DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 021992/S-031

SUPPLEMENT APPROVAL

Pfizer Inc.
Attention: Maria A. Pias
Associate Director, Worldwide Regulatory Strategy
445 Eastern Point Road
Groton, CT 06340

Dear Ms. Pias:

Please refer to the following Supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Pristiq (desvenlafaxine) 50 mg, 100 mg Extended-Release Tablets:

- **S-031,** dated and received November 15, 2011, a "Prior Approval" supplemental new drug application that proposes to update Section 7.7 Potential for Desvenlafaxine to Affect Other Drugs, i.e., midazolam, aripiprazole, tamoxifen and organize pharmacokinetic data in forest plots, in response to our request dated April 16, 2012.

We acknowledge receipt of your amendments dated:

April 19, 2012	November 2, 2012	February 28, 2013
May 8, 2012	November 30, 2012	October 29, 2013
May 25, 2012	December 5, 2012	December 6, 2013

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

We note that your May 25, 2012 submission includes final printed labeling (FPL) for your package insert and Medication Guide. We have not reviewed this FPL. You are responsible for assuring that the wording in this printed labeling is identical to that of the approved content of labeling in the structured product labeling (SPL) format.

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 (package insert and Medication Guide), 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 that includes labeling changes 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).

FULFILLMENT OF POSTMARKETING REQUIREMENT(S)/COMMITMENT(S)

We have received your submission dated August 19, 2013, containing the final report for the following postmarketing commitment listed in the February 29, 2008 approval letter.

1229-4 While it is clear that desvenlafaxine has a qualitatively negative effect on sexual function from the adverse events collected during your earlier trials, we do not have quantified sexual dysfunction data. You have agreed to assess sexual dysfunction in your planned lower dose study. If the lower dose study establishes that 50 mg/day is the lowest effective dose, you have agreed to conduct another acute, randomized controlled trial with placebo, 50, and 100 mg/day, and employ a validated and reliable outcome measure to assess for sexual dysfunction. This study could be conducted in parallel with the longer-term efficacy trial, and the results could be submitted approximately 5.5 years from the date of approval for this NDA.

We have reviewed your submission and conclude that the above commitment was fulfilled.

We remind you that the following postmarketing requirements listed in the February 29, 2008, and February 14, 2013, approval letters are still open.

1229-1 Deferred Pediatric Studies Under PREA You have agreed to conduct studies to assess the safety and effectiveness of desvenlafaxine succinate as a treatment for Major Depressive Disorder in pediatric patients ages 7 to 17 (children and adolescents). Both children (ages 7 to 11 years) and adolescents (ages 12 to 17

years) will be equally represented in the samples, and there will be a reasonable distribution of both sexes in these age strata.

In reference to the Pediatric Deferral Extension Granted letter, dated March 15, 2013, you are reminded that the Final Report Submission is December 29, 2017.

1229-2 Your NDA for desvenlafaxine succinate (DVS) demonstrates the effectiveness of doses as low as 50 mg as a treatment for Major Depressive Disorder (MDD), however, the available data for effectiveness for this drug in MDD suggests a flat dose response curve for efficacy between 50 and 400 mg/day. On the other hand, there is a clear dose response for adverse events as the dose increases from 50 to 400 mg/day. Therefore, there is a need to better understand the lower end of the dose response curve to determine if efficacy might be achieved at doses even lower than 50 mg/day. You have agreed to conduct and submit the results of a randomized controlled study including placebo and DVS doses of 10, 25, and 50 mg/day as a Postmarketing commitment. This study will assess efficacy in this dose range and will also include a validated and reliable outcome measure to assess for sexual dysfunction. You have agreed to submit the results of this trial no later than 3 years after the date of the approval for this NDA.

2053-1 Deferred pediatric study under PREA for the maintenance treatment of Major Depressive Disorder (MDD) in subjects age 7 to 17 years. You have agreed to meeting the following milestones:

Protocol Submission Date: June 30, 2018
Study Completion Date: December 31, 2024
Final Report Submission: June 25, 2025

Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

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
Office of Prescription Drug Promotion (OPDP)
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 Office of Prescription Drug Promotion (OPDP), see http://www.fda.gov/AboutFDA/CentersOffices/CDER/ucm090142.htm.

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, email Juliette Touré, PharmD, Senior Regulatory Project Manager, at Juliette.Toure@fda.hhs.gov.

Sincerely,

{See appended electronic signature page}

Mitchell V. Mathis, M.D.
CAPT, USPHS
Director (acting)
Division of Psychiatry Products
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/

MITCHELL V Mathis
12/10/2013