



[Home](#) > [Inspections, Compliance, Enforcement, and Criminal Investigations](#) > [Enforcement Actions](#) > [Warning Letters](#)

Inspections, Compliance, Enforcement, and Criminal Investigations

Isis Services, LLC 7/18/11



Department of Health and Human Services

Public Health Service
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

WARNING LETTER

July 18, 2011

VIA UNITED PARCEL SERVICE

Jon N. Cammack, Ph.D., DABT
President and Chief Executive Officer
ISIS Services, LLC
1031 Bing Street
San Carlos, CA 94070

Dear Dr. Cammack:

This Warning Letter is to inform you of objectionable conditions observed during the Food and Drug Administration (FDA) inspection conducted at your nonclinical laboratory, ISIS Services, LLC, in San Carlos, CA, from March 22, 2011, to April 7, 2011, by investigators from the FDA's San Francisco District Office. The FDA inspected the following nonclinical laboratory studies conducted by your facility: "[b](4)," and "[b](4)," involving the [b](4) System, Investigational Device Exemption (IDE)[b](4)]. The purpose of this inspection was to determine whether activities and procedures related to your participation in the nonclinical studies complied with applicable federal regulations. The [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 USC 321(h). This letter also discusses written responses from Jorge L. Garcia, DVM, Founder and Chief Scientific Officer, dated April 19, 2011, and May 24, 2011, to the noted observations on the Form FDA 483.

This inspection is a part of FDA's Bioresearch Monitoring Program, which includes inspections designed to verify compliance with Title 21 of the Code of Federal Regulations (21 CFR), Part 58 - Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies, which are requirements prescribed under section 520(g) (21 USC 360j(g)) of the Act. The regulation at 21 CFR Part 58 applies to nonclinical laboratory studies that support or are intended to support applications for research or marketing permits for products regulated by FDA [21 CFR 58.1(a)].

Our review of the inspection report prepared by the district office revealed serious violations of 21 CFR Part 58 - Good Laboratory Practice for Nonclinical Laboratory Studies. At the close of the inspection, the FDA investigators presented an inspectional observations Form FDA 483 to Dr. Garcia for review and discussed the observations listed on the form with Dr. Garcia. The deviations noted on the Form FDA 483, your company's written responses, and our subsequent review of the inspection report are discussed below:

Failure to ensure that each individual engaged in the conduct of or responsible for supervision of a nonclinical laboratory study has education, training, and experience, and failure to ensure that the testing facility maintains a current summary of training and experience. [21 CFR 58.29(a) and (b)]

Each individual engaged in the conduct of, or responsible for, the supervision of a nonclinical laboratory study shall have education, training, and experience, or a combination thereof, to enable that individual to perform the assigned functions. Additionally, each testing facility shall maintain a current summary of training and experience and a job description for each individual engaged in or supervising the conduct of a nonclinical laboratory study. Examples of your failure to adhere to the above-stated regulations include, but are not limited to, the following:

- [b](6)]. [b](6) Specialist, [b](6)., and [b](6). (Operating Room Technicians), and [b](6). [b](6) Technician lacked annual technical evaluations required by your facility's standard operating procedures (SOPs), "[b](4) Training and Evaluation Program," "[b](4) Technician Training and Evaluation Program," and "[b](4) Technician Training Program." Specifically, there are no evaluations for the above employees during the following time periods:
 - [b](6) - 2006, 2007, 2008, 2010;
 - [b](6) - 2003, 2004, 2005, 2006, 2007, and 2008;
 - [b](6) - 2005, 2006, 2007, and 2008;
 - [b](6) - 2007, 2008 and 2010; and
 - [b](6) - 2008, 2009, and 2010.

