February 3, 2012

WARNING LETTER

VIA- UPS OVERNIGHT
Michael Raya
Chief Executive Officer
West-Ward Pharmaceuticals Corp.
465 Industrial Way West
Eatontown, New Jersey 07724

Dear Mr. Raya:

During our June 13, 2011 through June 30, 2011 inspection of your pharmaceutical manufacturing facility, located at 465 Industrial Way West, Eatontown, New Jersey, inspectors from the Food and Drug Administration (FDA) identified significant violations of the Current Good Manufacturing Practice (CGMP) regulations for Finished Pharmaceuticals, Title 21, Code of Federal Regulations (CFR), 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 conformance with, CGMP.
We have reviewed your firm's response of July 21, 2011 and note that it lacks sufficient corrective actions.

The specific CGMP violations observed during the inspection include, but are not limited, to the following:

1. **Failure to establish control procedures that monitor the output and validate the performance of the manufacturing processes that may cause variability in the characteristics of in-process material and the drug product.** [21 C.F.R. § 211.110(a)] For example,

   a. The Standard Operating Procedure (SOP) PR-06, Tablet/Capsule Operation, Rev. D is inadequate in that it allows for drug product batches to be released with significant in-process quality defects, such as tablets produced outside of your firm's established specifications for thickness and hardness (these are also the specifications listed in your drug application). Your SOP PR-06 fails to provide adequate process control, as thickness and hardness results outside of the filed specification ranges are permitted provided that the (b)(4)-in-process testing of (b)(4) does not reveal more than (b)(4) that fail to meet the respective products' filed thickness or hardness specification. This could result in the release of a batch that had up to 25% of the units being out of specification without a follow-up investigation to determine the root cause of the high rate of process failures. It is essential that your firm's process controls and monitoring program are adequate to assure the uniform character and quality of each batch. An unreliable batch operation should be quickly detected, and deviations corrected to ensure that all units released for distribution meet predetermined specifications.

   Also, we note that your July 21, 2011 response fails to discuss why the batches showing a high degree of variability in-process testing do not have an impact on the products on the market. It appears that you agree to correct the manufacturing problem, but you do not address the potential impact on batches already released to the market. Please note that significant manufacturing variability or a pattern of deviations may indicate a fundamental flaw in your processes that may require that you redesign the process.

   b. Our review of manufacturing change control documents at your firm revealed that the manufacturing process for Lithium Carbonate Extended Release (ER) Tablets, USP 450 mg product has been changed at least (b)(4) times since November 25, 2008. The changes were implemented due to failures to meet the product's dissolution specifications at the (b)(4)

Your July 21, 2011 response appears generally adequate. Your firm commits to suspend manufacturing the product, Lithium Carbonate 450 mg ER tablets, and prepare a new development report assessing the impact of the process changes. However, your firm will also need to prospectively assess the adequacy of process controls through completion of successful process validation studies.

2. **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 been already distributed.** [21 C.F.R. § 211.192] For example,
a. As a result of your investigation into out-of-specification (OOS) dissolution results on March 22, 2011, at the (b)(4) for Lithium Carbonate ER Tablets USP, 450 mg, lot #CN66115A (24 month stability test station), your firm concluded that the (b)(4) of degassing was not equivalent to the USP method and therefore would invalidate the OOS results obtained from the (b)(4) our investigation concluded that the cause was the usage of this apparently incorrect degassing technique. You failed to include in your Quality Control Investigation Report (QCIR) #4028 a retrospective review of data generated using the (b)(4) apparatus and an impact assessment for your conclusion. Your firm also failed to assess the validity of the laboratory data generated by this apparatus for batches previously released.

b. A review of QCIR #3841 and #3857 investigations revealed that your firm obtained OOS dissolution results at the (b)(4) for Lithium Carbonate 450 mg ER tablets for lot #'s CN66113AC, CN6597AC, and CN66115 at the 6th month stability test station. Your firm determined that changing the dissolution medium degassing method from using (b)(4) to the USP method would obtain passing results. Your firm performed an informal equivalency study. This informal study concluded that the USP method and the (b)(4) method were not equivalent. Your firm chose to report the passing results obtained from the dissolution testing using the USP dissolution medium degassing method, based on the belief that this method was reliable, while the established (b)(4) degassing method was not. However, we are concerned that this (b)(4) degassing method is used in testing all other products at the firm. Further, while the original OOS results were invalidated on the assumption that the (b)(4) degassing method was incorrect, your investigation did not assess the impact on other batches tested by a method now designated by your firm to be invalid.

