



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

Dear Applicant:

Please refer to your New Drug Application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for **PRODUCT NAME**.

Since 2000, FDA has conducted several comprehensive inspections of bioequivalence studies in which the bioanalytical analysis was conducted by MDS Pharma Services (MDS) at the St. Laurent (Montreal) and Blainville sites in Quebec, Canada. The findings of these inspections raise significant concerns about the validity of the reported results of these analytical studies conducted in support of drug applications for marketing. Our findings from these inspections include, but are not limited to, the following:

- Failure to conduct a systematic and thorough evaluation to identify and correct sources of contamination.
- Failure to investigate anomalous results.
- Lack of assay reproducibility between original and repeat results.
- Assay accuracy not assured under the conditions of sample processing.
- Biased exclusion of study data resulting in the acceptance of failed runs.
- Failure to demonstrate the accuracy of analytical methods with appropriate validation experiments and documentation.

As a result of these findings, MDS agreed to conduct an audit of data from all its bioequivalence studies generated from January 2000 to December 2004. However, FDA identified significant deficiencies with the MDS audit during its most recent inspection. Thus, serious questions remain about the validity of any data generated by MDS in studies during this time period that have not been inspected by FDA. In view of these findings, FDA is informing holders of approved NDAs of these issues.

The impact of the data from these studies (which may include bioequivalence, pharmacokinetic, drug-drug interaction and others) cannot be assessed without knowing the details regarding the study and how the data in question were considered in the overall development and approval of your drug product. At this time, the Office of New Drugs is searching available documentation to determine which NDAs are impacted by the above findings.

To further expedite this process, we ask that you inform us within 30 days of receipt of this letter if you have submitted any studies conducted by MDS during the time period of concern (January 2000 through

December 2004). Please submit information on each of the studies submitted, including supplement number (if appropriate), study name/protocol number, and date of submission. This information should be submitted as correspondence to your NDA. In addition, please provide a desk copy to:

Office of New Drugs
Center for Drug Evaluation and Research
10903 New Hampshire Avenue
Bldg. 22, Room 6300
Silver Spring, MD 20993-0002

Once we have made an assessment regarding the potential impact of these data, we will contact you regarding the steps that need to be taken, if any, to assure the accuracy of the data submitted to your application.

If you have any questions, call NAME, Regulatory Project Manager, at 301-796-####.

Sincerely,

{See appended electronic signature page}

NAME
Director
Division of XX Products
Office of XX
Center for Drug Evaluation and Research