DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Central Region

Food and Drug Administration
Waterview Corporate Center
10 Waterview Blvd., 3rd Floor
Parsippany, NJ 07054

Telephone (973) 331-4993

May 22, 2013

VIA UNITED PARCEL SERVICE

Gerald Carlson, CEO
Phibro Animal Health Corporation
Glenpointe Centre East, 3rd Floor
300 Frank W. Burr Blvd., Suite 21
Teaneck, New Jersey 07666

Dear Mr. Carlson:

An FDA inspection of your corporate headquarters, Phibro Animal Health Corporation, for Type A medicated articles, was conducted from October 16-25, 2012 at Teaneck, New Jersey. This inspection focused on your firm's compliance with Field Alert Reporting (FAR) requirements and multiple assay Out-Of-Specification (OOS) results for finished product and stability samples since 2010. These incidents are related to Phibro's Stafac 20 (virginiamycin) Type A medicated article covered by NADA 091-467.

Your firm has entered into an agreement with a contract testing laboratory to test many of your products. This inspection documented significant deviations from the Current Good Manufacturing Practice (CGMP) for Type A medicated article manufacturers, Title 21, Code of Federal Regulations, Part 226 (21 CFR § 226.10 - 226.115). These CGMP deviations cause your Type A medicated articles to be adulterated within the meaning of section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act) [21 U.S.C. § 351(a)(2)(B)] in that the methods used in, or the facilities or controls used for, their manufacture, processing, packing, or holding do not conform to, or are not operated or administered in conformity with, CGMP.

We received your December 13, 2012 response to the FDA-483 observations and note that it lacks sufficient corrective actions. We have included applicable comments following each item listed below. Your firm distributes Type A medicated articles that are manufactured and tested for you by contract manufacturers and control testing laboratories. Your firm has responsibility for batch release and additional quality control unit (QCU) functions. Your firm's operations must satisfy the requirements of 21 C.F.R. § 226.58, but fail to do so. Specifically,

1) Your firm failed to establish adequate laboratory test procedures to check the specifications for Type A medicated articles in accordance with 21 CFR § 226.58(b). Your firm invalidated the original test results by repetitive retesting and failed to conduct appropriate investigations when Out-Of-Specification (OOS) results were obtained.

In 2011, your firm had approximately 140 initial OOS results for Stafac 20 (virginiamycin). Numerous lots failed specifications, were retested, and subsequently released. For example,

- Investigation 11-095 (August 2011) reported 20 lots with OOS results for Stafac 20. Six lots were rejected; however, 14 lots were retested and subsequently released.

- Investigation 11-097 (November 2011) reported 11 lots with OOS results. Three lots were rejected; however, eight lots were retested and subsequently released.

Repetitive retesting for your firm's products is permissible under the following OOS procedures:

- SOP QA 25.05, Handling Out of Specification and Out of Quality Assurance Action Level Results from Chemical Assays.

- SOP QA 24.06, Handling Out of Specification and Out of Quality Assurance Action Level Results from Microbiological Assays.

The above procedures are inadequate because the original OOS result should not be invalidated (and retested) without a proper investigation and without an assignable cause. In the previous examples and many other investigations, you did not identify the true root cause(s) of the various deficiencies. Accordingly, the actions taken often did not prevent recurrence of the problems. We remain concerned about the lots affected by the practice of repetitive retesting and subsequent release into distribution. The numerous OOS results are an indication that your firm's contract manufacturer does not have a well-controlled manufacturing process. In addition, it raises concerns about the quality of the batches that you released. Your response did not provide information to show that a thorough investigation to determine the cause of each unexplained discrepancy or failure to meet specifications was conducted.

In summary, we have concluded that your company did not conduct timely, comprehensive investigations to numerous OOS results obtained for Phibro products. Further, each investigation should include a root cause determination, corrective action plan, and evaluation of product impact.

2) Your firm failed to maintain appropriate laboratory controls to assure your Type A medicated articles conform to the appropriate standards of identity, strength, and purity in accordance as required by 21 CFR § 226.58.

For example, your firm invalidated (and retested) stability OOS retain samples for Stafac 20 until passing results were obtained.

