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Dockets Management Branch
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20857

CITIZEN PETITION

The undersigned submits this petition under section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. § 355(j)(2)(C)), which authority has been delegated to the Commissioner of Food and Drugs under 21 C.F.R. § 5.10. Petitioner requests that the Commissioner of Food and Drugs declare that abbreviated new drug applications ("ANDAs") may be submitted for combination oxycodone hydrochloride/acetaminophen tablet products in the strengths hereafter described.

A. Action Requested

King & Spalding requests that the Commissioner declare ANDAs may be submitted for combination oxycodone hydrochloride/acetaminophen tablet products in strengths of 15 mg/325 mg and 20 mg/325 mg.

B. Statement of Grounds

For reasons detailed in previous citizen petitions concerning combination oxycodone/acetaminophen tablet products (*e.g.*, Docket No. OOP-1270, requesting that ANDAs be permitted for combination oxycodone/acetaminophen tablets in strengths of 7.5 mg/325 mg and 10mg/325 mg (Attachment 1)), it is essential that medical professionals be able to titrate the opioid (*e.g.*, oxycodone) and non-opioid (*e.g.*, acetaminophen) components of combination therapies to best achieve the goal of safely and effectively managing moderate to moderately severe pain.

Addition of the currently proposed oxycodone/acetaminophen tablet strengths to the pharmaceutical armamentarium will enhance the ability of medical professionals to treat individual patients' pain. In particular, physicians and other health care providers will be able to upwardly titrate the opioid dosage for a patient (*e.g.*, depending on the severity of the patient's

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pain, the degree of tolerance the patient may have developed, and other physical and medical characteristics), while maintaining an effective, yet low, daily dose of acetaminophen, if appropriate. As FDA is aware, the daily dose of acetaminophen must not exceed 4000 mg per day to avoid **risk** of hepatotoxicity, and many doctors prefer to prescribe a lower daily dose of acetaminophen.

The reference listed drug upon which this petition is based is Endo Pharmaceuticals' Percocet® 10mg/325 mg oxycodone hydrochloride/acetaminophen combination tablets for oral administration (ANDA No. 40-434). In addition to the reference product, the Food and Drug Administration has approved Endo Pharmaceuticals' 2.5 mg/325 mg oxycodone hydrochloride/acetaminophen tablet, Endo's 5 mg/325 mg oxycodone hydrochloride/acetaminophen tablet, and Endo's 7.5 mg/325 mg oxycodone hydrochloride/acetaminophen tablet (*see* ANDA Nos. 40-330 and 40-434). The agency has thus recognized the importance of making available products combining various levels of oxycodone with 325 mg acetaminophen.

The proposed products are similar to the reference product in that the proposed products contain oxycodone hydrochloride in combination with 325 mg acetaminophen. The proposed products differ from the reference product in that, instead of the 10 mg oxycodone hydrochloride and 325 mg acetaminophen combination, the proposed products contain 15 mg or 20 mg oxycodone hydrochloride in combination with 325 mg acetaminophen.

The adult dosing of the proposed drugs is shown in Attachment 2. The usual adult dosage is one tablet every six hours as needed for pain. Dosing should be adjusted according to the severity of pain and the response of an individual patient. It may occasionally be necessary to exceed the usual dosage recommended in cases of more severe pain or in those patients who have become tolerant to the analgesic effect of opioids. The maximum daily dose of 15mg/325 mg oxycodone hydrochloride/acetaminophen would be four tablets. The maximum daily dose of 20 mg/325 mg oxycodone hydrochloride/acetaminophen would be three tablets. A side by side comparison of the dosing for the reference and proposed products is enclosed as Attachment 3,

There is no need for investigations to establish the safety and effectiveness of the proposed products, as oxycodone hydrochloride and acetaminophen will be present in the products in amounts known to provide safe and effective analgesia for the target population. The proposed acetaminophen dose of 325 mg is recognized by FDA as safe and effective both as a single entity and as a constituent of opioid combination analgesics. *See* 53 Fed. Reg. 46204 (1988). The safety and effectiveness of oxycodone at the proposed levels is established, among other ways, by FDA's approval of Roxicodone® immediate-release tablets, which provide 15 mg or 30 mg oxycodone hydrochloride per tablet (NDA No. 21-011). There is no reason to anticipate that the co-administration of oxycodone hydrochloride and acetaminophen in the proposed products will inhibit the safety or analgesic efficacy of either component.

This petition does not raise consideration of clinical studies pursuant to FDA's pediatric use regulation, as the proposed ANDAs do not contemplate a new active ingredient, indication, dosage form, dosing regimen, or route of administration. 21 C.F.R. § 314.55(a).

C. Environmental Impact

As provided in 21 C.F.R. § 25.31, neither an environmental assessment nor an environmental impact statement is required.

D. Economic Impact

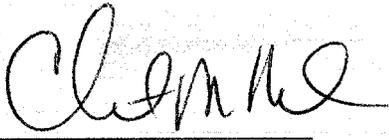
As provided in 21 C.F.R. § 10.30(b), economic impact information is to be submitted only when requested by the Commissioner following review of the petition.

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 us which are unfavorable to the petition.

Sincerely,

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Attachments