DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-419

Mallinckrodt, Inc.
Attention: Ronald T. Groman
Manager, Regulatory Affairs
675 McDonnell Boulevard
P.O. Box 5840
St. Louis, MO 63134

Dear Mr. Groman:

Please refer to your new drug application (NDA) dated July 31, 2001, received August 2, 2001, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Methylin® Oral Solution (methylphenidate hydrochloride oral solution), 5 mg/5 mL and 10 mg/5 mL.

We acknowledge receipt of your submission dated October 31, 2002.

The October 31, 2002, submission constituted a complete response to our May 31, 2002 action letter.

This new drug application provides for the use of Methylin® Oral Solution (methylphenidate hydrochloride oral solution) for the treatment of Attention-Deficit Hyperactivity Disorder (ADHD) and narcolepsy.

We have completed the review of this 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 Final Printed Labeling (FPL) dated October 31, 2002, for the package insert. Accordingly, the application is approved effective on the date of this letter.

Post Marketing Commitments

We remind you of your post marketing study commitments in your submission of October 31, 2002, to further qualify the impurities, (b)(4)---------- These commitments are listed below--

1. Genetic toxicity testing, Ames test and chromosomal aberration test:

   Final Report: Within 12 months of NDA approval

2. 14-Day General Toxicity Study in rats:

   Final Report: Within 12 months of NDA approval.

Please submit all clinical protocols to your IND for this product; and, all non-clinical and chemistry protocols and all final study reports to this NDA. In addition, under 21 CFR 314.81(b)(2)(vii) and 314.81(b)(2)(viii), please include a status summary of each commitment in your annual report to this NDA. This 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, the number of patients entered into each study. All submissions, including supplements, relating to these postmarketing study commitments must be prominently labeled, 'Postmarketing Study Protocol', 'Postmarketing Study Final Report', or 'Postmarketing Study Correspondence'.

We also encourage you to develop a patient package insert for this product to be consistent with the labeling for other recently approved products for the treatment of ADHD. This may be submitted as a labeling supplement post-approval.

Chemistry Issues

1. An 18 month expiry is granted for Methylin® Oral Solution.

2. We have not completed validation of the regulatory methods. However, we expect to continue to work with you to resolve any problems that may be identified.

In addition, please submit three copies of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print. Please submit one copy to this Division 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, Maryland 20857

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 H. Weikel, R.Ph., Regulatory Affairs Manager, at (301) 594-5535.

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

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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