Orchid HEALTHCARE

Plot No. B3-B6 & B11-B14
Sipcot Industrial Park, Irungattukottai,
Sriperumbudur (TK) - 602 105.
Kancheepuram District, Tamil Nadu, INDIA.

A Division of Orchid Chemicals & Pharmaceuticals Ltd.,

January 10, 2007

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

Re: Docket 2006P-0442 – Citizen Petition Supplement

Dear Sir or Madam:

Orchid Healthcare, a Division of Orchid Chemicals & Pharmaceuticals ("Orchid"), submits this supplement to its Citizen Petition filed on October 23, 2006 (2006P-0442) ("Citizen Petition") under Section 505(j)(2)(c) of the Federal Food, Drug and Cosmetic Act and 21 C.F.R. § 10.30.

The Citizen Petition requests that FDA issue a determination that Wyeth Pharmaceuticals, Inc. ("Wyeth") discontinued its previously-approved formulation of the Reference Listed Drug ("RLD") Zosyn® (piperacillin and tazobactam for injection), 40.5 gram bulk pharmacy vial, for reasons unrelated to safety and effectiveness. The Citizen Petition also requests that FDA accept Abbreviated New Drug Applications (ANDAs) for piperacillin and tazobactam for injection, 40.5 gram pharmacy bulk vial, equivalent to 36 grams of piperacillin and 4.5 grams of tazobactam sufficient for delivery of multiple doses, and ANDAs for piperacillin and tazobactam for injection, packaged in vials containing 2.25 grams, 3.375 grams and 4.5 grams of piperacillin sodium and tazobactam sodium, in each case without edetate disodium dihydrate (EDTA) and citric acid monohydrate. Finally, the Citizen Petition referenced the information contained in two separate citizen petitions requesting that FDA issue the same determinations with respect to the previously-approved formulation of the RLD Zosyn® packaged in vials containing 2.25 grams, 3.375 grams and 4.5 grams of piperacillin sodium and tazobactam sodium.[1]

On December 12, 2006, Wyeth submitted comments in response to the Citizen Petition. In sum, Wyeth's comments reiterate the position it has taken in its submissions to the Sandoz and Rakoczy citizen petition dockets, as well as in its own citizen petition addressing matters related to Zosyn®.[2] Wyeth claims that Orchid has failed to justify a request for a waiver of the requirement that an ANDA for a parenteral drug product contain the same inactive ingredient as the RLD, based on the exclusion of EDTA from the proposed generic product. In support of this argument, Wyeth focuses on a lack of discussion in the Citizen Petition of the particulate matter and compatibility issues that have repeatedly been raised in the prior submissions to the relevant citizen petition dockets.

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1 Sandoz Inc. (Sandoz) Citizen Petition, November 1, 2005 (2005P-0456); Rakoczy (Rakoczy) Molino Mazzochi Siwik LLP Citizen Petition, May 9, 2006 (2006P-0195).

2 Docket 2006P-0173.

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In making these arguments, Wyeth disregards Orchid's reference to and reliance on the information contained in the existing dockets on matters related to Zosyn® in support of this Citizen Petition. As Orchid previously noted, the information in the Sandoz and Rakoczy dockets provide ample – and unchallenged – support for the requests made in the Citizen Petition. Relevant filings from the dockets are provided as **Attachment A** and **Attachment B**, respectively, and are incorporated herein by reference. In sum, it is not in dispute that Wyeth withdrew the previous formulation of Zosyn® for reasons unrelated to safety and effectiveness. Indeed, Wyeth itself has stated that the level of particulates in the original formulation, without the additional EDTA and citric acid monohydrate, "did not present a clinically significant safety concern."[3] Thus, there is no question that the previously-approved formulation of Zosyn® is safe and effective when administered in accordance with its approved labeling.

Furthermore, as noted in the Rakoczy citizen petition, the "public health" concerns cited by Wyeth in connection with its arguments regarding compatibility and the appearance of particulate matter in the previously-approved formulation are both irrelevant and meritless with respect to the requests made in the Citizen Petition. Wyeth has proffered no evidence demonstrating that the particulate matter issues associated with its previous formulation of Zosyn® would necessarily occur in proposed generic versions of this formulation. The appearance of particulate matter in Wyeth's previous formulation may simply reflect a deficiency in Wyeth's processes and controls. As a result, the ability of a proposed generic product to comply with the particulate matter standard set forth in USP <788> should be addressed by the Office of Generic Drugs ("OGD") in connection with the review and approval of the ANDA for the proposed generic product. To that end, Orchid notes that its proposed generic formulation would comply with USP <788> as manufactured and under the conditions of use permitted under the label. Similarly, the difference in the compatibility profile between the previously-approved and current formulations of Zosyn® is irrelevant to a determination of whether the previously-approved formulation is safe and effective. The labeling of a proposed generic product will provide adequate protection against medication errors.

For these reasons, both these issues of compatibility and particulate matter are irrelevant for consideration of the determination requested in Orchid's Citizen Petition.

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[3] Docket 2005P-0456/C1 (Wyeth Comments to Sandoz Petition).

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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 is unfavorable to the petitioner.

Respectfully submitted,

Imtiyaz Basade January 10, 2007
Vice President – Regulatory Affairs
Orchid Healthcare

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