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Inspections, Compliance, Enforcement, and Criminal Investigations

Synergy Health Concepts, Inc 9/5/12



Department of Health and Human Services

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

WARNING LETTER

September 5, 2012

VIA UNITED PARCEL SERVICE

Michael A. Arata, M.D.
President/Principal Investigator
Synergy Health Concepts, Inc.
P.O. Box 12139
Newport Beach CA 92660

Dear Dr. Arata:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at Synergy Health Concepts, Inc. (Synergy Health) from April 10, 2012, to May 15, 2012, by an investigator from the FDA Los Angeles District Office. This inspection was conducted to determine whether activities by your firm as sponsor of the clinical studies: Venous Obstruction in Neurodegenerative Disorders Research Registry study (Registry study) and Radiographic and Intravascular (IVUS) Evaluation of Venous Morphology during CCSVI Treatment study (IVUS study), and your activities as clinical investigator of the IVUS study, comply with applicable federal regulations. The percutaneous transluminal angioplasty balloon dilation catheters and stents used in the Registry and IVUS studies are devices 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 they are 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 corrective action to address the violations cited and discusses the written response dated June 5, 2012, to the noted violations.

The inspection was conducted under a program designed to ensure that data and information contained in requests for Investigational Device Exemption (IDE), Premarket Approval (PMA) 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 serious violations of Title 21, Code of Federal Regulations (CFR) Part 812-Investigational Device Exemptions, and Part 50-Protection of Human Subjects, 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, John Joseph Hewett, M.D., Secretary and sub-investigator of the IVUS study, and Francis DeBarge-Igoe, RN, BSN, Practice Administrator. The deviations noted on the Form FDA 483, your written response, and our subsequent review of the inspection report, are discussed below:

Synergy Health in its role as a sponsor:

1. Failure to submit an application to the FDA and obtain IRB and FDA approval prior to allowing subjects to participate in an investigation [21 CFR 812.20, 21 CFR 812.40, and 21 CFR 812.42]

A sponsor must submit an IDE application for a significant risk device to the FDA (21 CFR 812.40), and shall not begin an investigation, or part of an investigation, until an Institutional Review Board (IRB) and FDA have both approved the application or supplemental application relating to the investigation or part of an investigation (21 CFR 812.42). Your firm failed to adhere to the above-stated regulations. An example of your firm's failure includes, but is not limited to, the following:

Your firm failed to submit an IDE application to the FDA and to obtain FDA approval before allowing subjects to participate in the Registry and IVUS studies. These clinical research studies investigated the safety or effectiveness of angioplasty balloon devices and stents for percutaneous transluminal angioplasty for treating extracranial venous obstructive lesions and their influence on the clinical outcomes of multiple sclerosis patients. Investigating angioplasty balloon devices and stents through the Registry and IVUS studies to determine the safety or effectiveness of this unapproved and uncleared use constitutes an investigation under 21 CFR 812.2. Accordingly, the angioplasty balloon devices and stents are investigational devices. Because using these devices to investigate a treatment for extracranial venous obstructive lesions and its affect on multiple sclerosis patients presents a potential for serious risk to the health, safety, or welfare of the subjects, the devices are significant risk devices, as defined in 21 CFR 812.3(m). As a result, your firm must submit an IDE application to FDA to use the significant risk devices in an investigation, as required by 21 CFR 812.20. This helps ensure that the rights, safety, and welfare of human subjects are adequately protected and that the trial is conducted in a way that ensures the integrity of the clinical data.

Your firm's Registry study administered an investigational device for percutaneous transluminal angioplasty on at least **(b)(4)** subjects without submitting an IDE application to FDA and obtaining FDA approval (21 CFR 812.20).

In addition, your firm's IVUS study administered an investigational device for percutaneous transluminal angioplasty on at least **(b)(4)** human subjects without submitting an IDE application to FDA and obtaining FDA approval (21 CFR 812.20).

Failure to furnish any notification or other material or information required by or under section 520(g) is a prohibited act under section 301(q)(1)(B) of the Act, 21 U.S.C. § 331(q)(1)(B).

2. Failure to maintain accurate, complete, and current device shipment records [21 CFR 812.140(b)(2) and 21 CFR 812.140(d)].

