CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

22-251

ENVIRONMENTAL ASSESSMENT

Food and Drug Administration
Center for Drug Evaluation and Research
Office of Pharmaceutical Science/Immediate Office

Memorandum

Date: February 1, 2008

From: Raanan A. Bloom, Ph.D.
OPS/IO/PARS

To: Martha Heimann
OPS/ONDQA/DPA I

Through: Jon Clark, M.S.
OPS/IO/PARS

Subject: LAMICTAL® ODT™ (Lamotrigine Orally Disintegrating Tablets)
Request for Categorical Exclusion

NDA 022-251
Submission Date: November 28, 2007; January 31, 2008 (amendment)

GlaxoSmithKline (GSK)
PO Box 13398
Research Triangle Park
North Carolina 27709-3398

Background

GlaxoSmithKline has filed a new drug application, NDA 22-251, to gain approval for LAMICTAL® ODT™ (Orally Disintegrating Tablets), indicated for the treatment of epilepsy and bipolar disorder.

GlaxoSmithKline has claimed a categorical exclusion under 21 CFR 25.31(b) for the present application based on the expected introduction concentration (EIC) of lamotrigine of less than 1 µg/L. In addition, as required under 21CFR25.15(d), GlaxoSmithKline states that there are no known "extraordinary circumstances" for the proposed action.

The applicant has calculated the EIC of lamotrigine based on the five-year (2008-2012 - anticipated Lamictal® ODT market entry in 2008) maximum amount of drug substance projected to be used in the United States market for all approved products and dosage forms. With approval of this action, the projected maximum annual production of lamotrigine for all

GSK products in the US market is predicted to be [redacted] with the peak year being is 2008; thereafter production of lamotrigine is expected to decline steeply.

Review of the Current Submission

An Environmental Assessment (EA; dated August 02, 2006) was previously submitted by GSK for Lamictal® (NDA 20-241 SE5-032; Submission Date: November 29, 2006). A FONSI was granted on May 10, 2007. The EA cross references EAs previously submitted and approved for Lamictal® Tablets (NDA 20-241) and Lamictal® Dispersible Tablets (NDA 20-764). The EA predicted sales of Lamictal® a [redacted], The present submission indicates that reduced sales are expected; 5 year projections are [redacted] with the peak year being 2008. Assuming a daily discharge of 1.214×10^{11} liters water from sewage treatment facilities in the United States, an EIC of <1.0 µg/L (ppb) is estimated. This value meet the concentration-based categorical exclusion criteria of $\leq$ 1 µg/L as stated at 21CFR25.31(b).

Comments and Conclusions

Based on an evaluation of the provided information, this application qualifies for a categorical exclusion under 21 CFR 25.31 (b).

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/s/

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2/1/2008 02:58:43 PM
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2/13/2008 05:02:20 PM
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