

# Procter & Gamble

The Procter & Gamble Company  
Health Care Research Center  
8700 Mason-Montgomery Road, Mason, Ohio 45040-9462

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January 24, 2002

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Draft Guidance for Industry on Food-Effect Bioavailability and Fed Bioequivalence Studies:  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; Availability

Dear Sir or Madam:

Reference is made to the Draft Guidance for Industry entitled, Food-Effect Bioavailability and Fed Bioequivalence Studies: Study Design, Data Analysis, and Labeling; Availability. Submitted herewith, are comments from Procter & Gamble Pharmaceuticals regarding the draft guidance. We appreciate the opportunity to respond to the Agency's request for comments.

## Comments

### A. Section II: Background

1. It is unclear in part B whether BCS Class I drug substances are exempt from food effect bioavailability (BA) and fed bioequivalence (BE) studies or whether the Agency is simply stating that the BA of this class of drugs is less likely than other classes to be affected by food and studies determining food effects are still required.
2. If the Agency intends to waive food effect studies for BCS class I drugs, the question arises as to whether currently there are sufficient data available to support this decision and whether the two additional FDA sponsored studies can definitively determine that BCS Class I drug substances are "unlikely to be bioequivalent" under fed conditions.

### B. Section III: Recommendations for Food-Effect BA and Fed BE Studies

1. It is unclear from the statement beginning in line 123 as to the direction being given by the Agency for performing BE studies for immediate-release drug products. Although line 123 states that BE studies for changes in dosage formulation between the clinical trial product and the to-be-marketed product should be performed under fasting conditions, the next sentence seems to imply that if BE is not established under fasting conditions, the sponsor has the option to perform an additional study under fed conditions. Clarification is needed as to the purpose of performing a second study under fed conditions when the BE study performed under fasting conditions failed.

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Will a BE study under fed conditions be the basis for approving a new formulation when a fasted BE study failed? The statement "it is important to determine food effects"(lines 124-126 and 160-164) is vague and implies that understanding the affect of food on the BA of to-be-marketed formulation is sufficient and that demonstrating BE between the to-be-marketed form and the clinical studies drug is not necessary.

To accurately assess the BE of the to-be-marketed product and clinical supplies under clinically appropriate conditions, the BE study should be performed under the dosage and administration recommendations stated in the label, e.g., if labeled to be taken with food, the BE study should be performed under fed conditions.

C. Section V: Data Analysis and Labeling

1. We agree that the data from the food-effect BA study should be factually reported in the CLINICAL PHARMACOLOGY section of the labeling. However, the dosing and administration recommendation in the DOSAGE AND ADMINISTRATION section of the labeling should reflect the dosing conditions used in the pivotal trials in order to best achieve similar safety and efficacy.
2. For better clarity and accuracy, it is recommended that the "are also similar" in line 307 be replaced with "do not demonstrate a clinically relevant difference".
3. It is recommended that consistency with abbreviations be used, e.g., AUC in line 317 should be  $AUC_{0-\infty}$  ( $AUC_{0-t}$ ).

Finally, we appreciate the clarification that is provided in line 118 as to whether or not sponsors can use relevant principles in the November 1995 Guidance for Industry: SUPAC-IR to determine whether in vivo BE studies are recommended for formulation changes prior to approval.

Thank you again for the opportunity to provide comments. If you have any questions, please feel free to contact me.

Sincerely,



Lenore Faulhaber, Ph.D., M.B.A.  
U. S. Regulatory Affairs Manager

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