DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 16-931/S-031 **SUPPLEMENT APPROVAL**

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

Dear Ms. Collins:

Please refer to your supplemental new drug application dated December 2, 2008, received December 2, 2008, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for R-Gene 10 (arginine hydrochloride, USP) Injection.

We acknowledge receipt of your submissions dated January 13, March 2 and 9, and June 16, 2009.

This "Prior Approval" supplemental new drug application provides for a response to our supplement request letters issued on September 3 and November 24, 2008. These letters requested changes to the package insert, container labeling and packaging configuration for this product in order to reduce the possibility of future medication errors. This supplemental application included significant changes made to the Description, Indications and Usage, Contraindications, Warnings, Precautions, Adverse Reactions, Overdosage, Dosage and Administration and How Supplied sections of the package insert. Additionally, the container label and packaging configuration were completely updated in accordance with our recommendations.

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed, agreed-upon labeling text and with the minor editorial revisions to the package insert listed below:

1. For further clarity to healthcare practitioners, insert a comma after the word "hyperventilation" in the first sentence in the Overdosage section as follows: "An overdosage may cause a transient metabolic acidosis with hyperventilation, which could lead to death (See "WARNINGS")."
2. In the Directions for Use subsection of the Dosage and Administration section, under the heading "For Pediatric Patients weighing 59 kg (130 lbs) or less", the word "verify" is spelled incorrectly. Please correct as follows: "The healthcare professional administering the dose should verify the accuracy of the dose prior to administration."

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)(1)(i)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to, except for including the revisions listed above, the enclosed labeling (text for the package insert). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, **"SPL for approved NDA 16-931/S-031**".

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed container labels that are identical to the enclosed container labels submitted on June 16, 2009, as soon as they are available, but no more than 30 days after they are printed. 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 (October 2005)*. 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 "**Final Printed Carton and Container Labels for approved NDA 16-931/S-031**." Approval of this submission by FDA is not required before the labeling is used.

PROMOTIONAL MATERIALS

All promotional materials for your drug product that include representations about your drug product must be promptly revised to make it consistent with the labeling changes approved in this supplement, including any new safety information [21 CFR 314.70(a)(4)]. The revisions to 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 following address or by facsimile at 301-847-8444:

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

In addition, as required under 21 CFR 314.81(b)(3)(i), you must submit your updated final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA-2253, directly to the above address. For instruction on completing the Form FDA 2253, see 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.

LETTERS TO HEALTH CARE PROFESSIONALS

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

MedWatch
Food and Drug Administration
5600 Fishers Lane, Room 12B05
Rockville, MD 20857

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 Jennifer Johnson, Regulatory Project Manager, at (301) 796-2194.

Sincerely,

{See appended electronic signature page}

Mary H. Parks, M.D.
Director
Division of Metabolism and Endocrinology Products
Office of Drug Evaluation II
Center for Drug Evaluation and Research

Enclosures:
Package Insert
Container Label

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-16931	SUPPL-31	PHARMACIA AND UPJOHN CO	R-GENE 10

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

/s/

MARY H PARKS
01/17/2010