CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-361

Bioequivalence Review(s)

BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 40-361 APPLICANT: Barr Laboratories, Inc.

DRUG PRODUCT: Dextroamphetamine Sulfate Tablets, 5 mg and 10 mg

The Division of Bioequivalence has completed its review and has no further questions at this time.

The dissolution testing will need to be incorporated into your stability and quality control programs as specified in USP 23.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Dale P. Conner, Pharm. D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

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Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

Dextroamphetamine Sulfate
5 mg and 10 mg Tablets
ANDA #40-361
Reviewer: Moheb H. Makary
File name: 40361DW.299

Barr Laboratories, Inc.
Pomona, NY
Submission Date:
February 18, 1999

Review of Dissolution Data and Waiver Requests

The firm has submitted waiver requests for its dextroamphetamine sulfate, 5 mg and 10 mg tablets. To support the requests, the firm has submitted comparative dissolution profiles on its products and reference listed drug, Dextrostat® 5 mg and 10 mg tablets (Shire Richwood Inc.).

Dextrostat® is indicated in narcolepsy and in attention deficit disorder with hyperactivity.

Dextroamphetamine Sulfate is coded as an AA drug in the therapeutic equivalence evaluation book.

Formulations:

The formulations of Dextroamphetamine Sulfate Tablets, 5 mg and 10 mg are shown in Table I.

Dissolution Testing: (USP method)

Apparatus: 1 (basket)
Speed: 100 rpm
Medium: Deaerated Water
Volume: 500 mL
Sampling times: 15, 30, 45 and 60 minutes
Number of Tablets: 12
Test product: Barr's Dextroamphetamine Sulfate Tablets
5 mg, lot #8R95204
10 mg, lot #8R95305
Reference product: Shire Richwood's Dextrostat^{R} Tablets
5 mg, lot #B4462
10 mg, lot #B4322
Specification: in 45 minutes

Dissolution testing results are shown in Table II.

Comments:

1. Dissolution results for Barr Laboratories, Inc., test products Dextroamphetamine Sulfate Tablets, 5 mg and 10 mg are acceptable as summarized in Table II.

2. Waivers of bioequivalence study requirements for the test products may be granted based on CFR 320.22 (c).

Recommendations:

1. The dissolution testing conducted by Barr Laboratories, Inc., on its dextroamphetamine sulfate, 5 mg and 10 mg tablets, lots #8R95204 and #8R95305, respectively, is acceptable. Waivers of *in vivo* of bioequivalence study requirements for the test products are granted based on CFR 320.22 (c). From the bioequivalence point of view, the Division of Bioequivalence deems Barr's dextroamphetamine sulfate, 5 mg and 10 mg tablets to be bioequivalent to Dextrostat[R] 5 mg and 10 mg tablets, respectively, manufactured by Shire Richwood Inc.

2. The dissolution testing should be incorporated into the firm's manufacturing controls and stability program. The dissolution testing should be conducted in 500 mL of water using USP 23 apparatus 1 (basket) at 100 rpm. The test product should meet the following specifications:

> Not less than __ of the labeled amount of the drug product is dissolved in 45 minutes.

The firm should be informed of the above recommendations.

Moheb H. Makary

Moheb H. Makary, Ph.D.
Division of Bioequivalence
Review Branch III

RD INITIALLED BDAVIT BDAVIT 4/2/99
FT INITIALLED BDAVIT Barbara M Davis Date: 4/2/99

Concur: Dale P. Conner Date: 4/2/99
Dale P. Conner, Pharm.D.
Director
Division of Bioequivalence

Table II. In Vitro Dissolution Testing

Drug (Generic Name): Dextroamphetamine Sulfate Tablet
Dose Strength: 5 mg and 10 mg
ANDA No.: 40-361
Firm: Barr Laboratories, Inc.
Submission Date: February 18, 1999
File Name: 40361DW.299

I. Conditions for Dissolution Testing: USP method

USP XXIII Basket: x Paddle: RPM: 100
No. Units Tested: 12
Medium: Water Volume: 500 mL
Specifications: in 45 minutes
Reference Drug: Dextrostat® Tablet (Shire Richwood Inc.)
Assay Methodology

II. Results of *In Vitro* Dissolution Testing:

Sampling Times (Minutes)	Test Product Lot #8R95204 Strength(mg) 5			Reference Product Lot #B4462 Strength(mg) 5		
	Mean %	Range	%CV	Mean %	Range	%CV
15	62		3.4	60		3.6
30	96		1.5	82		2.7
45	102		2.3	95		3.2
60	103		1.8	103		1.9

Sampling Times (Minutes)	Test Product Lot #8R95305 Strength(mg) 10			Reference Product Lot #B4322 Strength(mg) 10		
	Mean %	Range	%CV	Mean %	Range	%CV
15	50		4.5	54		2.6
30	84		3.8	84		3.0
45	98		2.4	102		1.1
60	101		2.3	102		0.9