

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**Approval Package for:**

*APPLICATION NUMBER:*

**NDA 19-872/S-006**

**Name:** Tylenol® (Acetaminophen) Arthritis Pain  
Extended Relief Geltabs, 650 mg

**Sponsor:** McNeil Consumer Healthcare

**Approval Date:** January 11, 2001

# CENTER FOR DRUG EVALUATION AND RESEARCH

*APPLICATION NUMBER:*  
**NDA 19-872/S-006**

## CONTENTS

|  |
|--|
| <b>Reviews / Information Included in this Review</b> |
|--|

|  |          |
|--|----------|
| <b>Approval Letter</b>                                     | <b>X</b> |
| <b>Approvable Letter</b>                                   | <b>X</b> |
| <b>Labeling</b>  | <b>X</b> |
| <b>Division Director's Memo</b>                            |          |
| <b>Labeling Review</b>                                     | <b>X</b> |
| <b>Medical Review</b>                                      |          |
| <b>Chemistry Reviews</b>                                   | <b>X</b> |
| <b>Environmental Assessment</b>                            |          |
| <b>Pharmacology / Toxicology Reviews</b>                   |          |
| <b>Statistical Reviews</b>                                 |          |
| <b>Microbiology Reviews</b>                                |          |
| <b>Clinical Pharmacology &amp; Biopharmaceutics Review</b> | <b>X</b> |
| <b>Administrative and Correspondence Documents</b>         | <b>X</b> |
|  |          |

**CENTER FOR DRUG EVALUATION AND RESEARCH**

***APPLICATION NUMBER:***

**NDA 19-872/S-006**

**APPROVAL LETTER**



NDA 19-872/S-006

McNeil Consumer Healthcare  
Attention: Paula J. Oliver  
Senior Director, Regulatory Compliance  
7050 Camp Hill Road  
Fort Washington, PA 19034-2299

Dear Ms. Oliver:

Please refer to your supplemental new drug application dated June 9, 1995, received June 12, 1995, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tylenol (acetaminophen) Arthritis Pain Extended Relief Geltabs, 650mg.

Please also refer to the Approvable letter that was issued for this supplemental new drug application on September 9, 1999. We acknowledge receipt of your submissions dated November 19, 1999 and September 7, 2000. Your submission of September 7, 2000 constituted a complete response to our September 9, 1999 action letter.

This supplemental new drug application provides for a geltab formulation.

We have completed the review of this supplemental new drug 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 labeling text dated September 7, 2000. 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 submitted draft labeling dated September 7, 2000, and must be formatted in accordance with the requirements of 21 CFR 201.66. Marketing the product with FPL that is not identical to the approved labeling text and "Drug Facts" format may render the product misbranded and an unapproved new drug.

Please submit 20 paper 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 heavyweight paper or similar material. Alternatively, you may submit the FPL electronically according to the guidance for industry titled *Providing Regulatory Submissions in Electronic Format - NDAs* (January 1999). For administrative purposes, this submission should be designated "FPL for approved supplement NDA 19-872/S-006." Approval of this submission by FDA is not required before the labeling is used.

We request that the following revisions in the labeling for this drug product be implemented within 180 days or at the next printing, whichever comes first:

1. For the 2-count pouch, under ***Other Information***, the temperature degree symbol should be

added to read "■ store at 20-25°C (68-77°F) ■ avoid excessive heat at 40°C (104°F)".

2. For the dispensit box for the 2-count pouches, under *Inactive ingredients*, the blank space at the end of the first line (listing of ingredients) should be filled.

3. You should remove the flag statement "New!" from the label since the drug product is not new.

In addition, please submit one copy 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. For administrative purposes, this submission should be sent to the NDA and should be identified as new correspondence to approved NDA 19-872.

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

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 call Thomas A. Parmelee, Pharm.D., Regulatory Project Manager, at (301) 827-2222.

Sincerely,

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

/s/

-----

Linda Katz

1/11/01 02:55:22 PM

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*

**NDA 19-872/S-006**

**APPROVABLE LETTER**



Food and Drug Administration  
Rockville MD 20857

NDA 19-872/S-006

SEP 9 1999

McNeil Consumer Healthcare  
Attention: Paula J. Oliver  
Senior Director, Regulatory Compliance  
7050 Camp Hill Road  
Fort Washington, PA 19034-2299

Dear Ms. Oliver:

Please refer to your supplemental new drug application dated June 9, 1995, received June 12, 1995, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tylenol (acetaminophen) Extended Relief tablets, 650 mg. Your supplemental new drug application provided for a geltab formulation.

We also acknowledge your submission dated March 8, 1999, received March 9, 1999. This submission constituted a complete response to our January 25, 1996 action letter.

We have completed the review of this supplemental new drug application, as amended, and it is approvable. Before this supplemental new drug application may be approved, however, it will be necessary for you to submit draft labeling consistent with the draft prototype labeling attached. Please note that the product name in the draft prototype label does not contain a reference to "arthritis," as the agency believes such reference to be misleading.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

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

Within 10 days after the date of this letter, you are required to amend the supplemental new drug application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the supplemental new drug application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this change prior to approval of this supplemental new drug application.

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

Sincerely,

  
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

Enclosure

Following this page, one page withheld in full - (b)(4) draft labeling

cc:

Archival NDA 19-872

HFD-560/Div. Files

HFD-560/K.Rothschild

HFD-560/Ganley/Katz/Cook

HFD-560/Lumpkins/Neuner/Mason/Roberts

HFD-550/Yaciw

HFD-830/Div Dir

DISTRICT OFFICE

*mm 9/7/99*  
*mm 9/11/99*

Drafted by: kgr/September 8, 1999

Initialed by:

final:

filename: 19872AZ.006

**APPROVABLE (AE)**

# **CENTER FOR DRUG EVALUATION AND RESEARCH**

***APPLICATION NUMBER:***  
**NDA 19-872/S-006**

**LABELING**



**Drug Facts (continued)**

If pregnant or breast-feeding, ask a health professional before use. Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

**Directions**

- do not take more than directed
- adults: take 2 tablets every 8 hours with water
- swallow whole - do not crush, chew or dissolve
- do not take more than 6 tablets in 24 hours
- do not use for more than 10 days unless directed by a doctor
- ask a doctor
- ask a doctor
- ask a doctor

**Drug Facts**

**Active ingredient (in each tablet)** Acetaminophen 650 mg Pain reliever

**Purpose** Pain reliever

**Uses** temporarily relieves minor aches and pains due to:

- the common cold
- flu
- headache
- muscular aches
- menstrual cramps

**Warnings**

**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain reliever/fever reducers. Acetaminophen may cause liver damage. Do not use with any other product containing acetaminophen.

**Stop use and ask a doctor if:**

- new symptoms occur
- itchiness or swelling is present
- pain gets worse or lasts for more than 10 days

**TYLENOL<sup>®</sup> Acetaminophen Extended Release ARTHRITIS PAIN**

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Gellabs**

6 Gellabs\* - 650 mg EACH Pain Reliever \*Gelatin-Coated Tablets

LASTS UP TO 8 HOURS

NDC 50580-505-XX

**TYLENOL<sup>®</sup> ARTHRITIS PAIN**

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Gellabs**

McNeil Consumer Healthcare  
DIVISION OF MCNEIL - PPC, INC.  
FORT WASHINGTON, PA 19034 USA  
© MCN-PPC, Inc. '00  
www.tylenol.com  
U.S. Pat. No. 4820522 and 5436026

**Drug Facts (continued)**

**Other information**

- do not use if carton is opened or red neck wrap or foil inner seal is imprinted with "Safety Seal" is broken
- store at 20-25°C (68-77°F)
- avoid excessive heat at 40°C (104°F)
- see end panel for lot number and expiration date

**Inactive ingredients**

benzyl alcohol, butylparaben, castor oil, cellulose, corn starch, edetate calcium disodium, FD&C Blue #1, FD&C Blue #2, FD&C Red #40, gelatin, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methylparaben, polyethylene glycol, propylparaben, sodium butyl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide

**Questions?**

Call 1-800-992-5387

**FPO**

0000000

**Labeling Format Information:**

|                                       |                  |
|---------------------------------------|------------------|
| <b>Fonts:</b> Helvetica regular, bold | and bold italic. |
| <b>Drug Facts:</b>                    | 8.25 pt          |
| <b>Header:</b>                        | 8 pt             |
| <b>Subheader:</b>                     | 6 pt             |
| <b>Body Text:</b>                     | 6 pt             |
| <b>Drug Facts (continued):</b>        | 6 pt             |
| <b>Leading:</b>                       | 6.5 pt           |
| <b>Bullets:</b>                       | 5 pt             |
| <b>Barlines:</b>                      | 2.5 pt           |
| <b>Hairlines:</b>                     | 0.5 pt           |

Horizontal Scale: 75%      Average Kerning: -15

**Active ingredient (in each tablet)** Acetaminophen 650 mg

**Purpose** Pain reliever

Uses temporarily relieves minor aches and pains due to:

- arthritis
- the common cold
- headache
- toothache
- muscular aches
- backache
- menstrual cramps

**Warnings**

**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage. Do not use with any other product containing acetaminophen.

**Stop use and ask a doctor if:**

- new symptoms occur
- redness or swelling is present
- pain gets worse or lasts for more than 10 days
- if pregnant or breastfeeding, ask a health professional before use

**Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.**

**Directions** Do not take more than directed adults: take 2 gels every 8 hours with water

- swallow whole - do not crush, chew or dissolve
- do not take more than 6 gels in 24 hours
- do not use for more than 10 days unless directed by a doctor
- under 18 years of age: ask a doctor

**Other information** do not use if red neck wrap or foil inner seal imprinted with "Safety Seal®" is broken

- store at 20 - 25°C (68 - 77°F)
- avoid excessive heat at 40°C (104°F)

**Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.**

**TYLENOL® ARTHRITIS PAIN**  
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN  
**Extended Relief Gels**

**Pain Reliever**

6 Gels\*  
650 mg EACH

\*Gelatin-Coated Tablets

NDC 50580-505-XX  
Lasts up to 8 Hours

NEW!

www.tylenol.com U.S. Pat. No. 4820522 and 5436026 © MCN-PPC, Inc. 00 XXXXXXXX

EXP. DATE: CONTROL:

