DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration
Silver Spring MD 20993

NDA 022565 **NDA APPROVAL**

Wyeth Consumer Healthcare
Attention: Erica Sinclair, MBA
Senior Manager, Global Regulatory Affairs
5 Giralda Farms
Madison, NJ 07940

Dear Ms. Sinclair:

Please refer to your new drug application (NDA) dated July 28, 2009, received July 28, 2009, submitted pursuant to section 505(b)(2) of the Federal Food, Drug, and Cosmetic Act, for Advil® Congestion Relief (200 mg ibuprofen /10 mg phenylepherine HCl) tablets.

We acknowledge receipt of your submissions dated August 7, 13, and 27, September 3 and 18, October 16, 23, and 27, 2009, February 17, March 16, April 14 and 22, May 10, 11, 18, and 26, 2010.

This new drug application provides for the use of Advil® Congestion Relief tablets for the temporary relief of the following symptoms associated with cold and flu: headache, fever, sinus pressure, nasal congestion, minor aches and pain, reduces swelling of the nasal passages, temporarily restores freer breathing through nose.

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.

LABELING

Submit final printed labeling as soon as they are available, but no more than 30 days after they are printed. The final printed labeling (FPL) must be identical to the (20-count carton (including piggy-back Drug Facts) and immediate container (10-count blister card) labels; 50-count (50 x 1-count pouch dispenser) carton and 1-count immediate container (pouch) labels submitted on May 26, 2010), and must be in the "Drug Facts" format (21 CFR 201.66), where applicable.

The final printed labeling should be submitted 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 Labeling for approved NDA 22565**." Approval of this submission by FDA is not required before the labeling is used.

Marketing the product with FPL that is not identical to the approved labeling text and in the required format may render the product misbranded and an unapproved new drug.

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 this application for ages 0 to 2 years for the temporary relief of common cold and flu symptoms because there is evidence suggesting that the drug product would be unsafe in this pediatric age group. FDA recommends that over-the-counter (OTC) cough and cold products should not be used for infants and children under 2 years of age because serious and potentially life-threatening side effects could occur.

We note that Advil is approved and labeled for use in children age 2 and above. We further note that the final monograph for cough, cold, allergy, bronchodilator, and antiasthmatic drug products (21 CFR part 341) currently provides dosing information for phenylephrine HCl for use in children age 2 and above (although we recognize that manufacturers have ceased marketing such monograph products in children under 4 years of age). Notwithstanding these facts, additional studies of Advil Congestion Relief are required under PREA for this new combination of active ingredients because there is no approved or monograph overlapping dosing interval for these two active ingredients in children ages 2 years to less than 12 years.

We are deferring submission of your pediatric studies ages 2 years to less than 12 years for this application, because this product is ready for approval for use in adults and the pediatric studies have not been completed.

Your deferred pediatric studies required under section 505B(a) of the Federal Food, Drug, and Cosmetic Act are required postmarketing studies. The status of these postmarketing studies must be reported annually according to 21 CFR 314.81 and section 505B(a)(3)(B) of the Federal Food, Drug, and Cosmetic Act. These required studies are listed below.

1643-1

You must conduct a PK trial in children 6 to < 12 who may benefit from the drug (i.e. not in otherwise healthy pediatric volunteers). You should conduct a single and multiple dose, dose ranging, PK trial that would evaluate the appropriate dosing interval based on pharmacokinetics, safety, and tolerability of phenylephrine in children, and in order to identify whether the dosing interval for phenylephrine can overlap with that of ibuprofen.

Final Protocol Submission:	April 2011
Final Study Report Submission:	May 2012

1643-2

You must conduct a randomized, double blind, placebo controlled clinical trial(s) in children 6 to < 12 years of age to evaluate PD response and clinical symptoms response of phenylephrine for temporary relief of nasal decongestion associated with the common cold. The objective of the trial should be to identify whether phenylephrine can be dosed appropriately so as to overlap with the dosing interval of ibuprofen in this pediatric age group. In order to accomplish this objective, this trial should evaluate clinical efficacy as well as safety of phenylephrine in this population, obtain data to support the appropriate dosing interval, and allow dosing to cover the expected period of clinical use (for example, up to 7 days). This study must include adequate representation of these age groups and be conducted in the target population, i.e. children with cough and cold symptoms.

Final Protocol Submission:	September 2012
Final Study Report Submission:	May 2014

1643-3

You must conduct a PK trial in children 2 to < 6 who may benefit from the drug (ie. not in otherwise healthy pediatric volunteers). You should conduct a single and multiple dose, dose ranging, PK trial that would evaluate the appropriate dosing interval based on pharmacokinetics, safety, and tolerability of phenylephrine in children, and in order to identify whether the dosing interval for phenylephrine can overlap with that of ibuprofen.

Final Protocol Submission:	April 2014
Final Study Report Submission:	May 2015

1643-4

You must conduct a clinical trial(s) in children 2 to < 6 years of age to evaluate PD response and clinical symptoms response of phenylephrine for temporary relief of nasal decongestion associated with the common cold. The objective of the trial should be to identify whether phenylephrine can be dosed appropriately so as to overlap with the dosing of ibuprofen in this pediatric age group. In order to accomplish this objective, this trial should evaluate clinical efficacy as well as safety of phenylephrine in this population, define the appropriate dosing interval, and allow dosing to cover the expected period of clinical use. This study must include adequate representation of these age groups and be conducted in the target population, i.e. children with cough and cold symptoms.

Final Protocol Submission:	September 2015
Final Study Report Submission:	May 2017

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

This product is appropriately labeled for use in children ages 12 to less than 17 years for these indications. Therefore, no additional pediatric studies are needed in this age group.

LETTERS TO HEALTH CARE PROFESSIONALS

If you decide to 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, at least 24 hours prior to issuing the letter, an electronic copy of the letter to this NDA, to CDERMedWatchSafetyAlerts@fda.hhs.gov, and to the following address:

MedWatch
Food and Drug Administration
Suite 12B-05
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 Janice Adams-King, Regulatory Project Manager, at (301) 796-3713.

Sincerely,

{See appended electronic signature page}

Joel Schiffenbauer, M.D.
Deputy Director
Division of Nonprescription Clinical Evaluation
Office of Drug Evaluation IV

ENCLOSURES:
Labeling

Application Type/Number	Submission Type/Number	Submitter Name	Product Name
NDA-22565	ORIG-1	WYETH CONSUMER HEALTHCARE	ADVIL COLD & SINUS PE(IBUPROFEN 200MG/PH

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

/s/

JOEL SCHIFFENBAUER
05/27/2010