# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*

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

# CORRESPONDENCE

CENTER FOR DRUG EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION

# FACSIMILE TRANSMISSION RECORD

DATE: 4/15/99

FROM: Kerry G. Rothschild, Esq.
Division of OTC Drug Products, HFD-560

PHONE: 301-827-2284 FAX: 301-827-2316 or
301-827-2315

TO: Name: Willie D. Pagsuyuin
Company: McNeil Consumer Healthcare
Phone: 215-~~233~~-7115
27

FAX #: 215-273-4049 No. Of Pages (including cover) 4

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**Message:** Please refer to your supplemental new drug application NDA 20-603/S-003, dated and received June 15, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Infants'Motrin (ibuprofen oral suspension) Concentrated Drops, 50 mg/mL. This supplemental new drug application provides for the the expanded use of Infant's Motrin Concentrated Drops to include dosing instructions for children 2 months to 3 years of age.

Please find attached, a revised mock-up of the product labeling which will constitute the basis for approval.

We request that you provide a commitment letter ASAP so that the action letter for this supplemental NDA may be completed. In your letter, please acknowledge the following:

1. That the enclosed labeling serves as a basis of approval for NDA 20-603/S-003; and

2. That you agree to submit Final Printed Labeling (FPL) that is identical to the enclosed labeling text.

If you have any questions, please contact Kerry Rothschild, Esq., Regulatory Project Manager, at 301-827-2284.

2 page(s) of revised draft labeling has been redacted from this portion of the review.

CENTER FOR DRUG EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION

# FACSIMILE TRANSMISSION RECORD

DATE: 4/8/99

FROM: Kerry G. Rothschild, Esq.
Division of OTC Drug Products, HFD-560

PHONE: 301-827-2284 FAX: 301-827-2316 or
301-827-2315

TO: Name: Willie D. Pagsuyuin
Company: McNeil Consumer Healthcare
Phone: 215-233-7115

FAX #: 215-273-4049 No. Of Pages (including cover) 5

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**This document is intended for the use of the party to whom it is addressed and may contain information that is privileged, confidential, and protected from disclosure under applicable law.** If you are not the addressee, or a person authorized to deliver the document to the addressee, you are hereby notified that any view, disclosure, copying, or other action based on the content of this communication is NOT authorized.

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**Message:** Please refer to your supplemental new drug application NDA 20-603/S-003, dated and received June 15, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Infants'Motrin (ibuprofen oral suspension) Concentrated Drops, 50 mg/mL. This supplemental new drug application provides for the the expanded use of Infant's Motrin Concentrated Drops to include dosing instructions for children 2 months to 3 years of age.

The User Fee goal date for this supplemental new drug application is April 15, 1999

Please find attached, a revised mock-up of the product labeling reflecting your response to a previous draft mock-up sent via FAX on April 12, 1999, and the reviewers comments.

We request that you provide a commitment letter ASAP so that the action letter for this supplemental NDA may be completed. In your commitment, please acknowledge the following:

1. That the enclosed labeling serves as a basis of approval for NDA 20-603/S-003; and

2. That you agree to submit Final Printed Labeling (FPL) that is identical to the enclosed labeling text.

If you have any questions, please contact Kerry Rothschild, Esq., Regulatory Project manager, at 301-827-2284.

2 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

CENTER FOR DRUG EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION

# FACSIMILE TRANSMISSION RECORD

DATE: 4/8/99

FROM: Kerry G. Rothschild, Esq.
Division of OTC Drug Products, HFD-560

PHONE: 301-827-2284 FAX: 301-827-2316 or
301-827-2315

TO: Name: Willie D. Pagsuyuin
Company: McNeil Consumer Healthcare
Phone: 215-233-7115

FAX #: 215-273-4049 No. Of Pages (including cover) 15

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**Message:** Please refer to your supplemental new drug application NDA 20-603/S-003, dated and received June 15, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Children's Motrin (ibuprofen oral suspension) Drops 50 mg/1.25 mL. This supplement provides for expanded use to include dosing instructions for children 2 months to 3 years of age. The supplement also provided for a change in the product name to Infants' Motrin Concentrated Drops. Draft labeling was also submitted.

The User Fee goal date for this supplemental new drug application is April 15, 1999

Please find attached, a copy of your draft labeling, complete with revisions identified by the review team. Please note that the requested dosing range has been modified to include dosing instructions for children 6 months to less than 2 years (23 months). Please also note that, while the change in the product name to Infants' Motrin Concentrated Drops is acceptable, the agency recommends the alternative name, "Baby Motrin Concentrated Drops," as the term "baby" is considered to be more universally understood.

