CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-802

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-802

Novartis Pharmaceuticals Corporation
Attention: Mara Stiles
Senior Associate Director
Drug Regulatory Affairs
One Health Plaza
East Hanover, New Jersey 07936-1080

Dear Ms. Stiles:
Please refer to your new drug application (NDA) dated July 28, 2004, received July 28, 2004, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Focalin XR (dexmethylphenidate hydrochloride) Extended-Release Capsules.

We acknowledge receipt of your additional submissions dated November 23, 2004, November 30, 2004, and May 9, 2004.

We also acknowledge receipt of your submission dated April 15, 2004. This submission was not reviewed for this action.

This new drug application provides for the use of Focalin XR 5, 10, and 20 mg capsules in the treatment of attention deficit hyperactivity disorder (ADHD) in children, adolescents, and adults.

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 agreed-upon labeling text.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert and text for the patient package insert). Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. Alternatively, you may submit 20 paper copies of the FPL as soon as it is available but no more than 30 days after it is printed. Individually mount 15 of the copies on heavy-weight paper or similar material. For administrative purposes, designate this submission "**FPL for approved NDA 21-802**." Approval of this submission by FDA is not required before the labeling is used.

Chemistry Manufacturing and Controls
Based on the stability data an 18 month expiry has been granted.

Office of Clinical Pharmacology and Biopharmaceutics

1. Biowaivers: A biowaiver for the 5 mg capsule is granted.

2. Dissolution: We remind you of your commitment to adopt the following regulatory dissolution methods and specifications for Focalin XR 5mg, 10 mg, and 20 mg Capsules emailed to you on May 24, 2005

Pediatric Research Equity Act (PREA)
All applications for new active ingredients, new dosage forms, new indications, new routes of administration, and new dosing regimens are required to contain an assessment of the safety and effectiveness of the product in pediatric patients unless this requirement is waived or deferred. We note that you have fulfilled the pediatric study requirement for this application.

Post Marketing Commitments
We remind you of the following postmarketing study commitments that you agreed to on May 26, 2005:

1. An *in vitro* interaction study with clinically relevant alcohol concentrations is requested to examine the effect of ethanol on dose dumping. Dissolution profiles for Focalin XR should be generated with the media, containing ethanol concentrations ranging from 0% to 24% in 4% increments, (n.b. both acid and buffer phases should have the same ethanol concentration). Please note that the effect of ethanol on drug degradation should also be addressed when performing these experiments.

Protocol Submission:	by 07/2005
Study Start:	by 09/2005
Final Report Submission:	by 10/2005

2. A thorough QT study examining relevant doses in adults is required.

Draft Protocol Submission:	by 09/2005
Protocol Submission:	by 11/2005
Study Start:	by 03/2006
Final Report Submission:	by 03/2007

3. Conduct a pediatric fixed-dose response study.

Draft Protocol Submission:	by 10/2005
Protocol Submission:	by 12/2005
Study Start:	by 05/2006
Final Report Submission:	by 12/2007

Submit clinical protocols to your IND for this product. Submit nonclinical and chemistry, manufacturing, and controls protocols and all study final reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), you should include a status summary of each commitment in your annual report to this NDA. The status summary should include expected summary completion and final report submission dates, any changes in plans since the last annual report, and, for clinical studies, number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled "**Postmarketing Study Commitment Protocol**", "**Postmarketing Study Commitment Final Report**", or "**Postmarketing Study Commitment Correspondence**."

Promotional Materials
In addition, submit three copies of the introductory promotional materials that you propose to use for this product. Submit all proposed materials in draft or mock-up form, not final print. Send one copy to this division/ the Division of Neuropharmacological Drug Products and two copies of both the promotional materials and the package insert directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-42
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857

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 Richardae C. Taylor, Pharm.D., Regulatory Health Project Manager, at (301) 594-5793.

Sincerely,

{See appended electronic signature page}
Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

Enclosure