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May 21, 2004

**OVERNIGHT COURIER 5/21/04**

Division of Dockets Management  
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 (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 Oxycodone and Acetaminophen Tablets, USP, 2.5 mg / 400 mg, 5 mg / 400 mg, 7.5 mg / 400 mg and 10 mg / 400 mg.

**A. Action Requested**

The petitioner requests that the Commissioner of the Food and Drug Administration make a determination that Oxycodone and Acetaminophen Tablet, USP combination drug products, in strengths of 2.5 mg / 400 mg, 5 mg / 400 mg, 7.5 mg / 400 mg and 10 mg / 400 mg are suitable for submission in an ANDA. The reference-listed drug product upon which this petition is based is PERCOCET® (Oxycodone and Acetaminophen Tablets USP), ANDA Number 85-106 (5 mg / 325 mg). PERCOCET® is held by Endo Pharmaceuticals. Therefore, this petition requests a change in the strength of the non-narcotic component, acetaminophen from 325 mg to 400 mg per tablet, along with 5 mg of oxycodone hydrochloride found in the reference-listed drug and to also include additional strengths of the narcotic component, hydrocodone bitartrate, 2.5 mg, 7.5 mg and 10 mg in combination with 400 mg of acetaminophen.

**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 strength 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 the strength of the non-narcotic active ingredient, acetaminophen, from 325 mg per tablet which is found in the reference-listed drug, PERCOCET® to 400 mg per tablet along with the same 5 mg of the narcotic component and the addition of 2.5 mg, 7.5 mg and 10 mg strengths of oxycodone hydrochloride to be combined with the changed 400 mg acetaminophen.

The listing of PERCOCET® (Oxycodone and Acetaminophen Tablets USP, 5 mg / 325 mg) can be found on page 3-7 of the 24<sup>th</sup> Edition of the Approved Drug Products with Therapeutic Equivalents Evaluation (commonly referred to as "The Orange Book"). Please see Attachment A.

According to the approved labeling of the reference-listed drug product, PERCOCET® (Oxycodone and Acetaminophen Tablets USP, 5 mg / 325 mg), the usual adult dosage is "one tablet every six hours. The total daily dose of acetaminophen should not exceed 4 grams." In addition, the approved labeling indicates that "[D]osage should be adjusted according to the severity of the pain and the response of the patient. It may occasionally be necessary to exceed usual dosage recommended [in the labeling] in cases of more severe pain or in patients who have become tolerant to the analgesic effects of opioids." For the 2.5 mg / 325 mg strength, the dosing instructions in the approved labeling of the RLD states: "take one or two tablets every 6 hours." It should be noted that Percocet is also approved in the following strengths:

2.5 mg / 325 mg  
5 mg / 325 gm  
7.5 mg / 500 mg  
10 mg / 650 mg

The approved package insert for PERCOCET® Tablets (Oxycodone Hydrochloride and Acetaminophen Tablets, 5 mg / 325 mg) is included in Attachment B. The dosage for the proposed product is consistent with the dosage approved in the reference-listed drug product's labeling. Also, numerous combination products containing greater than 325 mg of acetaminophen (i.e. from 500 mg – 750 mg) have been approved by the FDA as safe and effective. The restriction based on the maximum of a single 1000 mg dose of acetaminophen and a total daily dose of 4000 mg is maintained in the proposed labeling.

In summary, the proposed strength change of the non-narcotic component from that of the reference-listed drug (i.e. a change of acetaminophen from 325 mg to 400 mg) along with the currently approved 5 mg of oxycodone hydrochloride and the proposed change in strength of the narcotic component to also include 2.5 mg, 7.5 mg and 10 mg oxycodone hydrochloride to be included with 400 mg of acetaminophen will not raise questions of the safety or efficacy of the proposed products. The indication remains unchanged and the proposed dosing is consistent with that recommended in the labeling of the approved reference-listed drug product. The efficacy of a 400 mg dose of acetaminophen, in combination with equivalent doses of a narcotic analgesic, is supported by other FDA-approved products containing doses higher than 325 mg (i.e. from 500 mg – 750 mg). Therefore, the Agency should conclude that clinical investigations are not necessary to demonstrate the proposed product's safety or effectiveness.

The proposed labeling for Oxycodone and Acetaminophen Tablets, USP 2.5 mg / 400 mg, 5 mg / 400 mg, 7.5 mg / 400 mg and 10 mg / 400 mg is included as Attachment C. Labeling for the proposed product will be consistent with the approved labeling for the reference-listed drug, Percocet Tablets (Oxycodone and Acetaminophen Tablets, USP), the combination product upon which this petition is based. This proposed labeling includes four strengths of Oxycodone and Acetaminophen Tablets, USP, 2.5 mg / 400 mg, 5 mg / 400 mg; 7.5 mg / 400 mg and 10 mg / 400 mg.

For the aforementioned reasons, the undersigned requests that the Commissioner approve this petition and find that an application for Oxycodone and Acetaminophen Tablets, USP, 2.5 mg / 400 mg, 5 mg / 400 mg, 7.5 mg / 400 mg and 10 mg / 400 mg are suitable for submission in an ANDA.

**C. Environmental Impact**

The petitioner claims a categorical exclusion under 21 C.F.R. § 25.31.

**D. Economic Impact Statement**

According to 21 C.F.R. § 10.30(b), the 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,

  
Robert W. Pollock *PK*  
Vice President

RWP/pk

Attachments:

- A. Page 3-7, Approved Drug Products with Therapeutic Equivalence Evaluations, 24<sup>th</sup> Edition
- B. PERCOCET® (Oxycodone Hydrochloride and Acetaminophen Tablets) 5 mg / 325 mg Insert Labeling
- C. Draft Insert Labeling for Proposed Drug Product

cc: Emily Thakur (Office of Generic Drugs)

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