DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

DEC 29 2000

01 JAN -8

Paul Klopper
c/o Farmacy
Post Office Box 242
Forestville, CA 95436

Tod H. Mikuriya, M.D.
1168 Sterling Avenue
Berkeley, CA 94708

Re: Docket No. 99P-1865/CP1

Dear Mr. Klopper and Dr. Mikuriya:

This letter responds to your petition dated May 21, 1999, requesting that the Food and Drug and Administration (FDA) determine that 13 different cannabis-containing drugs are not new drugs, as defined in the Federal Food, Drug, and Cosmetic Act (the 1938 Act), and therefore are not subject to the new drug provisions of the 1938 Act. For the reasons set out below, your petition is denied.

In your petition, you correctly state that, under the 1938 Act's "grandfather" clause (21 U.S.C. 201(p)), if a drug was marketed under the Federal Food and Drugs Act of 1906 (the 1906 Act) prior to the enactment of the 1938 Act, and the drug's labeling regarding its use is the same as it was before the enactment of the 1938 Act, the drug is not a new drug. If it is not a new drug, it is not subject to the new drug provisions of the 1938 Act, such as the new drug application provisions found in section 505 of the 1938 Act (21 U.S.C. 355). For the Agency to determine that a drug product is not a new drug under the grandfather exemption, the following two questions must be answered affirmatively:

1. Was the drug product marketed between January 1, 1907, the effective date of the 1906 Act, and June 25, 1938, the enactment date of the 1938 Act?

2. Is the drug product at issue the same drug product that was marketed between January 1, 1907, and June 25, 1938, and does its labeling describe the same conditions of use?

Your petition presents significant evidence that versions of the 13 different cannabis-containing drug products were marketed between January 1, 1907, and June 25, 1938. The FDA will assume, for purposes of this response, that versions of all 13 drug products were marketed

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between January 1, 1907, and June 25, 1938. However, you do not present any evidence that the drug products at issue are the same drug products that were marketed between January 1, 1907, and June 25, 1938. For this reason, your petition must be denied.

The person seeking to show that a drug product comes within a grandfather exemption must prove every essential fact necessary for invocation of the exemption. See *United States v. An Article of Drug * * * "Bentex Ulcerine,"* 469 F.2d 875, 878 (5th Cir. 1972), *cert. denied*, 412 U.S. 938 (1973). Furthermore, the grandfather clause will be strictly construed against one who invokes it. See *id.*; *United States v. Allan Drug Corp.*, 357 F.2d 713, 718 (10th Cir.), *cert. denied*, 385 U.S. 899 (1966). A change in composition or labeling precludes the applicability of the grandfather exemption. See *USV Pharmaceutical Corp. v. Weinberger*, 412 U.S. 655, 663 (1973).

Section 314.200(e)(2) (21 CFR 314.200(e)(2)) specifies the information that must support a contention that a drug product is not a new drug because it was marketed under the 1906 Act. The required information addresses both when the drug in question was originally marketed and whether the drug that is currently marketed is the same as the drug marketed between January 1, 1907, and June 25, 1938. Section 314.200(e)(2) requires data showing the "exact quantitative formulation of the drug (both active and inactive ingredients) on the date of initial marketing of the drug" and a "statement whether such formulation has at any subsequent time been changed in any manner. If any such change has been made, the exact date, nature, and rationale for each change in formulation . . . should be stated . . . . If no such change has been made, a copy of representative documents or records showing the formula at representative points in time should be submitted to support the statement."

Additionally, § 314.200(e)(2) requires a "copy of each pertinent document or record to establish the identity of each item of written, printed, or graphic matter used as labeling on the date the drug was initially marketed" and

> A statement whether such labeling has at any subsequent time been discontinued or changed in any manner. If such discontinuance or change has been made, the exact date, nature, and rationale for each discontinuance or change and a copy of each pertinent document or record to establish each such discontinuance or change should be submitted . . . . If no such discontinuance or change has been made, a copy of representative documents or records showing labeling at representative points in time should be submitted to support the statement.

Finally, § 314.200(e)(2) requires a "copy of each pertinent document or record to establish the exact date the drug was initially marketed" and a "statement whether such marketing has at any

subsequent time been discontinued. If such marketing has been discontinued, the exact date of each such discontinuance should be submitted, together with a copy of each pertinent document or record to establish each such date."

As can be seen from the material quoted above, the determination of whether a drug product is or is not a new drug under the grandfather provision of the 1938 Act is a fact-intensive determination of whether a ***specific*** drug product is the same drug product marketed between January 1, 1907, and June 25, 1938. See *USV Pharmaceutical Corp. v. Weinberger*, 412 U.S. 655, 663 (1973).[1] Your petition and supporting documentation simply do not come close to giving the quantity and quality of information required for FDA to make a determination. To give just one example, you do not give the "exact quantitative formulation . . . (both active and inactive ingredients)" of any of the drugs marketed between January 1, 1907, and June 25, 1938, nor do you provide that data for any drug product whose new drug status you wish determined. Without this information, and much more, FDA cannot determine whether any specific drug product that is a member of one of the classes of drugs mentioned in your petition is or is not a new drug.[2]

FDA notes that marihuana is currently listed in Schedule I under the Controlled Substances Act (21 U.S.C. 812(c), 21 CFR 1308.11(d)(19)).[3] The labeling for all Schedule I drugs is required to bear the "C-I" symbol (21 CFR 1302.03). FDA would regard the inclusion of the "C-I" symbol on a product as a labeling change regarding the conditions of its use. This would mean that the drug product no longer qualified for the grandfather clause. This would be true even if marihuana were rescheduled and placed in Schedules II through V: the inclusion of the "C" symbol on the product would be viewed as a labeling change regarding the conditions of its use.

The Agency also denies your request that you be given a hearing prior to any adverse response to your petition (Petition at 5-6). There is no material issue of fact that requires a hearing. See 21 CFR 314.200(g).

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[1]The protection of the grandfather exemption extends only to the specific drug products on the market on the relevant date. A product marketed by a different manufacturer is not entitled to the exemption, even if the later product is virtually identical to the grandfathered product. See the *Federal Register* of May 4, 1982 (47 FR 19224).

[2]Note that the 1938 grandfather clause applies only to the new drug provisions of the Act and not to the adulteration or misbranding provisions (Sections 501 and 502 of the Act (21 U.S.C. 351 - 352)). Thus, the grandfather provision does not prevent the Agency from ensuring that any drug product, even if it might be grandfathered, is not adulterated or misbranded.

[3]Drugs in Schedule I have a high potential for abuse, have no currently accepted medical use in treatment in the United States, and there is a lack of accepted safety for use of the drugs under medical supervision (21 U.S.C. 812(b)(1)). Drugs listed in Schedule I may only be used in research (21 CFR 1301.13).

For the reasons stated above, your petition is denied.

Sincerely yours,

Dennis E. Baker
Associate Commissioner
for Regulatory Affairs