DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-835/S-014

Procter & Gamble Pharmaceuticals
Attention: Katherine McNeal
U.S. Regulatory Affairs Manager
Health Care Research Center
8700 Mason Montgomery Road
Mason, OH 45040-9462

Dear Ms. McNeal:

Please refer to your supplemental new drug application (NDA) dated August 22, 2003, received August 25, 2003, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Actonel (risedronate sodium) Tablets.

This "Changes Being Effected" supplemental new drug application provides for the following paragraph be added to the **Pregnancy** subsection of the **PRECAUTIONS** section of the package insert:

> "Bisphosphonates are incorporated into the bone matrix, from where they are gradually released over periods of weeks to years. The extent of bisphosphonate incorporation into adult bone, and hence, the amount available for release back into the systemic circulation, is directly related to the total dose and duration of bisphosphonate use. Although there are no data on fetal risk in humans, bisphosphonates do cause fetal harm in animals, and animal data suggest that uptake of bisphosphonates into fetal bone is greater than into maternal bone. Therefore, there is a theoretical risk of fetal harm (e.g., skeletal and other abnormalities) if a woman becomes pregnant after completing a course of bisphosphonate therapy. The impact of variables such as time between cessation of bisphosphonate therapy to conception, the particular bisphosphonate used, and the route of administration (intravenous versus oral) on this risk has not been established."

We have completed the review of this application. This application is approved, effective on the date of this letter, for use as recommended in the final printed labeling submitted on August 22, 2003.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

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

Sincerely,

{See appended electronic signature page}

David G. Orloff, M.D.
Director
Division of Metabolic and Endocrine Drug Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosure

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

/s/

David Orloff

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