DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 090505

Impax Laboratories, Inc.
Attention: Michelle P. Wong
Senior Director, Regulatory Affairs
30831 Huntwood Ave.
Hayward, CA 94544

Dear Madam:

This is in reference to your abbreviated new drug application (ANDA) dated March 18, 2008, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Doxycycline Hyclate Delayed-release Tablets USP, 75 mg (base) and 100 mg (base).

Reference is also made to your amendments dated June 13, October 10, and December 9, 2008; April 7, April 20, May 5, and May 13, 2009; and June 21, August 12, August 31, October 18, and November 9, 2010.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly the ANDA is approved, effective on the date of this letter. The Division of Bioequivalence has determined your Doxycycline Hyclate Delayed-release Tablets, 75 mg (base) and 100 mg (base), to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug (RLD), Doryx Tablets, 75 mg (base) and 100 mg (base), respectively, of Mayne Pharma International (Mayne).

Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application. The “interim” dissolution specifications are as follows:

Acid Stage:

Apparatus: USP Apparatus 1 (baskets), @50 rpm
Medium: 0.06 N hydrochloric acid, 37ºC
Volume: 900 mL

Specification:

Level 1- No individual value exceeds (b) (4) dissolved in 20 m
Level 2- NMT (b) (4) values of 12 tested are grea dissolved in 20 minutes.

Buffer Stage:

Apparatus: USP Apparatus 1 (baskets), @50 rpm
Medium: pH 5.5, neutralized phthalate buffer, 37ºC
Volume: 1000 mL

Specification: NLT (b) (4) (Q) of doxycycline is dissolved in 4 inutes.

The "interim" dissolution test(s) and tolerances should be finalized by submitting dissolution data from the first three production size batches. These data should be submitted as a "Special Supplement – Changes Being Effected" if there are no revisions to be made to the "interim" specifications, or if the final specifications are tighter than the "interim" specifications. In all other instances, the information should be submitted in the form of a Prior Approval Supplement.

The RLD upon which you have based your ANDA, Mayne's Doryx Tablets, is subject to a period of patent protection. As noted in the agency's publication titled Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book"), U.S. Patent No. 6,958,161 (the '161 patent) is scheduled to expire on December 15, 2022.

Your ANDA contains a paragraph IV certification under section 505(j)(2)(A)(vii)(IV) of the Act stating that the '161 patent is invalid, unenforceable, or will not be infringed by your manufacture, use, or sale of Doxycycline Hyclate Delayed-release Tablets, 75 mg (base) and 100 mg (base), under this ANDA. You have notified the agency that Impax Laboratories, Inc. (Impax) complied with the requirements of section 505(j)(2)(B) of the Act, and that litigation was initiated against Impax for infringement of the '161 patent in the United States District

Court for the District of New Jersey [Warner Chilcott Laboratories Ireland Limited, Warner Chilcott Company, Inc., Warner Chilcott (US), LLC and Mayne Pharma International Pty. Ltd. v. Impax Laboratories, Inc., Mylan Pharmaceuticals Inc., Mylan Inc., Mutual Pharmaceuticals Company, Inc., United Research Laboratories, Inc., and URL Pharma, Inc., Civil Action No.09-1233].[1]

With respect to 180-day generic drug exclusivity, we note that Impax, by virtue of its timely submission to a substantially complete ANDA of an amendment containing a paragraph IV certification to the '161 patent, is a "first applicant" with respect to its ANDA for Doxycycline Hyclate Delayed-release Tablets, 75 mg (base) and 100 mg (base).[2] Your ANDA was received by the agency on March 18, 2008, and was never granted tentative approval. This ANDA, therefore, was not granted tentative approval within the 30-month period described in section 505(j)(5)(D)(i)(IV). Nevertheless, the agency has determined that the failure to obtain tentative within the 30-month period was caused by a change in or a review of the requirements for approval of the application imposed after the date on which the application was filed.[3] We therefore conclude that the 180-day exclusivity period described in section 505(j)(5)(B)(iv) of the Act was not forfeited by Impax, and that with this approval Impax is eligible for 180 days of generic drug exclusivity for Doxycycline Hyclate Delayed-release Tablets USP, 75 mg (base) and 100 mg (base). This exclusivity, which is provided for

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[1] The '161 patent was not listed when the Office of Generic Drugs (OGD) received your ANDA on March 18, 2008, and your certification was submitted in an amendment to your ANDA. The agency has determined that, under these circumstances, there is no 30-month stay of approval.

[2] See part (b) of section 4 of the QI Supplemental Funding Act of 2008 (QI Act). These Transitional Rules provide that, with respect to patent information filed with the Secretary within the 60-day period after enactment of the QI Act --

> "each applicant that, not later than 120 days after the date of the enactment of this Act, amends an application that is, on or before the enactment of this Act, a substantially complete application … to contain a [paragraph IV certification] with respect to that patent shall be deemed to be a first applicant (as defined in paragraph (5)(B)(iv) of such section 505(j)."

[3] A citizen petition that was subject to section 505(q) of the Act was submitted that required the agency to review the requirements for approval for Doxycycline Hyclate Delayed-release drug products. See Docket No. FDA-2008-P-0586. Furthermore, the requirements for approval were changed when the RLD was approved for a scored tablet configuration; Impax was required to change to a scored tablet and conduct additional dissolution testing.

under section 505(j)(5)(B)(iv) of the Act, will begin to run from the date of the commercial marketing identified in section 505(j)(5)(B)(iv). Please submit correspondence to this ANDA informing the agency of the date of commercial marketing.

Under section 506A of the Act, certain changes in the conditions described in this ANDA require an approved supplemental application before the change may be made.

Please note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS. See section 505-1(i) of the Act.

Postmarketing reporting requirements for this ANDA are set forth in 21 CFR 314.80-81 and 314.98. The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Promotional materials may be submitted to FDA for comment prior to publication or dissemination. Please note that these submissions are voluntary. If you desire comments on proposed launch promotional materials with respect to compliance with applicable regulatory requirements, we recommend you submit, in draft or mock-up form, two copies of both the promotional materials and package insert directly 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

We call your attention to 21 CFR 314.81(b)(3) which requires that all promotional materials be submitted to the Division of Drug Marketing, Advertising, and Communications with a completed Form FDA 2253 at the time of their initial use.

As soon as possible, but no later than 14 days from the date of this letter, submit, using the FDA automated drug registration and listing system (eLIST), the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format, as described at http://www.fda.gov/ForIndustry/DataStandards/StructuredProductLabeling/default.htm, that is identical to the approved labeling (including the package insert, and any patient package insert and/or Medication Guide that may be required). 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/U_CM072392.pdf The SPL will be accessible via publicly available labeling repositories.

Sincerely yours,

{See appended electronic signature page}

Keith Webber, Ph.D.
Deputy Director
Office of Pharmaceutical Science
Center for Drug Evaluation and Research

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

/s/

ROBERT L WEST

12/28/2010

Deputy Director, Office of Generic Drugs
for Keith Webber, Ph.D.