Your response is inadequate. Your firm committed to cease manufacturing the product Lithium Carbonate 450 mg ER tablets until you identify the root cause and to perform a proper equivalency study. The response does not say what happens if the equivalency study determines that the (b)(4) and (b)(4) methods are not equivalent to the USP method. You did not commit to performing an impact assessment of lots that were released to the market with an unsuitable method.

c. Your firm did not initiate an investigation to address the root cause of the aberrant tablets when Digoxin 0.125 mg Tablets, lot #67009, #67010, #67366, and #67368 failed AQL sampling for overweight tablets. Your Quality Assurance investigation SOP QA-19, and I of Tablets, requires an investigation if (b)(4)

Your Quality Assurance "Hold" documents for the lots noted that lots were sorted in a thickness sorter in an effort to eliminate aberrant tablets as a corrective action. However, your firm did not document the number of aberrant tablets that were rejected during sorting or any examination of other batches that may have been impacted. In addition, your firm did not evaluate the state of control of the process, including whether it is capable of consistently producing tablets meeting specifications. Digoxin tablets have a narrow therapeutic range and over or underweight tablets can have a significant effect on the patient's health.

Your response failed to address this significant quality problem for Digoxin tablets. Additionally, your response does not address your failure to implement a global electronic
quality management system (QMS) system that you committed to implement as a corrective action in response to deficiencies in your firm's handling of investigations noted during our February 8 to March 1, 2010 inspection of your firm. You did not address inadequate investigations, including the potential impact on distributed batches.

3. Master production and control records lack a statement of theoretical yield including the maximum and minimum percentages of theoretical yield beyond which investigation is required. [21 C.F.R. § 211.186(b)(7)] For example,

Your firm does not calculate percent theoretical yields correctly at the conclusion of each appropriate phase of manufacture for numerous drug products. The batches outside the accountable yield specification have incurred a loss that your firm cannot account for. You add the amount of rejected product, losses due to sampling, and any other form of tailings, to the amount of good product produced from that phase of manufacture. This method of calculation makes the percent theoretical yields artificially high and not representative of the respective products' process capability.

In addition, your firm did not establish any specifications for acceptable yields beyond which an investigation would be required. Your July 21, 2011 response appears to partly address the deficiency. However, it is not clear if the revised master batch records or other new procedures will require an investigation if the new yield specifications are not met.

4. Equipment used in the manufacture, processing, packing or holding of drug products is not of appropriate design to facilitate operations for its intended use. [21 C.F.R. § 211.63)

For example,

a. Our review of the equipment qualifications for multiple automated Tablet Testing System (TTS) machines, used to conduct in-process tablet testing (weight, hardness and thickness) revealed that performance qualification was not conducted to ensure the accuracy of the machine at the various available speed settings. A February 2010 investigation of OOS tablet weights for Digoxin tablets revealed that the TTSs were giving incorrect tablet weights for lighter weight (< 200 mg) tablets when run at the default speed of (b)(4) and concluded it would give accurate results only when run at a speed of (b)(4) However, your firm failed to make a further assessment of the overall reliability of the TTS machines, including evaluating their accuracy with other products and other tablet weights at other speeds.

b. Your firm has not adequately qualified the in-line Pressure Control Device (PCD)-2 Automatic Tablet Weight Control System on the (b)(4) and (b)(4) tablet press machines. Your firm did not Qualifications (PQ) that are representative of all of the products run on the tablet presses to assure proper functioning, including evaluating the reject station timing in relation to tablet press rpm. There is no assurance that the PCD-2 system is accurately rejecting the "marked" OOS tablets throughout the compression run.

In your response, you fail to address interim measures to assure proper weight control of your tablet presses during batch manufacturing while you are qualifying the TTS and PTS systems.
The issues and violations cited in this letter are not intended to be an all-inclusive statement of violations that exist at your facility. We note that several deficiencies were cited in the February 2010 inspection and corrective actions were promised. The current inspection found that promised corrective actions have not occurred and the same deficiencies exist at your firm. 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.

If, as a result of receiving this Warning Letter or in general, you are considering making a decision that will result in a decreased number of finished drug products or active pharmaceutical ingredients produced by your manufacturing facility, FDA requests that you contact CDER's Drug Shortages Program immediately, as you begin your internal discussions, at drugshortages@fda.hhs.gov in order to ensure that your action(s) does not adversely affect the public health.

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 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: U.S. Food & Drug Administration, 10 Waterview Boulevard, 3rd Floor, Parsippany, New Jersey 07054, Attn: Andrew Ciaccia, Compliance Officer.

Sincerely,

/S/

Diana Amador-Toro
Director, New Jersey District