

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

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January 27, 2004

**OVERNIGHT COURIER 1/27/04**

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

**Amendment to Citizen Petition  
Docket Number 2003P-0464/CP1  
Inclusion of Pediatric Waiver Request**

Dear Sir or Madam:

The petition cited above was submitted on October 1, 2003. The petition requested the Commissioner of the Food and Drug Administration to declare that the drug product, Clonazepam Oral Solution, 1 mg / 5 mL is suitable for consideration in an abbreviated new drug application (ANDA).

In December of 2003, Congress passed the Pediatric Research Equity Act of 2003 that 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. The act also provided 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 reference listed drug product is currently available in a conventional immediate-release tablet, as well as in a wafer (orally disintegrating tablet). The wafer being an orally disintegrating tablet represents an available alternative to the proposed oral solution product. In addition, the reference-listed drug, as explained in the body of the petition, is already labeled for pediatric dosing for seizure disorders which includes dosing instructions for pediatric patients down to infants:

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Pediatric Patients – Klonopin is administered orally. In order to minimize drowsiness, the initial dose for infants and children (up to 10 years of age or 30 kg of body weight) should be between 0.01 and 0.03 mg / kg / day, but not to exceed 0.05 mg / kg / day given in two or three divided doses. Dosage should be increased by no more than 0.25 to 0.5 mg every third day until a daily maintenance dose of 0.1 to 0.2 mg / kg of body weight had been reached, unless seizures are controlled or side effects preclude further increase.

Clonazepam is not recommended for patients under 18 years of age for its other approved indication (i.e., panic attacks).

The change in dosage form to an oral solution from an immediate-release tablet would not likely result in use over that currently in the pediatric population, as there is currently also available a tablet for oral disintegration that is likely utilized for pediatric patients that cannot swallow tablets. The addition of an oral solution would permit ease of delivery to elderly patients and patients for that may require dosing via an NG tube. It will also provide for an alternative to the orally disintegrating tablet for pediatric patients that prefer the oral solution. Since the product is already labeled as safe and effective for pediatric patients, it is not likely that the proposed product would be used in a substantial number of pediatric patients for whom the product is not already labeled. In addition, there are other approved anticonvulsant products available in liquid forms, as well as the orally disintegrating tablet of clonazepam that can be used in the place of the proposed product, and therefore, it would not represent a meaningful benefit over existing therapies for the pediatric patient.

For the reasons stated above and consistent with the provisions of the Pediatric Research Equity Act of 2003, the petitioner respectfully requests that this waiver be granted. Due to the fact that the pending petition was submitted over 90 days ago, the undersigned requests that the review of this waiver request be conducted in an expeditious manner.

Sincerely,

pk

Robert W. Pollock  
Vice President  
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RWP/pk

cc: Emily Thomas (Office of Generic Drugs)  
Martin Shimer (Office of Generic Drugs)

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