**Active ingredient (in each tablet)** Acetaminophen 650 mg

**Purpose** Pain reliever

Uses temporarily relieves minor aches and pains due to:

- arthritis
- the common cold
- headache
- toothache
- muscular aches
- backache
- menstrual cramps

**Warnings**

**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage. Do not use with any other product containing acetaminophen.

**Stop use and ask a doctor if:**

- new symptoms occur
- redness or swelling is present
- pain gets worse or lasts for more than 10 days
- if pregnant or breastfeeding, ask a health professional before use

**Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.**

**Directions** Do not take more than directed adults: take 2 gels every 8 hours with water

- swallow whole - do not crush, chew or dissolve
- do not take more than 6 gels in 24 hours
- do not use for more than 10 days unless directed by a doctor
- under 18 years of age: ask a doctor

**Other information** do not use if red neck wrap or foil inner seal imprinted with "Safety Seal®" is broken

- store at 20 - 25°C (68 - 77°F)
- avoid excessive heat at 40°C (104°F)

**Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.**

**TYLENOL® ARTHRITIS PAIN**  
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN  
**Extended Release**

**Pain Reliever**

6 Gels\*  
650 mg EACH

\*Gelatin-Coated Tablets

NDC 50580-505-XX  
Lasts up to 8 Hours

NEW!

www.tylenol.com U.S. Pat. No. 4820522 and 5436026 © MCN-PPC, Inc. 00 XXXXXXXX

EXP. DATE: CONTROL:

200 % of size

**Labeling Format Information:**

Fonts: Helvetica regular, bold and bold italic.

**Drug Facts:** NA

**Header:** 4.5 pt

**Subheader:** 4.5 pt

**Body Text:** 4.5 pt

**Drug Facts (continued):** NA

**Leading:** 4.5 pt

**Bullets:** 3.5 pt

**Barlines:** 0 pt

**Hairlines:** 0 pt

Horizontal Scale: 60-63% Average Kerning: -30



**Labeling Format Information:**

|  |         |
|--|---------|
| <b>Fonts:</b> Helvetica regular, bold and bold italic. |         |
| <b>Drug Facts:</b>                                     | 8.25 pt |
| <b>Header:</b>   | 8 pt    |
| <b>Subheader:</b>                                      | 6 pt    |
| <b>Body Text:</b>                                      | 6 pt    |
| <b>Drug Facts (continued):</b>                         | 8 pt    |
| <b>Leading:</b>  | 6.5 pt  |
| <b>Bullets:</b>  | 5 pt    |
| <b>Barlines:</b>                                       | 2.5 pt  |
| <b>Hairlines:</b>                                      | 0.5 pt  |

Horizontal Scale: 100%      Average Kerning: 0

**NEW!**  
NDC 50580-505-24

*Lasts up to 8 Hours*

**TYLENOL<sup>®</sup>** Acetaminophen  
**ARTHRITIS PAIN** Extended Release

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Geltabs**

**Pain Reliever**

24 Geltabs\* - 650 mg EACH \*Gelatin-Coated Tablets

**Active ingredient (in each geltab) Purpose**  
Acetaminophen 650 mg.....Pain reliever

**Uses** temporarily relieves minor aches and pains due to: ■ arthritis ■ the common cold ■ headache ■ toothache ■ muscular aches ■ backache ■ menstrual cramps

**Warnings**  
Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage. Do not use ■ with any other product containing acetaminophen. Stop use and ask a doctor if ■ new symptoms occur ■ redness or swelling is present ■ pain gets worse or lasts for more than 10 days. If pregnant or breast-feeding, ask a health professional before use.

Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

**Directions** ■ do not take more than directed adults: ■ take 2 geltabs every 8 hours with water ■ swallow whole - do not crush, chew or dissolve ■ do not take more than 6 geltabs in 24 hours ■ do not use for more than 10 days unless directed by a doctor

**Other information** ■ ask a doctor under 18 years of age ■ do not use if red neck wrap or foil inner seal imprinted with "Safety Seal®" is broken ■ store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat at 40°C (104°F)

U.S. Pat. No. 4,820,522 and 5,430,226

EXP. DATE: XXXXXXXX

CONTROL: XXXXXXXX

**NEW!**  
NDC 50580-505-24

*Lasts up to 8 Hours*

**TYLENOL<sup>®</sup>** Acetaminophen  
**ARTHRITIS PAIN** Extended Release

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Geltabs**

**Pain Reliever**

24 Geltabs\* - 650 mg EACH \*Gelatin-Coated Tablets

**Active ingredient (in each geltab) Purpose**  
Acetaminophen 650 mg.....Pain reliever

**Uses** temporarily relieves minor aches and pains due to: ■ arthritis ■ the common cold ■ headache ■ toothache ■ muscular aches ■ backache ■ menstrual cramps

**Warnings**  
Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage. Do not use ■ with any other product containing acetaminophen. Stop use and ask a doctor if ■ new symptoms occur ■ redness or swelling is present ■ pain gets worse or lasts for more than 10 days. If pregnant or breast-feeding, ask a health professional before use.

Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

**Directions** ■ do not take more than directed adults: ■ take 2 geltabs every 8 hours with water ■ swallow whole - do not crush, chew or dissolve ■ do not take more than 6 geltabs in 24 hours ■ do not use for more than 10 days unless directed by a doctor

**Other information** ■ ask a doctor under 18 years of age ■ do not use if red neck wrap or foil inner seal imprinted with "Safety Seal®" is broken ■ store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat at 40°C (104°F)

U.S. Pat. No. 4,820,522 and 5,430,226

EXP. DATE: XXXXXXXX

CONTROL: XXXXXXXX

200% OF SIZE

**Labeling Format Information:**

Fonts: Helvetica regular, bold and bold italic.

**Drug Facts:** NA pt

**Header:** 4.5 pt

**Subheader:** 4.5 pt

**Body Text:** 4.5 pt

**Drug Facts (continued):** NA pt

**Leading:** 4.5 pt

**Bullets:** 3.5 pt

**Barlines:** 0 pt

**Hairlines:** 0 pt

Horizontal Scale: 74-75%

Average Kerning: -10



**NEW!**  
NDC 50580-505-50

*Lasts up to 8 Hours*  
**TYLENOL<sup>®</sup>** Acetaminophen  
**ARTHRITIS PAIN** Extended Release  
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Geltabs**

**Pain Reliever**

50 Geltabs\* - 650 mg EACH \*Gelatin-Coated Tablets

**Active ingredient (in each geltab) Purpose**  
Acetaminophen 650 mg.....Pain reliever

**Uses**  
temporarily relieves minor aches and pains due to:  
■ arthritis ■ the common cold ■ headache  
■ toothache ■ muscular aches ■ backache  
■ menstrual cramps

**Warnings**  
Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage.  
Do not use ■ with any other product containing acetaminophen  
Stop use and ask a doctor if ■ new symptoms occur ■ redness or swelling is present ■ pain gets worse or lasts for more than 10 days

If pregnant or breast-feeding, ask a health professional before use.  
Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

**Directions** ■ do not take more than directed adults: ■ take 2 geltabs every 8 hours with water ■ swallow whole - do not crush, chew or dissolve ■ do not take more than 6 geltabs in 24 hours ■ do not use for more than 10 days unless directed by a doctor under 18 years of age: ■ ask a doctor

**Other information** ■ do not use if red neck wrap or foil inner seal imprinted with "Safety Seal®" is broken ■ store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat at 40°C (104°F)

**Questions?** Call 1-800-962-5357

MON-EL - PPO, INC., FORT WASHINGTON, PA 19034 USA  
www.tylenol.com © MCK-PPO, Inc. 00 U.S. Pat. No. 482622 and 543928  
EXP. DATE: COUNTBOL: XXXXXXXX

**NEW!**  
NDC 50580-505-50

*Lasts up to 8 Hours*  
**TYLENOL<sup>®</sup>** Acetaminophen  
**ARTHRITIS PAIN** Extended Release  
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Geltabs**

**Pain Reliever**

50 Geltabs\* - 650 mg EACH \*Gelatin-Coated Tablets

**Active ingredient (in each geltab) Purpose**  
Acetaminophen 650 mg.....Pain reliever

**Uses**  
temporarily relieves minor aches and pains due to:  
■ arthritis ■ the common cold ■ headache  
■ toothache ■ muscular aches ■ backache  
■ menstrual cramps

**Warnings**  
Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage.  
Do not use ■ with any other product containing acetaminophen  
Stop use and ask a doctor if ■ new symptoms occur ■ redness or swelling is present ■ pain gets worse or lasts for more than 10 days

If pregnant or breast-feeding, ask a health professional before use.  
Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

**Directions** ■ do not take more than directed adults: ■ take 2 geltabs every 8 hours with water ■ swallow whole - do not crush, chew or dissolve ■ do not take more than 6 geltabs in 24 hours ■ do not use for more than 10 days unless directed by a doctor under 18 years of age: ■ ask a doctor

**Other information** ■ do not use if red neck wrap or foil inner seal imprinted with "Safety Seal®" is broken ■ store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat at 40°C (104°F)

**Questions?** Call 1-800-962-5357

MON-EL - PPO, INC., FORT WASHINGTON, PA 19034 USA  
www.tylenol.com © MCK-PPO, Inc. 00 U.S. Pat. No. 482622 and 543928  
EXP. DATE: COUNTBOL: XXXXXXXX

150% OF SIZE

**Labeling Format Information:**

Fonts: Helvetica regular, bold and bold italic.

|                                |      |                   |        |
|--------------------------------|------|-------------------|--------|
| <b>Drug Facts:</b>             | N/A  | <b>Leading:</b>   | 6.5 pt |
| <b>Header:</b>                 | 8 pt | <b>Bullets:</b>   | 5 pt   |
| <b>Subheader:</b>              | 6 pt | <b>Barlines:</b>  | 0 pt   |
| <b>Body Text:</b>              | 6 pt | <b>Hairlines:</b> | 0 pt   |
| <b>Drug Facts (continued):</b> | N/A  |                   |        |

Horizontal Scale: 70%      Average Kerning: -20



**Drug Facts**  
**Active ingredient (in each geltab) Purpose**  
 Acetaminophen 650 mg.....Pain reliever

**Uses**  
 temporarily relieves minor aches and pains due to  
 ■ arthritis  
 ■ the common cold  
 ■ headache  
 ■ toothache  
 ■ muscular aches  
 ■ backache  
 ■ menstrual cramps

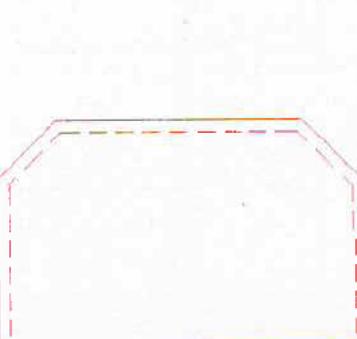
**Warnings**  
**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage.

