DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-835

Procter & Gamble Pharmaceuticals
Attention: Gary F. Galletta, Pharm.D.
U.S. Regulatory Affairs
Health Care Research Center
P.O. Box 8006, SB4-3C4
Mason, OH 45040-8006

WRITTEN REQUEST
Amendment #1

Dear Dr. Galletta:

Please refer to your correspondence dated July 19, 2002, submitted to IND 31,029, requesting changes to FDA's April 19, 2002, Written Request for pediatric studies for risedronate sodium.

We reviewed your proposed changes and are amending the below-listed sections of the Written Request. All other terms stated in our Written Request issued on April 19, 2002, remain the same.

- *Study endpoints*:

  Study 1: Pharmacokinetic parameters, such as AUC, Cmax, Tmax, CL/F, Vss/F, and $t_{1/2}$ should be evaluated. If possible, the effect of demographic covariates (e.g., age, gender, and body weight) on pharmacokinetic parameters will be assessed.

  Study 2: The primary endpoint should be the number of vertebral plus nonvertebral fractures after one year of treatment. Secondary endpoints should include total body and lumbar spine bone mineral content after one year of treatment.

- *Drug information*:

Dosage form:	Cellulose film-coated tablets
Route of administration:	Oral
Formulation:	2.5 and 5 mg tablets
Regimen:	To be determined from pharmacokinetic study results.

Timeframe for submitting reports of the studies: Reports of the studies that meet the terms of the Written Request dated April 19, 2002, as amended by this letter must be submitted to the Agency on or before January 31, 2009, in order to possibly qualify for pediatric exclusivity extension under Section 505A of the Act.

By this letter, we further confirm that we expect you to submit the final study report for study 2 following completion of the 3-year trial. A 1-year interim study report is not required.

Submit protocols for the above studies to an investigational new drug application (IND) and clearly mark your submission "**PEDIATRIC PROTOCOL SUBMITTED FOR PEDIATRIC EXCLUSIVITY STUDY**" in large font, bolded type at the beginning of the cover letter of the submission. Please notify us as soon as possible if you wish to enter into a written agreement by submitting a proposed written agreement. Clearly mark your submission "**PROPOSED WRITTEN AGREEMENT FOR PEDIATRIC STUDIES**" in large font, bolded type at the beginning of the cover letter of the submission.

Submit reports of the studies as a supplement to an approved NDA with the proposed labeling changes you believe would be warranted based on the data derived from these studies. When submitting the reports, please clearly mark your submission "**SUBMISSION OF PEDIATRIC STUDY REPORTS – PEDIATRIC EXCLUSIVITY DETERMINATION REQUESTED**" in large font, bolded type at the beginning of the cover letter of the submission and include a copy of this letter. In addition, send a copy of the cover letter of your submission, via fax (301-594-0183) or messenger, to the Director, Office of Generic Drugs, HFD-600, Metro Park North II, 7500 Standish Place, Rockville, MD 20855-2773.

If you wish to discuss any amendments to this Written Request, submit proposed changes and the reasons for the proposed changes to your application. Clearly mark submissions of proposed changes to this request **"PROPOSED CHANGES IN WRITTEN REQUEST FOR PEDIATRIC STUDIES"** in large font, bolded type at the beginning of the cover letter of the submission. We will notify you in writing if we agree to any changes to this Written Request.

We hope you will fulfill this pediatric study request. We look forward to working with you on this matter in order to develop additional pediatric information that may produce health benefits in the pediatric population.

If you have any questions, call Randy Hedin, Senior Regulatory Management Officer, at 301-827-6392.

Sincerely yours,

{See appended electronic signature page}

Robert J. Meyer, M.D.
Director
Office of Drug Evaluation II
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Robert Meyer

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