DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 010151/S-036

SUPPLEMENT APPROVAL

Pfizer Inc
Attention: Carol Haley
Director, Worldwide Regulatory Strategy
235 East 42nd Street
New York, NY 10017-5755

Dear Ms. Haley:

Please refer to your Supplemental New Drug Application (sNDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Dilantin® (phenytoin sodium, USP) injection.

Application	Submitted on:	Received on:
NDA 010151/S-036	October 27, 2008	October 27, 2008
This "Changes Being Effected" supplement provides for:		
• Revised labeling to include additional information in the Warnings and Precautions sections of the prescribing information with respect to skin reactions, hypersensitivity, and Anticonvulsant Hypersensitivity Syndrome.		

We also refer to our November 3, 2010 Joint Meeting of the Peripheral and Central Nervous System Drugs (PCNS) Advisory Committee and Drug Safety and Risk Management (DSRM) Advisory Committee.

We have completed our review of this supplemental application and in our review we have amended the labeling for NDA 10151, as amended, as follows: updating information regarding CYP450-mediated metabolism, revising the boxed important note to a boxed warning for cardiovascular risk associated with rapid infusion of parenteral phenytoin and strengthening the Warnings section regarding this risk, revising the Indications and Usage section and the Dosage and Administration section to recommend that parenteral Dilantin should be used only when oral phenytoin administration is not possible, adding information about Purple Glove Syndrome to the Warnings section, adding information regarding the risks with intramuscular administration of Dilantin, and additional revisions to the Drug Interactions section, to the Warnings section, and to the Adverse Reactions section. We have also incorporated additional recommendations from the Joint Advisory Committee to your proposed labeling. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text.

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).

CARTON AND IMMEDIATE CONTAINER LABELS

We also refer to your April 8, 2011 correspondence indicating that no current carton and container labels are available since you are no longer marketing the product.

As soon as you decide to remarket the product, you will need to submit the final printed carton and container labels that include the following revisions recommended by the PCNS/DRSM Advisory Committee, as soon as they are available, but no more than 30 days after they are printed:

Remove the (b) (4) statement. Additionally, change the information regarding route of administration to the verbatim statement, "For IV or IM use".

Please submit these labels electronically according to the guidance for industry titled "Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (June 2008)." Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Product Correspondence – Final Printed Carton and Container Labels for approved NDA 010151 S-036**." Approval of this submission by FDA is not required before the labeling is used.

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, call Su-Lin Sun, PharmD, Regulatory Project Manager, at (301) 796-0036.

Sincerely,

{See appended electronic signature page}

Russell G. Katz, M.D.
Division Director
Division of Neurology 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/

RUSSELL G KATZ
11/13/2011