LACHMAN CONSULTANT SERVICES, INC.
Westbury, NY 11590

ATTACHMENT D

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

FEB 13 2003

Lachman Consultant Services
Attention: Robert Pollock
1600 Stewart Avenue
Westbury, NY 11590

Docket No. 02P-0297/CP1

Dear Sir:

This is in response to your petition filed on June 28, 2002, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug product: Propoxyphene Hydrochloride, Acetaminophen and Caffeine Capsules, 65 mg/389 mg/ 32.4 mg. The listed drug product to which you refer in your petition is Darvon® Compound 65 (Propoxyphene Hydrochloride, Aspirin and Caffeine) Capsules, 65 mg/389 mg/32.4 mg, approved under NDA 10-996 held by AAI Pharma LLC.

Your request involves a change in one active ingredient for another active ingredient of the same pharmacologic class in a fixed combination listed drug product (i.e., substituting an equipotent dose of acetaminophen (APAP) for aspirin (ASA) in the listed drug products). The change you request is the type of change that is authorized under the Federal Food, Drug, and Cosmetic Act (Act).

We have reviewed your petition under Section 505(j)(2)(C) of the Act and have determined that it is approved. This letter represents the Food and Drug Administration's (FDA) determination that an ANDA may be submitted for the above-referenced drug product.

Under Section 505(j)(2)(C)(i) of the Act, the FDA must approve a petition seeking a change in one active ingredient for another active ingredient of the same pharmacologic class in a fixed combination listed drug product unless it finds that investigations must be conducted to show the safety and effectiveness of the differing active ingredients.

According to the Tentative Final Monograph (TFM), *Internal Analgesic, Antipyretic, and Antirheumatic Drug Products for Over-the-Counter Human Use*, published November 16, 1988 in the Federal Register (53 FR 46204), the Agency believes at this time that it is reasonable for APAP and ASA to have the same dosage and frequency of administration because, based upon the data submitted to the Panel, the safe and effective dosage ranges for APAP and ASA are the same—325 mg to 650 mg every 4 hours, not to exceed 4 g in 24 hours (TFM, 53 FR at 46236). Accordingly, the Agency finds that the change in active ingredient for the specific proposed drug product does not pose questions of safety or effectiveness because the uses, dose, and route of

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administration of the proposed drug product are the same as that of the listed drug product. When an ANDA is submitted for your proposed drug product, the proposed labeling should reflect the maximum number of tablets per day that can be administered for your proposed drug product. The total daily dose of the acetaminophen component should not exceed the maximum total daily dose for adults of 4000 mg established by the Agency for its safe and effective range. In addition, please consult the Labeling Review Branch at (301) 827-5846 if you have any questions regarding the proposed labeling for this specific drug product.

On October 17, 2002, the United States District Court for the District of Columbia ruled that the Food and Drug Administration (FDA) did not have the authority to issue the Pediatric Rule and enjoined FDA from enforcing it. (Civil Action 00-02898(HHK).[1] The government has decided not to appeal the decision; however, intervenors in the case have appealed. Because FDA is currently enjoined from enforcing the Pediatric Rule, you are under no obligation to conduct pediatric studies on your petitioned drug product at this time. Please be aware that if the decision to invalidate the Pediatric Rule is not upheld on appeal, an abbreviated new drug application (ANDA), submitted under an ANDA suitability petition[2], may be subject to the requirements of the Pediatric Rule in the future.[3] If the Pediatric Rule is reinstated and pediatric clinical studies are required for this product in the future, you will be notified as soon as possible. Under those circumstances, the petitioned product may not be eligible for approval under the ANDA approval authorities.

The FDA concludes, therefore, that investigations are not necessary in this instance. In addition, if shown to meet bioavailability requirements, the proposed drug product can be expected to have the same therapeutic effect as the listed reference drug product.

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1 The Pediatric Rule (rule) is codified at 21 CFR 314.55/21 CFR 601.27.

2 An ANDA suitability petition is a petition submitted pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act requesting permission to submit an ANDA for a new drug which has a different active ingredient, or whose route of administration, dosage form, or strength differ from that of the listed drug. Also see 21 C.F.R.§ 314.93.

3 While it was in effect, the Pediatric Rule required that all applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens must contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred (21 CFR 314.55).

The approval of this petition to allow an ANDA to be submitted for the above-referenced drug product does not mean that the FDA has determined that an ANDA will be approved for the drug product. The determination of whether an ANDA will be approved is not made until the ANDA itself is submitted and reviewed by the FDA.

To permit review of your ANDA submission, you must submit all information required under Sections 505(j)(2)(A) and (B) of the Act. To be approved, the drug product will, among other things, be required to meet current bioavailability requirements under Section 505(j)(2)(A)(iv) of the Act. We suggest that you submit your protocol for this drug product to the Office of Generic Drugs, Division of Bioequivalence prior to the submission of your ANDA. During the review of your application, the FDA may require the submission of additional information.

The listed drug product to which you refer in your ANDA must be the one upon which you based this petition. In addition, you should refer in your ANDA to the appropriate petition docket number cited above, and include a copy of this letter in the ANDA submission.

A copy of this letter approving your petition will be placed on public display in the Dockets Management Branch, Room 1061, Mail Stop HFA-305, 5630 Fishers Lane, Rockville, MD 20852.

Sincerely yours,

Gary J. Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

From: Westbury Office (516)683-1881
LACHMAN CONSULTANT SERVICES
1600 STEWART AVE
SUITE 604
WESTBURY, NY, 11590

REVENUE BARCODE

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Food and Drug Administration
Dept. of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD, 20852

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