**Do not use**  
 ■ with any other product containing acetaminophen

**Stop use and ask a doctor if**  
 ■ new symptoms occur  
 ■ redness or swelling is present  
 ■ pain gets worse or lasts for more than 10 days

**If pregnant or breast-feeding,** ask a health professional before use.

**Keep out of the reach of children.** In case of overdose get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.



**Drug Facts**  
**Active ingredient (in each geltab) Purpose**  
 Acetaminophen 650 mg.....Pain reliever

**Uses**  
 temporarily relieves minor aches and pains due to  
 ■ arthritis  
 ■ the common cold  
 ■ headache  
 ■ toothache  
 ■ muscular aches  
 ■ backache  
 ■ menstrual cramps

**Warnings**  
**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage.

**Do not use**  
 ■ with any other product containing acetaminophen

**Stop use and ask a doctor if**  
 ■ new symptoms occur  
 ■ redness or swelling is present  
 ■ pain gets worse or lasts for more than 10 days

**If pregnant or breast-feeding,** ask a health professional before use.

**Keep out of the reach of children.** In case of overdose get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.



**Drug Facts (continued)**

**Directions** ■ do not take more than directed  
 adults  
 ■ take 2 geltabs every 8 hours with water  
 ■ swallow whole – do not crush, chew or dissolve  
 ■ do not take more than 6 geltabs in 24 hours  
 ■ do not use for more than 10 days unless directed by a doctor  
 under 18 years of age ■ ask a doctor

**Other information**  
 ■ do not use if carton is opened or red neck wrap or foil inner seal imprinted with "Safety Seal®" is broken  
 ■ store at 20 - 25°C (68 - 77°F)  
 ■ avoid excessive heat at 40°C (104°F)  
 ■ see end panel for lot number and expiration date

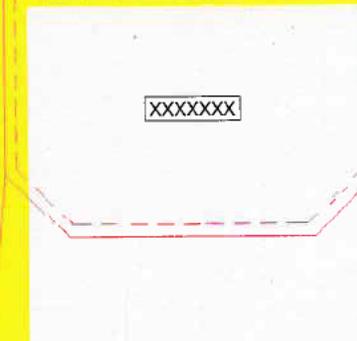
**Inactive ingredients**  
 benzyl alcohol, butylparaben, castor oil, cellulose, corn starch, edetate calcium disodium, FD&C Blue #1, FD&C Blue #2, FD&C Red #40, gelatin, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methylparaben, povidone, propylparaben, sodium lauryl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide

**Questions?** Call 1-800-962-5357

**What makes Tylenol® Arthritis Pain Extended Relief Geltabs different?**  
 • Uses a unique, patented bi-layer geltab. The first layer dissolves quickly to provide prompt relief while the second layer is time released to provide up to 8 hours of relief.  
 • The makers of Tylenol® do not manufacture store brands.  
 For more information or questions, visit our website [www.tylenol.com](http://www.tylenol.com).

100 Geltabs\* - 650 mg EACH  
**TYLENOL®**  
 Acetaminophen Extended Release  
**ARTHRITIS PAIN**  
 FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN  
 Extended Relief Geltabs  
 Pain Reliever  
 \*Gelatin-Coated Tablets  
**NEW!**  
 Lasts up to 8 Hours

100 Geltabs\* - 650 mg EACH  
**TYLENOL®**  
 Acetaminophen Extended Release  
**ARTHRITIS PAIN**  
 FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN  
 Extended Relief Geltabs  
 Pain Reliever  
 \*Gelatin-Coated Tablets  
**NEW!**  
 Lasts up to 8 Hours



100 Geltabs\* - 650 mg EACH  
**TYLENOL®**  
 Acetaminophen Extended Release  
**ARTHRITIS PAIN**  
 FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN  
 Extended Relief Geltabs  
 Pain Reliever  
 \*Gelatin-Coated Tablets  
**NEW!**  
 Lasts up to 8 Hours  
 XXXXXXXX  
 McNeil Consumer Healthcare  
 DIVISION OF MCNEIL-PPC, INC.  
 FORT WASHINGTON, PA 19034 USA  
 www.tylenol.com  
 © MCN-PPC, Inc. '00  
 U.S. Pat. No. 4,926,822  
 and 5,459,026



**Labeling Format Information:**  
 Fonts: Helvetica regular, bold and bold italic.  
**Drug Facts:** 8.5 pt  
**Header:** 8 pt  
**Subheader:** 6 pt  
**Body Text:** 6 pt  
**Drug Facts (continued):** 8 pt  
 Horizontal Scale: 85-87%  
 Average Kerning: -15

**NEW!**  
NDC 50580-505-10

**TYLENOL<sup>®</sup> ARTHRITIS PAIN**  
Acetaminophen Extended Release  
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Gelfabs**

**Pain Reliever**

100 Gelfabs\* - 650 mg EACH \*Gelatin-Coated Tablets

**Active ingredient (in each gelfab) Purpose**  
Acetaminophen 650 mg.....Pain reliever

**Uses**  
temporarily relieves minor aches and pains due to:  
■ arthritis ■ the common cold ■ headache  
■ toothache ■ muscular aches ■ backache  
■ menstrual cramps

**Warnings**  
Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage.  
**Do not use** ■ with any other product containing acetaminophen  
**Stop use and ask a doctor if** ■ new symptoms occur ■ redness or swelling is present ■ pain gets worse or lasts for more than 10 days  
If pregnant or breast-feeding, ask a health professional before use.

Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.  
**Directions** ■ do not take more than directed adults: ■ take 2 gelfabs every 8 hours with water ■ swallow whole - do not crush, chew or dissolve ■ do not take more than 6 gelfabs in 24 hours ■ do not use for more than 10 days unless directed by a doctor under 18 years of age: ■ ask a doctor  
**Other information** ■ do not use if red neck wrap or foil inner seal imprinted with "Safety Seal<sup>®</sup>" is broken ■ store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat at 40°C (104°F)  
**Inactive ingredients** benzyl alcohol, butylparaben, castor oil, cellulose, corn starch, edetate calcium disodium, FD&C Blue #1, FD&C Blue #2, FD&C Red #40, gelatin, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methylparaben, povidone, propylparaben, sodium lauryl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide  
**Questions?** Call 1-800-962-5352

Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.  
**Directions** ■ do not take more than directed adults: ■ take 2 gelfabs every 8 hours with water ■ swallow whole - do not crush, chew or dissolve ■ do not take more than 6 gelfabs in 24 hours ■ do not use for more than 10 days unless directed by a doctor under 18 years of age: ■ ask a doctor  
**Other information** ■ do not use if red neck wrap or foil inner seal imprinted with "Safety Seal<sup>®</sup>" is broken ■ store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat at 40°C (104°F)  
**Inactive ingredients** benzyl alcohol, butylparaben, castor oil, cellulose, corn starch, edetate calcium disodium, FD&C Blue #1, FD&C Blue #2, FD&C Red #40, gelatin, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methylparaben, povidone, propylparaben, sodium lauryl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide  
**Questions?** Call 1-800-962-5352

**NEW!**  
NDC 50580-505-10

**TYLENOL<sup>®</sup> ARTHRITIS PAIN**  
Acetaminophen Extended Release  
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Gelfabs**

**Pain Reliever**

100 Gelfabs\* - 650 mg EACH \*Gelatin-Coated Tablets

**Active ingredient (in each gelfab) Purpose**  
Acetaminophen 650 mg.....Pain reliever

**Uses**  
temporarily relieves minor aches and pains due to:  
■ arthritis ■ the common cold ■ headache  
■ toothache ■ muscular aches ■ backache  
■ menstrual cramps

**Warnings**  
Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage.  
**Do not use** ■ with any other product containing acetaminophen  
**Stop use and ask a doctor if** ■ new symptoms occur ■ redness or swelling is present ■ pain gets worse or lasts for more than 10 days  
If pregnant or breast-feeding, ask a health professional before use.

Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.  
**Directions** ■ do not take more than directed adults: ■ take 2 gelfabs every 8 hours with water ■ swallow whole - do not crush, chew or dissolve ■ do not take more than 6 gelfabs in 24 hours ■ do not use for more than 10 days unless directed by a doctor under 18 years of age: ■ ask a doctor  
**Other information** ■ do not use if red neck wrap or foil inner seal imprinted with "Safety Seal<sup>®</sup>" is broken ■ store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat at 40°C (104°F)  
**Inactive ingredients** benzyl alcohol, butylparaben, castor oil, cellulose, corn starch, edetate calcium disodium, FD&C Blue #1, FD&C Blue #2, FD&C Red #40, gelatin, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methylparaben, povidone, propylparaben, sodium lauryl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide  
**Questions?** Call 1-800-962-5352

**Labeling Format Information:**  
**Fonts:** Helvetica regular, bold and bold italic.  
**Drug Facts:** N/A  
**Header:** 8 pt  
**Subheader:** 6 pt  
**Body Text:** 6 pt  
**Drug Facts (continued):** N/A  
**Leading:** 6-6.25 pt  
**Bullets:** 5 pt  
**Barlines:** 0 pt  
**Hairlines:** 0 pt  
 Horizontal Scale: 70%  
 Average Kerning: -20

150% OF SIZE

To Open: While Folded on Line, Tear At Slit

**TYLENOL**® *Lasts up to 8 Hours*  
**ARTHRITIS PAIN** Acetaminophen Extended Release  
*Extended Relief Gellabs*  
**FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN**  
 2 Gellabs\* - 650 mg EACH Pain Reliever \*Gelatin-Coated Tablets

