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DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

JUN 28 2005

WARNING LETTER

CERTIFIED MAIL
RETURN RECEIPT REQUESTED

Donal T.M. Tierney
Chief Executive Officer
Bimeda MTC Animal Health Inc.
420 Beaverdale Road
Cambridge, Ontario, Canada N3C2W4

Dear Mr. Tierney:

This letter is regarding the U.S. Food and Drug Administration (FDA) inspection of your Bimeda MTC Animal Health pharmaceutical manufacturing facility in Cambridge, Ontario, Canada conducted by Consumer Safety Officers Linda K. Cline and Kevin D. Kallander from February 9-16, 2005. A comprehensive current Good Manufacturing Practice (cGMP) and pre-approval inspection of your veterinary drug manufacturing facility was performed. As part of the inspection, a preapproval inspection was conducted covering the following products:

[ ]

The inspection revealed significant deviations from cGMP under Title 21 of the Code of Federal Regulations (21 CFR), Parts 210 and 211. At the conclusion of the inspection, a ten-item FDA-483, Inspectional Observations, was issued to Mr. Gavin L. Tierney, President. These cGMP deviations cause your firm's approved animal drug products to be adulterated within the meaning of [21 U.S.C. 351(a)(2)(B)] Section 501(a)(2)(B) of the Federal Food, Drug, and Cosmetic Act (the Act). [21 U.S.C. 351(a)(2)(B)] Section 501(a)(2)(B) of the Act requires that the methods used in and the facilities and controls used for the manufacturing, processing, packing and holding of drugs be in conformity with cGMP. No distinction is made between human and animal drugs, and the failure of either to comply with cGMP constitutes a failure to comply with the requirements of the Act.

We reviewed your firm's March 14 and May 2, 2005 responses to the FDA-483 observations, which were signed by Ms. Arun Malaviya, Vice-President of Quality Affairs and Compliance. We found that the responses still lack sufficient detail, explanation, documentation or substantive corrective action plans to adequately address the deviations noted during the February 2005 inspection of your manufacturing facility in Cambridge, Ontario, Canada.

We acknowledge that your firm has made some changes and corrections in response to Agency findings and requests. However, we have found that while some individual cGMP deficiencies may have been corrected, your firm has failed to institute sufficient corrections to achieve cGMP compliance for a drug facility.

Our concern includes, but is not limited to, the following:

A. Container closure systems do not provide adequate protection against foreseeable external factors in storage and use that can cause deterioration or contamination of the drug product. **[21 CFR 211.94 (b)]**

In your response to the FDA-483 items, you stated that your firm has addressed all the concerns that the FDA investigators raised during the inspection. One of the FDA investigators' major concerns was that your firm has not adequately addressed the product failures of the [ ], which prior to the inspection were identified by several consumer complaints. As a result of the FDA February, 2005 inspection, your firm examined and determined the container/closure system had a twenty-percent failure rate. Your firm subsequently recalled over 100,000 units. From your response, the corrective action for this product was to conduct a process validation study and to add [ ] to the production line. Your response is inadequate and we require the following additional documentation:

- The process validation protocol and the data generated from the process validation showing how the [ ] will be effective on a routine basis.
- A description of how you intend to evaluate the effectiveness of the [ ] on eliminating the product failures.
- An updated batch record that incorporates the use of the [ ]
- A new SOP covering the following items: [ ] and the training of employees on the new procedures.
- Submit the methodology used and any raw statistical data collected in determining the twenty-percent failure rate of the [ ]

Your responses promised additional numerous corrective actions and procedural revisions. These revisions and corrective actions should be documented to FDA with copies of any protocols, reports, procedures, records, and documentation referenced as well as copies of any raw data generated. In addition, our review has identified specific areas that will require additional information for a complete evaluation of your corrections. We require the following additional documentation:

- Your firm utilized the running of media fills in [ ] as a primary tool to indicate sterility for the [ ] product. The Center for Veterinary Medicine (CVM) does not accept media fill qualification using [ ] Your response stated that the media fill protocol, P37 will be amended to [ ] Submit a copy of the revised media fill protocol and the media fill data performed using the revised protocol.
- The qualification of disinfectants is being revised to included additional disinfectants. Submit a copy of the revised disinfectant qualification protocol and resulting data to FDA when completed.
- Submit a copy of the revised SOP# 006-025 titled, "Issue of Dockets to Production".

The cGMP deviations identified above or on the FDA-483 issued to your firm at the close of the recent inspection are not to be considered an all inclusive list of the deficiencies at your facility. FDA inspections are audits and are not intended to determine or disclose all problems or deviations that exist at a firm. We recommend that you continually evaluate your facility on an overall basis to determine cGMP compliance.

You should take prompt action to correct these violations. Failure to promptly correct these violations may result in regulatory action being initiated by the Food and Drug Administration without further notice. These actions include, but are not limited to, seizure, injunction, and/or civil penalties. Further, if corrections are not made, we will recommend that your firm's products be placed on import alert and be denied entry into the United States. Articles can be refused admission pursuant to [21 U.S.C. 381(a)(3)] Section 801(a)(3) of the Act if it appears that the articles are adulterated in that the methods and controls used in their manufacture do not appear to conform to current good manufacturing practice within the meaning of [21 U.S.C. 351(a)(2)(B)]Section 501(a)(2)(B) of the Act.

Please notify this office in writing within 15 days of the specific steps you have taken to correct the noted violations, including an explanation of each step being taken to identify and make correction to any underlying systems problems necessary to assure that similar violations will not recur. Please include any and all documentation to show that adequate correction has been achieved. In case of future corrections, an estimated date of completion, and documentation showing

plans for correction should be included with your response to this letter. Please address your response and any questions to the Food and Drug Administration, Center for Veterinary Medicine, William Bargo, Compliance Officer, 7519 Standish Place, Room 103, Rockville, Maryland 20855.

Until such time as FDA can confirm compliance with 21 CFR Part 210 and 211, current Good Manufacturing Practice, and that correction of the deficiencies noted above has been achieved, we will recommend a pending correction status of any NADA/INAD applications for your firm.

Remember to include your Firm Establishment Indicator number (3001603179) in all your correspondence.

Sincerely,

Gloria J. Dunnavan, Director
Division of Compliance (HFV-230)
Office of Surveillance and Compliance
Center for Veterinary Medicine