- Facility management failed to maintain training documentation of the "[(b) (4)] Training Course" required by "Study Directorship: A [(b) (4)]," procedures 3004 and 33791 for [(b) (6)] [(b) (6)] study [(b) (6)] of ANS 1376, [(b) (6)] [(b) (6)] study director of ANS 1376 and [(b) (6)] of ANS 1393, and [(b) (6)] (replacement study director of ANS 1393).
- Facility management failed to maintain GLP training records as required by your SOP for the following individuals engaged in or supervising the conduct of a nonclinical laboratory study:
 - [(b) (6)], and [(b) (4)], study [(b) (6)] for ANS 1376 and 1393, and V.A., [(b) (6)] I Specialist 2008 and 2009 GLP training records.
- Facility management failed to maintain the curriculum vitae (CV) for [(b) (6)].

In your company's April 19, 2011, response, Dr. Garcia provided certificates of training for study [(b) (6)]. And [(b) (6)]; however, he failed to provide training certificates for [(b) (6)], and [(b) (6)]. Furthermore, he stated, "After discussing this observation with our team, it was clear training and evaluation have been done more often, in fact, on a continuous basis. Because of this, we have updated that SOP to reflect current practice." However, he failed to provide certificates of training for [(b) (6)], and [(b) (6)]. Please provide a copy of dates of training and a list of staff trained.

Failure of testing facility management and study directors to fulfill their responsibilities. [21 CFR 58.31(a), 58.31(f), and 58.33(f)]

For each nonclinical laboratory study, testing facility management shall designate a study director before the study is initiated and ensure that personnel clearly understand the functions they are to perform. The study director shall ensure that all raw data, documentation, protocols, specimens, and final reports are transferred to the archives during or at the close of the study.

- ISIS permitted the sponsor to designate study directors prior to initiation of the ANS 1376 and 1393 studies. ISIS then failed to provide study personnel with proper instructions. As a result, the study directors failed to prepare final reports and transfer all study records.

Your company's April 19, 2011, response included an updated SOP for Study Directorship: [(b) (6)], effective date April 18, 2011. The SOP lists criteria for [(b) (6)] a study director. However, Dr. Garcia failed to include documentation to show that study directors were trained on the SOP and that their personnel records are up-to-date. Please provide a copy of dates of training, list of staff trained, and evidence of their updated training records.

We emphasize that Isis Services LLC is a testing facility and is responsible for designating a study director affiliated with Isis for each study. In addition, it is your responsibility to ensure that study directors are properly trained and training documents are properly recorded and maintained.

- The study directors did not ensure that all raw data, final study reports, and study-related correspondence were transferred to the archives. Examples of information that were not archived include, but are not limited to, the following:
 - For ANS 1376 and 1393, correspondence between the study directors and testing facility personnel, and
 - Final study reports for ANS 1313, 1338, 1375, 1376, and 1393.

In your company's April 19, 2011, response, Dr. Garcia stated that some of the studies are still open pending receipt of a final study report from the study director, all study directors were contacted, and failure to respond will result in non-compliance and potential reassignment of the study director. In the response dated May 24, 2011, Dr. Garcia provided copies of final reports for ANS 1376 and 1393. However, he failed to provide SOPs for study director non-compliance and potential reassignment and an updated master schedule with projected end dates. Please provide a copy of the new SOPs as well as documentation of the date implemented, dates of training, and a list of staff trained. In addition, provide an updated master schedule listing of all FDA-regulated device nonclinical laboratory research for the last five years, including the name of the study and test article, the names of the study director and sponsor, and the current status of the studies for the last five years.

Failure of the quality assurance unit to determine that no deviations from approved protocols or SOPs were made without proper authorization and documentation, and to review the final study report to assure that such report accurately describes the methods and SOPs. [21 CFR 58.35(b)(5) and (6)]

The quality assurance unit (QAU) shall determine that no deviations from approved protocols or standard operating procedures were made without proper authorization and documentation. In addition, the QAU shall review the final study report to assure that it accurately describes the methods and standard operating procedures, and that the reported results accurately reflect the raw data of the nonclinical laboratory study. Examples of these failures include, but are not limited to, the following:

- There is no documentation to show that the QAU reviewed the final study reports for ANS 1376 and 1393.
- [(b) (6)] wrote the contributing scientist reports for ANS 1376 and 1393; however, there is no documentation of him participating in the studies, nor were there any amendments adding him to the studies.

