Inspections, Compliance, Enforcement, and Criminal Investigations

Scientific Protein Laboratories, LLC 1/20/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Minneapolis District Office
Central Region
250 Marquette Avenue, Suite 600
Minneapolis, MN 55401
Telephone: (612) 758-7112
FAX: (612) 334-4142

January 20, 2011
Warning Letter
WL 11-09

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

David G. Strunce, President and CEO
Scientific Protein Laboratories LLC
700 E.Main Street
Waunakee, Wisconsin 53597-1440

Dear Mr. Strunce:

During our July 28, 2010 - September 3, 2010, inspection of your active pharmaceutical ingredient (API) manufacturing facility, Scientific Protein Laboratories LLC, located at 700 E. Main Street, Waunakee, WI, investigators from the Food and Drug Administration (FDA) identified significant deviations from Current Good Manufacturing Practice (CGMP) for the manufacture of drugs. These deviations cause your drugs 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.

The FDA has reviewed your firm's post-inspectional correspondence with the agency, including your response of September 13, 2010, and note that it lacks sufficient corrective actions.

Specific deviations observed during the inspection include, but are not limited to, the following:

1. Failure to investigate all quality related complaints whether received orally or in writing according to a written procedure.

For example, your firm failed to conduct a formal investigation concerning a complaint identifying potential contamination with Oversulfated Chondroitin Sulfate (OSCS) in a lot of Heparin Sodium USP (lot 1035-0778) on October 9, 2008. Your firm did not initiate a formal investigation until September 9, 2009. In addition, at that time, your firm failed to extend your investigations to other lots of Heparin Sodium USP manufactured using the same crude lot identified with OSCS contamination. Your investigation did not consider the other lot of Heparin Sodium USP that was associated with the same contaminated crude lot until May 26, 2010, eight months after initiating a formal investigation (i.e., lot 1035-0780, which tested negative for OSCS in June 2010).[1] We acknowledge that you initiated a voluntary recall of Heparin Sodium USP that included lots 1035-0778 and 1035-0780 on October 13, 2010.

In your response, your firm notes that you have revised your procedure to state, "Any SPL employee will inform QA of a customer complaint." However, this response does not address the fundamental issues that allowed the delays in communications and investigation to occur. Your handling of the heparin contamination complaint suggests the need to evaluate training across all departments about the types of information requiring prompt reporting to the quality unit. Further, your response does not address how you will ensure that complaint investigations are handled in a timely manner.

The manner in which you addressed this problem is very worrisome with respect to the timeliness of the investigation, the identification of all potentially affected drugs, and implementing appropriate actions to resolve these issues. Be advised that your firm has the responsibility to ensure the quality, safety, and integrity of its drugs. FDA expects that your corporate management will immediately undertake a comprehensive evaluation of your quality system to ensure comprehensive compliance with CGMP.

2. Your firm failed to properly evaluate a contract laboratory to ensure GMP compliance of operations occurring at the contract site.

For example, our investigators identified that your firm had failed to audit the contract testing laboratory, **(b)(4)** utilized in testing your pancreatin product, as required in your Standard Operating Procedure (SOP) 65-9663, "Qualification and Use of Contract Laboratories." As a result, your firm conducted an audit of the contract laboratory prior to the close of the FDA inspection and identified "Critical and Major" deficiencies.

As a result of your failure to ensure that **(b)(4)** was in compliance with GMP you submitted data to FDA that was not accurate. For example, in numerous instances, **(b)(4)** reported passing results to your firm after failing results were obtained. In your response, your firm states that you have updated your procedures to ensure contract laboratories are completely qualified prior to submitting samples for release testing. Your response appears to be adequate, but we will verify the adequacy of your compliance with your procedures during the next inspection.

However, we are concerned about your firm's fundamental understanding of what is required by your Quality Unit and the regulatory expectations for a firm that enters into agreements with contract testing laboratories. Although you have agreements with other firms that may delineate specific responsibilities to each party, you are ultimately responsible for the quality of your products and the reliability of test results. Regardless of who tests your products or the agreements in place, you are required to manufacture these products in accordance with section 501(a)(2)(B) of the Act to assure their identity, strength, quality, purity, and safety.

