Inspections, Compliance, Enforcement, and Criminal Investigations

Amresco LLC 2/26/13

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Cincinnati District Office
Central Region
6751 Steger Drive
Cincinnati, OH 45237-3097
Telephone: (513) 679-2700
FAX: (513) 679-2771

February 26, 2013

WARNING LETTER
CIN-13-392384-15

VIA UPS

Manuel A.H. Brocke-Benz
President and CEO
VWR International, LLC
Randor Corporate Center
Building 1, Suite 200
100 Matsonford Road
Radnor, PA 19087-8660

Dear Mr. Brocke-Benz:

During an inspection of your firm, Amresco LLC located at 30175 Solon Industrial Parkway, Solon, OH 44139,on October 15 through December 18, 2012, an investigator from the United States Food and Drug Administration (FDA) determined that your firm is a contract manufacturer of in-vitro diagnostic kit reagents. Under section 201(h) of the Federal Food, Drug, and Cosmetic Act (the Act), 21 U.S.C. § 321(h), these products are devices 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 inspection revealed that these devices are adulterated within the meaning of section 501(h) of the Act (21 U.S.C. § 351(h)), in that the methods used in, or the facilities or controls used for, their manufacture, packing, storage, or installation are not in conformity with the Current Good Manufacturing Practice (CGMP) requirements of the Quality System (QS) regulation found at Title 21, Code of Federal Regulations (CFR), Part 820. We received a response from Michael J. Mascali, President of Amresco LLC dated January 7, 2013, concerning our investigator's observations noted on the Form FDA 483, List of Inspectional Observations (FDA 483) that was issued to you. We address this response below, in relation to each of the noted violations. These violations include, but are not limited to, the following:

1. Failure to adequately validate a process whose results cannot be fully verified by subsequent

inspection and test, as required by 21 CFR 820.75(a). Specifically,

a) The mixing instructions for Reagent A and Reagent B, which are part of **(b)(4)** in-vitro diagnostic kits, have not been quantified or validated for the following:

- A mixing time range has not been established for the addition of several raw materials used to manufacture Reagent A and Reagent B. For example, Validation Protocol P-05-002 for Reagent A, and P-05-001 for Reagent B have numerous ambiguous mixing instructions of "allow to mix until dissolved".

- The mixing speed of 50%-70% has not been validated. The validation studies for Reagent A and Reagent B were conducted using a mixing speed of 60%.

- The mixing time of 15-60 minutes has not been validated for Reagent A and Reagent B.

b) Two out of specification pH results documented during the validation of Reagent A were crossed out and new results with acceptable readings were documented. An investigation and the steps taken in order to achieve an acceptable pH were not documented.

c) Ten of the fifteen out of specification testing results for cap torque documented during the validation of Reagent B were accepted as is with no investigation or corrective actions taken.

d) The automated line filling system, used to fill, cap and label in-vitro diagnostic reagents, has not been validated for the capping operation. A review of three device history records revealed the following out-of-specification (OOS) results for the torque removal in-process checks: 82% OOS for lot 2372C466; 87% OSS for lot 1572C237; and 88% OOS for lot 3192C242.

The response dated January 7, 2013 cannot be assessed at this time. Your response states that containment measures will be implemented by February 4, 2013 and will remain in effect until these processes are revalidated. Additionally, all process validation procedures and all process validations will be reviewed and revised as necessary to ensure compliance with the applicable regulations. Please inform us, if the timeframes listed in your response cannot be met.

2. Failure to establish and maintain procedures for analyzing processes, work operations, concessions, quality audit reports, quality records, service records, complaints, returned product, and other sources of quality data to identify existing and potential causes of nonconforming product, or other quality problems, as required by 21 CFR 820.100(a) (1). Specifically,

During the manufacturing of in-vitro diagnostic reagents, materials that are rejected then reworked for issues such as labeling, capping issues, fill volume, and leaking are not being captured as quality data for potential corrective actions.

