



Firm
Attention: Point of contact
Address
City, State, zip code

Dear ANDA Holder/Applicant:

We are writing to you as the sponsor of approved abbreviated new drug application(s) (ANDAs) supported by bioequivalence studies in which the bioanalytical analysis was conducted by Cetero Research at the Houston, Texas site.

FDA has conducted several comprehensive inspections of bioequivalence studies conducted by Cetero Research. The findings of these inspections raise significant concerns about the validity of the reported results of these analytical studies conducted between April 2005 and June 2010 in support of drug applications. Please refer to the Notice for Industry on the CDER website at: <http://www.fda.gov/Drugs/DrugSafety/ucm265559.htm>

FDA is contacting you as a holder of approved ANDA(s) to inform you of these issues and what steps you need to take, to demonstrate the bioequivalence of your product(s). Accordingly, with respect to these studies submitted in your application(s), within 6 months of the date of this letter you must supplement your application(s) with data derived from one of the following options:

1. New bioequivalence studies.
2. Re-assay the samples from the original BE study. For this option to be accepted, the stability of the analyte in the original samples must be demonstrated throughout the entire frozen storage period.

We are also recommending for all of the above options that the blood/plasma level results obtained in the studies be compared to any published literature or other relevant information that is publicly available. If you will be unable to submit the information to re-establish the bioequivalence of your product within six months of this notice, you may request an extension. Requests for extension must be in writing and must explain why an extension is necessary and provide an estimated date of completion. The FDA reserves the right to reject or modify a request for extension if there is not adequate justification provided by the sponsor.

The new bioequivalence data should be submitted as a supplement to your approved application(s). Please find attached the list of your approved applications with studies conducted at Cetero Research during the specified time period. If your company has other applications with studies performed at Cetero Research, Houston during the time period in the FDA letter cited

above, that are not on the attached list, you should consider that this request applies to those applications as well.

As noted, we are recommending that the results of the bioequivalence studies, or re-assays, be submitted to your application within 6 months of the date of this letter. If the necessary information is not submitted within the recommended timeframe or the new information does not support a finding of bioavailability/bioequivalence, the FDA will consider downgrading the therapeutic equivalence evaluation of approved applications in the Agency's publication, Approved Drug Products with Therapeutic Equivalence Evaluations (Orange Book) from an "AB" to a "BX" rating. See Orange Book, Section 1.10 (describing the change from an "AB" to a "BX" rating "as a result of new information raising a significant question as to bioequivalence").

If you have any questions regarding this letter, please contact Cecelia Parise, Regulatory Policy Advisor to the Director, Office of Generic Drugs, at 240-276-9310.

Sincerely,

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Sciences
Center for Drug Evaluation and Research

Firm's ANDAs with studies conducted at Cetero:

ANDA #	Drug	Approved
ANDA #	Drug	Approved
ANDA #	Drug	Approved