In order to facilitate a timely action on the supplemental new drug application, please respond with a letter confirming your intent to implement the labeling revisions, or with your comments, by 12:00 noon, Tuesday, April 13, 1999.

If you have any questions, please contact Kerry Rothschild, Esq., Regulatory Project Manager, at 301-827-2284. Thank you.

cc: Original N20-603/S-003
HFD-560/Div. File
HFD-550/Rothschildk/Masons/Lumpkins/Neuner/Cookr/Katzl/Horowitz

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-603/S-001

McNeil Consumer Products Company
7050 Camp Hill Road
Fort Washington, PA 19034-2299

JUL 3 1997

Attention: Vivian A. Chester
Vice President, Regulatory Affairs

Dear Mr. Chester:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Children's Motrin® (ibuprofen) Drops, 40mg/mL

NDA Number: 20-603

Supplement Number: S-001

Date of Supplement: June 20, 1997

Date of Receipt: June 23, 1997

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on August 22, 1997 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Center for Drug Evaluation and Research
Division of Over-the-Counter Drug Products, HFD-560
Office of Drug Evaluation V
Attention: Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

/S/

Maria Rossana R. Cook, M.B.A.
Chief, Project Management Staff
Division of Over-the-Counter Drug Products, HFD-560
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
Original NDA 20-603/S-001
HFD-560/Div. Files
HFD-560/CSO/S. Mason

SUPPLEMENT ACKNOWLEDGEMENT

ORIGINAL

McNEIL

McNEIL CONSUMER PRODUCTS COMPANY, 7050 CAMP HILL ROAD, FORT WASHINGTON, PA 19034-2299 (215) 233-7000

JUN 20 1997

Debra L. Bowen, MD
Director
Division of Over-the-Counter Drug Products (HFD-560)
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850



RE: Children's MOTRIN® (ibuprofen) Drops, 40mg/mL
NDA 20-603
Special Supplement - Changes Being Effected

NDA NO. 20603 REF. NO. S-001
NDA SUPPL FOR Draft

Dear Dr. Bowen:

In accordance with 21 CFR 314.70(C)(2), we are submitting changes to our labeling for Children's MOTRIN Drops to incorporate the latest version of the Aspirin Sensitive Warnings, per FDA letter of March 31, 1997 (copy attached). Accordingly, the warnings are revised as follows:

***FROM:***

**ASPIRIN SENSITIVE CHILDREN:**

- **This product contains no aspirin, but may cause a severe reaction in people allergic to aspirin.**
- **Do not use this product if your child has had an allergic reaction to aspirin such as asthma, swelling, shock or hives.**

***TO:***

**ASPIRIN SENSITIVE CHILDREN:**
Although this product does not contain aspirin, it may cause a severe reaction in people allergic to aspirin. Children's MOTRIN® may cause:

- asthma
- hives
- shock (low blood pressure)
- allergy
- shortness of breath
- swelling of the face

Children's MOTRIN can cause serious reactions, similar to those listed above, requiring immediate medical attention. These reactions can occur after taking a single dose or any subsequent dose in persons both with, and without, a prior reaction to Children's MOTRIN or other pain reliever/fever reducer.

In addition, we are making the following labeling changes:

1. We are making the labeling consistent with the approved OTC labeling for Children's/Junior Strength MOTRIN Chewable Tablets (NDA 20-601, approved 11/15/96) with regards to the USES and storage conditions:

| *FROM:* | *TO:* |
|---|---|
| **USES:**<br>**For Temporary Relief of:**<br>• **Fever**<br>• **Minor aches and pains** due to colds, flu, sore throat, headaches and toothaches | **USES:**<br>**For Temporary:**<br>• **Reduction of Fever**<br>• **Relief of minor aches and pains** due to colds, flu, sore throat, headaches and toothaches |
| *FROM:* | *TO:* |
| **Store at controlled room temperature:**<br>**15° - 30°C (59° - 86°F)** | **Store at room temperature:**<br>**15° - 30°C (59° - 86°F)** |

2. We have revised the declaration of net quantity of contents on all the product labels:

| *FROM:* | *TO:* |
|---|---|
| ____ mL (___ fl oz) | ____ fl oz (___ mL) |

3. We have added a statement under the DIRECTIONS, as follows:

| *FROM:* | *TO:* |
|---|---|
| 2. Measure dose with dropper provided. | 2. Measure dose with dropper provided. **Use enclosed dropper only.** |

4. We have revised the IMPORTANT statement on the bottle labels:

| *FROM:* | *TO:* |
|---|---|
| **IMPORTANT:** See box for complete information and save for future use. | **IMPORTANT: See box for complete WARNINGS and other information and save box for future use.** |

5. We have made the following revisions on the carton labels:

- Deleted the flag "NEW" on the front panel.
- Deleted the sell copy on the side panel.
- Changed the color of the bar around "For Ages 2-3" from gold to pink.