3. Failure to have equipment for the manufacture of APIs of appropriate design for its intended use.

For example, your firm uses inappropriate equipment to remove pancreatin wet cake stored in **(b)(4)** drums. Significantly, utensils with the potential to scrape the **(b)(4)** drums and introduce particles into the drug substance and impact the quality of the storage containers were used. As a result, our investigators observed blue plastic shavings in the pancreatin wet cake (lot 1208-1779) during the inspection.

In your response, your firm states that you have initiated a visual inspection program of the drums, changed the **(b)(4)** utilized. Further,

you state that each lot that was produced utilizing the **(b)(4)** drums will undergo **(b)(4)** phase "100% visual inspection" for plastic shavings. Your response also states that you will reject any lots where plastic shavings are found in **(b)(4)** phase of the inspection.

Your response, however, is deficient in that you do not adequately describe the visual inspection acceptance criteria or provide any data to demonstrate that a visual inspection is an adequate technique to identify plastic shavings of various sizes and colors. In addition, your firm has not demonstrated that the proposed corrective action is adequate to ensure that your product is not contaminated with foreign material. Reliance on a visual inspection of the **(b)(4)** drums to identify wear does not prevent the introduction of foreign material.

4. Failure to follow procedures for evaluating suppliers of critical materials.

For example, your firm failed to audit your suppliers at least once every two years as required by your SOP 50-0044. Your firm uses porcine pancreas glands obtained from multiple slaughterhouses as a raw material for your pancreatin product. Our inspection identified the following facilities that have not been audited within the past two years:

- **(b)(4)** - Last audit 02/28/2008 (29 months prior to the initiation of the FDA inspection)
- **(b)(4)** - Last audit 06/18/2008 (over 25 months prior to the initiation of the FDA inspection)
- **(b)(4)** - Last audit 06/19/2008 (over 25 months prior to the initiation of the FDA inspection)

Only after FDA notified you of these findings did you complete audits of the suppliers as a corrective action.

In your response, your firm states that you have updated your SOPs to require management approval of the supplier audit schedule, and to include vendor qualification status as a specification for the incoming glands. Your response appears to be adequate, but we will verify your compliance with the procedures in these SOPs during the next inspection.

The deviations detailed in this letter are not intended to be an all-inclusive statement of deviations that exist at your facility. You are responsible for investigating and determining the causes of the deviations identified above and for preventing their recurrence and the occurrence of other deviations. It is your responsibility to ensure compliance with all requirements of federal law and FDA regulations.

We remind you that any addition, deletion, or change to the information in your Drug Master File (DMF) is required to be submitted to the FDA under 21 CFR 314.420. Additionally, you are required to notify each person authorized to reference the information in your DMF of the pertinent changes. You updated the information in your DMF only after an FDA request that you reflect that **(b)(4)**.

You should take prompt action to correct the deviations detailed in this letter. Failure to promptly correct these deviations may result in legal action without further notice including, without limitation, seizure and injunction. Other federal agencies may take this Warning Letter into account when considering the award of contracts. Additionally, FDA may withhold approval of requests for export certificates or approval of pending drug applications listing your facility, until the above deviations are corrected. FDA may re-inspect to verify corrective actions have been completed.

Within 15 working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct deviations. Include an explanation of each step being taken to prevent the recurrence of deviations and copies of supporting documentation. If you cannot complete corrective action within 15 working days, state the reason for the delay and the date by which you will have completed the correction. Additionally, your response should state if you no longer manufacture or distribute the drug product(s) manufactured at this facility, and provide the date(s) and reason(s) you ceased production.

Your reply should be sent to the following address:

Food and Drug Administration
Minneapolis District Office
Central Region
Attention: Pamela B. Schweikert
250 Marquette Avenue, Suite 600
Minneapolis, MN 55401

Sincerely,

/S/

Gerald J. Berg
Director
Minneapolis District

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1. Furthermore, we note that your September 2010 follow-up investigation to this inspectional finding revealed positive OSCS test results for another Heparin Sodium USP lot (lot 1035-0771). These test results had been generated by your R&D group in February of 2009, but were only addressed via voluntary recall on October 13 2010.

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