothy A. Ulatowski
Director
Office of Compliance
Center for Devices and
Radiological Health