We intend to implement these changes beginning third quarter of 1997. In support of this SSCBE, attached are 16 copies of final labeling, in mechanical form. For reference, we have also included a photocopy of representative final printed labeling which is currently being used for Children's MOTRIN Drops.

Should you have any questions, please call Willie D. Pagsuyuin at (215) 233-7115 or me at (215) 233-7010.

Very truly yours,

McNEIL CONSUMER PRODUCTS COMPANY

/S/

Vivian A. Chester
Vice President, Regulatory Affairs

WDP:dtg
Attachment

cc: Ms. Stephanie Mason (HFD-560)

p:\nda\corresp\bowen3.doc

NDA 20-603
NDA SUPPL NO: 2

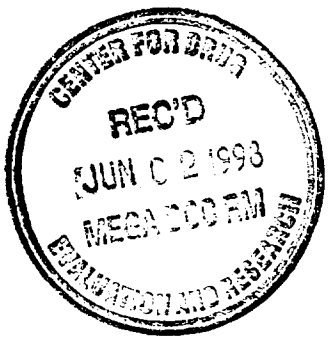
McNEIL

ORIGINAL

McNEIL CONSUMER PRODUCTS COMPANY, 7050 CAMP HILL ROAD, FORT WASHINGTON, PA 19034-2299 (215) 233-7000

JUN 1 1998

Debra L. Bowen, MD
Director
Division of Over-the-Counter Drug Products (HFD-560)
Food and Drug Administration
9201 Corporate Blvd.
Rockville, MD 20850




RE: Children's Motrin® Drops, 40mg/mL
NDA 20-603
Special Supplement - Changes Being Effected

Dear Dr. Bowen:

We wish to supplement NDA 20-603 for Children's Motrin Drops to provide for the following labeling changes which, in accordance with 21 CFR 314.70(c)(2), are intended to help in the safe use of the product:

(a) The warnings have been revised to clarify the possible occurrence of allergic reactions in patients who take ibuprofen, as well as in aspirin-sensitive patients who take ibuprofen.

*From*: "**WARNINGS**
**ASPIRIN SENSITIVE CHILDREN:** Although this product does not contain aspirin, it may cause a severe reaction in people allergic to aspirin. Children's Motrin may cause:

| | |
|---|---|
| -asthma | -hives |
| -shock (low blood pressure) | -allergy |
| -shortness of breath | -swelling of the face |

Children's Motrin can cause serious reactions, similar to those listed above, requiring **immediate** medical attention. These reactions can occur after taking a single dose or any subsequent dose in persons both with, and without, prior reaction to Children's Motrin or other pain reliever/fever reducer."

*To*: "**WARNINGS**

**ALLERGIC REACTIONS**: Children's Motrin may cause a severe allergic reaction which may include:

-wheezing (asthma) -shortness of breath
-hives -swelling of the face
-fast, irregular pulse or heartbeat -changing color of the skin (shock)

**ASPIRIN-SENSITIVE PATIENTS**: Although Children's Motrin does not contain aspirin, it may cause a severe reaction, similar to that listed above, in people allergic to aspirin or other pain relievers/fever reducers.

**Any of these reactions could be serious. Stop using this product and get emergency medical help immediately.** These reactions can occur after taking a single dose or any subsequent dose in persons both with, and without, prior reaction to Children's Motrin or other pain relievers/fever reducers."

(b) Information regarding what to do if stomach upset occurs while taking the product (which is found in the IMPORTANT section of the current labeling) has been moved to the DIRECTIONS and CALL YOUR DOCTOR IF sections, per FDA request.

Accordingly, we have added the information to the DIRECTIONS section:
"7. If stomach upset occurs while taking this product, give with food or milk."

And as fourth bullet statement in the CALL YOUR DOCTOR IF section:
"Stomach upset gets worse or lasts."

