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CONSULTANTS TO THE PHARMACEUTICAL AND ALLIED INDUSTRIES

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November 10, 2004

OVERNIGHT COURIER 11/10/04

Division of Dockets Management (HFA-305)
Food and Drug Administration
Department of Health and Human Services
5360 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

The undersigned submits this petition in quadruplicate under Section 505 (j) of the Federal Food, Drug and Cosmetic Act, 21 CFR §10.20 and §10.30, and 21 CFR §314.93, to request the Commissioner of Food and Drug Administration to amend the *Approved Drug Products with Therapeutics Equivalence Evaluations* (commonly known as the Orange Book) 24th edition to designate DiaBeta (glyburide) Tablets, 5 mg, as a second reference-listed drug product. DiaBeta Tablets are listed in FDA's Orange Book with a BX rating. DiaBeta Tablets are not currently designated as an RLD. The product currently designated as the RLD is Micronase[®] Tablets manufactured by Pharmacia & Upjohn.

A. Action Requested

By this petition, the undersigned requests that the Commissioner of Food and Drugs designate DiaBeta Tablets, 5 mg, as a second RLD for the purposes of submitting an ANDA for a duplicate version of that RLD product.

B. Statement of Grounds

The Food and Drug Administration maintains a list of drug products that are eligible for submission as abbreviated new drug applications. That list, referred to as the "Orange Book", contains all FDA approved drug products. The FDA has decided through the comment and rule making process that it will designate all reference-listed drug (RLD) products, and that the designated reference-listed drug products will be the same drug products selected by the Agency as the reference standard for bioequivalence testing for a duplicate generic version of the RLD (57 FR 17954). FDA's intention in this regard was to designate a single reference-listed drug against which all generic versions must be shown to be bioequivalent, and thus avoid possible variations among generic drugs and their brand name counterparts (57 FR 17954). For multiple source NDA drug products or multiple source drug products without an NDA, the FDA has decided to generally designate the market leader as the reference-listed drug (57 FR 17958).

2004P.0504

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However, for multiple source drug products, a product **not** designated as the reference-listed drug and **not** shown to be bioequivalent (i.e., not having an "A" rating) to the designated reference-listed drug product selected by the Agency may be shielded from direct generic competition. This is indeed the situation in regard to this request.

In the current edition of the electronic Orange Book (relevant printed pages attached), there are two NDA products, Micronase (NDA 17-498) and DiaBeta (NDA 17-532) for glyburide that are of the same dosage form, active ingredient, strength and route of administration (i.e., representing pharmaceutical equivalents). The Micronase product is designated by the Agency as the RLD and is AB rated to a number of approved generic equivalents. However, the Agency does not designate DiaBeta as an RLD and assigns the therapeutic equivalence code as "BX". Thus, based on the Agency's advice to the public, DiaBeta is not rated as therapeutically equivalent to other glyburide approved products. Therefore, at this point in time, any ANDA applicant seeking approval of a glyburide tablet in strengths of 1.25 mg, 2.5 mg and 5 mg must cite Pharmacia / Upjohn's Micronase as the RLD, since the Agency on its own has designated this product as the RLD. This effectively shields the Aventis' DiaBeta product from direct competition. The petitioner believes that the market share for DiaBeta is significant and against which it would like to compete. Therefore because:

- 1) DiaBeta Tablets had total sales of approximately \$4 million in 2003. While DiaBeta Tablets has a relatively small share of the glyburide tablet market, this share represents sales that should not be shielded from direct generic competition;
- 2) there is currently no AB rated generic version of DiaBeta Tablets;
- 3) an *in-vivo* bioequivalence study and *in-vitro* dissolution testing will be conducted to support the application;
- 4) Glyburide Tablets will be labeled identically to DiaBeta Tablets;

the petitioner requests the Agency to designate DiaBeta as a RLD in the Orange Book.

C. Environmental Impact

Petitioner claims a categorical exclusion from the requirement of an environmental assessment or environmental impact statement pursuant to 21 CFR § 25.31.

D. Economic Impact

According to 21 CFR §10.30(b), the petitioner will, upon request by the Commissioner, submit economic impact information.

E. Certification

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

Sincerely,



Robert W. Pollock *pk*
Vice President
Lachman Consultant Services, Inc.
1600 Stewart Avenue
Westbury, NY 11590

RWP/pk

Attachment: 1. Approved Drug Products with Therapeutic Equivalence Evaluations
24th Edition (electronic)

cc: Don Hare (Office of Generic Drugs)
Martin Shimer (Office of Generic Drugs)

M19P4315

ATTACHMENT 1

Proprietary Name Search Results from "OB_Rx" table for query on "diabeta."

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
<u>017532</u>	BX	No	GLYBURIDE	TABLET; ORAL	1.25MG	DIABETA	AVENTIS PHARMS
<u>017532</u>	BX	No	GLYBURIDE	TABLET; ORAL	2.5MG	DIABETA	AVENTIS PHARMS
<u>017532</u>	BX	No	GLYBURIDE	TABLET; ORAL	5MG	DIABETA	AVENTIS PHARMS

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Active Ingredient Search Results from "OB_Rx" table for query on "glyburide".

