DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 018482/S-049

SUPPLEMENT APPROVAL

Pfizer, Inc.
Attention: Michele Burtness
Manager, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017

Dear Ms. Burtness:

Please refer to your Supplemental New Drug Application (sNDA) dated and received April 6, 2011, submitted under section 505(b)(1) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Procardia (nifedipine) 10 mg Capsules.

We acknowledge receipt of your amendment dated September 9, 2011.

This "Changes Being Effected" supplemental new drug application provides for labeling revised as follows:

1. Under **DESCRIPTION,** the words (b) (4) were deleted from the second paragraph. The paragraph now reads:

   > Nifedipine is a yellow crystalline substance, practically insoluble in water but soluble in ethanol. It has a molecular weight of 346.3. PROCARDIA capsules are formulated as soft gelatin capsules for oral administration, each containing 10 mg nifedipine.

2. Under **WARNINGS**, the following paragraph was relocated from the fourth paragraph within this section to the second paragraph:

   > Severe hypotension and/or increased fluid volume requirements have been reported in patients receiving PROCARDIA together with a beta-blocking agent who underwent coronary artery bypass surgery using high dose fentanyl anesthesia. The interaction with high dose fentanyl appears to be due to the combination of PROCARDIA and a beta blocker, but the possibility that it may occur with PROCARDIA alone, with low doses of fentanyl, in other surgical procedures, or with other narcotic analgesics cannot be ruled out. In PROCARDIA treated patients where surgery using high dose fentanyl anesthesia is contemplated, the physician should be aware of these potential problems and, if the patient's condition permits, sufficient time (at least 36 hours) should be allowed for PROCARDIA to be washed out of the body prior to surgery.

3. Under **WARNINGS**, the third paragraph was relocated after the section titled "Increased Angina and/or myocardial infarction" and changed from:

(b) (4)

To:

Use in Essential Hypertension
PROCARDIA and other immediate-release nifedipine capsules have also been used for the long-term control of essential hypertension, although PROCARDIA capsules have not been approved for this purpose and no properly controlled studies have been conducted to define an appropriate dose or dose interval for such treatment.
PROCARDIA capsules should not be used for the control of essential hypertension.

4. Under **WARNINGS**, the following paragraph was relocated from the third paragraph to the fifth paragraph:

   Several well-controlled, randomized trials studied the use of immediate-release nifedipine in patients who had just sustained myocardial infarctions. In none of these trials did immediate-release nifedipine appear to provide any benefit. In some of the trials, patients who received immediate-release nifedipine had significantly worse outcomes than patients who received placebo. PROCARDIA capsules should not be administered within the first week or two after myocardial infarction, and they should also be avoided in the setting of acute coronary syndrome (when infarction may be imminent).

5. Under **ADVERSE REACTIONS**, the sentence "Acute generalized exanthematous pustulosis also has been reported" was added to the end of the fourteenth paragraph. The paragraph now reads:

   In post-marketing experience, there have been rare reports of exfoliative dermatitis caused by nifedipine. There have been rare reports of exfoliative or bullous skin adverse events (such as erythema multiforme, Stevens-Johnson Syndrome, and toxic epidermal necrolysis) and photosensitivity reactions. Acute generalized exanthematous pustulosis also has been reported.

6. There are multiple editorial changes too numerous to mention individually (i.e. Procardia changed to PROCARDIA, the word "those" added to the paragraph titled "Congestive Heart Failure", the word "since" added to the third paragraph of the section titled "Drug Interactions", the word "were" replacing the word "are" in the section titled "Pregnancy", the word United States spelled out rather than using the abbreviation U.S., "were" replacing "was", bolding and unbolding of text).

7. The revision date and version number were updated.

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

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format using the FDA automated drug registration and listing system (eLIST), as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm. Content of labeling must be identical to the enclosed labeling (text for the package insert), with the addition of any labeling changes in pending "Changes Being Effected" (CBE) supplements, as well as annual reportable changes not included in the enclosed labeling.

Information on submitting SPL files using eLIST may be found in the guidance for industry titled "SPL Standard for Content of Labeling Technical Qs and As" at http://www.fda.gov/downloads/DrugsGuidanceComplianceRegulatoryInformation/Guidances/UCM072392.pdf.

The SPL will be accessible from publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for this NDA, including CBE supplements for which FDA has not yet issued an action letter, with the content of labeling [21 CFR 314.50(l)(1)(i)] in MS Word format, that includes the changes approved in this supplemental application, as well as annual reportable changes and annotate each change. To facilitate review of your submission, provide a highlighted or marked-up copy that shows all changes, as well as a clean Microsoft Word version. The marked-up copy should provide appropriate annotations, including supplement number(s) and annual report date(s).

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit the following, in triplicate, (1) a cover letter requesting advisory comments, (2) the proposed materials in draft or mock-up form with annotated references, and (3) the package insert(s) to

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

You must submit final promotional materials and package insert(s), accompanied by a Form FDA 2253, at the time of initial dissemination or publication [21 CFR 314.81(b)(3)(i)]. Form FDA 2253 is available at http://www.fda.gov/opacom/morechoices/fdaforms/cder.html; instructions are provided on page 2 of the form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

All promotional materials that include representations about your drug product must be promptly revised to be consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions in your promotional materials should include prominent disclosure of the important new safety information that appears in the revised package labeling. Within 7 days of receipt of this letter, submit your statement of intent to comply with 21 CFR 314.70(a)(4) to the address above or by fax to 301-847-8444.

REPORTING REQUIREMENTS

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, please call:

Lori Anne Wachter
Regulatory Project Manager
(301) 796-3975

Sincerely,

{See appended electronic signature page}

Mary Ross Southworth, Pharm.D.
Deputy Director for Safety
Office of Drug Evaluation I
Center for Drug Evaluation and Research

ENCLOSURE:
Content of Labeling

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

/s/

MARY R SOUTHWORTH
09/27/2011