DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 50-006/S-086
NDA 50-007/S-027
NDA 50-480/S-052
NDA 50-533/S-042

SUPPLEMENT APPROVAL

Pfizer, Inc.
Attention: Shia Srulovich, RPh, PharmD
Senior Manager
Worldwide Safety & Regulatory
235 East 42nd Street
New York, NY 10017

Dear Dr. Srulovich:

Please refer to your Supplemental New Drug Applications (sNDAs) dated April 28, 2014, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act (FDCA) for the following:

NDA 50-006/S-086	Vibramycin Monohydrate (doxycycline monohydrate) for Oral Suspension
NDA 50-007/S-027	Vibramycin (doxycycline hyclate) Capsules
NDA 50-480/S-052	Vibramycin Calcium (doxycycline calcium oral suspension) Syrup
NDA 50-533/S-042	Vibra-Tabs (doxycycline hyclate) Film Coated Tablets

We acknowledge receipt of your amendments dated August 22, 2014.

These "Prior Approval" supplemental applications propose changes to the **PRECAUTIONS** and **WARNINGS** sections of the package insert in response to an Agency Prior Approval Supplement Request Letter dated March 5, 2014.

APPROVAL & LABELING

We have completed our review of these supplemental applications, as amended. They are 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 (underlined for additions and strikethrough for deletions) listed below and added to the enclosed labeling which Pfizer agreed to in an email communication dated September 5, 2014.

WARNINGS

Intracranial hypertension (IH, pseudotumor cerebri) has been associated with the use of tetracyclines including Vibramycin. Clinical manifestations of IH include headache, blurred vision, diplopia, and vision loss; ~~and~~ papilledema can be found on fundoscopy. Women of childbearing age who are overweight or have a history of IH are at greater risk for developing tetracycline associated IH. Concomitant use of isotretinoin and Vibramycin should be avoided because isotretinoin is also known to cause pseudotumor cerebri.

Although IH typically resolves after discontinuation of treatment, ~~it is possible that~~ the possibility for permanent visual loss exists ~~can occur~~. If visual disturbance occurs ~~symptoms develop~~ during treatment, prompt ophthalmologic evaluation is warranted. Since intracranial pressure can remain elevated for weeks after drug cessation patients should be monitored until they stabilize.

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, except with the revisions indicated in 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 via publicly available labeling repositories.

Also within 14 days, amend all pending supplemental applications for these NDAs, 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 with the revisions indicated above approved in these supplemental applications, as well as annual reportable changes, and annotate each change. To facilitate review of your submissions, 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).

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 Carmen DeBellas, Regulatory Project Manager, at (301) 796-1203.

Sincerely,

{See appended electronic signature page}

Sumathi Nambiar, MD, MPH
Director
Division of Anti-Infective Products
Office of Antimicrobial Products
Center for Drug Evaluation and Research

ENCLOSURE(S):
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/

SUMATHI NAMBIAR
09/12/2014