

Food and Drug Administration
Rockville MD 20857

MAY 26 2005 5 MAY 27 09:45

Nico Worldwide, LLC
Attention: Barry Sugarman
1730 Michael Lane
Pacific Palisades, CA 90272-2037

Docket No. 2004P-0280/CP1

Dear Mr. Sugarman:

This is in response to your petition filed on July 7, 2004, requesting permission to file an Abbreviated New Drug Application (ANDA) for the following drug products: Nicotine Polacrilex Oral Solution, 2 mg(base)/240 mL and 4 mg(base)/240 mL. The listed drug products to which you refer in your petition are Commit® (Nicotine Polacrilex) Troches/Lozenges, 2 mg(base) and 4 mg(base), manufactured by GlaxoSmithKline.

Your request involves a change in dosage form (i.e., from troches/lozenges to oral solution) from that of the listed drug products. The change that you request is the type of change that is authorized under Section 505(j)(2)(C) of the Act.

This petition was reviewed pursuant to Section 505(j)(2)(C) of the Federal Food, Drug, and Cosmetic Act (Act). In addition, the comments dated October 1, 2004, filed by Ropes & Gray LLP, on behalf of GlaxoSmithKline Consumer Healthcare, LP, were also considered. Under Section 505(j)(2)(C)(i) of the Act, such a petition will be approved unless the Agency finds that investigations must be conducted to show the safety and effectiveness of the proposed drug products, or of any of the active ingredients, the route of administration, the dosage form, or strength which differ from the listed drug products.

The Agency has determined that your proposed change in dosage form raises questions of safety and effectiveness, and has concluded that clinical trials are required for these specific drug products. Your proposed products will not be approved for the same conditions of use as the listed drugs because of the large volume of fluid that must be taken to comply with the dosing instructions for the proposed products. There is a safety concern that ingesting such a large volume of fluid may present a risk to certain target populations (e.g., those with renal compromise). As a result, clinical investigations will be required for the proposed products and the proposed products will have to be labeled with appropriate instructions and warnings not present in the Commit® labeling. Given the large volume of fluid to be consumed in the

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formulation proposed, consumer compliance in the OTC setting is also a concern with the proposed products. Actual use studies would be required to demonstrate consumer compliance with the proposed dosing regimen.

In addition, due to the difference in their respective sites of absorption, the proposed oral solution is unlikely to be bioequivalent to the approved lozenge. Nicotine absorption from the lozenge is in large part due to buccal absorption and would not be subject to a first pass metabolic effect that would occur with an oral solution which is absorbed through the GI tract.¹ As a result, it is expected that the buccal absorption of the lozenge would result in higher systemic levels of nicotine and the GI absorption of the oral solution would lead to lower systemic levels of nicotine (for equivalent amounts of active ingredient). Therefore, clinical trials are needed to determine the safety and effectiveness of the proposed products.

Thus, FDA is denying the petition under Section 505(j)(2)(C)(i) because clinical investigations are necessary to show the safety and effectiveness of the proposed drug products and under 21 CFR 314.93(e)(iv) because “the proposed changes from the listed drug would jeopardize the safe or effective use of the product so as to necessitate significant labeling changes to address the newly introduced safety of effectiveness problem.”

As noted above, this petition is being denied because clinical trials in adults are required for the approval of the requested change to the listed drug products. Therefore, the question of whether pediatric clinical studies are necessary under the Pediatric Research Equity Act (PREA) for the change proposed has not been evaluated. However, it should be noted that pediatric studies have been requested for other nicotine products and cannot be waived without justification. Please contact the Division of Over-The-Counter Drug Products at 301-827-2265 if you wish to pursue approval of your products under Section 505(b) of the Act.

If you disagree with our determination concerning the acceptability of your petition as originally submitted, you may seek a reconsideration of the denial following the procedures set forth in 21 CFR 10.33. Requests for reconsideration must be based solely on the information contained in your original petition and must be submitted in accordance with 21 CFR Section 10.20, in the format outlined in Section 10.33 and no later than 30 days after the date of the decision involved. Petitions for reconsideration should be filed with the Dockets Management Branch at the address listed below. If there is additional information, not included as part of your original submission that you would like the Agency to consider, you should submit a new petition including all the necessary information to the Dockets Management Branch.

¹ Molander L, Lunell E. Pharmacokinetic investigation of a nicotine sublingual tablet. *Eur J Clin Pharmacol.* 56(11):813-9, 2001

A copy of this letter denying 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,

A handwritten signature in black ink that reads "Gary Buehler". The signature is written in a cursive style with a large, stylized initial "G".

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