CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-076

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-076

Bayer Corporation, Consumer Care Division
Attention: Craig Hammes
Director, Regulatory Affairs
36 Columbia Road
P.O. 1910
Morristown, NJ 07962-1910

NOV 29 1999

Dear Mr. Hammes:

Please refer to your new drug application (NDA) dated January 28, 1999, received January 29, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Aleve Cold and Sinus (naproxen sodium and pseudoephedrine hydrochloride extended-release tablet) 220mg/120mg.

We acknowledge receipt of your submissions dated March 5, April 15(2), 28(2), May 21, June 2, 11, July 13(2), 20, 26, August 12, 16, 18, 26, 30, September 30, October 4, 11(2), 12,16, 18, 19, 20, November 12, 16, 18, 22, 23, 24, and 29, 1999 .

This new drug application provides for the over-the-counter use of Aleve Cold and Sinus (naproxen sodium and pseudoephedrine hydrochloride extended-release tablet) 220mg/120mg for the temporary relief of cold, sinus and flu symptoms.

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 draft labeling dated November 24, 1999, with the revisions listed below. Accordingly, the following components: 10- and 20- count carton, blister pack and the consumer insert leaflet are approved with the changes listed below. The approval is effective on the date of this letter.

As agreed in your communication dated November 29, 1999, the revisions are as follows:

Under ***Warnings***, the subsection entitled **"Stop use and ask a doctor if"** should be revised to read and appear as follows:

Stop use and ask a doctor if
- an allergic reaction occurs. Seek medical help right away.
- you get nervous, dizzy, or sleepless
- you develop heartburn
- nasal congestion lasts more than 7 days
- symptoms continue or get worse
- you have trouble swallowing or the caplet feels stuck in your throat
- new or unexpected symptoms occur
- stomach pain occurs with use of this product or if even mild symptoms persist
- fever lasts for more than 3 days

These revisions are terms of the NDA approval. Marketing the product before making these revisions in the product's final printed labeling (FPL) may render the product misbranded and an unapproved new drug. We also want to remind you that the flag "NEW" is not allowed for more than 6 months after initial introduction to the market place.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FPL for approved NDA 21-076." Approval of this submission by FDA is not required before the labeling is used.

We remind you of your Phase 4 commitments specified in your submission dated October 20, 1999. These commitments, along with any completion dates agreed upon, are listed below.

1. The product dissolution method and specifications will be _____ performance.

2. The _____ specification _____ for the finished product _____

These commitments are to be met within 1 year from the date of this letter.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as correspondence. In addition, under 21 CFR 314.81(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

In addition, please submit four 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 send one copy to this division, one to the Division of Over-the-Counter Drug Products, and two copies of both the promotional materials and the consumer insert leaflet directly to:

Division of Drug Marketing, Advertising,
and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Validation of the regulatory methods has not been completed. At the present time, it is the policy of the Center not to withhold approval because the methods are being validated. Nevertheless, we expect your continued cooperation to resolve any problems that may be identified.

Be advised that, as of April 1, 1999, 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 (63 *FR* 66632). We note that you have not fulfilled the requirements of 21 CFR 314.55. We are waiving the requirement to provide data on the safety and effectiveness of Aleve Cold and Sinus in pediatric patients under the age of two years on this application. We are deferring submission of pediatric studies for patients aged two through eleven years until December 1, 2001. However, in the interim, please submit your pediatric drug development plans as soon as possible unless you believe a waiver is appropriate.

If you believe that this drug qualifies for a waiver of the pediatric study requirement, you should submit a request for a waiver with supporting information and documentation in accordance with the provisions of 21 CFR 314.55 within 60 days from the date of this letter. We will notify you within 120 days of receipt of your response whether a waiver is granted. If a waiver is not granted, we will ask you to submit your pediatric drug development plans within 120 days from the date of denial of the waiver.

Pediatric studies conducted under the terms of section 505A of the Federal Food, Drug, and Cosmetic Act may result in additional marketing exclusivity for certain products (pediatric exclusivity). You should refer to the *Guidance for Industry on Qualifying for Pediatric Exclusivity* (available on our web site at www.fda.gov.cder/pediatric) for details. If you wish to qualify for pediatric exclusivity you should submit a "Proposed Pediatric Study Request" (PPSR) in addition to your plans for pediatric drug development described above. FDA generally will not accept studies submitted to an NDA before issuance of a Written Request as responsive to a Written Request. Sponsors should obtain a Written Request before submitting pediatric studies to an NDA. If you do not submit a PPSR or indicate that you are interested in pediatric exclusivity, we will proceed with the pediatric drug development plan that you submit and notify you of the pediatric studies that are required under section 21 CFR 314.55. Please note that satisfaction of the requirements in 21 CFR 314.55 alone may not qualify you for pediatric exclusivity. FDA does not necessarily ask a sponsor to complete the same scope of studies to qualify for pediatric exclusivity as it does to fulfill the requirements of the pediatric rule.

Please submit one market package of the drug product when it is a available.

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