**Drug Facts**

| Active ingredient (in each gellab) | Purpose       |
|------------------------------------|---------------|
| Acetaminophen 650 mg               | Pain reliever |

**Uses** temporarily relieves minor aches and pains due to: arthritis the common cold headache toothache muscular aches backache menstrual cramps

**Warnings**

**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers.

MCNEIL - PPG, INC., FORT WASHINGTON, PA 19034 USA  
 www.tylenol.com U.S. Pat. No. 4820522 and 5436026 © MCN-PPG, Inc. '00

SAMPLE • NOT TO BE SOLD

XXXXXX

**Drug Facts (continued)**

Acetaminophen may cause liver damage. Do not use with any other product containing acetaminophen. Stop use and ask a doctor if new symptoms occur redness or swelling is present pain gets worse or lasts for more than 10 days if pregnant or breast-feeding, ask a health professional before use. Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

**Directions** do not take more than directed. adults take 2 gellabs every 8 hours with water swallow whole - do not crush, chew or dissolve do not take more than 6 gellabs in 24 hours do not use for more than 10 days unless directed by a doctor. under 18 years of age: ask a doctor

**Inactive ingredients** benzyl alcohol, butylparaben, castor oil, cellulose, corn starch, edetate calcium disodium, FD&C Blue 1, FD&C Blue 2, FD&C Red 40, gelatin, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methylparaben, povidone, propylparaben, sodium lauryl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide

**Other information** do not use if pouch is opened store at 20 - 25C (68 - 77F) avoid excessive heat at 40C (104F)

150% OF SIZE

To Open: While Folded on Line, Tear At Slit

**TYLENOL**® *Lasts up to 8 Hours*  
**ARTHRITIS PAIN** Acetaminophen Extended Release  
*Extended Relief Gellabs*  
**FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN**  
 2 Gellabs\* - 650 mg EACH Pain Reliever \*Gelatin-Coated Tablets

**Drug Facts**

| Active ingredient (in each gellab) | Purpose       |
|------------------------------------|---------------|
| Acetaminophen 650 mg               | Pain reliever |

**Uses** temporarily relieves minor aches and pains due to: arthritis the common cold headache toothache muscular aches backache menstrual cramps

**Warnings**

**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers.

MCNEIL - PPG, INC., FORT WASHINGTON, PA 19034 USA  
 www.tylenol.com U.S. Pat. No. 4820522 and 5436026 © MCN-PPG, Inc. '00

SAMPLE • NOT TO BE SOLD

XXXXXX

**Drug Facts (continued)**

Acetaminophen may cause liver damage. Do not use with any other product containing acetaminophen. Stop use and ask a doctor if new symptoms occur redness or swelling is present pain gets worse or lasts for more than 10 days if pregnant or breast-feeding, ask a health professional before use. Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

**Directions** do not take more than directed. adults take 2 gellabs every 8 hours with water swallow whole - do not crush, chew or dissolve do not take more than 6 gellabs in 24 hours do not use for more than 10 days unless directed by a doctor. under 18 years of age: ask a doctor

**Inactive ingredients** benzyl alcohol, butylparaben, castor oil, cellulose, corn starch, edetate calcium disodium, FD&C Blue 1, FD&C Blue 2, FD&C Red 40, gelatin, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methylparaben, povidone, propylparaben, sodium lauryl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide

**Other information** do not use if pouch is opened store at 20 - 25C (68 - 77F) avoid excessive heat at 40C (104F)

**Labeling Format Information:**

|   |                   |
|---|-------------------|
| Fonts: Helvetica med, bold and bold italic. |                   |
| Drug Facts: 9.0 pt                          | Leading: 6.5 pt   |
| Header: 8 pt                                | Bullets: 5 pt     |
| Subheader: 6 pt                             | Barlines: 2.5 pt  |
| Body Text: 6 pt                             | Hairlines: 0.5 pt |
| Drug Facts (continued): 8 pt                |                   |

Horizontal Scale: 70% Average Kerning: -20

For Professional Use Only  
Not For Retail Sale

Lasts up to 8 Hours

**NEW!**

**TYLENOL** Acetaminophen  
Extended Release  
**ARTHRITIS PAIN**

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Geltabs** 

**Pain Reliever**

650 mg EACH

\*Gelatin-Coated Tablets

Lasts up to 8 Hours

**NEW!**

**TYLENOL** Acetaminophen  
Extended Release  
**ARTHRITIS PAIN**

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Geltabs** 

**Pain Reliever**

650 mg EACH

\*Gelatin-Coated Tablets

Lasts up to 8 Hours

**NEW!**

**TYLENOL** Acetaminophen  
Extended Release  
**ARTHRITIS PAIN**

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Geltabs** 

**Pain Reliever**

650 mg EACH

\*Gelatin-Coated Tablets

Lasts up to 8 Hours

**NEW!**

**TYLENOL** Acetaminophen  
Extended Release  
**ARTHRITIS PAIN**

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief Geltabs** 

**Pain Reliever**

650 mg EACH

\*Gelatin-Coated Tablets

**Prompt Pain Relief That  
Lasts Up To 8 Hours**

**34 POUCHES OF 2 SOLID GELTABS EACH**

*Lasts up to 8 Hours*  
**TYLENOL** Acetaminophen  
**ARTHRITIS PAIN** Extended Release  
 Pain Reliever <sup>\*Gelatin-Coated Tablets</sup>

650 mg EACH

**Drug Facts**

**Active ingredient (in each tablet)**  
 Acetaminophen 650 mg **Purpose**  
Pain reliever

**Uses** Temporarily relieves minor aches and pains due to:  
 ■ arthritis ■ the common cold ■ headache ■ toothache  
 ■ muscular aches ■ backache ■ menstrual cramps

**Warnings**  
**Alcohol warning:** If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take acetaminophen or other pain relievers/fever reducers. Acetaminophen may cause liver damage.

**Do not use**  
 ■ with any other product containing acetaminophen

**Stop use and ask a doctor if**  
 ■ new symptoms occur  
 ■ redness or swelling is present  
 ■ pain gets worse or lasts for more than 10 days

**If pregnant or breast-feeding, ask a health professional before use.**  
**Keep out of the reach of children.** In case of overdose, get medical help or contact a Poison Control Center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

**Directions**  
 ■ do not take more than directed  
 adults ■ take 2 tablets every 8 hours with water  
 ■ swallow whole - do not crush, chew or disperse  
 ■ do not take more than 6 tablets in 24 hours  
 ■ do not use for more than 10 days unless directed by a doctor  
 under 18 years of age ■ ask a doctor

**Other information**  
 ■ do not use if pouch is opened  
 ■ store at 20 -25°C (68 -77°F)  
 ■ avoid excessive heat at 40°C (104°F)  
 ■ see and panel for lot number and expiration date

**Inactive ingredients**  
 benzyl alcohol, butylparaben, croscellose, calcium carbonate, croscellose, croscellose calcium dihydrate, FD&C Blue #1, FD&C Blue #2, FD&C Red #40, gelatin, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, methylparaben, polydioxane, propylparaben, sodium lauryl sulfate, sodium propionate, sodium starch glycolate, titanium dioxide

**Questions?** Call 1-800-942-5357

**McNeil**  
 McNeil Consumer Healthcare  
 DIVISION OF MCNEIL-PPC, INC., FORT WASHINGTON, PA 1904 USA  
 REG. U.S. PAT. & TM. OFF. © 1999 McNeil-PPC, Inc. U.S. Pat. No. 6,270,622 and 6,400,022

**Labeling Format Information:**

Front: Helvetica regular, bold and bold italic.  
 Drug Facts: 6.25 pt  
 Header: 6.25 pt  
 Subheader: 6 pt  
 Body Text: 6 pt  
 Drug Facts (continued): 6 pt  
 Horizontal Scale: 100%  
 Average Kerning: 0

# **CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*  
**NDA 19-872/S-006**

**LABELING REVIEWS**

## LABELING REVIEW OF NDA SUPPLEMENT

SEP 3 1999

**NDA:** 19-872

**Supplement:** SCF-006(AZ)

**Submission Date:** March 8, 1999

**Received:** March 9, 1999

**Review Date:** August 31, 1999

**Applicant:**

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

**Applicant's Representative:**

Paula J. Oliver  
Senior Director, Regulatory Compliance  
(215-273-7878)

**Drug:**

Tylenol® (b)(4) Geltabs  
Acetaminophen Extended Relief Tablets, 650 mg

**Pharmacologic Category:**

(b)(4)

**Submitted:**

Representative draft color labeling for 100 count  
bottle and carton

**Reviewer:**

Debbie Lumpkins

**Background:** The current chemistry supplement is in response to the Agency's non-approval letter dated January 1, 1995. This submission constitutes McNeil's response to the deficiencies cited in the FDA-483 dated October 5, 1995. The specific modifications include: drug product specifications and analytical methods, stability, and revised draft labeling.

The submission includes draft color labeling revised to be consistent with Tylenol® Extended Pain Relief Caplets. According to the sponsor, the labeling has been revised in the following ways:

- product name changed from Tylenol® (b)(4) Geltabs to Tylenol® (b)(4) (b)(4) Geltabs
- back panel of carton updated to bullet format
- alcohol warning revised in accordance with the final rule published in the FEDERAL REGISTER of October 23, 1998 (63 FR 56789)
- changed company name to McNeil Consumer Healthcare.

**Reviewer's comments:**

*Principle display panel (carton and bottle):*

1. As with the name for the sponsor's caplet product, the new product name for the gelcaps is not acceptable as it promotes or implies (b)(4)

(b) (4). The name should be modified to emphasize the treatment of pain and not the  
(b) (4). The sponsor should be referred to the prototype provided to the sponsor  
for its caplet product.

2. In accordance with 21 CFR 201.61(b) and (c) the principal display panel is required to include a statement of identity in terms of the established name of the drug followed by accurate description of the pharmacologic category or intended purpose of the product. The established name of the drug should be "acetaminophen extended release tablets" and the pharmacologic category should be "(b) (4)". These statements should be presented in bold type and be in a print size reasonably related to the most prominent printed matter on the panel.

3. The term "geltab" is not an Agency or USP recognized dosage form. In the net contents statement the term "geltab" needs to be followed by an asterisk and defined as a "gelatin-coated tablet."

