U.S. Food and Drug Administration



## Inspections, Compliance, Enforcement, and Criminal Investigations

### Formatech Inc. 2/10/11

Department of Health and Human Services

Public Health Service
Food and Drug Administration
One Montvale Avenue
Stoneham, Massachusetts 02180
Phone: (781) 587-7500
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**WARNING LETTER**

**NWE-09-11W**

VIA UPS Next Day Air

February 10, 2011

Ms. Indu S. Javeri
Chief Executive Officer
Formatech, Inc.
200 Bullfinch Drive
Andover, MA 01810

Dear Ms. Javeri:

During our August 25, 2010 to October 15, 2010 inspection of your clinical supply manufacturing facility, Formatech, Inc., located at 200 Bullfinch Drive, Andover, Massachusetts, investigators 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 products 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 November 3, 2010, and note that it lacks sufficient corrective actions.

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

1. Your firm has not thoroughly investigated the failure of a batch or any of its components to meet its specifications whether or not the batch has already bee distributed [21 C.F.R. § 211.192]. For example,

a) Your firm has routinely failed to thoroughly investigate and identify root causes when environmental monitoring data exceeds the action limit.

In your response, your firm states that you have hired a consultant to assess the environmental data and subsequently, repaired the facility. Your response, however, is inadequate because your firm failed to investigate adequacy of your disinfectant procedures, frequencies, and preparation as part of your investigation for environmental samples that exceeded action levels in the critical and supporting clean areas. For example, your firm's disinfection program included insufficient use of sporicidal agents. It is essential that environmental control is continually maintained throughout your aseptic processing facility.

Furthermore, we evaluated your environmental data from 2008 to 2010 and are concerned with the lack of comprehensive investigations when mold and bacteria were identified in your aseptic filling facility that exceeded action levels. Your aseptic process relies on manual manipulations and interventions where personnel are in close proximity to open product, and poor environmental control poses a significant risk of contamination.

Your risk assessment for microbial and particulate contamination of products produced at your facility failed to properly evaluate excursions associated with the filling room area adjacent to the lyophilizer in which vials are manually transferred from the filling line to the lyophilizer. Furthermore, your assessment did not provide a plan of action to effectively investigate future environmental excursions.

b) Your firm has failed to thoroughly investigate the cause of repeated leaks of heat transfer fluid around shelf 3 in your lyophilizer and its impact on product.

In your response, your firm states that you will develop methods to detect the transfer fluid in product and evaluate the medical risk of the transfer fluid. Your response, however, is inadequate because your proposal only relies on the detection of heat transfer fluid. Your proposal fails to take corrective actions that ensure the source of the leak (e.g., tubing) is addressed and whether engineering measures will be taken to prevent the leak from occurring in the future. Furthermore, your firm has failed to adequately identify all impacted lots.

2. Your firm has failed to maintain buildings used in the manufacture, processing, packing, or holding of a drug product in a good state of repair [21 C.F.R. § 211.58].

For example, holes, cracks, chipping and peeling paint were observed in your aseptic facility that could lead to contamination and increase the risk to product quality.

In your response, your firm states that you will repair the facility defects and implement a Standard Operating Procedure (SOP) to identify defects in the future. It is important that you create and institute an environment that will ensure that employees are encouraged and are responsible to identify and report quality issues when first observed. Furthermore, your response did not establish engineering controls (e.g., measures to prevent damage to walls, alternate construction materials that reduce the need for repairs, etc.) to prevent the reoccurrence of facility defects.

3. Your firm has failed to establish separate or defined areas or such other control systems for your firm's aseptic processing areas, including a system for monitoring environmental conditions [21 C.F.R. § 211.42(c)(10)(iv)].

For example, your firm has failed to include the communication devices and a transfer cart as part of your environmental monitoring program. These items are used in your filling suite and are not sterilized, which could compromise product sterility.

In your response, your firm states that you will revise procedures for sanitizing equipment that is transferred into the filling suite and require sampling after use in the filling suite. Your response, however, is inadequate because you did not indicate whether you will qualify this sanitization process.

4. Your firm has failed to establish separate or defined areas or such other control systems for your firm's aseptic processing areas, including temperature and humidity controls [21 C.F.R. § 211.42(c)(10)(ii)].

For example, your firm fails to control the humidity in your clean rooms which is necessary to protect the drug product and minimize the risk of environmental contamination.

In your response, your firm justifies the lack of humidity control by relying on humidity monitoring and obtaining client concurrence when high values are obtained. Your response is inadequate because it is your responsibility to ensure that appropriate humidity controls are in place.

The violations cited in this letter are not intended to be an all-inclusive statement of violations that exist at your facility. You are responsible for investigating and

determining the causes of the violations identified above and for preventing their recurrence and the occurrence of other violations. It is your responsibility to assure compliance with all requirements of federal law and FDA regulations.

You should take prompt action to correct the violations cited in this letter. Failure to promptly correct these violations 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 violations are corrected. FDA may re-inspect to verify corrective actions have been completed.

Within fifteen working days of receipt of this letter, please notify this office in writing of the specific steps that you have taken to correct violations. Include an explanation of each step being taken to prevent the recurrence of violations and copies of supporting documentation. If you cannot complete corrective action within fifteen working days, state the reason for the delay and the date by which you will have completed the correction.

Your reply should be sent to the following address: Food and Drug Administration, One Montvale Avenue, 4th floor, Stoneham, MA 02180, Attention: Karen Archdeacon, Compliance Officer.

Sincerely,

/s/

Mutahar S. Shamsi
District Director
New England District

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