In your company's April 19, 2011, response, Dr. Garcia explained that the QAU did review and sign off on the contributing scientist reports prior to release to the sponsor, but the sponsor has yet to submit the final study report even though the firm has made several attempts to retrieve it. However, he failed to provide SOPs to address the QAU's responsibilities in the event when the sponsor fails to produce the final report or the actions that the QAU will take to ensure that the final report is retrieved from the sponsor and reviewed prior to the end of the study. Furthermore, he recognized that no documentation was available to show [(b) (6)]'s relationship to the studies, and an amendment to the contributing scientist report explaining [(b) (6)]'s responsibilities to the studies was filed on March 29, 2011. However, your company failed to provide SOPs explaining preventive actions for recurrence of this issue. Please provide a copy of the new SOPs as well as documentation of the date implemented, dates of training, and a list of staff trained.

Failure to retain final reports generated as a result of the nonclinical laboratory study. [21 CFR 58.190(a)]

- Final reports generated as a result of a nonclinical laboratory study must be retained. Your facility did not retain copies of final reports for ANS 1313, 1338, 1375, 1376, and 1393.

We acknowledge that in your company's May 24, 2011, response, Dr. Garcia provided copies of final reports for ANS 1376 and 1393 as indicated earlier; however, we note that these final reports were not available during the inspection of your facility.

Failure to provide a sufficient number of animal rooms or areas to assure proper quarantine of animals. [21 CFR 58.43(a)(3)]

A testing facility shall have a sufficient number of animal rooms or areas, as needed, to assure proper quarantine of animals. An example of this failure includes, but is not limited to the following:

- Your facility does not have a dedicated quarantine room to assure proper separation of quarantined animals.

Your company's responses are inadequate. You failed to include a copy of an updated floor plan of your facility to show that you have a dedicated quarantine room for proper separation of animals. Please provide an updated floor plan of your facility to show dedicated quarantine rooms.

The violations described above are not intended to be an all-inclusive list of problems that may exist with nonclinical laboratory studies conducted by your facility. It is your responsibility as a testing facility to ensure compliance with the Act and all applicable regulations.

You must address these violations and establish procedures to ensure that any ongoing or future studies are conducted in compliance with the Act and applicable FDA regulations.

Within fifteen working days of receipt of this letter, you must provide written documentation of the specific additional corrective actions that you have taken or will take to address all of the violations noted above and to prevent recurrence of similar violations in current or future nonclinical laboratory studies conducted by your facility. Any submitted corrective action plan must include projected completion dates for each action to be accomplished. In addition, please provide a complete list of all nonclinical laboratory research of FDA-regulated devices for the last five years, including the name of the study and the test article, the names of the study director and sponsor, and the current status of the studies.

We will review your company's response and determine whether it is adequate. Failure to respond to this letter and take appropriate corrective action could result in FDA taking regulatory action without further notice to you, including disqualification proceedings in accordance with 21 CFR 58.202.

Your response should reference "CTS # G080182/E004" and be sent to:

Attention:
Linda D. Godfrey
Food and Drug Administration
Center for Devices and Radiological Health
Office of Compliance
Division of Bioresearch Monitoring
10903 New Hampshire Avenue
Building 66, Room 3462
Silver Spring, Maryland 20993-0002

A copy of this letter has been sent to the San Francisco District Office, 1431 Harbor Bay Parkway, Alameda, CA 94502. Please send a copy of your response to that office.

For further information about the Bioresearch Monitoring program, please visit our Internet homepage. Valuable links to related information are included at this site. <http://www.fda.gov/cdrh/comp/bimo.html>¹.

If you have any questions, please contact Branch Chief, Linda D. Godfrey, by telephone at (301) 796-5490 or via email at Linda.Godfrey@fda.hhs.gov.

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

Links on this page:

1. <http://www.fda.gov/cdrh/comp/bimo.html>