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June 27, 2002

OVERNIGHT DOCUMENT 6/27/02

Dockets Management Branch
Food and Drug Administration
Department of Health and Human Services
5630 Fishers Lane, Room 1061
Rockville, MD 20852

CITIZEN PETITION

The undersigned, on behalf of a client, submits this petition in quadruplicate under Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act ("the FDC Act"), 21 U.S.C. § 355(j)(2)(C), and 21 C.F.R. §§ 10.20, 10.30, and 314.93 to request that the Commissioner of Food and Drugs make a determination that an Abbreviated New Drug Application (ANDA) may be submitted for Propoxyphene Hydrochloride Acetaminophen and Caffeine Capsules 65 mg / 389 mg / 32.4 mg.

A. Action Requested

The petitioner requests that the Commissioner of Food and Drugs make a determination that a Propoxyphene Hydrochloride, Acetaminophen and Caffeine Capsule, 65 mg / 389 mg / 32.4 mg combination drug product is suitable for submission as an ANDA. The reference-listed drug product upon which this petition is based is DARVON[®] Compound 65 (Propoxyphene Hydrochloride, Aspirin and Caffeine Capsules, 65 mg / 389 mg / 32.4 mg), NDA Number 10-996 manufactured by Lilly. Therefore, this petition requests the substitution of an equipotent dose of one of the active ingredients for another of the same therapeutic class (i.e., 389 mg of Aspirin to 389 mg of Acetaminophen) in the above-referenced combination product.

This petition also requests that the FDA grant a waiver of the pediatric study requirements for the proposed product. This waiver is sought under 21 CFR 314.55(c)(2)(i). The basis for this request is that the newly proposed combination product will not offer a meaningful therapeutic benefit over existing treatments for pediatric patients and the new product is not expected to be utilized in a significant number of pediatric patients. There are numerous approved products, many in dosage forms more appropriate for use in treating pain in pediatric patients (e.g., acetaminophen with codeine solution and Hydrocodone Bitartrate and Acetaminophen Elixir where dosing recommendations down to 2 years of age are provided). It is not anticipated that the simple substitution of an equipotent dose of acetaminophen for

aspirin in the existing combination product will likely promote the use of the product in pediatric patients. In addition, this product will, by nature of its composition, be of a relatively large capsule size (greater than 500 mg) and would contain a dose of 389 mg of acetaminophen. Both of these factors would not appear to be particularly useful in treating pediatric patients especially with other more convenient (liquid) dosage form products available in the marketplace.

B. Statement of Grounds

Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act provides for the submission of an ANDA for a new drug that differs in active ingredient from a listed drug, provided that the FDA has approved a petition seeking permission to file such an application. This petition requests a change in one of the active ingredients (aspirin) of DARVON[®] Compound 65 (Propoxyphene Hydrochloride, Aspirin and Caffeine Capsules, 65 mg / 389 mg / 32.4 mg) to contain an equipotent dose 389 mg of acetaminophen. The reference-listed drug is manufactured by Lilly.

The listing of the reference listed drug product, DARVON[®] Compound 65 (Propoxyphene Hydrochloride, Aspirin and Caffeine Capsules, 65 mg / 389 mg / 32.4 mg) can be found on page 3-34 of the 22nd Edition of the Approved Drug Products with Therapeutic Equivalents Evaluation (commonly referred to as the "Orange Book"). (See Attachment A.)

According to the approved labeling of the reference listed drug product, the usual dosage is "65 mg Propoxyphene Hydrochloride, 389 mg aspirin and 32.4 mg caffeine" or one capsule "every four hours if needed for pain". The maximum recommended dose of Propoxyphene Hydrochloride is 390 mg / day or 6 capsules a day. The approved package insert for DARVON[®] Compound 65 (Propoxyphene Hydrochloride, Aspirin and Caffeine Capsules, 65 mg / 389 mg / 32.4 mg) is included as Attachment B. The dosage for the proposed product is the same as that of the reference listed drug (i.e., one capsule every 4 hours if needed for pain with a maximum of 6 capsules recommended per day). In addition, because the dose-limiting component expressed in the labeling of the reference-listed drug product appears to be Propoxyphene Hydrochloride (i.e., daily dose not to exceed 390 mg), the maximum total daily dose of acetaminophen will be 2334 mg, which is well below the total daily-recommended limit of 4000 mg for this component. Therefore, there should be no safety or efficacy concern regarding the substitution of acetaminophen in the proposed product.

The proposed labeling for Propoxyphene Hydrochloride, Acetaminophen and Caffeine Capsules, 65 mg / 389 mg / 32.4 mg is included as Attachment C. Labeling for the proposed product will be consistent with the approved labeling for other Propoxyphene and Acetaminophen combination products and the labeling of the reference-listed drug.

In summary, the proposed substitution of an equipotent dose of one active ingredient component for another of the same therapeutic class from that of the reference-listed drug will not affect the product's safety or efficacy. The indication remains unchanged and the proposed dosing is consistent with dosing recommendations in the labeling of the approved reference-listed drug product's labeling. Therefore, the Agency should conclude that investigations are not necessary to demonstrate the proposed product's safety or effectiveness and grant the petition.

C. Environmental Impact

The petitioner claims a categorical exclusion under 21 CFR 25.31.

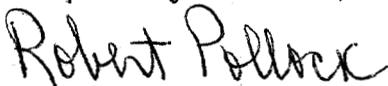
D. Economic Impact Statement

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

E. Certification

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

Respectfully submitted,



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- Attachments:
- A. Page 3-34, *Approved Drug Products with Therapeutic Equivalence Evaluations, 22nd Edition*
 - B. Darvon Compound 65 (Propoxyphene Hydrochloride, Aspirin and Caffeine) Insert Labeling
 - C. Draft insert labeling for proposed drug product

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