3. Failure to establish and maintain procedures to control product that does not conform to specified requirements, as required by 21 CFR 820.90(a). Specifically,

A total of 6 of the 9 device history records reviewed had out of specification results for the torque removal of the cap. These out of specification products were not identified as a nonconforming product, segregated, dispositioned and trended as required by your "Control of Non-Conforming Product Procedure", QSP 8.6. All of these products were distributed and two complaints have been received on leaking vials from these lots.

The response dated January 7, 2013 cannot be assessed at this time. Your response states that all procedures relating to control of nonconforming product and device history record will be reviewed for product release. Additionally, a review of torque specifications to ensure proper use of application and/or removal torque is employed and the associated acceptable torque ranges clearly documented will be completed. Please inform us, if the timeframes listed in your response cannot

be met.

4. Failure to establish and maintain procedures to ensure that sampling methods are adequate for their intended use and to ensure that when changes occur the sampling plans are reviewed, as required by 21 CFR 820.250(b). Specifically,

The sampling method of taking 3 samples at 15 minutes and 60 minutes during manufacturing from the top, middle and bottom of the tank for a total of 18 samples during the validations of Reagents A and B, which are part of **(b)(4)** in-vitro diagnostic kits, is not based on a valid statistical rationale.

The response dated January 7, 2013 is not adequate. Although the response states that manufacturing processes will be revalidated, it does not address the statistical rationale for your sampling plans.

5. Failure to define the type and extent of control to be exercised over the product, services, suppliers, contractors, and consultants, based on the evaluation results, as required by 21 CFR 820.50(a)(2). Specifically,

Your supplier, which was used to fill ampoules was disqualified for this service due to quality issues, but was left on your approved suppliers list because the supplier is still approved for other services. The supplier remained on the approved supplier list for all products, and/or services. There is no method for disqualifying suppliers from providing specific products and/or services.

The response dated January 7, 2013 cannot be assessed at this time. Your response states that all supplier evaluation and control procedures will be revised to include an appropriate mechanism to ensure suppliers are qualified and disqualified on a product or service-specific basis. These procedures will also be reviewed to assure compliance with the Quality System Regulation. Additionally, you will also electronically prevent the issuance of purchase orders unless a supplier is approved for a specific product or service. Please inform us, if the timeframes listed in your response cannot be met.

You should take prompt action to correct the violations addressed in this letter. Failure to promptly correct these violations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil money penalties. Also, federal agencies are advised of the issuance of all Warning Letters about devices so that they may take this information into account when considering the award of contracts. Additionally, premarket approval applications for Class III devices to which the Quality System regulation deviations are reasonably related will not be approved until the violations have been corrected. Requests for Certificates to Foreign Governments will not be granted until the violations related to the subject devices have been corrected.

Please notify this office in writing within fifteen working days from the date you receive this letter of the specific steps that you have taken to correct the noted violations, including an explanation of how you plan to prevent these violations, or similar violations, from occurring again. Include documentation of the corrective action you have taken. If your planned corrections will occur over time, please include a timetable for implementation of those corrections. If corrective action cannot be completed within 15 working days, state the reason for the delay and the time within which the corrections will be completed.

Your response should be sent to: Ms. Gina Brackett, Compliance Officer, Food and Drug Administration, 6751 Steger Drive, Cincinnati, Ohio 45237. If you have any questions about the content of this letter please contact Ms. Brackett at (513) 679-2700, ext. 2167, or by facsimile at (513) 679-2773.

Finally, you should know that this letter is not intended to be an all-inclusive list of the violations at your facility. It is your responsibility to ensure compliance with applicable laws and regulations administered by FDA. The specific violations noted in this letter and in FDA 483 issued at the closeout of the inspection may be symptomatic of serious problems in your firm's manufacturing and quality assurance systems. You should investigate and determine the causes of the violations, and take prompt actions to correct the violations and to bring your products into compliance.

Sincerely yours,
/S/
Paul J. Teitell
District Director
Cincinnati District

CC: Michael J. Mascali
President
Amresco, LLC
P.O. Box 3098
Solon, OH 44139

Page Last Updated: 03/11/2013
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