The data generated in support of the assigned expiration dating period for your Type A medicated articles should be from long-term studies under appropriate storage conditions. Proper statistical analysis of long-term stability data collected should support the expiry date for each of your firm's products. Your products should meet specifications to establish a valid expiration dating period. Also, your stability studies include data from unrelated retain samples from different batches which is not considered an acceptable method to verify expiry dating. Finally, your firm's practice of averaging hides the variability of assay test results.

Your response, however, is inadequate because your revised SOP QA 22.11, Stability Studies and Assignment of Expiration Dates, dated December 12, 2012, Section 6.3, states that you will conduct additional testing of retain lots to obtain a passing result. This SOP is inadequate because the original OOS result should not be invalidated (and retested) without a proper investigation and without an assignable cause. As this is a repeat observation from the November 2005 inspection, your response failed to provide an effective corrective action(s).

3) Your firm failed to submit Field Alert Reports (FARs) as required by 21 CFR § 514.80(b)(1). For example, distributed batches of Stafac 20 failed to meet specifications and were not reported to FDA. Specifically, you failed to submit FARs to FDA following long-term stability failures (Lots N10390429VK, N10690767VK, N91481824, N91591963VK, N92793320VK, and N92643120VK) after receiving information from your contract laboratory.

Your response is inadequate because SOP RA 11.00, Field Alert Reporting, dated December 12, 2012, failed to address timeframes for submission of 3-day FARs to FDA. Also, your response failed to adequately address the insect issues revealed in your stability test samples. Your firm's Quality System has failed to adequately evaluate the insect problem apparently revealed at your contract manufacturing and/or contract testing facilities. It is your responsibility to properly investigate the impact of the insect issue on your stability study and the marketed lots of your firm's Type A medicated articles. Further, your evaluation should include scientific justification for methods used to control insects revealed in your stability testing samples (i.e., freezing samples) and the impact of those methods on the stability study. In addition, your response failed to address any corrective and preventive actions for appropriate handling of potential future insect problems. FDA believes an effective audit system at your contract facilities will evaluate whether a firm is ensuring daily adherence to CGMP's. Without such a quality feedback system in place, the Quality System cannot provide the basic assurance of product quality.

Initial OOS results received from your contract laboratory should be sent as a FAR within three working days to FDA. As noted above, additional testing to obtain passing results is not considered an acceptable practice. Finally, we expect that your corrective actions will include a comprehensive evaluation of your firm's reporting of post-marketing studies for all Type A medicated articles for which your firm holds an approved application.

In summary, your firm should have agreements in place with your contract manufacturer(s) and testing laboratories. Your firm is ultimately responsible for the quality of your products. Regardless of who manufactures and tests your products, you are required to ensure these products meet predefined specifications prior to distribution and that they are manufactured in accordance with the Act, and its implementing regulations, including CGMP regulations for Type A medicated articles, Title 21, Code of Federal Regulations, Part 226. Anyone that distributes an adulterated drug, which includes type A medicated articles, not manufactured in conformance with the CGMP regulations, has committed a prohibited act under the Act.

Be advised that we will confirm the implementation and adequacy of all corrective actions upon reinspection of your facilities.

Neither this letter nor the observations noted in this letter are intended to be an all-inclusive statement of deficiencies that may exist at your contract facilities. It is your responsibility to ensure that all facilities under your control comply with all of the requirements of the Act and the regulations promulgated under it. The specific deviations noted in this letter are serious and may be symptomatic of underlying post-marketing reporting failures and an underlying failure to comply with Type A medicated article CGMPs.

Please notify this office in writing, within 30 working days of receipt of this letter, of the specific steps that you have taken to correct the noted deviation, including an explanation of each step being taken to prevent the recurrence of similar deviations. If corrective actions cannot be completed within 30 working days, state the reason for delay and provide timeframes or a schedule detailing when these corrections will be completed.

Your reply should be sent to the Food and Drug Administration, New Jersey District Office, 10 Waterview Boulevard, Parsippany, New Jersey 07054, to the attention of Erin McCaffery, Compliance Officer. If you have any questions about the content of this letter please contact: Erin McCaffery at (973) 331-4993, or email at erin.mccaffery@fda.hhs.gov.

Sincerely,

Diana Amador-Toro

Diana Amador Toro
District Director
New Jersey District