DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 21-514

Noven Pharmaceuticals, Incorporated
Co-development partner Shire Pharmaceuticals
Attention: Harris Rotman, Ph.D.
Senior Manager, Regulatory Affairs
725 Chesterbrook Boulevard
Wayne, PA 19087

Dear Dr. Rotman:

Please refer to your new drug application (NDA) dated and received June 27, 2000, submitted pursuant to section 505(b)(2)of the Federal Food, Drug, and Cosmetic Act for Daytrana (methylphenidate) Transdermal System.

We acknowledge receipt of your submissions dated December 27, 2005, January 6, 2006, January 11, 2006, February 8, 2006, and February 9, 2006. Your submission dated February 9, 2006 constituted a complete response to our December 23, 2005 action letter.

This new drug application provides for the use of Daytrana (methylphenidate) Transdermal System for attention deficit hyperactivity disorder (ADHD) in pediatric patients aged 6-12 years old.

We have completed our review of this application, as amended, and it is approved, effective on the date of this letter, for use as recommended in the enclosed labeling text agreed-upon in a communication dated April 3, 2006.

The final printed labeling (FPL) must be identical to the enclosed labeling (text for the package insert) and/or submitted labeling. 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.

Please submit an electronic version of the FPL according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDA*. For administrative purposes, designate this submission "**FPL for approved NDA 21-514**." Approval of this submission by FDA is not required before the labeling is used.

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 are waiving the pediatric study requirement for ages 2 to 5 years and deferring pediatric studies for ages 13 to 17 years for this application.

Phase 4 Commitments
We remind you of your postmarketing commitments agreed upon in communications dated February 9, 2006, and April 5, 2006.

1. Deferred pediatric studies under PREA

   Your deferred pediatric studies required under section 2 of the Pediatric Research Equity Act (PREA) are considered required postmarketing study commitments. The status of this postmarketing study shall be reported annually according to 21 CFR 314.81. This commitment is listed below.

   Deferred pediatric study under PREA for the treatment of attention deficit hyperactivity in pediatric patients ages 13 to 17 years.

   Final Report Submission: 3 years from the date of approval of this application.

   Submit final study reports to this NDA. For administrative purposes, all submissions related to this pediatric postmarketing study commitment must be clearly designated "**Required Pediatric Study Commitments**".

2. Contact Sensitization Study

   We note your agreement to conduct a study for estimating the risk of sensitization in a clinical setting.

   Protocol Submission: 2 months from the date of approval of this application.
   Final Report Submission: 2 and one-half years from the date of approval of this application.

Monitoring and Reporting on Abuse, Misuse or Diversion with Methylphenidate Transdermal System (MTS)

We note your agreement to submit all serious outcome cases of abuse, misuse, or diversion on an expedited basis (15-day).

Additionally, we note your agreement to summarize in a section of the Periodic Report all cases of abuse, misuse, and diversion regardless of whether an adverse event occurred. Sources of such cases include, but are not limited to, the MTS toll-free line, the Internet Monitoring Program, News/Media monitoring, and your general information phone lines and direct emails to you.

Dissolution Methods and Specifications

Please adopt the following dissolution method and specifications for all strengths of Daytrana.

Apparatus:	(b)(4)
Medium:	(b)(4)
Temperature:	
Volume:	
Rotation Speed:	
Sampling Times:	
Acceptance Criteria:	

A 26 month expiry (which includes a 24 month shelf life and a 2 month in use period) is granted for all strengths of Daytrana.

Comments and Recommendations on Container Labels, Tray, Carton and Insert Labeling
Our Division of Medication Errors and Technical Support (DMETS), Office of Drug Safety has the following comments and recommendations:

(b)(4) (b)(4)

(b)(4) (b)(4)

[redacted]

[redacted]

[redacted]

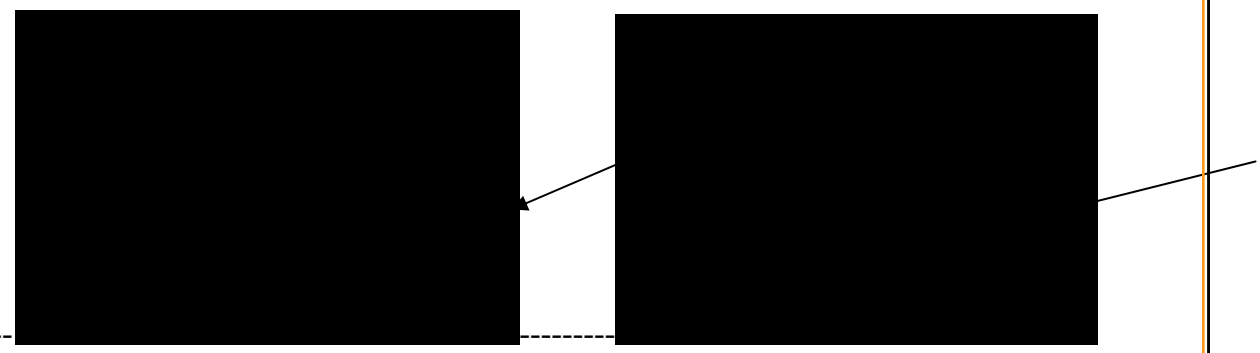
(b)(4)

(b)(4)

(b)(4)

(b)(4)

(b)(4)



(b)(4)

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(b)(4)

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 the Division of Psychiatry Products and two copies of both the promotional materials and the package insert(s) directly to:

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

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 Susan Player, M.S., A.P.R.N., B.C., Regulatory Project Manager, at (301) 796-1074.

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

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
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