Each firm listed in the subject announcement has been furnished a copy of the Academy's report.

Recommendation

That the enclosed Federal Register document (Tab A) be signed.

REVIEW OF A BIOAVAILABILITY STUDY

IONAMIN 15 AND 30 CAPSULES RESIN COMPLEX CONTAINING 15 AND 30 MG. OF PHENTERMINE, NBA 11-613, PENNWALT CORP. AF 13-769. SUBMISSION MAY 30, 1973

1. Submitted are clinical studies to show efficacy of the product, and bioavailability studies to demonstrate the availablity of the product. If the clinical studies were done with the present formulation and show satisfactory efficacy, there is no need to consider the bioavailability studies. However, in case the bioavailability studies are needed, they are briefly reviewed below.

2. Eighteen subjects were used. Eights were crossed over at the 30 mg. and six at the 15 mg. does. The reference products were capsules containing 10, 15, or 30 mg. of phentermine. The 10 mg. phentermine capsules were given to four subjects at the 10 x 3 mg. dose. It is not clear if this was given all at once or in separate dosages of 10 mg. each. Blood samples were taken at 0.5, 1, 2, 3, 5, 6, 7, 9, 11, 12, 16, 24, 36, 43 and 72 hours. The essay used was a gas caromatographic method as described in volume 1.3 beginning on page 00136.

The phentermine capsules produced an average peak blood level in 5 hours of 51.5 and 199.2 mg/al for the 15 and 30 mg. dosages respectively. The corresponding values for the resinated product were 50.3 and 93.0 nc/my. the peaks being at 9 hours. The 10 x 3 dose produced peaks of 75.5 ag/my at 11 hours. The average areas under the curve for the 30 mg. dose was 253.75 and 2413.88 ng-ar/ml for the reference and ionamin products respectively. The blood level curves for the test and reference products were very similar.

Comments and recommendations

The bioavailability data for the test and reference products show similar blood levels. Acceptance of the bioavailability studies are recommended provided the company can satisfactorily answer such questions as how the reference products were prepared. However, if the clinical studies are satisfactory, there is no need to pursue the bioavailability studies any further. They were done in 1971 and the details of the studies may not still be available.

The company should not be allowed to make claims that their resin-complex product produces better or more prolonged blood levels than the nonresinated preparations.

HAROLD R. MURDOCK, Ph. D.,
Clinical Research Branch/DCR.

MEDICAL OFFICER'S REVIEW OF NDA 11-613

ANNUAL REPORT R-11 (5/30/73)

Date assigned to me: June 21, 1973.
Date review completed: October 2, 1973.
Sponsor: Pennwalt Corp., Rochester, N.Y.
Name of drug: Trade: Ionamin '15' and '30': Generic: phentermine resin.
Dosage forms (per capsule): phentermine—15 mg; 30 mg.
Route of administration: Oral.
Category: Anorectic.
Adverse reaction reports:

1. A young female taking Ionamin for her obesity became jittery, insomniac and complained of dry mouth. "She had become addicted to it." She had a "nervous breakdown accompanied by a catatonic condition". She was admitted to a State Hospital in N. J. for 3 months. Other details not given.