*Drug Facts format (carton and bottle)*

1. While the sponsor has attempted to put the Drug Facts information in a bulleted format, the proposed format is not in compliance with the final rule for labeling format published in the FEDERAL REGISTER of March 17, 1999 (64 FR 13254). There are a number of changes that are needed to make the label format comply to the final rule.

- a. All information needs to be enclosed by a 2.5 point barline.
- b. The "Drug Facts" title needs to be added in a minimum 14 point type size and left justified. The title needs to be separated from the rest of the information by a 0.5 point horizontal barline that extends to within 2 spaces on either side of the drug facts box.
- c. "Drug Facts (continued)" needs to appear on all subsequent panels of the Drug Facts information. "Drug Facts" needs to appear in 8 point bold italicized print and "continued" needs to be presented in 8 point regular type. The title is to be separated from subsequent information by a 0.5 point horizontal barline that extends to within 2 spaces on either side of the drug facts box.
- d. Headings, i.e., Active ingredients, Purposes, Uses, Warnings, Directions, etc. need to be in italicized print and appear in minimum 8 point type size.
- e. Only the first letter of each heading and subheading should be capitalized.
- f. The colons following the headings and subheadings should be deleted.
- g. On the carton only, the heading "Purpose" and the information that immediately follows needs to be right justified.

- h. Only the first letter of the purpose statement should be capitalized, i.e., (b) (4)  
(b) (4).
- i. The heading "Warnings" needs to be left justified.
- j. The alcohol warning should not be presented as a bulleted statement. The warning should immediately follow the heading on the same line. Only the "A" in the heading should be capitalized, i.e., "Alcohol warning."
- k. The directions are included in a table. While a table format is not required for dosing directions (b) (4), it is acceptable. However, the information contained in the tables should be revised to omit upper case text. The sponsor should be referred to the prototype for the caplets product for guidance on the revision of the table contents.
- l. The heading "Other information" should be added for the storage conditions statement and the tamper evident statement. This heading should be in bold italicized type. The information in this sections needs to be separated from the other headings by a 2.5 point barline.
- m. On the carton only, the inactive ingredients listing should be contained within the drug facts area with a graphic on the last panel directing consumers to the information on the end flap of the carton.
- n. On the carton only, the listing of inactive ingredients should begin with the heading of "Inactive ingredients" in bold italicized print. This information needs to be separated from the rest of the headings by a 2.5 point hairline.
- o. The listing of the inactive ingredients should all be lower case.

*Drug Facts content (bottle and carton)*

1. Under the heading "Uses," the bulleted statement "(b) (4)" is redundant with the statement before and should be revised to "arthritis." The revised "Uses" statement should be as follows:

*Uses* temporarily relieves minor aches and pains due to: ■ arthritis ■ the common cold  
■ headache ■ toothache ■ muscular aches ■ backache ■ menstrual cramps

(b) (4)

2. The wording of the alcohol warning is acceptable.
3. The subheading "Do not use" is intended for absolute contraindications. None of the bullets currently listed under this subheading are absolute contraindications. Therefore, this subheading should be deleted and the information included under other subheadings as indicated below.

4. A new subheading “(b) (4)” should be added. The information about the use of the product with other products containing acetaminophen should be included under this heading as follows:

(b) (4) any other product containing acetaminophen

5. The heading “(b) (4)” should be revised to “**Stop use and ask a doctor if.**” The bullets “(b) (4)” and “(b) (4)” previously listed under the subheading “Do not use” should be included under this subheading as follows:

**Stop use and ask a doctor if**

- new symptoms occur
- redness or swelling is present
- pain gets worse or lasts for more than 10 days

(b) (4)

It should be noted that the first bullet under this subheading, i.e., “(b) (4)” has been revised as shown above.

6. The highlighted statement “(b) (4)” should be revised to “do not take more than directed” and should be included as the first bullet under the heading “Directions.”

7. The pregnancy/nursing warning should precede the overdose warning and should be revised as follows:

**If pregnant or breast feeding,** ask a health professional before use.

8. The overdose warning should be revised as follows:

**Keep out of the reach of children.** In case of overdose, get medical help or contact a Poison Control center right away. Quick medical attention is critical for adults as well as for children even if you do not notice any signs or symptoms.

9. (b) (4)

(b) (4)

(b) (4)

10. On the carton only, the tamper evident statement should be moved from its current location, i.e., immediately following directions, and placed under the heading indicated below.

11. The promotional statements following the "Directions" section area should be moved outside the "Drug Facts" area.

12. An additional heading, "Other information" should be added. For the carton, the following information should be under this heading:

**Other information**

- store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat 40°C (104°F)
- do not use if the carton is opened or red neck wrap or foil inner seal imprinted with "Safety Seal®" is broken
- see other end panel for lot number and expiration date

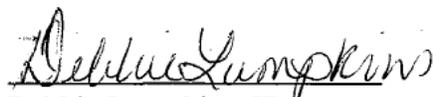
The bottle label should contain the following:

**Other information**

- store at 20 - 25°C (68 - 77°F) ■ avoid excessive heat 40°C (104°F)

Note the revision of the storage statements to be consistent with the current recommendations for storage condition statements for all OTC drug products from the Division of New Drug Chemistry.

**Recommendations:** The product name is not acceptable and should be modified to avoid any suggestion that the product is useful for (b) (4). The sponsor should be informed that the labeling as submitted is not approvable. The revisions listed above will be provided to the sponsor. In addition, the sponsor should be referred to the prototype label developed for the Tylenol® Arthritis Extended Relief Caplets product for additional guidance on the labeling of this product.

  
Debbie Lumpkins, IDS  
Leader, Team 3

  
Stephanie A. Mason, IDS

cc:  
NDA 19-872  
HFD-560/Div Files  
HFD-560/KRothschild

N19-872 SCF-006(AZ)

page 6

HFD-560/SMason

HFD-560/DLumpkins

HFD-560/LKatz *JK*

Doc:19872.gel

*9/31/97*

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*  
**NDA 19-872/S-006**

**CHEMISTRY REVIEWS**

ORIGINAL

JAN 11 1996

|   |   |   |
|---|---|---|
| <b>Chemistry Review</b>   | <b>1. Division</b><br>HFD-550                 | <b>2. NDA Number</b><br>19-872                                      |
| <b>3. Name and Address of Applicant</b><br>McNeil Consumer Products Company<br>7050 Camp Hill Road<br>Fort Washington, PA 19034-2299  |   | <b>4. Supplement Number</b> <b>Date</b><br>SCF006            6/9/95 |
| <b>5. Name of Drug</b> Tylenol ER   | <b>6. Nonproprietary Name</b> acetaminophen   |   |
| <b>7. Supplement Provides for:</b> The use of gelating as an alternate coating  |   | <b>8. Amendment(s)</b><br>12/11/95                                  |
| <b>9. Pharmacological Category</b> analgesic  | <b>10. How Dispensed</b><br>OTC               | <b>11. Related Documents</b>  |
| <b>12. Dosage Form</b> coated bilayer tablets   | <b>13. Potency(ies)</b>                       |   |
| <b>14. Chemical Name and Structure</b> see USAN   |   |   |
| <b>15. Comments</b>   |   |   |
| <p>It is stated in the cover letter that</p> <p>“The <sup>(b)(4)</sup> of the proposed product is identical to the approved formulation. The proposed product differs from the approved product in the shape of the tablet and the addition of a gelatin coating to the tablet.”</p> <p>The shape change requires only different tooling. The proposed coating is reviewed in the attached Notes.</p> <p>GMP clearance was requested 8/8/95 and a withhold recommendation from the district office (Philadelphia) was received on 10/24/95. An inspection of the manufacturing line for the tablet <sup>(b)(4)</sup> revealed problems which prompted the issuance of a Form FDA 48</p> <p>Other problems were also cited. See the attached documents. None of these problems have been addressed in this supplement.</p> |   |   |
| <b>16. Conclusions and Recommendations</b> Issue an non-approval letter. (A PK review is also required for this supplement)   |   |   |
| <b>17. Name</b><br>Charlotte A. Yaciw   | <b>Signature</b><br><i>Charlotte A. Yaciw</i> | <b>Date</b><br>12/26/95   |
| <b>Concurrence</b>  |   |   |

cc:

NDA 19-872/S006  
HFD-550/Division File  
HFD-550/C Yaciw  
HFD-550/SRairodski

Doc ID: n19872s.006

*EP Steiner*  
1-11-96

Following this page, one page withheld in full - (b)(4)

A LOA from <sup>(b) (4)</sup> was submitted for the <sup>(b) (4)</sup> materials (page 08 000066) along with some analytical information.

The manufacturing directions for the gelcoat are in volume 14 of the supplement.

---

For the NA letter:

This supplement is not approvable since you have failed to show that you have the necessary control over your manufacturing procedures for this product.

CHEMIST REVIEW #2  
OF SUPPLEMENT

- 1. ORGANIZATION HFD-560
- 2. NDA NUMBER: 19-872
- 3. SUPPLEMENT NUMBERS/DATES: SCF-006

Letter date: 6/9/95  
 Stamp date: 6/12/95  
 Due date: 9/9/99

SEP 8 1999

- 4. AMENDMENTS/REPORTS/DATES:  
 This document is covered by this review: AZ  
 Letter date: 3/8/99  
 Stamp date: 3/9/99

5. RECEIVED BY CHEMIST: 3/18/99

6. APPLICANT NAME AND ADDRESS: McNeil Consumer Healthcare  
 7050 Camp Hill Road  
 Fort Washington, PA 19034-2299

- 7. NAME OF DRUG: Tylenol® Extended Release Tablets
- 8. NONPROPRIETARY NAME: acetaminophen
- 9. CHEMICAL NAME/STRUCTURE: see USP
- 10. DOSAGE FORM(S): extended release tablet (bilayer)
- 11. POTENCY: 650 mg
- 12. PHARMACOLOGICAL CATEGORY: analgesic
- 13. HOW DISPENSED: OTC
- 14. RECORDS & REPORTS CURRENT: yes
- 15. RELATED IND/NDA/DMF: na
- 16. SUPPLEMENT PROVIDES FOR: a gelatin coated tablet
- 17. COMMENTS

This supplement was originally submitted in 1995 and was not approved due to serious problems revealed during the inspection of the site. See Review #1 for the details. This amendment is in response to the 1/25/96 NA letter from HFD-550 and the Form 483 issued by the inspector. The line has been reinspected and found to be acceptable. This product will be known as Geltabs. See the attached review notes.

