



U.S. Food and Drug Administration
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Inspections, Compliance, Enforcement, and Criminal Investigations

Endogastric Solutions, Inc. 8/1/12



Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Ave.
Silver Spring, MD 20993-0002

WARNING LETTER

JUN 8, 2012

VIA UNITED PARCEL SERVICE

Michael M. Kleine
President & Chief Executive Officer
Endogastric Solutions, Inc.
555 Twin Dolphin Drive, Ste. 650
Redwood City, CA 94065

Dear Mr. Kleine:

The purpose of this Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at Endogastric Solutions, Inc., from February 10, 2012, to February 29, 2012, by an investigator from the FDA San Francisco District Office. This inspection was conducted to determine whether your firm's activities as sponsor of the clinical study, "A Randomized Controlled Trail of **(b)(4)** Patients to Reduce Regained Weight," Investigational Device Exemption (IDE) **(b)(4)**, complied with applicable federal regulations. **(b)(4)** 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), because it is intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or function of the body. This letter also requests prompt action to address the observed violations and discusses your firm's written response to the violations dated March 12, 2012.

The inspection was conducted under a program designed to ensure that data and information contained in requests for IDEs, premarket approval applications, and premarket notification 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 prepared by the district office revealed several violations of Title 21, Code of Federal Regulations (CFR) Part 812 - Investigational Device Exemptions, which concerns requirements prescribed under section 520(g) of the Act, 21 U.S.C. § 360j(g).

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 violations noted

on the Form FDA 483, your firm's March 12, 2012, written response, and our subsequent review of the inspection report are discussed below:

1. Failure to provide investigators with the information they need to conduct the investigation properly, ensure proper monitoring of the investigation, and ensure that any reviewing IRB and FDA are promptly informed of significant new information about an investigation. [21 CFR 812.40]

Sponsors are responsible for providing investigators with the information that they need to conduct the investigation properly, ensuring proper monitoring of the investigation, and ensuring that any reviewing Institutional Review Board (IRB) and FDA are promptly informed of significant new information about an investigation. Examples of your firm's failure to meet these requirements include, but are not limited to, the following:

a. Endogastric Solutions failed to follow the monitoring schedule as specified in the protocol (at least every 6-8 weeks or enrollment of every 10 subjects, whichever occurs first).

Site 01 (b)(6):

- Enrolled 14 subjects between the September, 2009 (day not specified) and November 17, 2009 monitoring visits.
- Enrolled 39 subjects between the November 17, 2009, and July 26, 2010, monitoring visits (34 weeks elapsed).
- 22 weeks elapsed between the December 1, 2010, and May 10, 2011, monitoring visits.

Site 02 (b)(6)

- Enrolled 14 subjects between the December 9, 2009, and July 13, 2010, monitoring visits (30 weeks elapsed).

b. Endogastric Solutions failed to promptly inform the reviewing IRB and FDA of significant new information about its investigation, which was put on hold due to questionable effectiveness of the **(b)(4)** investigational device. Specifically, Endogastric Solutions notified **(b)(6)** during a meeting on November 30, 2010, and notified **(b)(6)** during a meeting on December 1, 2010, that enrollment was being put on hold. However, the IRB was not notified until April 2011 about this decision and FDA was not notified at all.

c. Endogastric Solutions failed to provide clinical investigators with the information that they need to conduct the investigation properly. Specifically, Endogastric Solutions did not provide for **(b)(6)**.

Lack of proper monitoring can put subjects at risk because monitoring can identify problems or deviations that occur during the study. These include: potential defects with the device and its performance; protocol deviations that may affect subject safety and data integrity; and adverse events, which can also affect subject safety. Proper monitoring ensures that any adverse events and safety concerns have been captured appropriately so that the sponsor can convey necessary information to all sites. Delaying monitoring visits can expose subjects to unnecessary risks if the investigator failed to promptly communicate events or safety concerns to the sponsor.

In addition, your firm's delay in notifying the IRB and failure to notify FDA about putting enrollment on hold are clinically-significant violations. The lack of timely information compromises the IRB's ability to ensure that appropriate human subject protection measures are in place for the enrolled subjects. In addition, failure to notify FDA limits the agency's ability to ensure that the enrolled subjects are adequately protected.

Lastly, your firm's failure to provide **(b)(6)** may have compromised subject safety and data quality. If an investigator has not received adequate training to conduct the study, the safety of study subjects may be placed at risk and the quality of the data collected may not be assured.

Your firm's March 12, 2012, written response is inadequate because the preventative actions are not sufficiently detailed. Please provide a preventative action plan detailing how management oversight will ensure that monitors are less independent and more accountable to prevent recurrence of improper monitoring. Additionally, describe the title of personnel who will be responsible (e.g., clinical project manager) for reporting significant new information to the IRB and FDA and the timing of those reports. Lastly, for investigators who are absent when training is provided, describe how these investigators will receive the training they missed.

2. Failure to notify FDA within 30 working days of termination of an investigation of a significant risk device. [21 CFR 812.150(b)(7)]

Sponsors of a significant risk device are responsible for notifying FDA within 30 working days of the completion or termination of the investigation. Endogastric Solutions **(b)(4)** investigational device is a significant risk device as defined in 21 CFR 812.3. Your firm failed to notify FDA within the required timeframe. Specifically, on June 2, 2011, **(b)(6)** and **(b)(6)** were notified that the study was being "cancelled"; however, FDA was not notified of study termination until July 15, 2011 (43 days later).

Your firm's delay in notifying FDA that the study had been terminated compromised FDA's ability to evaluate the reasons for the termination and to determine, in a timely manner, whether any measures were necessary to ensure safety of the enrolled subjects. A delay of this kind can have a clinically significant impact on subject safety.

Your firm's March 12, 2012, response regarding notification to FDA is inadequate because it is not sufficiently detailed. Please identify the title of personnel who will report information (e.g., clinical project manager) to FDA and provide a detailed preventative action plan to describe how you will prevent recurrence. 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 15 working days of receiving this letter, please provide documentation of the additional actions that you have taken or will take to correct these violations and to prevent the recurrence of similar violations in current or future studies for which you are the study sponsor. Any submitted preventative action plan must include projected completion dates for each action to be accomplished as well as a plan for monitoring the effectiveness of your preventative actions. Failure to respond to this letter and take appropriate preventative action could result in the FDA taking regulatory action without further notice to you.

Your response should reference "CTS# **(b)(4)**" and be sent to:

Attention: Anne Hawthorn
Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
10903 New Hampshire Avenue
Building 66, Room 3504
Silver Spring, Maryland 20993-0002

A copy of this letter has been sent to FDA's San Diego District Office, 1431 Harbor Bay Pkwy, Alameda, CA 94502-7070. Please send a copy of your response to that office.

The Division of Bioresearch Monitoring has developed introductory training modules in FDA-regulated device clinical research practices, which are available on the FDA website. The modules are for persons involved in FDA-regulated device clinical research activities. These modules are located at the following website address: <http://www.fda.gov/Training/CDRHLearn/ucm162015.htm>¹.

If you have any questions, please contact Anne Hawthorn at (301) 796-6561 or anne.hawthorn@fda.hhs.gov.

Sincerely yours,
/S/
Steven D. Silverman
Director
Office of Compliance
Center for Devices and
Radiological Health

Page Last Updated: 09/21/2012

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1. <http://www.fda.gov/Training/CDRHLearn/ucm162015.htm>