A sponsor is responsible for maintaining accurate, complete, and current records relating to the shipment and disposition of the devices. 21 CFR 812.140(b)(2). Such records shall include the name and address of the consignee, type and quantity of device, date of shipment, and batch number or code mark. Also, a sponsor is responsible for maintaining the records required by 21 CFR 812.140(b) during the investigation, for a period of 2 years after the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of

supporting a PMA application, whichever is later (21 CFR 812.140(d)). Specifically, your firm failed to maintain and could not produce during the inspection the device accountability records described above because, as noted in your **(b)(4)**, affidavit, your firm is unable to **(b)(4)**.

These records are necessary to ensure that the use of investigational devices is consistent with the conduct of clinical research, limited to the investigational use, and traceable to individual subject exposure.

As a clinical investigator:

1. Failure to ensure that informed consent was obtained in accordance with 21 CFR Part 50 [21 CFR 50.27(a)].

Informed consent shall be documented by the use of a written consent form approved by the IRB and signed and dated by the subject or the subject's legally authorized representative at the time of consent. You failed to ensure that informed consent was obtained from subjects and documented in accordance with 21 CFR Parts 50 and 56. Specifically, in the IVUS study, you failed to use the IRB-approved written consent form dated **(b)(4)**, for at least **(b)(4)** subjects and the IRB-approved written consent form dated **(b)(4)**, for at least **(b)(4)** subjects.

A valid informed consent process ensures that research subjects have a clear understanding of risks of participation in a research protocol, have sufficient opportunity to consider whether to participate in the study, and make an informed decision if they decide to participate.

2. Failure to maintain accurate, complete, and current records related to your participation in the investigation [21 CFR 812.140(a)(2); 21 CFR 812.140(a)(3)(iii); and 21 CFR 812.140(d)].

As a clinical investigator, you are responsible for maintaining accurate, complete, and current records of study-related matters, including receipt and use of devices that relate to the type and quantity, dates of receipt, batch number or code mark (21 CFR 812.140(a)(2)). You are also required to maintain records of each subject's case history and exposure to the device (21 CFR 812.140(a)(3)(iii)). Also, a clinical investigator is responsible for maintaining the records required by 21 CFR 812.140(a) during the investigation, for a period of 2 years after the date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a PMA application, whichever is later (21 CFR 812.140(d)). Specifically, between **(b)(4)**, and **(b)(4)**, you failed to maintain and could not produce during the inspection the **(b)(4)** records, described above, in the IVUS study for at least **(b)(4)** subjects.

These records are necessary to ensure and document that the use of investigational devices is limited to the clinical study and that subjects can be notified in the event of any need for additional follow-up, e.g., exposure to an unanticipated risk.

Response to FDA Form 483:

The response submitted June 5, 2012, on your behalf by C. Humphrey and Associates P.A., states that FDA has no jurisdiction to inspect or review Synergy Health's studies. This is incorrect. The Registry and IVUS studies are subject to FDA jurisdiction because they involve the investigational use of medical devices by experts qualified by scientific training and experience to investigate the safety and effectiveness of such devices (see section 520(g) of the Act, 21 U.S.C. § 360j(g)).

Synergy Health must apply for an IDE in accordance with the regulations in 21 CFR Part 812 to conduct these studies. The June 25, 2012 response is inadequate in that:

1. it does not acknowledge that a clinical study of a significant risk device requires an IDE and FDA approval of the IDE before allowing subjects to participate, as required by 21 CFR 812.20 and 812.42;

2. it does not acknowledge that clinical investigators must obtain and document informed consent using an IRB-approved informed consent document, as required by 21 CFR 50.27; and
3. it does not address how you will correct the failure to maintain adequate device shipment records and the records related to your participation in these studies.

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

Within 15 working days of receiving this letter, please provide documentation of the actions that you firm and 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 your firm is the study sponsor and you are a clinical investigator. Any submitted corrective action plan must include projected completion dates for each action to be accomplished as well as a plan for monitoring the effectiveness of all corrective actions. Failure to respond to this letter and take appropriate corrective action could result in the FDA taking regulatory action without further notice to your firm or you.

Your response should reference CTS - EC120258/E001 and be sent to:

Attention: Anne T. 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 Los Angeles District Office, 19701 Fairchild, Irvine, CA 92612. 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 T. 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

cc:

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