18. CONCLUSIONS AND RECOMMENDATIONS:

This supplement may be approved contingent on acceptance of the labeling by HFD-560.

19. REVIEWER NAME  
 Charlotte Yaciw

SIGNATURE  
*Charlotte A. Yaciw*  
*Bonnie B. Owen*

DATE COMPLETED  
 9/3/99  
 9/8/99

*for* Concurrency: Hasmukh Patel

- cc: Original: NDA 19-872
- HFD-560/Division File
- HFD-560/PM/KRothschild
- HFD-560/Dep. Dir./LKatz
- HFD-550/Chem/CYaciw
- HFD-830/Dir/CWChen

Doc. ID: n19872\_006r2.doc

31-AUG-1999

Page 1 of 1

FDA CDER EES  
ESTABLISHMENT EVALUATION REQUEST  
SUMMARY REPORT

|  |  |                      |
|--|--|----------------------|
| Application: <b>NDA 19872/006</b>                            | Priority: <b>3S</b>                                | Org Code: <b>560</b> |
| Stamp: <b>12-JUN-1995</b> Regulatory Due: <b>09-SEP-1999</b> | Action Goal:                                       | District Goal:       |
| Applicant: <b>MCNEIL CONSUMER</b>                            | Brand Name: <b>TYLENOL (ACETAMINOPHEN)</b>         |                      |
| <b>1 CAMP HILL RD</b>  | <b>EXTENDED-RELIEF</b>                             |                      |
| <b>FORT WASHINGTON, PA 19034</b>                             | Established Name:                                  |                      |
|  | Generic Name: <b>ACETAMINOPHEN</b>                 |                      |
|  | Dosage Form: <b>SRT (SUSTAINED RELEASE TABLET)</b> |                      |
|  | Strength: <b>650 MG</b>                            |                      |

|               |                                |                     |                         |
|---------------|--------------------------------|---------------------|-------------------------|
| FDA Contacts: | <b>K. ROTHSCHILD (HFD-560)</b> | <b>301-827-2284</b> | <b>,Project Manager</b> |
|               | <b>C. YACIW (HFD-830)</b>      | <b>301-827-2296</b> | <b>,Review Chemist</b>  |
|               | <b>H. PATEL (HFD-550)</b>      | <b>301-827-2507</b> | <b>,Team Leader</b>     |

---

Overall Recommendation:

**ACCEPTABLE on 27-AUG-1999 by M. EGAS (HFD-322) 301-594-0095**

---

|                                    |          |
|------------------------------------|----------|
| Establishment: <b>2510184</b>      | DMF No:  |
| <b>MCNEIL CONSUMER PRODUCTS CO</b> | AADA No: |
| <b>1 CAMP HILL RD</b>              |          |
| <b>FORT WASHINGTON, PA 19034</b>   |          |

|  |                         |  |
|--|-------------------------|--|
| Profile: <b>TTR</b>                      | OAI Status: <b>NONE</b> | Responsibilities: <b>FINISHED DOSAGE</b> |
| Last Milestone: <b>OC RECOMMENDATION</b> |                         | <b>MANUFACTURER</b>                      |
| Milestone Date: <b>26-AUG-1999</b>       |                         |  |
| Decision: <b>ACCEPTABLE</b>              |                         |  |
| Reason: <b>DISTRICT RECOMMENDATION</b>   |                         |  |

---

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*  
**NDA 19-872/S-006**

**CLINICAL PHARMACOLOGY & BIOPHARMACEUTICS**  
**REVIEW**

**ACETAMINOPHEN**

TYLENOL® ER 650 mg Caplet

McNEIL Consumer Products Company

SNDA 19-872 (SCS-006)

Camp Hill Rd., Fort

Washington, PA 19034

Reviewer: Ahmed El-Tahtawy, R.Ph., Ph.D.

Date of Submission: Jun. 12, 1995

---

**1. BACKGROUND:**

---

The firm is seeking approval of TYLENOL® ER 650 mg Caplet for the OTC market. This supplemental NEW Drug Application provides for the addition of a round gelatin-coated tablet form of TYLENOL® Extended Relief 650 mg Caplet. The proposed product differs from the approved product in the shape of the tablet and the addition of a gelatin coating to the tablet instead of the <sup>(b) (4)</sup> film.

On March, 1995, the firm submitted this application as an ANDA to the Office of Generic Drugs (OGD). On May, 1995, OGD issued a "refuse to file" letter and recommend filing the application as an SNDA to NDA 19-872.

**2. OBJECTIVE:**

This SNDA seeks approval of a round gelatin-coated extended release tablet. The reference drug is a capsule-shaped, film coated extended release tablet. The tablet <sup>(b) (4)</sup> product consists of immediate and extended release layers. The <sup>(b) (4)</sup> of the proposed product is identical in formulation to that of the approved drug product.

**3. FORMULATION:**

The acetaminophen ER Geltab and the acetaminophen ER caplet were designed to consist of immediate- and extended-release layers, which are <sup>(b) (4)</sup>



#### 4. DISSOLUTION:

The pKa of acetaminophen lies in the range of 9.0 to 10.0 which is outside the range of physiological pH's and we should not expect any changes in the solubility of the drug due to shifts in the pH. The firm tested the dissolution of the Acetaminophen ER Geltabs in four different media (see attached Table) and determined that the dissolution of Acetaminophen ER Geltabs is pH independent as expected.

The conditions employed for the dissolution testing were as follows:

USP Apparatus II at 50 rpm

900 ml Simulated Gastric Fluid w/o Pepsin, pH 1.2

Number of capsules used: 12

Sampling times: 30, 90, 240 min..

#### Proposed Dissolution Specification (firm's)

| Time (min) | Mean<br>(% of Claim)   |
|------------|------------------------|
| 30         | (b) (4)                |
| 90         | (b) (4)                |
| 240        | not less than (b) (4)% |

#### RECOMMENDATION:

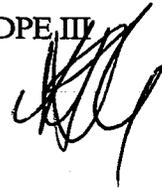
From the biopharmaceutical point of view the firm has met the requirements of an in vitro dissolution testing with an appropriate reference product, and the application is acceptable.

The Division of Biopharmaceutics recommends the following dissolution specification for tablets:

| Time (min) | Mean<br>(% of Claim)   |
|------------|------------------------|
| 30         | (b) (4)                |
| 90         | (b) (4)                |
| 240        | not less than (b) (4)% |

Method: USP Apparatus II at 50 rpm in 900 ml of SGF w/o Pepsin, pH 1.2 at 37°C.

Ahmed El-Tahtawy, R.Ph., MS., Ph.D.  
Pharmacokineticist, DPE, III



---

RD,FT Initialed by, Dennis Bashaw, Pharm. D. *Ed* 12/12/95

Distribution List:

CC: NDA 20-584 (ORIG)

HFD-460/DIV/File

HFD-460/CSO/S. Guchenheimer

HFD-460/PK files/El-Tahtawy (X2)

HFD-344/Viswanathan

HFD-880/Drug, Chron, Reviewer, N. Fleischer (X4)

R/D Init. By: DBashaw/ 12/6/95

**CENTER FOR DRUG EVALUATION AND RESEARCH**

*APPLICATION NUMBER:*  
**NDA 19-872/S-006**

**ADMINISTRATIVE and CORRESPONDENCE**  
**DOCUMENTS**

NDA NO. 19-872 REF. NO. 006  
NDA SUPPL FOR SCF SCF

**McNEIL**

ORIGINAL

NDA SUPPLEMENT

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

Robert F. Bedford, MD  
Acting Director  
Pilot Drug Evaluation Staff (HFD-007)  
Document Control Room #9B-23  
Food and Drug Administration  
5600 Fishers Lane  
Rockville, MD 20857



RE: TYLENOL® Acetaminophen Extended Release Caplet, 650mg  
NDA 19-872  
Supplemental New Drug Application

Dear Dr. Bedford:

In accordance with 21 CFR 314.70(b)(2), enclosed is a Supplemental New Drug Application for TYLENOL® acetaminophen Extended Release (ER) Geltab, 650mg. This application provides for the addition of a round gelatin-coated tablet form of TYLENOL® Extended Relief to NDA 19-872, which was approved on June 8, 1994 for TYLENOL® Extended Relief Caplet, 650mg. The <sup>(b)(4)</sup> of the proposed product is identical to the approved formulation. The proposed product differs from the approved product in the shape of the tablet <sup>(b)(4)</sup> and the addition of a gelatin coating to the tablet.

This application was initially submitted to the Office of Generic Drugs as an ANDA on March 17, 1995. On May 19, 1995, the Office of Generic Drugs issued a letter refusing to file this ANDA because "it is the subject of a submission that is already covered by an approved prior application from the applicant for the proposed drug product [21 CFR 314.101(d)(8)(i)]" (letter attached). It was recommended by the Office of Generic Drugs and confirmed by the Pilot Drug Division (conversation with Ms. Susan Guckenheimer and Dr. Charlotte Yaciw on 5/31/95) that this product should be filed as an SNDA to NDA 19-872.

NDA 19-872  
Supplemental New Drug Application  
Page 2

In subsequent discussions with Ms. Susan Guckenheimer, it was agreed that this SNDA could be submitted in the ANDA format. Therefore, this submission is formatted in accordance with 21 CFR 314.94. The patent certification and the debarment and conviction certification have been removed from Section III because these are not applicable to an SNDA. Furthermore, as requested by the reviewing chemist, Dr. Charlotte Yaciw, the stability section (Section XVII) has been updated to report six months stability data for the test batch.

---

Please contact Janet A. Uetz at (215) 233-8368 or me at (215) 233-7010 for any questions or requests regarding this application.

Sincerely,

McNEIL CONSUMER PRODUCTS COMPANY



Vivian A. Chester  
Executive Director, Regulatory Affairs

cc: (Cover Letter and Section XVII):  
Debra Pagano, Philadelphia District Office, PAI Coordinator

Enclosures:

Archival Copy (Sections I through XXI)  
Biopharmaceutics Review Copy (Sections I through VII)  
Chemistry Review Copy (Sections I through V, VII through XXI)  
Methods Validation Package (Sections VIII (Active Ingredient), XV, XVI and XIX)  
(3 Copies)

\jau002.ltr



W.H.I.

