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December 17, 2001

CERTIFIED MAIL/RETURN RECEIPT REQUESTED

Dockets Management Branch (HFA-305)
Food and Drug Administration
5630 Fishers Lane, rm. 1061
Rockville, MD 20852

RE: **Docket No. 01D-0488**
Draft Guidance for Industry on Food-Effect Bioavailability and Fed
Bioequivalence Studies: Study Design, Data Analysis, and Labeling

Upsher-Smith Laboratories, Inc. would like to comment on the above referenced Draft Guidance.

Lines 123-126 and Lines 160-164. As written, these sections are confusing and inconsistent with current FDA requirements. It appears that a sponsor of a NDA may fail a fasting bioequivalence study between the to-be-marketed formulation and the clinical trial material when a change is made to their clinical trial formulation and still obtain FDA approval based solely on a successful food-effect study. This is inconsistent with the Office of Generic Drugs (OGD) current policy that require an ANDA applicant to pass both fasted and food-effect BE studies even when the package insert states take with food. This would mean generic manufacturers are being held to a tighter standard than the innovators. We do not believe this is the intent of the FDA and suggest that these two sentences be rewritten to clarify the FDA's intent.

Lines 236-237. The draft guidance states "Following an overnight fast of at least 10 hours, subjects should be given the recommended meal 30 minutes before dosing. The meal should be consumed over 30 minutes...". We recommend changing the wording to "Following an overnight fast of at least 10 hours, subjects should be served the test meal and ingest this meal within 30 minutes." as the previous draft guidance states. Study participants eat at varying rates and would be very difficult to regulate that the subjects consume the meal evenly over 30 minutes.

Lines 258-259. The draft guidance states that the data should be analyzed using average criterion. We suggest that analyzing the data with individual bioequivalence criterion should be an option for highly variable drugs.

01D-0488

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Lines 315-317. We feel that the requirement for 90% CI to be within the limits of 80-125% for AUC and Cmax is too restrictive and will make passing BE more difficult especially with highly variable drugs. The CI limits should be expanded to prevent the need for excessive subject numbers and limit the exposure to investigational medications.

Please take our comments into consideration before finalizing this Guidance.

Sincerely,
Upsher-Smith Laboratories, Inc.

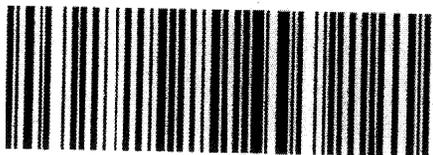
A handwritten signature in black ink, appearing to read 'Mark S. Robbins', with a long horizontal flourish extending to the right.

Mark S. Robbins, Ph.D., J.D.
Vice President, Scientific Affairs

CERTIFIED MAIL

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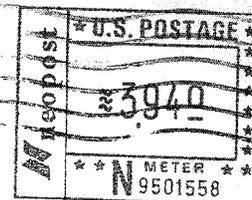
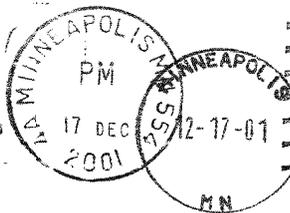
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