



NDA 21-121/S-004

ALZA Corporation
Attention: Tracy Lin
Associate Director, Regulatory Affairs
1900 Charleston Road
P.O. Box 7210
Mountain View, CA 94039-7210

Dear Ms. Lin:

Please refer to your supplemental new drug application dated November 30, 2001, received December 3, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for CONCERTA™ (methylphenidate hydrochloride) Extended-release Tablets.

We acknowledge receipt of your submissions dated February 14, March 1 and 4, 2002

This supplemental new drug application provides for an additional 27 mg dosage strength to be manufactured at the Vacaville manufacturing site and the requisite changes in the labeling for this new strength. In addition, the phrase, 'esophageal motility disorders' has been added to 'Potential for Gastrointestinal Obstruction' in the WARNINGS section of the labeling.

We have completed the review of this supplemental application, as amended, and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the submitted labeling text dated November 30, 2001. Accordingly, this supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the submitted draft labeling (package insert submitted November 30, 2001).

Please submit 20 paper copies of the FPL as soon as it is available, in no case more than 30 days after it is printed to each application. Please individually mount ten of the copies on heavy-weight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved supplement NDA 21-121/S-004". Approval of this submission by FDA is not required before the labeling is used.

BIOPHARMACEUTICS

The previously approved *in vitro* specifications are also recommended for the 27 mg methylphenidate HCl OROS® formulation. The recommended *in vitro* specifications are as follows:

Time Point	Specification of label claim(%range) Specification
at 1 h	(b)(4)-----
at 4 h	-----
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The *in vitro* testing is performed with USP Type VII dissolution apparatus with oral extended release tablet holder (spring holder) in pH 3 water with a fixed agitation rate of 30 cycles per minute, maintained at a temperature of 37±0.5° C.

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you should have any questions, please call, Ms. Anna Marie Homonnay, Regulatory Project Manager, at (301) 594-5535.

Sincerely,

Russell Katz, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

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

/s/

Russell Katz

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