# Memorandum

Date **NOV 15 1995**

From **Branch Chief  
Investigations and Preapproval Compliance  
Branch, HFD-324**

Subject **Recommendation to Withhold Approval** Firm **McNeil Consumer Products  
Company  
7050 Camp Hill Road  
Fort Washington, PA 19034**

To **Charlotte Yaciw  
Division of Pilot Drug Evaluation, HFD-007**

We have completed our review of the Establishment Inspection Report (EIR) for McNeil Consumer Products Company of 7050 Camp Hill Road, Fort Washington, PA 19034. The facility was inspected by the FDA Philadelphia District Office on October 2 and 6, 1995. The inspection was conducted in response to your Establishment Evaluation Request (EER) dated August 8, 1995.

The Division of Manufacturing and Product Quality (DMPQ) concurs with the District's recommendation to withhold approval of NDA 19-872/S-006. Significant CGMP deficiencies noted during the inspection include, but are not limited to the following:

1. The production process for Acetaminophen Extended Release Geltabs, 650 mg is not described in sufficient detail, as follows:
  - A. Specific equipment has not been identified.
  - B. The Composition of Acetaminophen Extended Release Geltabs (Formula (b)(4))  
[REDACTED]  
However, the firm has not conducted development studies to support the (b)(4).
  - C. The final (b)(4) has not been identified.

Page 2  
McNeil Consumer Products Company

2. There is no assurance of [REDACTED] <sup>(b) (4)</sup> for Acetaminophen Extended Release Geltabs, 650 mg after [REDACTED] <sup>(b) (4)</sup>

At the conclusion of the inspection, McNeil was presented with a Form FDA 483, which listed 9 observations. On October 23, 1995, McNeil submitted a response to the observations. The response indicates that the firm has recently established a [REDACTED] <sup>(b) (4)</sup>

listed in NDA 19-872.

A copy of the EIR and the firm's response are attached for your review.

If you have any questions please contact John M. Singer or me at (301) 827-0062.

  
Mark A. Lynch

Attachment - EIR and McNeil Response

DEPARTMENT OF HEALTH AND HUMAN SERVICES  
Public Health Service  
FOOD AND DRUG ADMINISTRATION

ESTABLISHMENT EVALUATION REQUEST

|   |  |                                |                       |   |
|---|--|--------------------------------|-----------------------|---|
| TEST TYPE (Check One)<br><input checked="" type="checkbox"/> Original <input type="checkbox"/> Follow-Up <input type="checkbox"/> FUR   |  | Date August 8, 1995            | Phone No.<br>443-4250 | EER ID #<br>8604  |
| REQUESTOR'S NAME<br>Charlotte Yaciw   |  | DIVISION<br>PDES               |                       | MAIL CODE<br>HFD-007  |
| APPLICATION AND SUPPLEMENT NUMBER 19-872/SCF 006  |  |                                |                       |   |
| BRAND NAME Tylenol® Extended Relief   |  | ESTABLISHED NAME acetaminophen |                       |   |
| DOSAGE FORM AND STRENGTH extended release bi-layer tablets, 650 mg  |  |                                |                       | STERILE<br><input type="checkbox"/> YES <input type="checkbox"/> NO |
| PROFILE CLASS TTR   |  | PRIORITY CLASSIFICATION 3S     |                       |   |
| APPLICANT'S NAME McNeil Consumer Products Company   |  |                                |                       |   |
| ADDRESS 7050 Camp Hill Road<br>Fort Washington, Pennsylvania 19034-2299   |  |                                |                       |   |
| COMMENTS Provides for the gel-coating (gelatin coating) <sup>(b) (4)</sup> , a different coating technology from the currently marketed product which is film coated. Other products are also gel-coated at this site.<br><del>Use for due date is 12/12/95</del> |  |                                |                       |   |

ILITIES TO BE EVALUATED

| Name and Complete Address |   | RESPONSIBILITY                            | DMF NUMBER/<br>PROFILE CODE | F KEY/<br>CIRTS ID | HFD-324 USE ONLY |
|---------------------------|---|---|-----------------------------|--------------------|------------------|
| 1.                        | McNeil Consumer Products Company<br>7050 Camp Hill Road<br>Fort Washington, Pennsylvania 19034-2299 | manufacture,<br>package and QC<br>tablets | TTR                         | MENF<br>21089      | UN<br>10/6/95    |
| 2.                        |   |   |                             |                    |                  |
| 3.                        |   |   |                             |                    |                  |
| 4.                        |   |   |                             |                    |                  |
| 5.                        |   |   |                             |                    |                  |

|                               |   |                          |
|-------------------------------|---|--------------------------|
| FOR<br>HFD-324<br>USE<br>ONLY | CSO<br><i>Shirnette Ferguson</i>            | DATE RECEIVED<br>8/11/95 |
|                               | CGMP COMPLIANCE STATUS<br><i>acceptable</i> | DATE<br>11/15/95         |

**McNEIL**

**NDA SUPPL AMEND**

SCF-006 (BB)

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

DEC 11 1995

Michael Weintraub, MD  
Acting Director  
Division of Anti-Inflammatory, Analgesic,  
and Dental Products (HFD-550)  
Central Document Room  
Food and Drug Administration  
9201 Corporate Blvd.  
Rockville, MD 20850



RE: **TYLENOL® acetaminophen ER Geltab**  
**Amendment No. 1 to NDA 19-872/S-006**

Dear Dr. Weintraub:

We are submitting this amendment in follow up to a telephone request by Dr. Ahmed El Tahtawy, reviewing pharmacokineticist. Dr. El Tahtawy requested that we provide an additional analysis for Bioavailability Study 132, "A Comparison of Acetaminophen Extended Release Geltabs with Acetaminophen Extended Release Caplets Following Single Fasted and Fed Doses (Protocol 94-409)". The reanalysis and results are discussed in the attached document.

If you have any questions regarding the information provided, please contact Paula J. Oliver at (215) 233-7878 or me at (215) 233-7010.

Very truly yours,

McNEIL CONSUMER PRODUCTS COMPANY

A handwritten signature in cursive script that reads "Vivian A. Chester".

Vivian A. Chester  
Executive Director, Regulatory Affairs

cc: **S. Raigrodski, CSO, Letter Only (HFD-550)**  
**A. El Tahtawy, Review Copy (HFD-550)**



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

NDA 19-872/S-006

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

JAN 25 1996

Attention: Vivian A. Chester  
Executive Director, Regulatory Affairs

Dear Ms. Chester:

Please refer to your June 9, 1995, supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tylenol® (acetaminophen) Extended Release Caplets, 650 mg.

We acknowledge receipt of your amendment dated December 11, 1995.

We have completed our review and find the information presented is inadequate, and the supplemental application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). The deficiencies may be summarized as follows:

This supplement is not approvable since you have failed to show that you have the necessary control over your manufacturing procedures for this product.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the supplemental application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment, nor will the review clock be reactivated until all deficiencies have been addressed.

Should you have any questions, please contact:

---

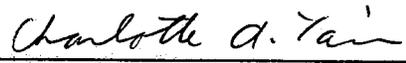
Susan I. Raigrodski  
Consumer Safety Officer  
Telephone: (301) 827-2090

---

Sincerely yours,

Review Team  
Division of Anti-Inflammatory, Analgesic,  
and Dental Drug Products, HFD-550  
Office of Drug Evaluation V  
Center for Drug Evaluation and Research

 1/19/96  
\_\_\_\_\_  
Ahmed El-Tahtawy, R.Ph., Ph.D.  
Pharmacokineticist

 1/19/96  
\_\_\_\_\_  
Charlotte A. Yaciw  
Chemistry Team Leader

cc:

Original NDA 19-872/S-006

District Office

HFD-550/Div File

*SJR 1/19/96*

HFD-550/SRaigrodski/CYaciw/AEI-Tahtawy/SSchmidt

*1/19/96*

HFD-80

HFD-830/ESheinin

*1/23/96*

HFD-550/SCook/1-16-96

S Cook/1-16-96/nda19872.s6

RD init. by:SSchmidt-1/19/96

FT by:MMatheny-1/19/96

**NOT APPROVABLE**



SCF  
S006 (AZ)

McNeil Consumer Healthcare, 7050 Camp Hill Road, Fort Washington, PA 19034-2299 (215) 273-7000

Debra L. Bowen, MD  
Acting Director  
Division of OTC Drug Products (HFD-560)  
Center for Drug Evaluation and Research  
Document Control Room  
Food and Drug Administration  
9201 Corporate Blvd., Room S-212  
Rockville, MD 20850

MAR 8 1999



RE: Acetaminophen Extended Relief Geltab, 650 mg  
Amendment No. 2 to NDA 19-872/S-006

Dear Dr. Bowen:

We are submitting this amendment in response to a non-approvable letter that was issued by the division on January 1, 1995 (copy attached). It is also being submitted to address several items that were listed on an FDA-483 at the conclusion of a Pre-Approval inspection (PAI) at our Ft. Washington facility on October 6, 1995. In our October 23, 1995 response to the FDA-483, we indicated to the Philadelphia District Office that an amendment would be filed and additional process optimization work would be completed. We are now at the point where the process optimization work has been completed.

To aid in the review of this amendment, we have attached the FDA-483 that was issued to McNeil on October 6, 1995 and our written response dated October 23, 1995. Items 4 and 5 only on the FDA-483 dealt with acetaminophen extended release gels, the subject of this amendment.

As a result of the developmental work that has been completed during the interval from the 9/95 Pre-Approval Inspection to date, we have revised the following sections of our application:

- Drug Product, including the quantitative composition, inactive ingredient specifications and the manufacturing requisitions.
- Specifications and Analytical Methods to provide for [REDACTED] (b) (4) controls and a modified/re-validated analytical method.
- Stability data to include updated data (36 months) on the primary stability batch (which is also the biobatch) and new data on a second batch through 36 months.
- Revised draft labeling.

