

**Appendix A**

**APPENDIX A.**

**DOCKET NO. 2004P-0390  
SUITABILITY PETITION SUBMITTED BY LACHMAN CONSULTANT  
SERVICES, INC. ON AUGUST 31, 2004**

**LACHMAN CONSULTANT SERVICES, INC.**  
CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

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August 31, 2004

**OVERNIGHT COURIER 8/31/04**

Division of Dockets Management  
Food and Drug Administration (HFA-305)  
Department of Health and Human Services  
5630 Fishers Lane, Room 1061  
Rockville, MD 20852

**Citizen Petition**

Dear Sir or Madam:

The undersigned submits this petition, in quadruplicate, pursuant to section 505(j)(2)(C) of the Federal Food, Drug and Cosmetic Act and in accordance with 21 CFR 10.30 on behalf of a client requesting the Commissioner of the Food and Drug Administration to declare that the drug products, Doxycycline Hyclate Tablets 75 mg and 100 mg, are suitable for consideration in an abbreviated new drug application (ANDA).

**A. Action Requested**

The petitioner requests that the Commissioner of the Food and Drug Administration declare that Doxycycline Hyclate Tablets, 75 mg and 100 mg are suitable for submission in an ANDA. The listed reference drug product (RLD) upon which this petition is based is Doryx® (doxycycline hyclate), Capsules (coated pellets) 100 mg. Doryx® is also approved in a 75 mg strength. Therefore, the petitioner seeks a change in dosage form (from capsule to tablet) from that of the listed drug product.

**B. Statement of Grounds**

The RLD product is a capsule product containing (coated pellets) 75 mg or 100 mg of doxycycline hyclate. The listing for Doryx® Capsules appears on page 3-135 of the 24<sup>th</sup> edition of the Approved Drug Products with Therapeutic Equivalence Evaluations (better known as the Orange Book) (Attachment A). The proposed drug product represents a tablet dosage form of the same strengths and same active ingredient. The petition is thus seeking a change in dosage form (from capsule to tablet) from that of the RLD.

In support of the change in dosage form requested in this petition, we refer to other FDA approved "doxycycline" drug products that are available in a tablet dosage form (i.e., other doxycycline hyclate tablet products). However, in this instance, citing any of those products as the RLD would not be appropriate, since the purpose of this petition is to seek the ability to file a different dosage form (tablet) that is bioequivalent to Doryx® (doxycycline hyclate) Capsules (coated pellets). The petitioner is seeking this change in dosage form in an effort to make an alternate dosage form (tablet) available for those individuals that either have difficulty in

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swallowing a capsule or who prefer a tablet dosage form as an alternative to Doryx® (doxycycline hyclate), Capsules (coated pellets).

In further support of our proposed product, the petitioner would like to point out that the Agency has previously approved ANDA suitability petitions allowing for a change in dosage form (from capsule to tablet) in many instances. The labeling of the proposed product will be the same as that of the RLD with the exception of the obvious change in dosage form sought in this petition. The uses, doses and indications for the proposed product are also the same as those of the RLD. Draft labeling for the proposed product is included in Attachment B and labeling of the RLD is included in Attachment C.

Therefore, the petitioner's request for the Commissioner to find that a change in dosage form from capsule to tablet for Doxycycline Hyclate 75 mg and 100 mg should raise no questions of safety or effectiveness, and the Agency should approve the petition.

#### **Pediatric Waiver Request**

In any petition seeking a change in dosage form, it is necessary to address the provisions of the Pediatric Research Equity Act (PREA) of 2003. PREA amended the Federal Food, Drug and Cosmetic Act, to provide the Agency authority to require drug firms to study certain drugs in pediatric patients if the Agency felt that such study would provide beneficial health data for that patient population. In that regard, please consider this request for a full waiver for the need to conduct pediatric studies for the proposed drug product under PREA for the reasons outlined below.

The act provides a provision for a waiver from such requirement if:

- (iii) the drug or biological product,
  - (I) does not represent a meaningful therapeutic benefit over existing therapies for pediatric patients; and
  - (II) is not likely to be used in a substantial number of pediatric patients.

The petitioner hereby requests that a waiver from the conduct of pediatric patient be granted for the approval of this petition to permit subsequent ANDA filing.

The labeling of the RLD clearly supports the use of the doxycycline hyclate in pediatric patients above 8 years of age.

"The recommended dosage schedule for pediatric patients weighing 100 pounds or less is 2 mg/lb of body weight divided into two doses on the first day of treatment, followed by a 1 mg/lb of body weight given as a single daily dose or divided into two doses on subsequent days. For more severe infections, up to 2 mg/lb of body weight may be used. For pediatric patients over 100 pounds, the usual adult dose should be used."

However, the lack of dosing recommendations for pediatric patients under 8 years of age should not be construed as a need to study this drug in lower age groups since the product contains warnings against use in younger patients.

"The use of drugs of the tetracycline class during tooth development (last half of pregnancy, **infancy and childhood to the age of 8 years**) may cause permanent discoloration of the teeth (yellow-gray-brown). This adverse reaction is more common during long-term use of the drug but has been observed following repeated short-term courses. Enamel hypoplasia has also been reported. Tetracycline drugs, therefore, should not be used in this age group, except for Anthrax, including inhalational anthrax (post exposure) unless other drugs are not likely to be effective or are contraindicated." (Emphasis added)

Clearly then, this drug product should not be utilized in other than the pediatric population for whom it is currently labeled (age 8 or older) and based on the fact that inhalational anthrax is an extremely rare disease, the product would not likely be used in a substantial number of pediatric patients. Therefore, a waiver should be granted exempting pediatric studies on the proposed product.

**C. Environmental Impact**

The petitioner claims a categorical exclusion under 21 CFR 25.31.

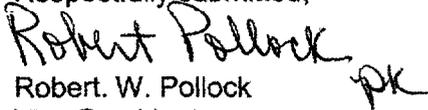
**D. Economic Impact**

The petitioner does not believe that this is applicable in this case, but will agree to provide such an analysis if requested by the Agency.

**E. Certification**

The undersigned certifies, that to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the petitioner, which are unfavorable to the petition.

Respectfully submitted,

  
Robert W. Pollock  
Vice President  
Lachman Consultant Services, Inc.  
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RWP/pk

- Attachments: A. page 3-135 of the 24<sup>th</sup> edition of the Approved Drug Products with Therapeutic Equivalence Evaluations  
B. Proposed Labeling  
C. Doryx (RLD) Labeling

cc: Emily Thomas (OGD)

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