DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-064/S-017

Procter & Gamble Pharmaceuticals, Inc.
Health Care Research Center
Attention: Victoria Ireland
U.S. Regulatory Affairs
8700 Mason-Montgomery Road
Mason, Ohio 45040-9462

Dear Ms. Ireland:

Please refer to your supplemental new drug application dated March 16, 2007, received March 19, 2007, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Macrobid® Capsules (nitrofurantoin monohydrate/macrocrystals).

We acknowledge receipt of your submission dated March 16, 2007.

We also note in this submission that you communicated with Lonnie Smith, Project Specialist, Office of Information Management and Randy Levin, MD, Director for Health and Regulatory Data Standards, Associate Director for Medical informatics regarding the active ingredient of Macrobid SPL being posted on the DailyMed website incorrectly.

This "Changes Being Effected" supplemental new drug application provides for the following changes to the label:

1. The following paragraphs were added to the end of the **WARNINGS** section:

   "*Clostridium difficile* associated diarrhea (CDAD) has been reported with use of nearly all antibacterial agents, including nitrofurantoin, and may range in severity from mild diarrhea to fatal colitis. Treatment with antibacterial agents alters the normal flora of the colon leading to overgrowth of *C. difficile*.

   C. difficile produces toxins A and B which contribute to the development of CDAD. Hypertoxin producing strains of *C. difficile* cause increased morbidity and mortality, as these infections can be refractory to antimicrobial therapy and may require colectomy. CDAD must be considered in all patients who present with diarrhea following antibiotic use. Careful medical history is necessary since CDAD has been reported to occur over two months after the administration of antibacterial agents.

   If CDAD is suspected or confirmed, ongoing antibiotic use not directed against *C. difficile* may need to be discontinued. Appropriate fluid and electrolyte management, protein

supplementation, antibiotic treatment of *C. difficile*, and surgical evaluation should be instituted as clinically indicated."

2. The following paragraph was added to the end of the **Information for Patients** section:

   "Diarrhea is a common problem caused by antibiotics, which usually ends when the antibiotic is discontinued. Sometimes after starting treatment with antibiotics, patients can develop watery and bloody stools (with or without stomach cramps and fever) even as late as two or more months after having taken the last dose of the antibiotic. If this occurs, patients should contact their physician as soon as possible."

We completed our review of this application, as amended. This application is approved, effective on the date of this letter, for use as recommended in the agreed-upon labeling text.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH
Food and Drug Administration
5515 Security Lane
HFD-001, Suite 5100
Rockville, MD 20852

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call Kyong Hyon, Regulatory Project Manager, at (301) 796-0734.

Sincerely,

{See appended electronic signature page}

Janice M. Soreth, MD
Director
Division of Anti-Infective and Ophthalmology Products
Office of Antimicrobial Products
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/

Janice Soreth

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