(c) The DIRECTIONS section is further revised to improve product dosing instructions:

*From*: "**DIRECTIONS:**

1. Find right dose on chart below. If possible, use weight to dose; otherwise use age.
2. Measure dose with dropper provided. **Use enclosed dropper only**.
3. Repeat dose every **6-8 hours**, if needed.
4. Do not use more than **4 times a day**."

[Dosing Chart]

*To*: "**DIRECTIONS:**

1. Shake well before using.
2. Find right dose on chart below. If possible use weight to dose; otherwise, use age.
3. Only use enclosed dropper; fill to prescribed level and dispense liquid slowly into child's mouth, toward inner cheek.
4. Replace original bottle cap to maintain child resistance.
5. If needed, repeat dose every **6-8 hours**
6. Do not use more than **4 times a day**.
7. If stomach upset occurs while taking this product, give with food or milk.

[Dosing Chart]

**Attention: Specially designed for use with enclosed dropper. Use only enclosed dropper to dose this product. Do not use any other dosing device."**

(d) To strengthen adherence to the recommended dosing regimen, we have elaborated the overdose warning under the IMPORTANT section of the labeling:

*From*: **"IMPORTANT**
**Keep this and all drugs out of the reach of children. If case of accidental overdose, seek professional assistance or contact a poison control center immediately."**

*To*: **"IMPORTANT**
**Do not exceed recommended dose.** Taking more than the recommended dose (overdose) may not provide more relief and could cause serious health problems. **Keep this and all drugs out of the reach of children. In case of accidental overdose, seek professional assistance or contact a poison control center immediately "**

(e) We are adding "Concentrated" to the Children's Motrin Drops name to better differentiate the product in name from the less concentrated Children's Motrin Suspension.

(f) We have made the following revision advising consumers that they can contact *other* health care professionals about the product:

*From*: "**Questions or Comments**?...Or ask your Pharmacist, Doctor or Health Care Professional."

*To*: "**Questions or Comments**?...Or ask your Pharmacist, Doctor or other Health Care Professional."

(g) The tamper-evident packaging statement on the label has been revised.

*From*: **"DO NOT USE:**
**If plastic bottle wrap imprinted with "Safety Seal®" is broken."**

*To:* **"DO NOT USE:**
**If plastic bottle wrap imprinted "Safety Seal®" and "Use With Enclosed Dropper Only" is broken or missing."**

(h) All inactive ingredients, including colorants, are now in alphabetical order.

*From*: "**Inactive Ingredients**: Citric acid, cornstarch, artificial flavors, glycerin, polysorbate 80, purified water, sodium benzoate, sorbitol, sucrose, xanthan gum, FD&C Red #40."

*To*: "**Inactive Ingredients**: Citric acid, cornstarch, FD&C Red #40, artificial flavors, glycerin, polysorbate 80, purified water, sodium benzoate, sorbitol, sucrose, xanthan gum."

The changes described in this SSCBE are being implemented immediately. Please note that a similar supplement reflecting pertinent labeling changes is being submitted under separate cover to each of our approved NDAs for OTC ibuprofen products.

In support of this supplement, attached are 12 copies of final labeling, in mechanical form.

Should you have any questions, please call me at (215) 233-7010.

Very truly yours,

McNEIL CONSUMER PRODUCTS COMPANY

Vivian A. Chester
Vice President, Regulatory Affairs

Attachments

p:\nda\corresp\bowdrop.doc

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-603/S-002

8 1998

McNeil Consumer Products Company
7050 Camp Hill Road
Fort Washington, PA 19034

Attention: Vivian A. Chester
Vice President, Regulatory Affairs

Dear Ms. Chester:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Children's Motrin® Oral Drops, 40mg/mL

NDA Number: 20-603

Supplement Number: S-002

Date of Supplement: June 1, 1998

Date of Receipt: June 2, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on August 1, 1998 in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

Food and Drug Administration
Division of Over-the-Counter Drug Products, HFD-560
Office of Drug Evaluation V
Center for Drug Evaluation and Research
Attention: Document Control Room
5600 Fishers Lane
Rockville, MD 20857

Sincerely,

/S/

Maria Rossana R. Cook, M.B.A.
Chief, Project Management Staff
Division of Over-the-Counter Drug Products, HFD-560
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
Original NDA 20-603/S-002
HFD-560/Div. Files
HFD-560/CSO/Mason, S.

SUPPLEMENT ACKNOWLEDGEMENT