U.S. Food and Drug Administration

Inspections, Compliance, Enforcement, and Criminal Investigations

Cephazone Pharma LLC 4/25/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
Los Angeles District
Pacific Region
19701 Fairchild
Irvine, CA 92612-2506
Telephone: 949-608-2900
FAX: 949-608-4415

Warning Letter

WL: 34-11

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

April 25, 2011

Avinash G. Ghanekar
Director of Operations
Cephazone Pharma, LLC
250 E Bonita Avenue
Pomona, CA 91767-1924

Dear Mr. Ghanekar:

During our July 12, 2010 to August 26, 2010 inspection of your pharmaceutical manufacturing facility, Cephazone Pharma, LLC, located at 250 E Bonit Avenue, Pomona, CA, investigator(s) from the Food and Drug Administration (FDA) identified significant violations of Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations, Parts 210 and 211. These violations cause your drug product(s) 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 have reviewed your firm's response of September 2, 2010, and note that it lacks sufficient corrective actions. In addition, we acknowledge your written responses, dated September 23, 2010, October 11, 2010, October 28, 2010, and December 16, 2010, to the Form FDA 483. However, because these responses were received more than 15 business days after the Form FDA 483 was issued; these responses have not been considered. We plan to evaluate your additional responses to the Form FDA 483, along with any other written material provided, as a direct response to this Warning Letter.

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

1. Your firm does not have appropriate laboratory testing to determine if each batch of drug products, purporting to be sterile, conform to such requirements [21 C.F.R. § 211.167(a)].

For example, your firm only uses **(b)(4)** IU of the required **(b)(4)** IU of beta-lactamase neutralizing agent (as per your validation studies) for the purpose of inhibiting the antimicrobial properties of Ceftriaxone during sterility testing. In addition, your firm does not include *Escherichia coli* as part of your test organisms despite your protocol, "Validation of Antibiotic Neutralizer Effectiveness," **(b)(4)**, stating that *Escherichia coli* is the most sensitive challenge organism for evaluating if the antibiotic was effectively neutralized.

In your response, your firm provided protocol **(b)(4)**, "Method Validation Protocol for Recovery studies from PVDF Filter Membrane of Steritest EZ Sterility Testing System Surfaces," that describes the amount of Ceftiofur Sodium recovered from the Steritest EZ Sterility Testing System and correlates it to the amount of neutralizer required by your original neutralizer effectiveness study. Your response, however, is inadequate because you firm has failed to provide any scientific data to justify the correlation between the use of **(b)(4)** IU of beta-lactamase to **(b)(4)** of Ceftiofur Sodium or the use of **(b)(4)** IU of beta-lactamase to **(b)(4)** of Ceftiofur Sodium.

Please provide scientific data to justify the correlation between the amount of beta-lactamase required to neutralize a specific amount of Ceftiofur drug product. Further, please provide information that demonstrates the beta-lactamase effectiveness at this concentration. Future validations should ensure that you include the rationale for your choice of cephalosporin(s) included in the validation. In addition, future validations should include those products that proved to be most difficult to neutralize in your original validation.

2. Your firm has not established appropriate written procedures designed to prevent microbiological contamination of drug products purporting to be sterile [21 C.F.R. § 211.113(b)].

For example, your firm's written procedures for environmental monitoring, disinfection, and your process simulation media have not been validated. Specifically, your firm has not demonstrated the ability of reconstituted beta-lactamase at a concentration of **(b)(4)** IU (0.1ml/1L Sterile Water for Injection) to neutralize cephalosporins in the Tryptic Soy Broth (TSB) used in aseptic process simulation studies (i.e., media fills) or in your surface swab sampling solution. Furthermore, you have not demonstrated the ability of the neutralizing agents in the surface sampling plates purchased by your firm to neutralize the cephalosporin drug products manufactured at your firm.

In your response, you state that you will determine the residual amount of cephalosporin and then determine the amount of neutralizing agent required. Your response is inadequate because you have not provided a scientific rationale that demonstrates a correlation between the residual cephalosporin recovered to the necessary amount of beta-lactamase.

In addition, your firm provided procedure **(b)(4)**, "Cephalosporin Residue Determination during Filling Process," to demonstrate the effectiveness of the amount of penase enzyme used to neutralize residual antibiotic during environmental surface sampling. We cannot determine the adequacy and/or effectiveness of your corrective action because you have not provided the data from this study.