DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 22-108 **NDA APPROVAL**

Biovail Laboratories International SRL
Attention: John B. Dubeck, U.S. Agent
1001 G Street NW, Suite 500W
Washington, DC 20001

Dear Mr. Dubeck:

Please refer to your new drug application dated September 27, 2006, received September 28, 2006, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act for Aplenzin (Bupropion Hydrobromide) Extended-release tablets 174mg, 348mg, and 522mg.

We acknowledge receipt of your submissions dated:

October 23, 2007	March 18, 2008	April 16, 2008
November 29, 2007	March 31, 2008	April 17, 2008
March 17, 2008	April 11, 2008	April 18, 2008

The October 23, 2007 submission constituted a complete response to our July 19, 2007 action letter.

This new drug application provides for the use of Aplenzin (Bupropion Hydrobromide) Extended-release tablets for Major Depressive Disorder (MDD).

We have completed our review of this application, as amended. It is approved, effective on the date of this letter, for use as recommended in the enclosed agreed-upon labeling text.

REQUIRED PEDIATRIC ASSESSMENTS

Under the Pediatric Research Equity Act (PREA) (21 U.S.C. 355c), all applications for new active ingredients, new indications, new dosage forms, new dosing regimens, or new routes of administration are required to contain an assessment of the safety and effectiveness of the product for the claimed indication(s) in pediatric patients unless this requirement is waived, deferred, or inapplicable.

We are waiving the pediatric study requirement for ages 0 to 6 years because necessary studies are impossible or highly impractical due to the difficulty of diagnosing MDD in this age group. We are deferring submission of your pediatric study for ages 7 to 17 years for this application because this product is ready for approval for use in adults and the pediatric study has not been completed.

Your deferred pediatric study required by section 505B(a) of the Food, Drug, and Cosmetic Act (FDCA) is a required postmarketing study. The status of this required pediatric postmarketing study must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the FDCA. This required study is listed below.

1. Deferred pediatric study under PREA for the treatment of Major Depressive Disorder in pediatric patients ages 7 to 17.

   Final Report Submission: 5 years from the date of approval

Submit final study reports to this NDA 22-108. For administrative purposes, all submissions related to this required pediatric postmarketing study must be clearly designated "**Required Pediatric Assessment**".

RISK EVALUATION AND MITIGATION STRATEGIES (REMS) REQUIREMENT

Title IX, Subtitle A, Section 901 of FDAAA amends the FDCA to authorize FDA to require the submission of a Risk Evaluation and Mitigation Strategy (REMS) if the Secretary determines that such a strategy is necessary to ensure that the benefits of the drug outweigh the risks (section 505-1(a)(1)). This provision took effect on March 25, 2008.

In accordance with section 505-1 of FDCA, as one element of a REMS, FDA may require the development of a Medication Guide as provided for under 21 CFR Part 208. Pursuant to 21 CFR Part 208, FDA has determined that Aplenzin poses a serious and significant public health concern requiring the distribution of a Medication Guide. The Medication Guide is necessary for patients' safe and effective use of Aplenzin. FDA has determined that Aplenzin is a product that has serious risks of which patients should be made aware because information concerning the risks could affect patients' decisions to use Aplenzin. Antidepressants, including bupropion hydrobromide, are associated with an increased risk of suicidality in children, adolescents, and young adults in short-term studies of MDD and other psychiatric disorders. Under 21 CFR 208, you are responsible for ensuring that the Medication Guide is available for distribution to patients who are dispensed Aplenzin.

Your proposed REMS, submitted on April 21, 2008, is approved. The REMS consists of the Medication Guide included with this letter and the timetable for submission of assessments of the REMS included in your April 21, 2008 submission. The timetable you submitted is as follows:

1st FDAAA assessment: November 2009 (18 months from approval)
2nd FDAAA assessment: May 2011 (3 years from approval)
3rd FDAAA assessment: May 2015 (7 years from approval)

Information needed for assessment of the REMS may include:

a. Survey of patients' understanding of the serious risks of Aplenzin
b. Report on periodic assessments of the distribution and dispensing of the Medication Guide in accordance with 21 CFR 208.24
c. Report on failures to adhere to distribution and dispensing requirements, and corrective actions taken to address noncompliance

DISSOLUTION METHOD AND SPECIFIATION

Method:

Medium:	900 ml 0.1N HCl
Apparatus 1:	Basket
Speed:	75 rpm
Sampling Times:	2, 4, and 8 hrs

Specification:

Time	Criteria
2 hours	
4 hours	
8 hours	NLT

EXPIRY DATE

An expiration date of 24 months has been granted for the 174 mg & 348 mg tablets and an expiration date of 12 months has been granted for the 522 mg tablet.
We are waiving the requirements of 21 CFR 201.57(d)(8) regarding the length of Highlights of prescribing information. This waiver applies to all future supplements containing revised labeling unless we notify you otherwise.

CONTENT OF LABELING

As soon as possible, but no later than 14 days from the date of this letter, please submit the content of labeling [21 CFR 314.50(l)] in structured product labeling (SPL) format as described at http://www.fda.gov/oc/datacouncil/spl.html that is identical to the enclosed labeling (text for the package insert and Medication Guide). Upon receipt, we will transmit that version to the National Library of Medicine for public dissemination. For administrative purposes, please designate this submission, "SPL for approved NDA 22-108."

CARTON AND IMMEDIATE CONTAINER LABELS

Submit final printed carton and container labels as soon as they are available, but no more than 30 days after they are printed. Please submit these labels electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format – Human Pharmaceutical Product Applications and Related Submissions Using the eCTD Specifications (October 2005)*. Alternatively, you may submit 12 paper copies, with 6 of the copies individually mounted on heavy-weight paper or similar material. For administrative purposes, designate this submission "**Final Printed Carton and Container Labels for approved NDA 22-108**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product(s) with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

PROMOTIONAL MATERIALS

You may request advisory comments on proposed introductory advertising and promotional labeling. To do so, submit, in triplicate, a cover letter requesting advisory comments, the proposed materials in draft or mock-up form with annotated references, and the package insert(s) to:

Food and Drug Administration
Center for Drug Evaluation and Research
Division of Drug Marketing, Advertising, and Communications
5901-B Ammendale Road
Beltsville, MD 20705-1266

As required under 21 CFR 314.81(b)(3)(i), you must submit final promotional materials, and the package insert(s), at the time of initial dissemination or publication, accompanied by a Form FDA 2253. For instruction on completing the Form FDA 2253, see page 2 of the Form. For more information about submission of promotional materials to the Division of Drug Marketing, Advertising, and Communications (DDMAC), see www.fda.gov/cder/ddmac.

LETTERS TO HEALTH CARE PROFESSIONALS

If you issue a letter communicating important safety related information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit an electronic copy of the letter to both this NDA and to the following address:

MedWatch
Food and Drug Administration
Suite 12B05
5600 Fishers Lane
Rockville, MD 20857

REPORTING REQUIREMENTS

We remind you that you must comply with reporting requirements for an approved NDA (21 CFR 314.80 and 314.81).

If you have any questions, call LCDR Renmeet Grewal, Pharm.D., Senior Regulatory Project Manager, at (301) 796-1080.

Sincerely,

{See appended electronic signature page}

Thomas Laughren, M.D.
Director
Division of Psychiatry Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure : Package Insert & Medguide

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Thomas Laughren
4/23/2008 12:08:39 PM