Appl No	TE Code	RLD	Active Ingredient	Dosage Form; Route	Strength	Proprietary Name	Applicant
<u>075947</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE	AMIDE PHARM
<u>075947</u>	AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE	AMIDE PHARM
<u>075947</u>	AB	No	GLYBURIDE	TABLET; ORAL	6MG	GLYBURIDE	AMIDE PHARM
<u>017532</u>	BX	No	GLYBURIDE	TABLET; ORAL	1.25MG	DIABETA	AVENTIS PHARMS
<u>017532</u>	BX	No	GLYBURIDE	TABLET; ORAL	2.5MG	DIABETA	AVENTIS PHARMS
<u>017532</u>	BX	No	GLYBURIDE	TABLET; ORAL	5MG	DIABETA	AVENTIS PHARMS
<u>074591</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	CLONMEL HLTHCARE
<u>074591</u>	AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	CLONMEL HLTHCARE
<u>074591</u>	AB	No	GLYBURIDE	TABLET; ORAL	4.5MG	GLYBURIDE (MICRONIZED)	CLONMEL HLTHCARE
<u>074591</u>	AB	No	GLYBURIDE	TABLET; ORAL	6MG	GLYBURIDE (MICRONIZED)	CLONMEL HLTHCARE
<u>076257</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.25MG	GLYBURIDE	COREPHARMA
<u>076257</u>	AB	No	GLYBURIDE	TABLET; ORAL	2.5MG	GLYBURIDE	COREPHARMA
<u>076257</u>	AB	No	GLYBURIDE	TABLET; ORAL	5MG	GLYBURIDE	COREPHARMA
<u>075890</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	HIKMA
<u>075890</u>	AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	HIKMA

<u>075890</u> AB	No	GLYBURIDE	TABLET; ORAL	6MG	GLYBURIDE (MICRONIZED)	HIKMA
<u>074792</u> AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	MYLAN
<u>074792</u> AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	MYLAN
<u>074792</u> AB	No	GLYBURIDE	TABLET; ORAL	6MG	GLYBURIDE (MICRONIZED)	MYLAN
<u>017498</u> AB	No	GLYBURIDE	TABLET; ORAL	1.25MG	MICRONASE	PHARMACIA AND UPJOHN
<u>020051</u> AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYNASE	PHARMACIA AND UPJOHN
<u>017498</u> AB	No	GLYBURIDE	TABLET; ORAL	2.5MG	MICRONASE	PHARMACIA AND UPJOHN
<u>020051</u> AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYNASE	PHARMACIA AND UPJOHN
<u>017498</u> AB	Yes	GLYBURIDE	TABLET; ORAL	5MG	MICRONASE	PHARMACIA AND UPJOHN
<u>020051</u> AB	Yes	GLYBURIDE	TABLET; ORAL	6MG	GLYNASE	PHARMACIA AND UPJOHN
<u>075174</u> AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	SANDOZ
<u>075174</u> AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	SANDOZ
<u>074388</u> AB	No	GLYBURIDE	TABLET; ORAL	1.25MG	GLYBURIDE	TEVA
<u>074686</u> AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	TEVA
<u>074388</u> AB	No	GLYBURIDE	TABLET; ORAL	2.5MG	GLYBURIDE	TEVA
<u>074686</u> AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	TEVA

<u>074686</u> AB	No	GLYBURIDE	TABLET; ORAL	4.5MG	GLYBURIDE (MICRONIZED)	TEVA
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<u>074388</u> AB	No	GLYBURIDE	TABLET; ORAL	5MG	GLYBURIDE	TEVA
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<u>074686</u> AB	No	GLYBURIDE	TABLET; ORAL	6MG	GLYBURIDE (MICRONIZED)	TEVA
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Proprietary Name Search Results from "OB_Rx" table for query on "glyburide".

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<u>076257</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.25MG	GLYBURIDE	COREPHARMA
<u>074388</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.25MG	GLYBURIDE	TEVA
<u>075947</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE	AMIDE PHARM
<u>076257</u>	AB	No	GLYBURIDE	TABLET; ORAL	2.5MG	GLYBURIDE	COREPHARMA
<u>074388</u>	AB	No	GLYBURIDE	TABLET; ORAL	2.5MG	GLYBURIDE	TEVA
<u>075947</u>	AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE	AMIDE PHARM
<u>076257</u>	AB	No	GLYBURIDE	TABLET; ORAL	5MG	GLYBURIDE	COREPHARMA
<u>074388</u>	AB	No	GLYBURIDE	TABLET; ORAL	5MG	GLYBURIDE	TEVA
<u>075947</u>	AB	No	GLYBURIDE	TABLET; ORAL	6MG	GLYBURIDE	AMIDE PHARM
<u>075890</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	HIKMA
<u>074792</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	MYLAN
<u>075174</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	SANDOZ
<u>074686</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	TEVA
<u>074591</u>	AB	No	GLYBURIDE	TABLET; ORAL	1.5MG	GLYBURIDE (MICRONIZED)	CLONMEL HLTHCARE
<u>074686</u>	AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	TEVA

<u>075174</u> AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	SANDOZ
<u>075890</u> AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	HIKMA
<u>074792</u> AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	MYLAN
<u>074591</u> AB	No	GLYBURIDE	TABLET; ORAL	3MG	GLYBURIDE (MICRONIZED)	CLONMEL HLTHCARE
<u>074591</u> AB	No	GLYBURIDE	TABLET; ORAL	4.5MG	GLYBURIDE (MICRONIZED)	CLONMEL HLTHCARE
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