CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

20-603/S-001, S-002, S-003

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-603/S-001

JUN 12 1998

McNeil Consumer Products Company
Attention: Vivian A. Chester
Vice President, Regulatory Affairs
7050 Camp Hill Road
Fort Washington, Pennsylvania 19034-2299

Dear Ms. Chester:

Please refer to your new supplemental drug application dated June 20, 1997, received June 23, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Children's Motrin Drops (ibuprofen oral suspension), 40 mg/mL.

This new supplemental drug application provides for the incorporation of the latest version of the Aspirin Sensitive Warnings as specified in the Agency letter dated March 31, 1997, and other labeling changes that you have proposed.

We have completed the review of this new supplemental application, including the submitted draft labeling, 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 enclosed. Accordingly, the application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed draft labeling. 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 "FINAL PRINTED LABELING" for approved NDA 20-603/S-001. Approval of this submission by FDA is not required before the labeling is used.

Please revise the labeling for this drug product at the time of the next printing or within 180 days, which ever comes first as follows:

New or revised language is accented.

A. Read Product Information Statement (All cartons)

Read all product information before using. Keep this box for important information. This product is intended for use in children ages 2-3 years.

B. Headings (All cartons and containers)

All headings and information presented in all capital letters (IMPORTANT, ACTIVE

INGREDIENT, USES, DIRECTIONS, WARNINGS, SHAKE WELL BEFORE USING, ASPIRIN SENSITIVE CHILDREN, CALL YOUR DOCTOR IF, DO NOT USE, and AGE, WEIGHT, AND DOSE in the dosing table) should be revised to upper and lower case.

C. Use Statement (All cartons and containers)

The current uses statement should be deleted and replaced with the following statement:

The "Uses" section should be revised as follows:

Uses: Temporarily:

- **reduces fever**
- **relieves minor aches and pains due to the common cold, flu, sore throat, headaches, and toothaches**

D. Directions (All cartons and containers)

A fifth statement should be added under "Directions" as follows:

5. **If stomach upset occurs while taking this product, give with food or milk.**

E. Dosing Table (All cartons and containers)

The dosing table should be revised as shown.

Weight (lb)	Age (yr)	Dose (mL)
Under 24	Under 2	Consult Doctor
24-35	2-3	2 Dropperfuls (2.5 mL)
One Dose Last 6-8 Hours		

F. Aspirin Sensitive Statement (All cartons and containers)

Aspirin sensitive children: Although this product does not contain aspirin, it may cause a severe reaction in people allergic to aspirin. Do not give to children who have had any of the following reactions to any pain reliever/fever reducer:

- allergic reaction
- difficulty breathing
- shock
- asthma
- hives
- swelling

G. Call Your Doctor If Statements (All containers and cartons)

- stomach upset gets worse or lasts

(Statement to immediately follow bullet concerning a lack of relief or worsening of symptoms.)

H. Stomach Upset statement (All cartons)

The following statement should be deleted from the "Warnings Section":

"If stomach upset occurs while taking this product, give with food or milk. If stomach irritation gets worse or lasts, call your doctor."

The information contained in the statements in H. above have been modified (refer to D. and G.).

Should additional information relating to the safety and effectiveness of the drug become available, revision of the labeling may be required.

Should a letter communicating important information about this drug product (i.e., "Dear Doctor" letter) be issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20852-9787

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

If you have any questions, please contact Stephanie Mason, Project Manager, at (301) 827-2275.

Sincerely yours,

/S/

Debra L. Bowen, M.D.
Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure

cc:
Original NDA 20-603
HFD-560/Div. files
HFD-560/CSO/S.Mason
HFD-560/Lumpkins/Yoder/Chang/Neuner
HFD-002/ORM (with labeling)
HFD-105/Office Director
HFD-101/L.Carter
HFD-830/ONDC Division Director
DISTRICT OFFICE
HF-2/Medwatch (with labeling)
HFD-92/DDM-DIAB (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-735/DPE (with labeling) - for all NDAs and supplements for adverse reaction changes.
HFI-20/Press Office (with labeling)

JSI 6/11/98

Drafted by: Smason/March 31, 1998/chester9.wpd
Initialed by:RCook:4/23/98
Final typed:SMason:6/2/98

APPROVAL (AP)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

SEP 13 1999

NDA 20-516/S-004
NDA 20-601/S-002
NDA 20-602/S-003
NDA 20-603/S-002

McNeil Consumer Healthcare
Attention: Janet Uetz
Associate Director, Regulatory Affairs
7050 Camp Hill Road
Fort Washington, PA 19034

Dear Ms. Uetz:

Please refer to your supplemental new drug applications dated June 1, 1998, received June 2, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act, providing for revised labeling for the following products:

NDA 20-516/S-004 Children's Motrin (ibuprofen) oral suspension 100 mg/5 mL;
NDA 20-601/S-002 Children's/Junior Strength Motrin (ibuprofen) chewable tablets, 50 and 100 mg;
NDA 20-602/S-003 Junior Strength Motrin (ibuprofen) tablets, 100 mg; and
NDA 20-603/S-002 Childrens Motrin (ibuprofen) drops, 50 mg/1.25 mL.