ORIGINAL

In providing these revised sections, we have included specific equipment, deleted the (b) (4), identified (b) (4), revised and updated the master manufacturing requisitions (batch records), updated the stability data, revised and revalidated the analytical methods, and made a minor variation in the product formula. A reviewers guide detailing changes precedes each modified section.

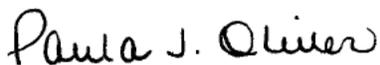
Additionally, we have revised the labeling for this product to make it consistent with the revised labeling on TYLENOL® Arthritis Extended Relief Caplet, 650 mg, submitted to the agency on December 8, 1998 under S-009. This labeling supplement is currently "pending" in HFD-560, Division of OTC Drug Products.

With the submission of this amendment, we have addressed all outstanding items that have been brought to our attention and we are requesting that the division reactivate the review of this supplemental application.

If you have any questions, please contact me at (215) 273-7878 or Jackie Linse at (215) 273-8733.

Very truly yours,

McNEIL CONSUMER HEALTHCARE



Paula J. Oliver  
Senior Director, Regulatory Compliance

PJO:dtg  
Attachment

cc: D. Pagano, Pre-Approval Manager, Philadelphia District



ARCHIVAL  
COPY

McNeil Consumer Healthcare, 7050 Camp Hill Road, Fort Washington, PA 19034-2299 (215) 273-7000

Charles Ganley, MD, Director  
Division of Over-the-Counter Drug Products (HFD-560)  
Center for Drug Evaluation and Research  
Document Control Room, Room S-212  
9201 Corporate Boulevard  
Rockville, MD 20850

NOV. 19 1999

SUPPL AMENDMENT  
SCF-006/BL

RE: Acetaminophen Extended Relief Tablet (Geltab), 650 mg  
NDA 19-872  
Supplemental NDA S-006  
Correspondence - Labeling Comments Dated 9/9/99



Dear Dr. Ganley:

This letter is being submitted to address agency comments on **TYLENOL®** labeling in **Drug Facts** format. Draft labeling was provided to McNeil on September 9, 1999 via an Approvable Letter (copy attached) for our geltab formulation. The division advised us to submit draft labeling consistent with the draft prototype attached to the Approvable Letter.

We have evaluated the agency's modifications to McNeil's version of the **TYLENOL®** extended release label in Drug Facts format. We concur with the modifications with the following exceptions:

**Concomitant Use Warning**

Inclusion of a concomitant use statement in the labeling of all **TYLENOL** products was voluntarily initiated in 1994 as a label phase in to address reports of adverse experiences following concomitant misuse of the product. The following was added to the Warnings section of the labeling:

"Do not use with other products containing acetaminophen"

In 1998, when we introduced bulleted text on our single ingredient adult and pediatric **TYLENOL** products, we maintained this same language but included it under a Warnings subheading titled "Do Not Use".

The draft **TYLENOL** labeling provided to McNeil on September 9, 1999 eliminated the "Do Not Use" subheading and modified the language to the following:

[REDACTED] (b) (4)

ORIGINAL

Charles Ganley, MD, Director  
NDA 19-872  
Page 2

The revised language differs in content from our current language. We believe our current language is clearer and more appropriate. Therefore, we would appreciate your reconsideration of this issue since it affects numerous McNeil labels, including all of our combination products.

**Directions**

As pointed out in our correspondence to the agency on SNDA-009 (Drug Facts submission on the caplet formulation), we currently include additional text in the Directions section of adult TYLENOL® labeling which reads as follows:



This is voluntary language that we added in 1998 to TYLENOL labeling to address reports of misuse of the product in children under 12. We would also appreciate your review of this language since, as with the concomitant use warning, it affects numerous labels, as discussed above and it was not included in the prototype provided to us.

The final rule on OTC labeling, as published in the *Federal Register* on March 17, 1999 acknowledges that manufacturers may add voluntary warnings to their OTC labeling and encourages manufacturers to discuss such warnings with the agency. Therefore, since voluntary warnings have been included in TYLENOL labeling for a number of years, we would like to discuss our situation with the agency at your earliest convenience.

If you have any questions regarding this correspondence, please contact me at (215) 273-7878.

Very truly yours,

McNEIL CONSUMER HEALTHCARE

A handwritten signature in black ink, appearing to read "Paula J. Oliver".

Paula J. Oliver  
Senior Director, Regulatory Compliance

PJO:dtg  
Attachment

cc: L. Katz, MD (HFD-560)  
K. Rothschild, Esquire (HFD-560)

CENTER FOR DRUG EVALUATION AND RESEARCH  
FOOD AND DRUG ADMINISTRATION

PJO  
SEP 09 1999

**FACSIMILE TRANSMISSION RECORD**

DATE: 9/9/99

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: Paula J. Oliver  
Company: McNeil Consumer Healthcare  
Phone: 215-273-7878

FAX #: 215-273-4049 No. Of Pages (including cover) 3

\*\*\*\*\*  
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.  
\*\*\*\*\*

Message: Please find attached the action letter for your supplemental NDA 19-872/S-006.

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



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration  
Rockville MD 20857

NDA 19-872/S-006

McNeil Consumer Healthcare  
Attention: Paula J. Oliver  
Senior Director, Regulatory Compliance  
7050 Camp Hill Road  
Fort Washington, PA 19034-2299

SEP 9 1999

Dear Ms. Oliver:

Please refer to your supplemental new drug application dated June 9, 1995, received June 12, 1995, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tylenol (acetaminophen) Extended Relief tablets, 650 mg. Your supplemental new drug application provided for a geltab formulation.

We also acknowledge your submission dated March 8, 1999, received March 9, 1999. This submission constituted a complete response to our January 25, 1996 action letter.

We have completed the review of this supplemental new drug application, as amended, and it is approvable. Before this supplemental new drug application may be approved, however, it will be necessary for you to submit draft labeling consistent with the draft prototype labeling attached. Please note that the product name in the draft prototype label does not contain a reference to "arthritis," as the agency believes such reference to be misleading.

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

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

Within 10 days after the date of this letter, you are required to amend the supplemental new drug application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the supplemental new drug application. Any amendment should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

**NDA 19-872/S-006**

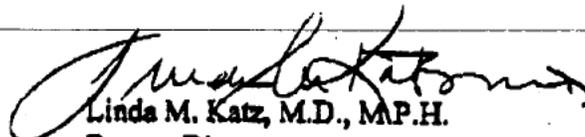
**Page 2**

**This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this change prior to approval of this supplemental new drug application.**

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

Sincerely,

---



**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**

**Enclosure**

Following this page, one page withheld in full - (b)(4) draft labeling

9/29/00 noted. NDA filed for medical content. R. Neuner MD

REVIEW COPY



NDA SUPPL AMENDMENT

McNeil Consumer Healthcare, 7050 Camp Hill Road, Fort Washington, PA 19034-2299 (215) 273-7000

Charles Ganley, MD, Director  
Division of Over-the-Counter Drug Products (HFD-560)  
Center for Drug Evaluation and Research  
Document Control Room, Room S-212  
9201 Corporate Boulevard  
Rockville, MD 20850

SEP 7 2000

NDA SUPPL AMENDMENT

AL  
SCF-006



RE: Acetaminophen Extended Release Geltab, 650mg  
NDA 19-872  
Amendment #3 to SNDA S-006  
Complete Response to Approvable Letter -  
Revised Labeling in **Drug Facts** Format

Dear Dr. Ganley:

We are submitting this amendment to our pending Supplemental New Drug Application (S-006) in response to the Division's Approvable Letter dated September 9, 1999 (copy attached).

Labeling for our 6, 24, 50 and 100 count bottles as well as our 2 count pouch and dispensit box for the pouch have been prepared in **Drug Facts** format, taking into account the labeling that was approved on July 25, 2000 for the caplet dosage form.

The tradename on this product has been revised to Tylenol Arthritis Pain Extended Relief Geltab with a prominent descriptor line underneath the name reading "For the temporary relief of minor arthritis pain".

**Attachment 1** provides copies of thermals for the package sizes previously referenced.

**Attachment 2** provides a copy of the labeling text in **Drug Facts** format. The type size for required elements is indicated directly on the thermals.

If there are any questions, please contact me at 215-273-7878.

Very truly yours,  
McNEIL CONSUMER HEALTHCARE

Paula J. Oliver

Paula J. Oliver  
Senior Director, Regulatory Compliance

DUPLICATE

cc: Thomas J. Parmelee, Pharm. D, Project Manager

PJO:joc

Pjo009

ARCHIVAL  
COPY



McNeil Consumer Healthcare, 7050 Camp Hill Road, Fort Washington, PA 19034-2299 (215) 273-7000

Charles Ganley, MD, Director  
Division of Over-the-Counter Drug Products (HFD-560)  
Center for Drug Evaluation and Research  
Document Control Room, Room S-212  
9201 Corporate Boulevard  
Rockville, MD 20850

INDASOPTIG AMENDMENT

SEP 7 2000

AL  
S OF 006



RE: Acetaminophen Extended Release Geltab, 650mg  
NDA 19-872  
Amendment #3 to SNDA S-006  
Complete Response to Approvable Letter –  
Revised Labeling in **Drug Facts** Format

Dear Dr. Ganley:

We are submitting this amendment to our pending Supplemental New Drug Application (S-006) in response to the Division's Approvable Letter dated September 9, 1999 (copy attached).

Labeling for our 6, 24, 50 and 100 count bottles as well as our 2 count pouch and dispensit box for the pouch have been prepared in **Drug Facts** format, taking into account the labeling that was approved on July 25, 2000 for the caplet dosage form.

The tradename on this product has been revised to Tylenol Arthritis Pain Extended Relief Geltab with a prominent descriptor line underneath the name reading "For the temporary relief of minor arthritis pain".

**Attachment 1** provides copies of thermals for the package sizes previously referenced.

**Attachment 2** provides a copy of the labeling text in **Drug Facts** format. The type size for required elements is indicated directly on the thermals.

If there are any questions, please contact me at 215-273-7878.

Very truly yours,  
McNEIL CONSUMER HEALTHCARE

*Paula J. Oliver*

Paula J. Oliver  
Senior Director, Regulatory Compliance

ORIGINAL

cc: Thomas J. Parmelee, Pharm. D, Project Manager

PJO;joc

Pjo009