We also acknowledge receipt of your communications dated October 23, 1998 and February 19, 1999.

We have completed the review of these supplemental new drug applications, as amended, and have concluded that adequate information has been presented to demonstrate that the drug products are safe and effective for use as recommended in the draft labeling dated June 1, 1998. Accordingly, these supplemental new drug applications are approved effective on the date of this letter.

For each supplemental NDA, 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, these submissions should be designated as FPL for approved supplemental NDA 20-516/S-004, 20-601/S-002, 20-602/S-003, 20-603/S-002, as applicable. Approval of these submissions by FDA is not required before the labeling is used.

As agreed during the telephone conversation of February 11, 1999, between Kerry Rothschild and Willie Pagsuyuin, and confirmed in Mr. Pagsuyuin's letter of February 19, 1999, the

following revisions in the labeling of each product will be made at the time of the next printing or within 180 days of receipt of an approval letter, whichever comes first:

1. The header "Important" should be deleted. The phrase "Do not exceed recommended dose..." should be revised to read "Do not take more than directed." This should be placed under the "Directions" section as the first bullet. The second sentence following "Do not exceed recommended dose" should be deleted.

2. The storage statement should be modified to read "Store between 20-25°C (68-77°F)."

3. The flag statement "See New Label" should be removed after 6 months.

You are further reminded that the "Aspirin Sensitive Children" statement should have been replaced with the "Allergy alert" statement required by the agency's letter of September 15, 1998, in accordance with the time frame outlined in that letter.

Please also reformat the labeling of these products in accordance with the provisions of the March 17, 1999 FEDERAL REGISTER document "Over-The-Counter Human Drugs; Labeling Requirements; Final Rule" (64 FR 13254).

Should additional information relating to the safety and effectiveness of these drugs become available, further revision of the labeling may be required.

This approval affects only those changes specifically submitted in these supplemental new drug applications. Other changes that may have been approved or are pending evaluation are not affected.

In addition, please submit three copies of the introductory promotional materials that you propose to use for these products. 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 inserts directly to:

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

If a letter communicating important information about any of these drug products (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to the subject NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 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 have any questions regarding these applications, please contact Kerry Rothschild, Esq., Regulatory Project Manager, at (301) 827-2284.

Sincerely yours,

/S/

Linda M. Katz, M.D., M.P.H.
Deputy Director
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
Archival NDAs 20-516, 20-601, 20-602, 20-603
HFD-560/Div. Files
HFD-560/K.Rothschild
HFD-560/Mason
HFD-560/Lumpkins
HFD-560/Cook /S/ 9/9/99
HFD-560/Katz
HFD-105/Bowen
HF-2/MedWatch (with labeling)
HFD-002/ORM (with labeling)
HFD-105/ADRA (with labeling)
HFD-40/DDMAC (with labeling)
HFD-613/OGD (with labeling)
HFD-21/ACS (with labeling) - for drug discussed at advisory committee meeting.
HFD-95/DDMS (with labeling)
HFD-830/DNDC Division Director
DISTRICT OFFICE

Drafted by: KGR/February 11, 1999
Initialed by:
final:

APPROVAL (AP)

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-603/S-003

APR 15 1999

McNeil Consumer Healthcare
Attention: Vivian A. Chester
7050 Camp Hill Road
Fort Washington, PA 19034-2299

Dear Ms. Chester:

Please refer to your supplemental new drug application dated and received June 15, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Infant's Motrin (ibuprofen oral suspension) Concentrated Drops, 50 mg/1.25 mL.

We acknowledge receipt of your correspondences dated April 14 and 15, 1999.

This supplemental new drug application provides for the the expanded use of Infant's Motrin (ibuprofen oral suspension) Concentrated Drops, 50 mg/1.25 mL to include dosing instructions for children 6 months to 23 months of age.

The user fee goal (10 months) for this supplemental new drug application is April 15, 1999.

We have completed the review of this supplemental new drug application 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 enclosed agreed upon labeling text. Accordingly, the supplemental new drug application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed labeling text. Marketing the product with FPL that is not identical to the approved labeling text may render the product misbranded and an unapproved new drug.

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 supplement NDA 20-603/S-003." Approval of this submission by FDA is not required before the labeling is used.

If additional information relating to the safety or effectiveness of this drug product becomes available, revision of the labeling may be required.

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 the Division of Over-the-Counter Drug Products and two copies of both the promotional materials and the labeling directly to:

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

If a letter communicating important information about this drug product (i.e., a "Dear Health Care Practitioner" letter) is issued to physicians and others responsible for patient care, we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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 fulfilled the pediatric study requirement at this time.

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

If you have any questions regarding this application, please contact Kerry Rothschild, Esq., Regulatory Project Manager, at (301) 827-2222.

Sincerely yours,

/S/

Linda M. Katz, M.D., M.P.H.
Deputy Director 4/15/99
Division of Over-the-Counter Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure