

CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

NDA 19-872/S-009

Name: Tylenol (Acetaminophen)
Extended Release Caplet, 650 mg

Sponsor: McNeil Consumer Healthcare

Approval Date: July 25, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-872/S-009

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-872/S-009

APPROVAL LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville MD 20857

NDA 19-872/S-009

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

JUL 25 2000

Dear Ms. Oliver:

Please refer to your supplemental new drug application dated December 8, 1998, received December 9, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tylenol (acetaminophen) Extended Release Caplet, 650mg.

Please also refer to the Approvable letter that was issued for this supplemental new drug application on April 13, 2000. We acknowledge receipt of your submissions dated October 1, 1999, and April 24, July 5, and July 14, 2000. Your submissions of July 5 and July 14, 2000 constitute a complete response to our April 13, 2000 action letter.

This supplemental new drug application provides for the following:

1. Change the product tradename to Tylenol Arthritis Pain;
2. Update the alcohol Warning to meeting the requirements of the Final Rule published October 23, 1998 (63 FR 56789); and
3. To change the company name to McNeil Consumer Healthcare.

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

The final printed labeling (FPL) must be identical to the enclosed labeling 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.

As of the date of this letter there should be no further production of this drug product, intended for interstate commerce, that contains unapproved labeling.

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 heavy-weight paper or similar

(Lm 7-26-00)

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-009." Approval of this submission by FDA is not required before the labeling is used.

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:

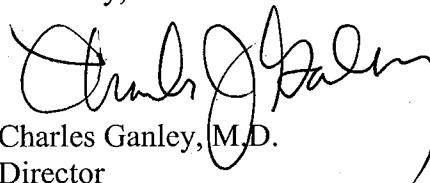
MEDWATCH, HF-2
FDA
5600 Fishers Lane
Rockville, MD 20857

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

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

If you have any questions, call Thomas A. Parmelee, Pharm.D., Regulatory Project Manager, at (301) 827-2271.

Sincerely,



Charles Ganley, M.D.

Director

Division of Over-the-Counter Drug Products

Office of Drug Evaluation V

Center for Drug Evaluation and Research

Enclosure

NDA 19-872/S-009

Page 3

cc:

Archival NDA 19-872

HFD-560/Div. Files

HFD-560/PM/Parmelee

HFD-560/Ganley/Katz/Neuner/Lumpkins/Mason

HF-2/MedWatch (with labeling)

HFD-002/ORM (with labeling)

HFD-105/ADRA (with labeling)

HFD-42/DDMAC (with labeling)

HFI-20/Press Office (with labeling)

HFD-400/OPDRA (with labeling)

HFD-613/OGD (with labeling)

HFD-095/DDMS-IMT (with labeling)

HFD-830/DNDC Division Director

DISTRICT OFFICE

Drafted by: tap/July 24, 2000

Initialed by:

final:

filename: 19872AP

APPROVAL (AP)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-872/S-009

APPROVABLE LETTER



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-872/S-009

APR 13 2000

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

Dear Ms. Oliver:

Please refer to your supplemental new drug application dated December 8, 1998, received December 9, 1998, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Tylenol (acetaminophen) Extended Relief Caplet, 650 mg.

We acknowledge receipt of your communications dated December 17, 1998; July 15, October 1, and December 28, 1999; and January 14 and 21, 2000.

This supplemental new drug application proposes the following changes to the product labeling:

To change the product name to Tylenol Arthritis (b) (4) Caplet;

To update the alcohol Warning to meet the requirements of the Final Rule published October 23, 1998 (63 FR 56789); and

To change the company name to McNeil Consumer Healthcare.

We have completed the review of this supplemental new drug application, as amended, and it is approvable. Before this supplemental NDA may be approved, however, it will be necessary to reach resolution regarding the tradename for this product. The proposed tradename "Tylenol Arthritis (b) (4) Caplet" and the proposed alternative "Tylenol Arthritis Pain" are considered to be unacceptable for the following reasons:

One of the approved Uses of the product is for the temporary relief of the minor pain of arthritis. The name Tylenol Arthritis (b) (4) Caplet and Tylenol Arthritis Pain do not convey this message. This is reflected in the October 1, 1999 survey results submitted by you. Although 78 of 103 consumers

surveyed indicated that the product was for pain, they did not necessarily distinguish the severity of pain. Twenty six out of these 78 stated that it was for "arthritis" or was an "anti-inflammatory" product. This is an important distinction because a consumer may be led to believe that this particular product is somehow unique in its treatment of arthritis compared to other Tylenol products that are marketed with the same use, the temporary relief of the minor pain of arthritis. The only unique aspect of this product compared to other single ingredient Tylenol products is the difference in pharmacokinetics which allows for less frequent daily dosing. This dosing regimen would not only benefit individuals with arthritis but also other individuals with symptoms associated with other conditions of several days duration listed on the labeling (e.g., common cold, menstrual cramps).

Other troubling aspects of the survey suggest, as noted above, that the product was (b) (4) arthritis. This product has not demonstrated these types of benefit and, in fact, highlights our concern about possible consumer confusion. Much of this consumer confusion is likely attributable to the name of the product and to the lack of clarifying information on the principal display panel.

Furthermore, the name that you have proposed promotes off-label use of this product as (b) (4) the OTC indication is for the temporary relief of minor arthritis pain (not to exceed 10 days use).

The Directions section of the label includes instructions for dosing (b) (4) (b) (4). While this may be appropriate for the other conditions listed in the Uses section of the label, it raises concerns for this product because the product name emphasizes arthritis. The treatment of arthritis (b) (4) (b) (4) should be diagnosed and managed by a physician. The Division (b) (4) has made this distinction in the past for the treatment of other diseases (b) (4) that require a physician's recommendation before use. Most recently, your Motrin Migraine Pain product was approved with Directions instructing consumers under 18 years of age to ask a doctor before using. It would be inappropriate to suggest to the consumer that the treatment of arthritis (b) (4) (b) (4) can be treated without first getting the advice of a doctor.

In addition, it will be necessary to submit for review labeling that is formatted consistent with the requirements 21 CFR 201.66 (See the March 17, 1999 FEDERAL REGISTER document "Over-The-Counter Human Drugs; Labeling Requirements; Final Rule" (64 FR 13254) (OTC labeling final rule).

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

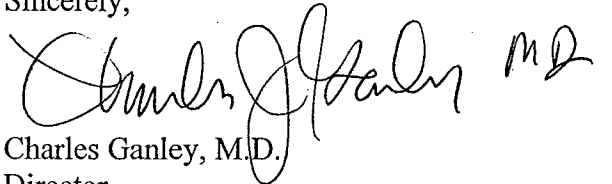
In addition, please submit one copy of the introductory promotional materials that you propose to use for this product. All proposed materials should be submitted in draft or mock-up form, not final print.

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 these changes prior to the 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,

A handwritten signature in black ink, appearing to read "Charles Ganley M.D.", with a stylized flourish at the end.

Charles Ganley, M.D.
Director

Division of Over-the-Counter Drug Products
Center for Drug Evaluation and Research

CC:

Orig NDA 19-872

HFD-560/Div File

HFD-560/Central File

HFD-560/Ganley

HFD-560/Katz/4/12/2000

HFD-560/RothschildK/Lumpkins/Mason/Neuner/Roberts

HFD-613/OGD

DISTRICT OFFICE

Drafted by: kgr/January 14, 2000

Revised March 23, 2000

Final: April 13, 2000

APPROVABLE (AE)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-872/S-009

LABELING

APPROVED

JUL 25 2000

Drug Facts

Active ingredient (in each caplet) 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.

Lasts up to 8 Hours

TYLENOL[®] Acetaminophen
Extended Release

ARTHRITIS PAIN

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

Extended Relief Caplets

100 Caplets • 650 mg EACH Pain Reliever *Capsule-Shaped Tablets

XXXXXX

Lasts up to 8 Hours

TYLENOL[®] Acetaminophen
Extended Release

ARTHRITIS PAIN

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

Extended Relief Caplets

100 Caplets • 650 mg EACH Pain Reliever *Capsule-Shaped Tablets

NDC 50580-112-10

Lasts up to 8 Hours

TYLENOL[®] Acetaminophen
Extended Release

ARTHRITIS PAIN

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

Extended Relief Caplets

McNeil

McNeil Consumer Healthcare © MCN-PPC, Inc. 100
 DIVISION OF MCNEIL - PPC, INC. U.S. Pat. No. 4820522
 FORT WASHINGTON, PA 19034 USA
 www.tylenol.com

Drug Facts (continued)

Directions ■ do not take more than directed
 ■ take 2 caplets every 8 hours with water
 ■ swallow whole - do not crush, chew or dissolve
 ■ do not take more than 6 caplets in 24 hours
 ■ do not use for more than 10 days unless directed by a doctor
 ■ 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
 corn starch, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, powdered cellulose, pregelatinized starch, sodium starch glycolate, titanium dioxide, triacetin

Questions? Call 1-800-962-5357

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

FPO
00000000

Labeling Format Information:

Fonts: Helvetica regular, bold and bold italic.

Drug Facts:	8.5 pt	Leading:	7 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: 85% Average Kerning: -15

NDC 50580-112-10

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.

TYLENOL[®]
Acetaminophen
Extended Release
ARTHRITIS PAIN
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

Extended Relief
Caplets

Pain Reliever

100 Caplets* 650 mg EACH *Capsule-Shaped Tablets

Active ingredient (in each caplet) 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.

Directions ■ do not take more than directed adults ■ take 2 caplets every 8 hours with water ■ swallow whole — do not crush, chew or dissolve ■ do not take more than 6 caplets 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)

Inactive ingredients corn starch, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, powdered cellulose, pregelatinized starch, sodium starch glycolate, titanium dioxide, triacetin

Questions? Call 1-800-962-5357

McNeil Consumer Healthcare, DIVISION OF MCNEIL - PPC, INC.
FORT WASHINGTON, PA 19034 USA www.tylenol.com
© MCN-PPC, Inc. '00 U.S. Pat. No. 4,820,522 XXXXXX

150% OF SIZE

NDC 50665-112-10

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.

TYLENOL[®]
Acetaminophen
Extended Release
ARTHRITIS PAIN
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

Extended Relief
Caplets

Pain Reliever

100 Caplets* 650 mg EACH *Capsule-Shaped Tablets

Active ingredient (in each caplet) 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.

Directions ■ do not take more than directed adults ■ take 2 caplets every 8 hours with water ■ swallow whole — do not crush, chew or dissolve ■ do not take more than 6 caplets 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)

Inactive ingredients corn starch, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, powdered cellulose, pregelatinized starch, sodium starch glycolate, titanium dioxide, triacetin

Questions? Call 1-800-962-5357

McNeil Consumer Healthcare, DIVISION OF MCNEIL - PPC, INC.
FORT WASHINGTON, PA 19034 USA www.tylenol.com
© MCN-PPC, Inc. '00 U.S. Pat. No. 4,820,522 XXXXXX

APPROVED
JUL 25 2000

Labeling Format Information:

Fonts: Helvetica regular, bold and bold italic.			
Drug Facts:	8.5 pt	Leading:	6.25 pt
Header:	7 pt	Bullets:	5 pt
Subheader:	6 pt	Barlines:	0 pt
Body Text:	6 pt	Hairlines:	0 pt
Drug Facts (continued):	0 pt		

Horizontal Scale: 70%

Average Kerning: -20

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-872/S-009

LABELING REVIEWS

29-1

JUL 22 1999

LABELING REVIEW OF NDA SUPPLEMENT

NDA: 19-872

Supplement: SLR-009

Submission Date: December 8, 1998
Received: December 9, 1998
Review Date: December 21, 1998
Amended: January 6, 1999
Amended: January 11, 1999
Amended: February 21, 1999
Amended: March 3, 1999
Amended: June 7, 1999
Amended: July 22, 1999

Applicant:

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

**Applicant's
Representative:**

Paula J. Oliver
Senior Director, Regulatory Compliance
(215-233-7878)

Drug:

Tylenol Arthritis Acetaminophen
Extended Relief Caplets, 650 mg

**Pharmacologic
Category:**

Pain reliever (b) (4)

Submitted:

Supplemental NDA - Expedited Review
Revised color labeling for 100 count
Bottle and carton

Reviewer:

Stephanie A. Mason

Background: McNeil has re-launched Tylenol extended release originally approved on June 8, 1994 under the new name Tylenol Arthritis Extended Relief. This supplemental submission is in response to a teleconference held on November 18, 1998, with Dr. Linda Katz, Ms. Marina Chang, Ms. Debbie Lumpkins and Ms. Stephanie Mason, to discuss labeling submitted in the annual report dated June 1998. For review purposes, draft labeling was submitted for only one package size (100 count bottle). Per the sponsor, all other package sizes will be consistent with the 100 count size. The sponsor provided two versions of the revised labeling, one in bullet format (Attachment 2).

The sponsor has indicated that the following changes have been made:

- (1) The word (b) (4) has been added in the product name to read: Tylenol Arthritis (b) (4) Caplets" in place of "Tylenol Arthritis Extended Relief

Caplets.”

- (2) The alcohol warning has been updated per the final rule dated October 23, 1998.
- (3) The name of company has been changed from McNeil Consumer Products Company to McNeil Consumer Healthcare per McNeil's correspondence dated November 2, 1998.

Reviewer's comments: The renaming of the product is not acceptable as it promotes or implies use of the product as (b) (4) arthritis. Changes #2 and #3 are acceptable. The following additional changes/concerns are noted:

Label Attachment 1 (old labeling format) is the same as Label Attachment 2 (modified labeling format) with the exception of the following:

1. On the back side panel of the carton where required language is located, the sponsor added the following after the “Warnings” section:

- (b) (4) **Tylenol Arthritis Extended Relief Caplets use a unique, patented bi-layer caplet.** The first layer dissolves quickly to provide prompt relief while the second layer is time released to provide up to 8 hours of relief.
- (b) (4)
- (b) (4)
- (b) (4)

Comments: The above information should be deleted from the required information section and located elsewhere on the label. Of note, in an Agency letter dated March 31, 1997, the sponsor was requested to delete the promotional statements in bullets number 2 and 3 above from its Extra Strength Tylenol product (NDA 17-552, recently withdrawn and now under the monograph. No clinical studies were designed to test the (b) (4)

Thus, statements related to (b) (4) claims not supported by clinical data should be deleted from the

labeling.

2. The flag statement “(b) (4)” is misleading since the proposed claims that modify the “(b) (4)” are no different from the original claim of providing relief of pain (i.e., work up to 8 hours).
3. In accordance with 21 CFR 201.61(b) and (c), an accurate statement of the general pharmacological categories of the drug (i.e., pain reliever (b) (4)) must follow the established name (i.e., acetaminophen extended release tablets). This statement should be presented in bold face type and be in a print size reasonably related to the most prominent printed matter on such panel.
4. A location for the lot number on the carton needs to be designated.

Label Attachment 2 - McNeil's preferred version

Principal display panel:

1. On the principal display panel under the declaration of net quantity of content statement, the asterisk on “Caplets” is absent with no footnote stating “Capsule-Shaped Tablet.” The term “caplet” is not an Agency or USP recognized dosage form nor is it in the dictionary.

Comments: The sponsor needs to define “caplet” with an asterisk as “*capsule-shaped tablet” on the principal display panel under the declaration of net quantity of content statement.

Example: *caplet (*capsule-shaped tablet.)

Side flap and end flap of carton:

1. On the end flap of the carton under the patent information, the sponsor has added their web site address (www.tylenol.com). This is acceptable.
2. On the side panel where required language is located, the sponsor added the following information after “Directions”:

(b) (4)
• (b) (4)

The reviewer notes that the word “(b) (4)” was not included as part of the name.

Comments: An “s” should be added to the word “(b) (4)” to read “(b) (4).” As stated above the name “Tylenol Arthritis (b) (4) Caplets” should be modified to ensure that it does not emphasize the (b) (4).

(b) (4)

(b) (4)

Comments: A “s” should be added to the word “(b) (4)” to read “(b) (4)s” in the bulleted statement. In addition, the words “(b) (4)” should be deleted and replaced with “(b) (4)”
“(b) (4)” The above information should be deleted from the required information section and located elsewhere on the label.

In addition, the above statements are promotional information and should be deleted from within the Drug Facts area and placed elsewhere in the labeling.

Warnings:

1. The header “Warnings” should be flushed with the left margin and not centered. All headers (e.g., active ingredients, purposes, uses, warnings, directions, other information, and inactive ingredients) should be italicized.

Do not use:

1. The following bulleted statements found under the “Do not use” section should be deleted because the statements are not absolute contraindications for the use of the product:

“(b) (4)” and “(b) (4)”
“(b) (4)” Instead, the bulleted statements should be moved to the “Stop use and ask a doctor if” section and revised to read:

- pain gets worse or lasts for more than 10 days
- (b) (4)

Also, the statement “with any other product containing acetaminophen” should be deleted from under the “Do not use” section and placed under the heading “Ask a doctor or pharmacist before use if you are” and revised to read: ▪ taking any other product containing acetaminophen.

Directions:

1. Under the “Directions” section, second bullet, the phrase “(b) (4)” should be deleted. It should be revised to read: “▪ (b) (4)”

Additional recommended changes:

1. The "Inactive ingredient(s)" statement should follow after the "Other information" section.
2. The Agency continues to allow flexibility as to where the tamper-evident statement appears in the labeling, and does not require that it appear within the "Drug Facts" area. However, if the sponsor prefers to place the statement within the "Drug Facts" area, the statement should be deleted from under the "Directions" section, and placed under the header "Other information." (See § 201.66(c)(7).)

Recommendations: All of the changes made by the sponsor in this submission are acceptable except for the renaming of the product. The name of the product is not acceptable, and should be modified to avoid any reference to arthritis treatment. The sponsor should be sent an approvable letter pending resolution of the name for the product. In addition, to support the new proposed name the following additional information should be included: review of all consumer complaints prior to and since the use of Tylenol Arthritis name, any reports of misuse and overdose, and any serious adverse events and deaths from the use of this product.

Conclusions:

The following labeling revisions can be made at the time of the next printing or 180 days whichever comes first:

1. The sponsor will need to modify their label to conform with the proper format and content of the "Drug Facts" format.
2. The sponsor needs to define "caplet" with an asterisk as "*capsule-shaped tablet" on the principal display panel.
3. The second bullet under the heading "Directions" should be revised to read:
 - (b) (4)
4. The information regarding promotional statements should be deleted from the required information section and located elsewhere on the label. The statements related to (b) (4) claims not supported by clinical data should be deleted from the labeling.
5. The flag statement " (b) (4) " should be removed (b) (4) . In addition, the (b) (4) " should be deleted from the **Directions** statement since the claims proposed are not (b) (4) .
6. The header "**Warnings**" should be flushed with the left margin and not centered.
7. A location for the lot number on the carton needs to be designated.

8. The following bulleted statements found under the "**Do not use**" section should be deleted because the statements are not absolute contraindications for the use of the product:

"(b) (4)" and "(b) (4)"
" (b) (4)." Instead, the bulleted statements should be moved to the "**Stop use and ask a doctor if**" section and revised to read:

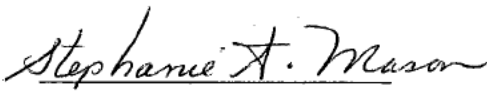
- pain gets worse or lasts for more than 10 days
- (b) (4)

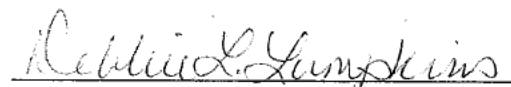
Also, the statement "with any other product containing acetaminophen" should be deleted from under the "**Do not use**" section and placed under the heading "**Ask a doctor or pharmacist before use if you are**" and revised to read: ■ taking any other product containing acetaminophen.

9. The statement of identity should include the dosage form to read: "Acetaminophen extended release tablets."

10. The tamper-evident statement "Do not use if carton is opened" should be deleted from under the "**Directions**" section and placed under the header "**Other information.**"

11. The storage condition statement should be modified to conform with the current recommendation for all OTC drug products given by the Division of New Drug Chemistry which states: "Store at 20 - 25°C (68 - 77°F)."


Stephanie A. Mason, IDS


Debbie L. Lumpkins, Microbiologist
Team Leader 3

cc:

NDA 19-872

HFD-560/Div files

HFD-560/K. Rothschild

HFD-560/S.Mason

HFD-560/D. Lumpkins:1/11/99:1/14/99:5/26/99

HFD-560/Dr. Katz:1/21/99:7/1/99:7/22/99:7/27/99:8/4/99

HFD-560/Dr. Neuner

HFD-560/Dr. Bowen:2/17/99

Rev:SMason:7/1/99:7/22/99

19-872la.wpd



3241
LABELING REVIEW OF NDA SUPPLEMENT No. 2-AMENDMENT

NDA: 19-872

Supplement: SLR-009/BL

SEP - 3 1999

Submission Date: July 15, 1999

Received: July 16, 1999

Review Date: August 6, 1999

Applicant:

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

**Applicant's
Representative:**

Paula J. Oliver
Senior Director, Regulatory Compliance
(215-233-7878)

Drug:

Tylenol Arthritis Acetaminophen
(b) (4) Caplets, 650 mg

**Pharmacologic
Category:**

Pain reliever (b) (4)

Submitted:

Supplement-minor amendment-draft labeling
Expedited Review
Revised drug facts format of color labeling
for 8, 24, 50, and 100 count bottles and 2 count
pouch and dispensit box for the pouch (diskette)

Reviewer:

Stephanie A. Mason

Background: On December 8, 1998, the sponsor submitted a supplemental NDA (S-009) which provided for revised labeling on the above referenced drug that included: (1) The change in product name, (2) revised alcohol warning, and (3) change in the company name. Review of this labeling supplement was completed on August 4, 1999. (Other revisions and recommendations regarding the Tylenol Arthritis labeling were pointed out extensively in the August 4, 1999 review, and therefore, will not be repeated again.) (See prototype labeling attached for convenience of the reader.)

This supplemental application (S-009/BL) provides for updated labeling reformatted into *Drug Facts* format as required in the OTC Labeling Requirements final rule dated March 17, 1999; 64 FR 13254. The 2 count pouch and 8 count bottle labeling are for professional use. Also, the sponsor wishes to include additional text under *Directions* for (b) (4). An expedited review was requested by the sponsor in order to be in compliance with the revised alcohol warning for this product by October 22, 1999.

We have the following comments:

1. The alcohol warning is acceptable.

Carton labeling for 8, 24, and 50 counts - Modified Format
Font type sizes:

1. For the *Drug Facts* title, the sponsor uses 8.5 point type size for the 8 and 50 counts carton and 8.25 point type size for the 24 count carton. The headers (e.g., *active ingredients*, *purposes*, *uses*, *warnings*, *directions*, and *other information*) are set in 7 point type size. To accommodate smaller packaging, the Agency is allowing headings to be presented in a minimum 7 point or greater type size to meet the format requirements.

Bottle labeling - Modified format
8 count

1. The font used is Helvetica regular bold, the type size is 4.5 for the title *Drug Facts*, headers, subheaders and body text. While the type style is appropriate, the type size is not. Per the OTC Labeling Requirements final rule (at 13254 at 13264), we recommend that the *Drug Facts* title appear in a type size greater than the largest type size used within the *Drug Facts* area.
2. We recommend that the header *Purposes* be right justified.
3. Per the final rule, we recommend that the bulleted information start on the same line with headings and subheadings, but not with the *Warnings* header. (This also applies to the 24 and 50 count bottle labeling and the 2 pouch.)

Carton label for 100 counts - Standard Format

1. The font type sizes are acceptable.

Other comments for all submitted labeling:

1. Other labeling revisions and recommendations stated in the Agency's review dated August 4, 1999, should be incorporated in all representative labeling that the sponsor intends to market.
2. We note that the sponsor rearranged the instructions under *Directions* from that which was previously submitted in December 1998:

From:

(b) (4)

(b) (4) ”

To: “take 2 caplets every 8 hours with water; swallow whole - do not crush, chew or dissolve; do not take more than 6 caplets in 24 hours.” This is acceptable.

3. Under *Uses*, the bulleted statement “ (b) (4) ” should be revised to read:

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

(b) (4)

It is unnecessary to state: “ (b) (4) ”

4. Under the *Directions* for (b) (4), the sponsor proposes the following revision:

Adults (b) (4)	Take 2 caplets every 8 hours with water; swallow whole - do not crush, chew or dissolve. Do not take more than 6 caplets in 24 hours.
(b) (4)	(b) (4)

The additional text under the *Directions* section for (b) (4) is unnecessary and potentially confusing. Since this product is not (b) (4), it would be appropriate to use the following statement: “ (b) (4) ”

Recommendations: The *Drug Facts* labeling format is approvable. However, other labeling revisions and recommendations stated in the Agency’s review dated August 4, 1999, and those listed below will need to be incorporated for all representative labeling that the sponsor intends to market. We request a supplemental application which provides labeling that reflects these changes.

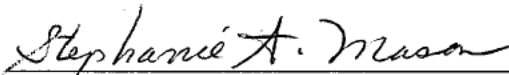
1. The additional text under the *Directions* section for (b) (4) should not be included in the labeling. The statement should be revised to read: “ (b) (4) ”

2. Under *Uses*, the bulleted statements should be revised to read:

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

(b) (4)

3. For the **8 count bottle** (professional sample), we recommend that the ***Drug Facts*** title appear in a type size greater than the largest type size used within the ***Drug Facts*** area, and that the header ***Purposes*** be right justified.
4. For the **8, 24, and 50 count bottle** labeling and **2 count pouch**, we recommend that the bulleted information not appear on the same line as the header ***Warnings*** but may start on the same line with headings and subheadings.



Stephanie A. Mason, IDS



Debbie L. Lumpkins, B.S., Microbiologist
Team Leader 3

cc:

NDA 19-872

HFD-560/Div files

HFD-560/K. Rothschild

HFD-560/S.Mason

HFD-560/D. Lumpkins:8/24/99

HFD-560/Dr.Ganley

HFD-560/Dr.Katz *jmu* 9/3/99

HFD-560/Dr.Neuner

HFD-560/L.Roberts

R/D:SMason:8/18/99:8/24/99

19-872bl.wpd

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

37.1

Review of a Labeling Supplement

NDA 19-872
SLR-009/NC

Date of Submission: April 20, 2000
Date CDER Rec'd: April 20, 2000
Date assigned: April 27, 2000
Date review initiated: April 27, 2000
Dates to Team Leader: May 1, 2000, May 2, 2000

Applicant: McNeil Consumer Healthcare
7050 Camp Hill Road
Fort Washington, PA 19034

Applicant's
Representative: Paula J. Oliver
Senior Director, Regulatory Compliance
(215-233-7878)

Drug: Tylenol Arthritis Acetaminophen
(b) (4) Caplets, 650 mg

Pharmacologic
Category: Pain reliever

Reviewer: Stephanie A. Mason

Background: The sponsor requested a meeting with the Agency to discuss the tradename and resolve labeling issues for Tylenol Arthritis Extended Relief Caplet and Geltab. In a letter dated April 13, 2000, the sponsor provided confirmation and background material for the meeting.

On April 20, 2000, the Agency received a facsimile from the sponsor that included a revised agenda, a list of attendees, and revised draft labeling for the Tylenol Arthritis product. On April 25, 2000, another facsimile was received by the Agency. In that facsimile, the sponsor provided the results of a consumer survey on the sponsor's proposed new label to compare with the survey results on the original label submitted on October 1, 1999.

The sponsor made the following revisions to its revised draft labeling:

1. The product name "Tylenol Arthritis Pain" along with the addition of "For the temporary relief of minor arthritis pain" on the principal display panel is acceptable since it now conveys the product's intended use.
2. All references to (b) (4) have been deleted from the labeling. The product's intended use is as a pain reliever only. This is acceptable.
3. Per the Agency's approvable letter dated April 13, 2000, the Directions for use were revised as follows:

adults	take 2 caplets every 8 hours with water; swallow whole – do not crush, chew or dissolve; do not take more than 6 caplets in 24 hours
under 18 years of age	ask a doctor

(*See below for recommended revision to the above Directions)

A meeting was held on April 27, 2000, and the following labeling changes were agreed upon:

Principal Display Panel:

1. The statement of identity (i.e., pain reliever, acetaminophen extended release), needs to be in a size reasonably related to the most prominent printed matter on the panel.
2. The term "Caplet" needs to be defined as "*capsule-shaped tablet."

Directions:


1. Although the statement "pain gets worse or lasts for more than 10 days" is located under the **Stop use and ask a doctor if** section, the duration for use needs to be emphasized in the **Directions** section also. The sponsor should add another bulleted statement under this section to read: "Do not use for more than 10 days unless directed by a doctor."

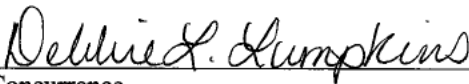
Other subsequent recommendations that should be made are as follows:

Use:

1. The bullet symbols need to be in alignment.
2. For consistency with other approved adult analgesic drug products, in the second sentence following the pregnant/breast-feeding statement, the word "(b) (4)" should be replaced with the word "Quick" to read "Quick medical attention is critical for adults...."

Recommendation: The sponsor should submit revised labeling for all package sizes to reflect the changes listed above.


Stephanie A. Mason, IDS Reviewer


Concurrence
Debbie L. Lumpkins, Microbiologist
Team Leader 3

Cc:

NDA 19-872

HFD-560/Div File

HFD-560/T.Parmelee

HFD-560/S.Mason

HFD-560/D.Lumpkins:5/11/00

HFD-560/M.Jackson

HFD-560/L.Katz *pink 7/17/00*

HFD-560/C.Ganley

Tylenolar.doc

JUL 13 2000

Review of a Labeling Supplement

NDA: 19-872/SLR-009/BL **Date of Submission:** July 5, 2000
Date CDER Rec'd: July 6, 2000
Date assigned: July 13, 2000
Date review initiated: July 13, 2000
Date to Team Leader:

Applicant: McNeil Consumer Healthcare
7050 Camp Hill Road
Fort Washington, PA 19034

Applicant's Representative: Paula J. Oliver
Senior Director, Regulatory Compliance
☎215-273-7878

Drug: Tylenol Arthritis Pain Acetaminophen
Extended Release Caplets, 650 mg

Pharmacologic Category: Pain reliever

Submitted: Color thermals for 24, 50, and 100-count
Carton and bottle labels, and labeling text
in Drug Facts format

Reviewer: Stephanie A. Mason

Background: This amendment to the pending supplemental NDA is in follow-up to: (1) The Agency's approvable letter dated April 13, 2000, and (2) changes provided in follow-up to the April 27, 2000 meeting. Based on the above correspondence, the sponsor made the following revisions to its labeling:

1. The trade name has been revised from "Tylenol Arthritis Extended Relief Caplet" to "Tylenol Arthritis Pain Extended Relief Caplet." To strengthen the intended use of the product, the statement "For the temporary relief of minor arthritis pain" has been added to the principal display panel (PDP), and placed underneath the product name "Tylenol Arthritis Pain."

2. The statement of identity (i.e., pain reliever) and the established name of the product (i.e., Acetaminophen extended release) have been increased in size on the PDP.

(La 7-26-00)

3. The term "caplet" has been defined as capsule-shaped tablet on the PDP.
4. Under the **Direction** section, the directions for use is now in bullet format, and the statement "do not use for more than 10 days unless directed by a doctor" has been added as the fourth bullet.
5. The bullet symbols located under **Uses** have been aligned.
6. The word "(b) (4)" has been replaced with the word "quick" in the statement "Quick medical attention is critical for adults...."

These changes are acceptable.

Reviewer's comments:

1. Regarding **Drug Facts** format, the pale yellow color used for the 0.5 hairlines, the visual cue, and the table format under **Directions** is hardly noticeable. To be in compliance with the final rule, the sponsor will need to correct this.
2. We note that promotional statements have been included in the labeling and are located outside of the **Drug Facts** area for the 50- and 100-count but not the 24. The first and last statements are acceptable. However, the second statement "(b) (4)"
(b) (4)
' is a concern. In an Agency letter dated March 31, 1997, the sponsor was told that no clinical studies were designed to test the (b) (4)
(b) (4) drug. Thus, the statement related to a (b) (4)
(b) (4) claim is not supported by clinical data, and should be deleted from the labeling.
3. The type size specifications provided for the carton and bottle labeling are acceptable per the final rule. However, when reading the carton label, the actual print size appears smaller and harder to read compared to draft labeling for Tylenol Arthritis that was previously included as background material for the April 27th meeting. In a telephone conversation with McNeil held on June 20, 2000, the sponsor stated that the labeling version submitted was scaled down, and assured the Agency that the specifications provided are the ones that will be used in the final printed labeling.

Recommendations: The labeling is approvable. However, the following revisions will need to be made before approval of this application is granted:

1. The pale yellow contrast color used for the 0.5 hairlines, the visual cue, and the table format under **Directions** are hardly noticeable. This is not acceptable. The sponsor will need to correct this.
2. The sponsor should increase the size of the statement "For the temporary relief of minor arthritis pain" on the PDP.
3. The promotional statement "(b) (4)"
" (b) (4)" should be deleted from the labeling since the claim is not supported by clinical data.
4. The sponsor should increase the size of the statement "For the temporary relief of minor arthritis pain" on the PDP.

Stephanie A. Mason

Stephanie A. Mason
IDS Reviewer

Debbie L. Lumpkins

Concurrence
Debbie L. Lumpkins, Microbiologist
Leader, Team 3

cc:

NDA 19-872
HFD-560/Div File
HFD-560/T.Parmelee
HFD-560/S.Mason
HFD-560/D.Lumpkins
HFD-560/L.Katz
HFD-560/C.Ganley
19-872s9bl.doc

JUL 20 2000

Review of a Labeling Supplement

NDA 19-872
SLR-009/AL
Amendment 5

Date of Submission: July 14, 2000
Date CDER Rec'd: July 18, 2000
Date assigned: July 20, 2000
Date review initiated: July 20, 2000
Dates to Team Leader: July 20, 2000

Applicant: McNeil Consumer Healthcare
7050 Camp Hill Road
Fort Washington, PA 19034

Applicant's Representative: Paula J. Oliver
Senior Director, Regulatory Compliance
(215-233-7878)

Drug: Tylenol Arthritis Acetaminophen
(b) (4) Caplets, 650 mg

Pharmacologic Category: Pain reliever

Submitted: 100 count size carton/label

Reviewer: Stephanie A. Mason

Background: In response to labeling comments relayed to the sponsor on July 13, 2000, via facsimile, the following revisions have been made to its Tylenol Arthritis product:

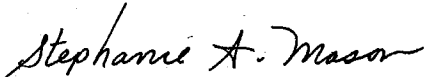
1. Added the letter "I" to the word "liver" on its bottle label for the 290 count size. (See S-010.)
2. Revised the contrast color from pale yellow to dark blue for the hairlines, the visual cue, and the table format under Directions to provide clearer contrast.
3. Delete the phrase " (b) (4)
4. Increased the print size of the indication "For the temporary relief of minor arthritis pain" on the principal display panel.


These changes are acceptable. In addition, the changes will also be implemented on the other package sizes covered by S-009 (i.e., 24 and 50 count size carton and bottle labels).

(Rm 7-76-00)

(NOTE: Regarding action for item 3, the sponsor believes there is adequate support for this statement, and intends to discuss with the Agency reinstitution of it on future versions of its labeling following approval of this SNDA. The sponsor was requested to provide background data that would support this statement.)

Recommendation: The labeling should be approved.


Stephanie A. Mason, IDS Reviewer


Concurrence
Debbie L. Lumpkins, Microbiologist
Team Leader 3

Cc:

NDA 19-872
HFD-560/Div File
HFD-560/T.Parmelee
HFD-560/S.Mason
HFD-560/D.Lumpkins
HFD-560/M.Jackson
HFD-560/L.Katz
HFD-560/C.Ganley
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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-872/S-009

MEDICAL REVIEW

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
CENTER FOR DRUG EVALUATION AND RESEARCH

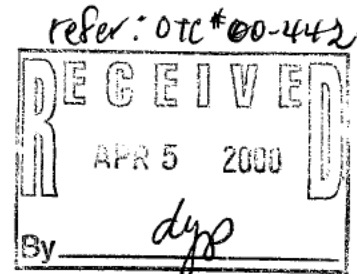
DATE: March 21, 2000

TO: Charles Ganley, MD
Div. Dir., DOTCDP
HFD-550

THROUGH: Linda M. Katz, MD, MPH
Dep. Div. Dir., DOTCDP
HFD-550

FROM: Rosemarie Neuner, MD, MPH
Medical Reviewer, HFD-550

SUBJECT: TYLENOL® Arthritis Extended Relief Caplets, 650 mg
NDA 19-872, SLR-009



Acetaminophen, an analgesic and antipyretic drug with weak anti-inflammatory properties at high doses, was approved for over-the-counter (OTC) marketing in the United States (U.S.) in 1965. It is indicated for the temporary relief of minor aches and pains associated with the common cold, headache, toothache, muscular aches, backache, for the minor pain of arthritis, for the pain of menstrual cramps and for the reduction of fever. Acetaminophen's effectiveness as an analgesic has been attributed to its ability to raise the pain threshold, while its antipyretic is due to its effect on the hypothalamic heat-regulating center.

On June 8, 1994 McNeil Consumer Products, sponsor of the TYLENOL® brand of acetaminophen, received agency approval to market a 650 mg extended-release formulation of their product called TYLENOL® Extended Relief (NDA 19-872). The recommended dose of TYLENOL® Extended Relief is two 650 mg caplets every 8 hours swallowed whole with water. The maximum daily dosage of TYLENOL® Extended Relief is 3,900 mg in a 24-hour period. On December 8, 1998, the sponsor submitted a supplemental NDA (S-009) that proposed the following labeling changes to this product:

1. Changing the product's name to TYLENOL® Arthritis (b) (4) Caplets.
2. Updating the Alcohol Warning as per the Final Rule (63 FR 56789) published October 23, 1998.
3. Changing the sponsor's name to McNeil Consumer Healthcare.

A labeling review of this submission was completed on July 22, 1999 by Ms. Stephanie Mason, a member of this division's inter-disciplinary science (IDS) reviewing staff who noted that although the last 2 proposed labeling changes were acceptable, the sponsor's proposed product name was not since it promotes or implies the use of

this product as (b) (4) arthritis. The comments in this medical reviewer's memo are limited to the first issue, the proposed change in the product's name, and to additional information sent into the agency by the sponsor in support of this change dated October 1, 1999, December 28, 1999 and January 24, 2000.

I. Proposed new name for product: TYLENOL® Arthritis Caplets.

The proposed new name for the product implies that (b) (4). The current labeling for OTC acetaminophen products is limited to the temporary relief of the minor pain of arthritis. Over-the-counter (OTC) analgesic products are not approved for (b) (4). Inclusion of the word "arthritis" in the product's proposed name is potentially misleading to consumers (b) (4).

In addition, adult formulations of OTC acetaminophen are labeled for use in (b) (4). Thus this product may erroneously be used by a parent or care giver to treat (b) (4) with new onset of symptomatic arthritis. Such cases need to be evaluated by a health care provider to rule out (b) (4) rheumatoid arthritis, lyme disease, neoplastic bone lesions, or soft tissue neoplasias. A delay in seeking medical treatment in such cases could potentially lead to life threatening or permanently disabling physical conditions.

The sponsor included a mock-up of the principle display panel (PDP) with the new proposed product name. (See the attached figure, Figure I.) Examination of the proposed PDP reveals that the caplet mg-strength listing is located too far from the product's statement of identity (SOI). Thus the proposed line extension of this product could potentially also lead to confusion in consumers who may think that the caplet mg-strength of this product is the same as the extra-strength (500 mg), or regular strength (325 mg) formulations marketed by the sponsor under the TYLENOL® brand name.

II. Consumer survey results regarding the proposed product's name change.

On October 1, 1999, the sponsor submitted an amendment to this supplemental NDA in support of their proposed product name change. This amendment contained the results of a consumer survey by (b) (4), that evaluated the perceptions of 103 consumers regarding the benefits gained from using TYLENOL® Arthritis (b) (4) formulation. The survey consisted of open-ended questions that were directed to the sponsor's proposed PDP and new name. Although the first and second most commonly recorded responses were "relieves pain" (78%) and "is long-lasting/8 hour/extended relief" (34%) respectively, the (b) (4)

Misrepresentation to consumers is also supported by 6% of the survey cohort who responded that the product was "designed for arthritis."

In addition to the survey results, this amendment contained the labels from 7 other OTC products where the term "arthritis" was contained in the products' name. The manufacturers of these 7 products are allowed to use the term "arthritis" in their products' names since these products are marketed under the Tentative Final Monograph (TFM) for Internal and External Analgesics. The agency has more regulatory oversight regarding the name that McNeal Consumer Products wishes to use for the product discussed in this memo since it was approved via the NDA-process.

III. New proposed product name and PDP mock-up.

On December 28, 1999, the sponsor submitted a third amendment to this SNDA which contained a new proposed product name (TYLENOL® Arthritis Pain) and a new mock-up of the proposed PDP as shown in the attachment, Figure II, at the end of this memo. Although the sponsor has corrected the linear alignment and location of the SOI and caplet mg-strength, the reasons why this new proposed name is unacceptable remain the same as stated in the above item, Item I.

IV. Correspondence submitted to the NDA regarding the proposed name change.

On January 21, 2000, in response to an agency question regarding pricing complaints, the sponsor reported that although they had received 17 complaints about price increases associated with the product's name change during the time period of September 1998 through August 1999. They state that they did not increase the price of the product. Any price increases noted by consumers was probably due to store pricing which the sponsor stated they do not control. The sponsor also reported that they received complaints from 16 consumers about the product's name change while the product remained the same. The sponsor also claimed that they had reviewed their internal adverse event database reporting system during this period, and did not find anything that was unusual or suggestive of a problem related to consumer confusion associated with the product's name change although they did not submit the data reviewed in support of this statement.

Final Recommendation: As stated above, the sponsor's proposed product name changes (i.e., TYLENOL® Arthritis (b) (4) Caplets and TYLENOL® Arthritis Pain) are unacceptable due to the possibility of misrepresentation to consumers regarding the (b) (4), and the potential that this product would be used in (b) (4) with new onset arthritis who need medical evaluation to rule-out serious illness. If the sponsor wants to use TYLENOL® Arthritis Pain Acetaminophen Extended Release, they will need to prominently display under the product's name on the PDP a clause that states "for the temporary relief of minor pain of arthritis."

CC:
NDA 19-872 file
Div. File

Following this page, two pages withheld in full - (b)(4) draft labeling.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:
NDA 19-872/S-009

OTHER REVIEW(S)

CONSULTATION RESPONSE
Office of Post-Marketing Drug Risk Assessment
(OPDRA; HFD-400)

DATE RECEIVED: January 13, 2000	DUE DATE: February 28, 2000	OPDRA CONSULT#: 00-0026
TO: Charles Ganley, M.D. Director, Division of OTC Drug Products HFD-560		
THROUGH: Kerry Rothschild, Project Manager HFD-560		
PRODUCT NAME: Tylenol Arthritis (b)(4) Caplet, Tylenol Arthritis Pain (acetaminophen extended release tablets) NDA #: 19-872	MANUFACTURER: McNeil Consumer Healthcare	
SAFETY EVALUATOR: Carol Pamer, R.Ph.		
SUMMARY: In response to a consult from the Division of OTC Drug Products (HFD-560), OPDRA conducted a review of the proposed proprietary names "Tylenol Arthritis (b)(4) Caplet" and "Tylenol Arthritis Pain" to determine the potential for confusion with approved proprietary and generic names as well as pending names.		
OPDRA RECOMMENDATION: From a safety perspective, OPDRA does not object to the use of the names "Tylenol Arthritis (b)(4) Caplet" or "Tylenol Arthritis Pain".		
<div style="display: flex; justify-content: space-between;"><div style="width: 45%;"><p><i>Jerry Phillips</i> 2/24/2000 Jerry Phillips, R.Ph. Associate Director for Medication Error Prevention Office of Post-Marketing Drug Risk Assessment Phone: (301) 827-3246 Fax: (301) 480-8173</p></div><div style="width: 45%;"><p><i>Jerry Phillips for /</i> 2-24-2000 Peter Honig, M.D. Deputy Director Office of Post-Marketing Drug Risk Assessment Center for Drug Evaluation and Research Food and Drug Administration</p></div></div>		

Office of Postmarketing Drug Risk Assessment (OPDRA)

HFD-400; Parklawn Building Room 15B-03

FDA Center for Drug Evaluation and Research

PROPRIETARY NAME REVIEW

DATE OF REVIEW: February 23, 2000

NDA NUMBER: 19-872

NAME OF DRUG: Tylenol Arthritis (b)(4) Caplet, Tylenol Arthritis Pain
(acetaminophen extended release tablets, USP)

NDA HOLDER: McNeil Consumer Healthcare

I. INTRODUCTION

This consult was written in response to a request from the Division of OTC Drug Products (HFD-560) for assessment of the tradenames "Tylenol Arthritis (b)(4) Caplet" and "Tylenol Arthritis Pain". The product for which the names were proposed is a marketed product that previously bore the name "Tylenol Extended Relief". The sponsor changed the product name to "Tylenol Arthritis Extended Relief Caplet" and informed the FDA in the December 1998 Periodic Safety Report. The Division (HFD-560) notified the sponsor of their objections to the use of this name. The sponsor then submitted for FDA approval the two proprietary names that are the subject of this review.

"Tylenol Arthritis Extended Relief Caplet" contains acetaminophen 650mg in a bilayer capsule-shaped tablet ("caplet"). The first layer is immediately released while the second layer is an extended release layer that is active over an 8-hour period. According to the PDR listing, the uses of Tylenol™ include "temporary relief of minor aches and pains associated with headache, muscular aches, backache, minor arthritis pain, common cold, toothache, menstrual cramps and for the reduction of fever". The usual dose for adults and children 12 years of age and older is 2 "caplets" every 8 hours, not to exceed 6 "caplets" in any 24-hour period.

II. RISK ASSESSMENT

The medication error staff of OPDRA conducted a search of several standard published drug product reference texts^{i,ii,iii} as well as several FDA databases^{iv} for existing drug names which

ⁱ MICROMEDEX Healthcare Intranet Series, 2000, MICROMEDEX, Inc., 6200 South Syracuse Way, Suite 300, Englewood, Colorado 80111-4740, which includes the following published texts: DrugDex, Poisindex, Martindale (Parfitt K (Ed), Martindale: The Complete Drug Reference. London: Pharmaceutical Press. Electronic version.), Emergindex, Reprodisk, index Nominum, and PDR/Physician's Desk Reference (Medical Economics Company Inc).

ⁱⁱ American Drug index, 42nd Edition, online version, Facts and Comparisons, St. Louis, MO.

ⁱⁱⁱ Facts and Comparisons, online version, Facts and Comparisons, St. Louis, MO.

sound alike or look alike to "Tylenol Arthritis (b) (4) Caplet" or "Tylenol Arthritis Pain" to a degree where potential confusion between drug names could occur under the usual clinical practice settings. A search of the electronic online version of the U.S. Patent and Trademark Office's Text and Image Database was also conducted^{iv}.

A. EXPERT PANEL DISCUSSION

A group discussion was held by OPDRA to gather professional opinions on the safety of these proprietary names. Potential concerns regarding drug marketing and promotion related to these proposed names were also discussed. This group is composed of FDA health professionals (pharmacists) from OPDRA and the Division of Drug Marketing and Advertising Communications (DDMAC). The group relies on their clinical and other professional experiences and a number of standard references when making a decision on the acceptability of a proprietary name.

A consensus was formed by the Expert Panel that, because there are currently a large number of "Tylenol" brand products marketed in the U.S. without a prescription, a high level of consumer confusion among the products seems likely. A separate consult has been requested by the Division of OTC Drug Products of the Division of Drug Risk Evaluation I and is in process to investigate some aspects of this concern. *Because this product has previously been marketed with two different names, it would be advisable for the firm to provide sufficient materials for pharmacies, distributors, and retail outlets to inform consumers and health professionals of the change in name of the product. Publishers of drug product reference texts should also be informed of this name change.*

In addition, a representative from DDMAC noted that the firm has encoded one of the FDA-approved indications, "arthritis pain", into the trade name for this product, which is a concern with reminder ads. However, this practice is widespread among OTC drug products. The regulation of promotion and advertising of OTC drug products currently falls under the jurisdiction of the Federal Trade Commission and not the FDA.

One noteworthy point regarding the reports of medication errors related to this product, a waiver was granted to McNeil for non-NDA Tylenol OTC products in 1987 whereby the firm is not required to submit MedWatch (3500a) form reports for any non-serious adverse drug experiences and non-fatal overdose reports. The waiver was approved with the stipulation that McNeil must submit any 3500a's if requested by FDA. Therefore, if consumer confusion among Tylenol products is occurring and reporting to McNeil is occurring, the FDA's Adverse Event Reporting System (AERS) database will not likely reflect the true nature and extent of this situation.

III. LABELING, PACKAGING, AND SAFETY RELATED ISSUES

Although complete labeling and packaging was not available with this review, it was noted that the term "caplet" is used throughout the PDR listing for this product. Although the term "caplet" has been used extensively in the OTC drug market, "caplet" is not an official USP dosage form. The established name should reflect the official USP dosage form "tablet". We

^{iv} Drug Product Reference File [DPR], the Established Evaluation System [EES], the AMF Decision Support System [DSS], the Labeling and Nomenclature Committee [LNC] database of Proprietary name consultation requests, New Drug Approvals 98-99, and the electronic online version of the FDA Orange Book.

^v WWW location <http://www.uspto.gov/tmdb/index.html>.

recommend that the established name be revised to read "acetaminophen extended release tablets". The term "caplet" may be retained in other appropriate sections of the labeling, with a footnote included that defines "caplet" as a capsule-shaped tablet.

IV. DISCUSSION

An OPDRA Expert Panel discussion was held to address the drug product names "Tylenol Arthritis ^{(b) (4)} Caplet" and "Tylenol Arthritis Pain". Consumers and health professionals have become familiar with this drug product under two different trade names: "Tylenol Extended Relief" and "Tylenol Arthritis Extended Relief Caplet". Multiple other Tylenol products are marketed in the U.S. These two factors may provide a significant source of confusion and medication errors for consumers. We urge the manufacturer to provide sufficient materials for pharmacies, distributors, and retail outlets to inform consumers and health professionals of the change in name of the product. Publishers of drug product reference texts should also be informed of this name change.

Some issues were raised in the Expert Panel discussion by DDMAC concerning the proposed names and drug promotion and advertising. However, FDA currently has no regulatory authority for non-NDA, OTC drug product advertising and promotion.

V. RECOMMENDATIONS

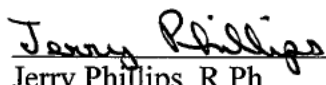
From a safety perspective, OPDRA does not object to the use of the proprietary names "Tylenol Arthritis ^{(b) (4)} Caplet" or "Tylenol Arthritis Pain". However, the established name should be changed to comply with official USP/NF dosage form designations.

OPDRA would appreciate feedback of the final outcome of this consult (e.g., copy of revised labels/labeling). We are willing to meet with the Division for further discussion as well. If you have any questions concerning this review, please contact Carol Pamer, R.Ph. at 301-827-3245.



Carol Pamer, R.Ph.
Safety Evaluator
Office of Postmarketing Drug Risk Assessment (OPDRA)

Concur:



Jerry Phillips, R.Ph.
Associate Director for Medication Error Prevention
Office of Postmarketing Drug Risk Assessment (OPDRA)

cc: NDA 19-872

HFD-560; Division Files/Kerry Rothschild, Project Manager

HFD-560; Charles Ganley, Division Director

HFD-040, Mark Askine, Senior Regulatory Review Officer, DDMAC

HFD-400; Carol Pamer, Safety Evaluator, OPDRA

HFD-400; Jerry Phillips, Associate Director, OPDRA

HFD-400; Peter Honig, Director, OPDRA (electronic copy)

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

NDA 19-872/S-009

ADMINISTRATIVE and CORRESPONDENCE
DOCUMENTS

SUPPL

NDA NO. 19-872 REF. NO. 209



NDA SUPPL FOR SLR

ORIGINAL

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

Robert DeLap, MD, PhD

Acting Director

Division of Anti-Inflammatory, Analgesic
and Ophthalmologic Drug Products (HFD-550)

Center for Drug Evaluation and Research

Central Document Room N115

Food and Drug Administration

9201 Corporate Boulevard

Rockville, MD 20850

DEC 8 1998

RE: Acetaminophen Extended Relief Caplet, 650 mg
NDA 19-872
Supplemental New Drug Application - Labeling
EXPEDITED REVIEW REQUESTED



Dear Dr. DeLap:

This supplemental application is being submitted in follow-up to a teleconference that was held on November 9, 1998 with Dr. Linda Katz, Ms. Marina Chang, Ms. Stephanie Mason and Ms. Debbie Lumpkins. During that teleconference, McNeil was advised to revise the labeling for "TYLENOL® Arthritis Extended Relief Caplet" to more clearly convey that the product is intended for the relief of arthritis pain rather than (b) (4).

In response to FDA's request, we have revised the product labeling (Attachment 1). Please note, for review purposes, that we have submitted labeling for only one package size (100 count bottle). All other package sizes will be consistent with the 100 count size.

In revising this labeling, we have made the following changes:

- Changed the product name from Tylenol Arthritis Extended Relief Caplet to Tylenol Arthritis (b) (4) Caplet.
- Updated our alcohol warning to meet the requirements of the final rule as published in the *Federal Register* on October 23, 1998.
- Changed the company name from McNeil Consumer Products Company to McNeil Consumer Healthcare, consistent with our NDA correspondence dated November 2, 1998.

Robert DeLap, MD, PhD
Page 2

Additionally, we are providing our revised labeling in bullet format (Attachment 2). We prefer the bulleted version (versus the text version) but wanted to provide both options for your review.

We are requesting an expedited review of this labeling in order to meet the deadline of the alcohol warning final rule. If there are any questions, please contact me at (215) 233-7878.

Very truly yours,

McNEIL CONSUMER HEALTHCARE

A handwritten signature in cursive script that reads "Paula J. Oliver".

Paula J. Oliver
Senior Director, Regulatory Compliance

PJO:dtg

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DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-872/S-009

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

DEC 29 1998

Attention: Paula J. Oliver, Senior Director, Regulatory Compliance

Dear Ms. Oliver:

We acknowledge receipt of your supplemental application for the following:

Name of Drug: Tylenol Arthritis ER Caplet (Acetaminophen Extended Relief Caplet, 650mg)

NDA Number: 19-872

Supplement Number: S-009

Date of Supplement: December 8, 1998

Date of Receipt: December 9, 1998

Unless we find the application not acceptable for filing, this application will be filed under Section 505(b)(1) of the Act on February 7, 1998, in accordance with 21 CFR 314.101(a).

All communications concerning this NDA should be addressed as follows:

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

Sincerely,

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

NDA 19-872/S-009

Page 2

cc:

Original NDA 19-872/S-009

HFD-560/Div. Files

HFD-560/CSO/K. Rothschild

SUPPLEMENT ACKNOWLEDGEMENT



ORIGINAL

SLR-009(BL)

NDA SUPPL AMEND

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
9201 Corporate Boulevard
Rockville, MD 20850

JUL 15 1999

RE: Acetaminophen Extended Relief Caplet, 650 mg
NDA 19-872
Amendment # 1 to SNDA S-009
Revised Labeling - **Drug Facts** - Expedited Review Requested



Dear Dr. Ganley:

On December 8, 1998, we submitted a Supplemental New Drug Application (S-009) which provided for revised labeling on the above referenced drug. The revisions we made included a change in product name from **TYLENOL® Arthritis Extended Relief Caplet** to **TYLENOL® Arthritis (b)(4) Caplet**, the revised alcohol warning to meet the requirements of the final rule dated 10/23/98 and a change in company name. S-009 is currently pending in the division.

We have now updated that labeling to meet the requirements of the final rule on OTC labeling as published in the March 19, 1999 *Federal Register*. The labeling has been reformatted into **Drug Facts** and we are requesting an expedited review since we need to implement the revised alcohol warning on this product in accordance with the October 22, 1999 deadline. Thermals are attached for our 8, 24, 50, and 100 count bottles, as well as our 2 count pouch and the dispensit box for the pouch.

Although not included in the text of the attached thermals, we would like to include additional text under the **Directions** heading of the labeling in the section for (b)(4). The entire Directions heading would thus read as follows:

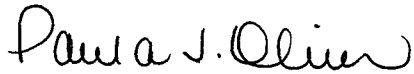
Directions	
Adults (b)(4)	Take 2 caplets every 8 hours with water; swallow whole - do not crush, chew or dissolve. Do not take more than 6 caplets in 24 hours.
(b)(4)	(b)(4)

Charles Ganley, MD
Page 2

If there are any questions on this submission, please contact me (215) 273-7878.

Very truly yours,

McNEIL CONSUMER HEALTHCARE

A handwritten signature in black ink, reading "Paula J. Oliver". The signature is written in a cursive, flowing style.

Paula J. Oliver
Senior Director, Regulatory Compliance

PJO:dtg
Attachment

cc: K. Rothschild, Project Manager

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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

OCT 1 1999



RE: Acetaminophen Extended Relief Caplet, 650 mg
NDA 19-872
Amendment #2 to SNDA S-009
Labeling – Product Name

SUPPL & AMENDMENT
SLR-009/BL

Dear Dr. Ganley:

On August 10, 1999 we were supplied (via telephone) with feedback on our revised labeling for this product as submitted to the agency on July 15, 1999. More specifically, we were advised that the product name, **TYLENOL® Arthritis** (b)(4) Caplet, was considered misleading. We were also advised that the agency believes that the name is confusing to consumers, intimating that the product (b)(4).

In follow-up to the feedback provided to us, we elected to conduct a survey of consumers to evaluate what they perceive as the benefits of using **TYLENOL® Arthritis**. In addition, we identified and collected representative labeling of other currently marketed products that have the word "arthritis" as part of their product name.

The results of the consumer survey conducted for McNeil by (b)(4) (b)(4), are provided as Attachment 1. They clearly indicate that consumers understand the product's indication.

In this survey, a total of 103 respondents were shown a color picture of the front panel of the **TYLENOL® Arthritis** package as it was submitted to the agency on July 15, 1999. Consumers were questioned as to the main reason why someone with arthritis would use the product and for what other reasons, if any, someone with arthritis would use the product. These were open ended questions, based only on reading of the front panel. The two most prevalent responses provided were that **TYLENOL® Arthritis** is being used because it "relieves pain" (78%) and because it offers "long lasting/extended relief" (34%). Not a single respondent indicated that the product (b)(4). A summary tabulation of the responses and a list of verbatim answers is included in Attachment 1, as well as demographic information, a copy of the labeling that was shown to consumers, and a copy of the questionnaire.

ORIGINAL

Based on the results of this consumer survey, it is evident that the name TYLENOL® Arthritis (b) (4) Caplet is not misleading to consumers and, in fact, clearly communicates the product's intended use. Clearly, consumers understand that this product is used to relieve pain. This is especially significant since consumers only reviewed the Principal Display Panel of the carton, which is a more rigorous test than review of the entire label, where they would have been exposed to the "Uses" section. Therefore, based on the results of our survey, we continue to believe that the product name is not misleading and therefore, request that it remain as submitted to the division on July 15, 1999 (SNDA S-009 Amendment #1).

Additionally, as previously referenced, we conducted a limited survey of other currently marketed products containing "arthritis" as part of the product name. A variety of products were identified, including the following:

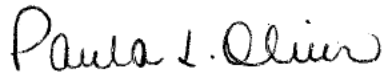
- Icy Hot Arthritis Therapy Gel with Capsaicin
- Arthritis Formula BenGay® NonGreasy Pain Relieving Cream
- Deep Penetrating Arthritis Hot® Pain Relief Creme
- Absorbine® Arthritis Strength Liquid-Fast Arthritis Pain Relieving Liquid with Capsaicin
- Bufferin® Arthritis Strength
- Arthritis Pain Formula Aspirin Pain Reliever
- Extra Strength Bayer® Arthritis Pain Regimen Formula...Arthritis Strength Aspirin

Representative labeling for these products is included with this correspondence as Attachment 2. It is very apparent that a variety of other products are being marketed with the arthritis benefit featured prominently in the product name.

We would like to review this issue with the division and would welcome a meeting to discuss the issue and our research results in more detail. We are interested in resolving this issue as quickly as possible since it also affects final approval of our gelta formulation (S-006) which is currently pending in the division. I can be reached at (215) 273-7878.

Very truly yours,

McNEIL CONSUMER HEALTHCARE



Paula J. Oliver

Senior Director, Regulatory Compliance

PJO:dtg

Attachments

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

K. Rothschild, Project Manager (HFD-560)

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

Charles J. Ganley, MD, Director
Division of OTC Drug Products (HFD-560)
Center for Drug Evaluation and Research
Document Control Room, Room S-212
Food and Drug Administration
9201 Corporate Boulevard
Rockville, MD 20850

DEC 28 1999



NEW COUNTRY
NC

RE: Acetaminophen Extended Release Caplet, 650mg
NDA 19-872
Amendment No.3 to SNDA S-009
Labeling-Product Name

Dear Dr. Ganley:

In response to a telephone conversation with Kerry Rothschild, Project Manager, on December 22, 1999, attached is an alternate product name for your review and consideration in conjunction with the division's ongoing review of the labeling for this product. This alternate product name was submitted to the division via fax on December 22, 1999.

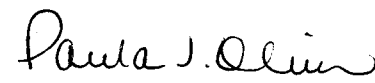
We would like to resolve the issues surrounding this labeling as quickly as possible since the labeling for our geltaab formulation (SNDA S-006) is still pending and we have also submitted a supplemental application for larger package sizes (SNDA S-010) that is under active review.

We believe that a meeting between McNeil personnel and the agency would facilitate resolution of this labeling. Therefore, we would like to request your consideration of our earlier request (October 1, 1999) for a meeting.

If there are any questions on the attached, or you need additional information, please contact me at 215-273-7878.

Very truly yours,

MCNEIL CONSUMER HEALTHCARE


Paula J. Oliver
Senior Director, Regulatory Compliance

ORIGINAL

PJO:rad
Attachment

cc: Kerry Rothschild, Project Manager (HFD-560)



ORIGINAL

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

Charles J. Ganley, MD
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

JAN 14 2000

NEW CORRESP

NC



Re: TYLENOL® Arthritis Extended Relief Caplet
NDA 19-872
Correspondence to NDA

Dear Dr. Ganley:

In follow-up to your request of 1/13/2000, attached is a copy of the regulatory chronology associated with the product name. This duplicates the information we submitted by fax.

You also raised a question regarding pricing of this product. McNeil's direct price did not change in conjunction with the product name change from TYLENOL Extended Relief to TYLENOL Arthritis Extended Relief in 1998. The direct price charged to our customers has remained the same from January 1998 (prior to name change) to present.

We are in the process of evaluating our consumer contact database and will provide additional information next week.

We appreciate your assistance in resolution of issues associated with this product's labeling. If there are any questions, please contact me at 215-273-7878 or Vivian A. Chester at 215-273-7010.

Very truly yours,

MCNEIL CONSUMER HEALTHCARE

Paula J. Oliver
Senior Director, Regulatory Compliance

cc: K. Rothschild (HFD-560)
PO000114:sco



ARCHIVAL
COPY

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

JAN 21 2000

Charles J. Ganley, MD
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

NEW CORRESP

NC



**Re: TYLENOL Arthritis Extended Relief Caplet
NDA 19-872
Correspondence to NDA**

Dear Dr. Ganley:

During our conversation on January 13, 2000, you inquired about consumer complaints on Tylenol Arthritis Extended Relief Caplets. We have reviewed the consumer contact database for the first year of this product's distribution, September 1998 through August 1999, and our findings are summarized below:

- In response to your question concerning pricing complaints, there were 17 complaints for this time period regarding a claimed price increase associated with the name change. As indicated in our correspondence of January 14, 2000, McNeil did not increase the price of this product when the name changed, and in fact, the price remains the same as that in effect in January 1998. The price increase referred to by consumers may reflect store pricing, over which McNeil has no control.
- There have been 16 complaints in which the consumer complained about the product's name or the name change. In general, these were from consumers who were complaining that the product name changed but the product remained the same.

To put these complaints into context, we note that there were (b) (4) packages of Tylenol Arthritis Extended Relief shipped during this time period. Further, a toll-free number appears on these packages to facilitate consumer feedback and to answer product questions.

In addition, our review of the consumer database indicates that there have been over 250 testimonials from consumers providing positive comments regarding the product and its efficacy in arthritis pain relief. Tylenol Arthritis Extended Relief received the highest number of favorable testimonials among all of our drug products during this time period. It has been extremely well-received by consumers.

ORIGINAL

TYLENOL Arthritis Extended Relief Caplet - NDA 19-872

Page 2

We also conducted a review of our adverse experience reporting database for the same time period. This review revealed that there have been no unusual findings suggestive of a problem with consumer confusion since the name change.

We hope this information is helpful in evaluating the Tylenol Arthritis Extended Relief name change. As I indicated during our telephone conversation, we believe it is extremely important that we resolve the name change issue, which we note has been pending since November 1998. We would appreciate a meeting in the near future to discuss this product's name, as well as other aspects of our labeling as explained in our correspondence of November 19, 1999.

If you have any questions, please contact me directly at 215/273-7010.

Sincerely,
MCNEIL CONSUMER HEALTHCARE

A handwritten signature in black ink, appearing to read "Vivian Chester", written over the printed name.

Vivian A. Chester
Vice President, Regulatory Affairs

cc: K. G. Rothschild (HFD-560)



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

APR 14 2000

Charles J. Ganley, MD
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

NEW CORRESP

NC to S009



Re: Acetaminophen Extended Release Caplet/Geltab, 650mg
NDA 19-872
Correspondence to SNDA S-009

Dear Dr. Ganley:

In response to FDA's letter of 4/13/00 (copy enclosed) and in accord with 21 CFR 314.110, we wish to advise you that we intend to amend the application.

Sincerely,

McNEIL CONSUMER HEALTHCARE

Paula J. Oliver
Senior Director, Regulatory Compliance

PJO0414:sco

ORIGINAL



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 S-212
9201 Corporate Boulevard
Rockville, MD

APR 20 2000

NEW CORRESP

NC



RE: Acetaminophen Extended Release Caplet/Geltab, 650 mg
NDA 19-872
Background Package REVISION

Dear Dr. Ganley:

Based on the Approvable Letter that was sent to McNeil on April 13, 2000, we are proposing a restructuring of the agenda and attendee list included in the Background Package for our 3:00 PM meeting on April 27, 2000.

We would like to focus the meeting on the following two items:

1. Resolution of the labeling
2. Mechanism for changing product names in the future

We are in the process of "revising" the labeling for our product, based on the comments in your letter. We will fax this draft labeling to your office on Monday morning, April 24, and would like to focus the meeting on any comments the agency may have with regard to the labeling.

We apologize for any inconvenience caused by this change in agenda; however, after reviewing the agency's comments, we feel that it will be more productive to spend the meeting time discussing revised labeling and the process to follow in the future when considering name changes.

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

Very Truly Yours,
MCNEIL CONSUMER HEALTHCARE

Paula J. Oliver
Senior Director, Regulatory Compliance

cc: K. Rothschild (HFD-560)
ganley4-20

ORIGINAL



5/19/00 Noted. See
labelling MDR
Review Rheum, MD

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

April 24, 2000

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



RE: Acetaminophen Extended Release Caplet/Geltab, 650mg
NDA 19-872
Background Package REVISION - Labeling

Labeling: SLR-011
NDA: 19-872 Pcd. 4-25-00
Reviewed by: DDR

SNC-009

Dear Dr. Ganley:

In follow-up to the revised Background Package that was submitted on April 20, 2000, attached are color copies of revised draft labeling (100 count size). We would like to discuss this labeling at our meeting on April 27, 2000.

If there are any questions, I can be reached at 215-273-7878.

Very truly yours,
McNEIL CONSUMER HEALTHCARE

Paula J. Oliver

Paula J. Oliver
Senior Director, Regulatory Compliance

noted
S. J. Mason
6/19/00

cc: Kerry Rothschild, Product Manager (HFD-560)

Attachment

PJO:joc

Pjo005

ORIGINAL

37.1

MINUTES OF A MEETING
April 27, 2000
Corporate Building, Room S-200A

Meeting Type: Feedback/Face-to-Face

NDA: 19-872 (Tylenol Arthritis Pain ER Caplets)

Project Manager: Tom Parmelee, Pharm.D.

FDA Participants:

Charles Ganley, M.D., Division Director
Linda Katz, M.D., M.P.H., Deputy Division Director
Bob DeLap, M.D., Director, Office of Drug Evaluation V
Mary Jane Walling, Associate Director, Office of Drug Evaluation V
Debbie Lumpkins, IDS Team Leader
Michelle Jackson, Ph.D., IDS reviewer
Stephanie Mason, IDS reviewer
Tom Parmelee, Pharm.D., Project Manager

Sponsor Participants:

Vivian Chester, Vice President, Regulatory Affairs and Project Management
William I. McComb, Vice President, Marketing and Professional Sales
Edward B. Nelson, M.D., Vice President, Medical/R&D
Anthony R. Temple, M.D., Vice President, Medical Affairs
Paula Oliver, Senior Director, Regulatory Compliance
Charles A. Martin, Director, Consumer Insights Group
Ashley C. McEvoy, Tylenol Franchise Manager

Objective:

To discuss labeling on Tylenol Arthritis Extended Relief Caplet/Geltab.

Discussion:

The sponsor provided a brief background summary of this product as well as input relating to the justification of its name. The sponsor stated this product provides a longer duration of effect and does not imply (b) (4) or other conditions related to Arthritis. The Agency representatives stated that it is imperative to provide consumers with appropriate drug product information that is not misleading or easily misinterpreted.

Recommendations:

The Agency representatives made the following preliminary recommendations to the sponsor:

- 1) The statement of identity on the principal display panel should be more prominent for consumer viewing.
- 2) The term "caplet" should be defined as a "capsule-shaped tablet" on the principal display panel.
- 3) The statement "Do not use more than 10 days unless directed by a doctor" should be added under the "Directions" section.

Action Items:

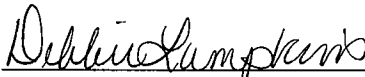
The Agency will finalize the review of the labeling and provide feedback and other recommendations to the sponsor.



Tom Parmelee, Pharm.D.

Minutes Preparer

Division of OTC Drug Products (HFD-560)



Debbie Lumpkins, Chair Concurrence

Division of OTC Drug Products (HFD-560)

cc: Original NDA File/19-872
HFD-560 Division File
HFD-560/C. Ganley/L. Katz/D. Lumpkins/T. Parmelee/S. Mason

MEETING MINUTES

**CENTER FOR DRUG EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION**

FACSIMILE TRANSMISSION RECORD

DATE: May 16, 2000

FROM: Thomas A. Parmelee, Pharm.D.
Division of OTC Drug Products, HFD-560

PHONE: (301) 827-2271 FAX: (301) 827-2315

TO: Paula Oliver
McNeil Consumer Healthcare
Phone: (215) 273-7878 FAX: (215) 273-4049

No. Of Pages (including cover) 2

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Message:

Here are the recommendations regarding labeling for the Tylenol product (NDA 19-872). Please note that any future submission addressing this issue should be labeled as a re-submission or a complete response to the approvable letter that was issued on April 13, 2000.

If you have any questions, please contact Thomas A. Parmelee, Pharm.D., Regulatory Project Manager, at 301-827-2271.

A meeting was held on April 27, 2000, and the following labeling changes were agreed upon:

Principal Display Panel:

1. The statement of identity (i.e., pain reliever, acetaminophen extended release), needs to be in a size reasonably related to the most prominent printed matter on the panel.
2. The term "Caplet" needs to be defined as "capsule-shaped tablet."

Directions:

1. Although the statement "pain gets worse or lasts for more than 10 days" is located under the Stop use and ask a doctor if section, the duration for use needs to be emphasized in the Directions section also. The sponsor should add another bulleted statement under this section to read: "Do not use for more than 10 days unless directed by a doctor."

Other subsequent recommendations that should be made are as follows:

Use:

1. The bullet symbols need to be in alignment.
2. For consistency with other approved adult analgesic drug products, in the second sentence following the pregnant/breast-feeding statement, the word "(b) (4)" should be replaced with the word "Quick" to read "Quick medical attention is critical for adults...."

Recommendation: The sponsor should submit revised labeling for all package sizes to reflect the changes listed above.



ARCHIVAL
COPY

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

NDA SUPPL AMENDMENT JUL - 5 2000

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

SLR-009 BL

RE: Acetaminophen Extended Release Caplet, 650mg
NDA 19-872
Amendment #4 to SNDA S-009
Complete Response to Approvable Letter –
Revised Labeling in **Drugs Facts** Format



Dear Dr. Ganley:

We are submitting this amendment to our pending Supplemental New Drug Application (S-009) in response to the Division's Approvable Letter dated April 13, 2000 (copy attached).

Labeling for the package sizes covered under this SNDA has been prepared in **Drug Facts** format, taking into account the labeling comments (attached) that were provided in follow-up to our April 27, 2000 meeting. The following changes have been made in the labeling:

Principal Display Panel

- The statement of identity (Pain Reliever) has been increased in size, as well as acetaminophen extended release
- Caplet has been defined as "capsule-shaped" tablet

Directions

- The Directions section has been revised to bullet format and a bullet reading "do not use for more than 10 days unless directed by a doctor" has been added.

Uses

- The bullets have been aligned

ORIGINAL

Warnings

- The word “quick” has been substituted for the word “(b) (4)” in the sentence reading “Quick medical attention is critical for adults ...”

Additionally, the tradename has been revised from Tylenol Arthritis Extended Relief Caplet to Tylenol Arthritis Pain Extended Relief Caplet with a prominent descriptor line underneath the name reading “For the temporary relief of minor arthritis pain”.

Attachment 1 provides copies of thermals for our 24, 50 and 100 count bottle labels and cartons. **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

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

PJO:joc

Pjo010

8/4/00. Noted. Refer to IDS review



REVIEW
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R. H. H. H. H.

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

NDA SUPPL AMENDMENT JUL - 5 2000

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

SLR-009 BL



RE: Acetaminophen Extended Release Caplet, 650mg
NDA 19-872
Amendment #4 to SNDA S-009
Complete Response to Approvable Letter -
Revised Labeling in **Drugs Facts** Format

Dear Dr. Ganley:

We are submitting this amendment to our pending Supplemental New Drug Application (S-009) in response to the Division's Approvable Letter dated April 13, 2000 (copy attached).

Labeling for the package sizes covered under this SNDA has been prepared in **Drug Facts** format, taking into account the labeling comments (attached) that were provided in follow-up to our April 27, 2000 meeting. The following changes have been made in the labeling:

Principal Display Panel

- The statement of identity (Pain Reliever) has been increased in size, as well as acetaminophen extended release
- Caplet has been defined as "capsule-shaped" tablet

Directions

- The Directions section has been revised to bullet format and a bullet reading "do not use for more than 10 days unless directed by a doctor" has been added.

Uses

- The bullets have been aligned

DUPLICATE

Warnings

- The word "quick" has been substituted for the word "(b)(4)" in the sentence reading "Quick medical attention is critical for adults ... "

Additionally, the tradename has been revised from Tylenol Arthritis Extended Relief Caplet to Tylenol Arthritis Pain Extended Relief Caplet with a prominent descriptor line underneath the name reading "For the temporary relief of minor arthritis pain".

Attachment 1 provides copies of thermals for our 24, 50 and 100 count bottle labels and cartons. **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
Senior Director, Regulatory Compliance

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

PJO:joc

Pjo010

CENTER FOR DRUG EVALUATION AND RESEARCH
FOOD AND DRUG ADMINISTRATION

FACSIMILE TRANSMISSION RECORD

DATE: July 13, 2000

FROM: Thomas A. Parmelee, Pharm.D.
Division of OTC Drug Products, HFD-560

PHONE: (301) 827-2271 FAX: (301) 827-2315

TO: Paula Oliver
McNeil Consumer Healthcare
Phone: (215) 273-7878 FAX: (215) 273-4049

No. Of Pages (including cover) 1

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Message:

Please refer to you supplemental new drug application NDA 19-872/S-010 for Tylenol Extended Release Caplets. We also acknowledge receipt of your amendment to NDA 19-872/S-010 on June 2, 2000.

The labeling reviewer has provided the following comments:

- 1) The letter "l" in the word "liver" should be added in the bottle label for the 290-count caplets.
- 2) The pale yellow contrast color used for the 0.5 hairlines, the visual graphic, and the table format, under **Directions**, are not significantly noticeable. This is unacceptable.
- 3) We have concerns regarding the promotional statement " (b) (4)
Please provide a detailed regulatory history regarding this statement. Were there clinical data to support this statement?
- 4) You will need to submit labeling for the 100-count caplet bottle size.
- 5) The size of the statement "For the temporary relief of minor arthritis pain" should be larger on the PDP.

In order to assure a timely action for this supplemental new drug application, we request that you address the aforementioned comments, and amend the labeling accordingly. If you have any questions, please contact Thomas A. Parmelee, Pharm.D., Regulatory Project Manager, at 301-827-2271.



ARCHIVAL
COPY

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

JUL 14 2000
NDA SUPPL AMENDMENT

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



RE: Acetaminophen Extended Release Caplet, 650mg
NDA 19-872
Amendment #5 to SNDA S-009
Revised Labeling in **Drugs Facts** Format

SLR-009 AL

Dear Dr. Ganley:

In response to the labeling comments (attached) that were provided to us on July 13, 2000, we agree to make the following changes:

1. Add an "l" to the word "liver" on the bottle label for the 290 count size. The 290 count size is covered by S-010.
2. Revise the contrast color from pale yellow to dark blue for the hairlines, the visual graphic and the table format under **Directions**. This color change should provide clear contrast.
3. Eliminate use of the phrase "[REDACTED]" We are eliminating this phrase at this time in order to expedite approval of this SNDA. Nonetheless, we believe there is adequate support for this statement and since the statement was specifically discussed with the agency and deemed appropriate for inclusion in the original NDA labeling, we wish to discuss with you reinstitution of it on future versions of this labeling following approval of this SNDA.
4. Submit an updated version of the 100 count caplet bottle size. Labeling for this size was submitted as amendment #4 to this SNDA on July 5, 2000 but has been revised again based on the agency's comments of July 13, 2000.
5. Increase the size of the statement "For the temporary relief of minor arthritis pain" on the PDP.


Representative revised thermals reflecting these changes are provided for the 100 count package size, including bottle label and carton (Attachment I). These changes will also be implemented on the other package sizes covered by S-009.

ORIGINAL

Acetaminophen Extended Release Caplet, 650mg
NDA 19-872
Amendment #3 to SNDA S-010
Revised Labeling in **Drug Facts** Format
Page 2

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

Very truly yours,
McNEIL CONSUMER HEALTHCARE



Paula J. Oliver
Senior Director, Regulatory Compliance

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

PJO:joc

Attachments
Pjo016

8/4/00, noted. Refer to ITS review



REVIEW
COPY

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

JUL 14 2000

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

NDA SUPPL AMENDMENT

RE: Acetaminophen Extended Release Caplet, 650mg
NDA 19-872
Amendment #5 to SNDA S-009
Revised Labeling in **Drugs Facts** Format

SLR-009 AL

Dear Dr. Ganley:

In response to the labeling comments (attached) that were provided to us on July 13, 2000, we agree to make the following changes:

1. Add an "l" to the word "liver" on the bottle label for the 290 count size. The 290 count size is covered by S-010.
2. Revise the contrast color from pale yellow to dark blue for the hairlines, the visual graphic and the table format under **Directions**. This color change should provide clear contrast.
3. Eliminate use of the phrase "(b) (4)". we are eliminating this phrase at this time in order to expedite approval of this SNDA. Nonetheless, we believe there is adequate support for this statement and since the statement was specifically discussed with the agency and deemed appropriate for inclusion in the original NDA labeling, we wish to discuss with you reinstitution of it on future versions of this labeling following approval of this SNDA.
4. Submit an updated version of the 100 count caplet bottle size. Labeling for this size was submitted as amendment #4 to this SNDA on July 5, 2000 but has been revised again based on the agency's comments of July 13, 2000.
5. Increase the size of the statement "For the temporary relief of minor arthritis pain" on the PDP.


Representative revised thermals reflecting these changes are provided for the 100 count package size, including bottle label and carton (Attachment I). These changes will also be implemented on the other package sizes covered by S-009.

DUPLICATE

Acetaminophen Extended Release Caplet, 650mg
NDA 19-872
Amendment #3 to SNDA S-010
Revised Labeling in **Drug Facts** Format
Page 2

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

Very truly yours,
McNEIL CONSUMER HEALTHCARE



Paula J. Oliver
Senior Director, Regulatory Compliance

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

PJO:joc

Attachments
Pjo016



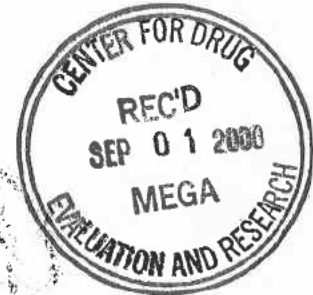
McNeil Consumer Healthcare, 7050 Camp Hill Road, Fort Washington, PA 19034-2299 (215) 273-7000

Charles J. Ganley, MD
Director
Division of OTC Drug Products (HFD-560)
Center for Drug Evaluation and Research
Document Control Room
Food and Drug Administration
9201 Corporate Boulevard, Room S-212
Rockville, MD 20850

NDA SUPPL AMENDMENT

FA
SLR 009

AUG 31 2000



Re: Tylenol® Arthritis Pain Caplet, 650mg
"FPL for Approved Supplement NDA 19-872/S-009"

Dear Dr. Ganley:

In response to the approval letter for S-009 to NDA 19-872 (copy attached), we are submitting 20 copies of FPL (sizes 24's, 50's and 100's bottle and carton label), 10 of which are mounted on heavy-weight paper. Also enclosed is one market package.

If any additional information is needed, please contact me at (215) 273-7878.

Sincerely,
McNEIL CONSUMER HEALTHCARE

Paula J. Oliver
Senior Director, Regulatory Compliance

Enclosure

MB0830/2:kt

ORIGINAL



DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-872/S-009

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

Dear Ms. Oliver:

We acknowledge receipt of your August 31, 2000 submission containing final printed labeling (FPL), in response to our July 25, 2000 letter approving your supplemental new drug application for Tylenol Arthritis Pain Caplet (acetaminophen caplet), 650 mg.

We have reviewed the labeling that you submitted in accordance with our July 25, 2000 letter, and we find it acceptable.

If you have any questions regarding your application, please contact Walter Ellenberg, Ph.D., Regulatory Project Manager, at (301) 827-2247.

Sincerely yours,

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

2/28/01 12:06:18 PM

original

NDA

19-872

a. 9.1.00

Reviewed by

Marshall

FEB 28 2001

EXP: 3 0045-0838-24 7

**Drug Facts** (continued)

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

- | | |
|-----------------------|--|
| adults | <ul style="list-style-type: none"> ■ take 2 caplets every 8 hours with water ■ swallow whole – do not crush, chew or dissolve ■ do not take more than 6 caplets in 24 hours ■ do not use for more than 10 days unless directed by a doctor |
| under 18 years of age | <ul style="list-style-type: none"> ■ ask a doctor |

Other information

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

24 Caplets*—650 mg EACH Pain Reliever

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

TYLENOL®
Acetaminophen
Extended Release
ARTHRITIS PAIN

Lasts up to 8 Hours

NDC 50580-172-24

24 tablets*—650 mg EACH **Pain Reliever**

TYLENOL[®]
Acetaminophen
Extended Release
ARTHRITIS PAIN
FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN
Extended Relief Caplets

Lasts up to 8 Hours

Drug Facts

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

Uses tempo

- 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.**

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

08717420

8717420

Michel Consumer Healthcare
 DIVISION OF MONEL - PPG, INC.
 FORT WASHINGTON, PA 19004 USA
 www.lybend.com

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 U.S. Pat. No. 4,823,622

Inactive ingredients: corn starch, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, powdered cellulose, pregelatinized starch, sodium starch glycolate, titanium dioxide, thioclacin

Drug Facts (continued)

Inactive ingredients com starch, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, polydioxane, powdered cellulose, pregelatinized starch, sodium starch glycolate, titanium dioxide, triacetin

Questions? Call 1-800-962-5357

Active ingredient (in each caplet)	Purpose
Acetaminophen 650 mg	Pain reliever
Uses temporarily relieves minor aches and pains due to: <ul style="list-style-type: none"> • arthritis • the common cold • headache • toothache • muscular aches • backache • menstrual cramps 	
Warnings	
<p>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 if you're taking other product containing acetaminophen.</p> <p>Stop use and ask a doctor if: you have • persistent or severe pain • redness or swelling is present • pain gets worse or lasts for more than 10 days</p> <p>If pregnant or breast-feeding, ask a health professional before use.</p>	

NDC 50580-112-2

Lasts up to 8 Hours

TYLENOL Acetaminophen
Extended Release

ARTHRITIS PAIN

FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN

**Extended Relief
Caplets**
Pain Reliever

24 Caplets*—650 mg EACH *Capsule-Shaped Tablets

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 capsules every 8 hours with water
- **swallow whole** – do not crush, chew or dissolve
- **do not take more than 6 capsules 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 by USP (6000)**

EXP. DATE: CONTROL: 7825940

Labeling: original
 NDANO. 19-872 Rcd. 9-1-00
 Review: M. h. h. 9

FEB 28 2001



Drug Facts (continued)

Directions ■ do not take more than directed

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

under 18 ■ ask a doctor
 years of age

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 corn starch, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, powdered cellulose, pregelatinized starch, sodium starch glycolate, titanium dioxide, triacetin

Questions? Call 1-800-962-5357

What makes Tylenol® Arthritis Pain Extended Relief Caplets different?

- Uses a unique, patented bi-layer caplet. The first layer dissolves quickly to provide prompt relief while the second layer is time released to provide up to 8 hours of relief.
- For more information or questions, visit our website www.tylenol.com.
- The makers of Tylenol® do not manufacture store brands.

50 Caplets* - 650 mg EACH **THIS PACKAGE IS FOR HOUSEHOLDS WITHOUT YOUNG CHILDREN** *Capsule Shaped Tablets

TYLENOL® Acetaminophen Extended Release
ARTHRITIS PAIN
 FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN
 Extended Relief Caplets
Lasts up to 8 Hours
 NDC 50580-112-50

50 Caplets* - 650 mg EACH **THIS PACKAGE FOR HOUSEHOLDS WITHOUT YOUNG CHILDREN** *Capsule Shaped Tablets

TYLENOL® Acetaminophen Extended Release
ARTHRITIS PAIN
 FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN
 Extended Relief Caplets
Lasts up to 8 Hours
 NDC 50580-112-50

Drug Facts

Active ingredient (in each caplet) 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.



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 McNeil Consumer Healthcare
 DIVISION OF MCNEIL - PPC, INC.
 FORT WASHINGTON, PA 19004 USA
 www.tylenol.com

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 U.S. Pat. No. 4,808,822

8717440

Active ingredient (in each caplet) 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

TYLENOL® Acetaminophen Extended Release
ARTHRITIS PAIN
 FOR THE TEMPORARY RELIEF OF MINOR ARTHRITIS PAIN
 Extended Relief Caplets
Lasts up to 8 Hours
 NDC 50580-112-50

50 Caplets* - 650 mg EACH *Capsule Shaped Tablets

THIS PACKAGE FOR HOUSEHOLDS WITHOUT YOUNG CHILDREN

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 caplets every 8 hours with water ■ swallow whole – do not crush, chew or dissolve ■ do not take more than 6 caplets 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

McNeil Consumer Healthcare, D. J. WISNIOFFSKIE, - PPC, INC.
 FORT WASHINGTON, PA 19004 USA www.tylenol.com
 © MCN-PPC, Inc. '00 U.S. Pat. No. 4,808,822 **77829550**
 EXP. DATE: _____ CONTROL: _____

FEB 28 2001



Drug Facts (continued)

Directions ■ do not take more than directed

adults ■ take 2 caplets every 8 hours with water
 ■ swallow whole - do not crush, chew or dissolve
 ■ do not take more than 6 caplets 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

corn starch, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, powdered cellulose, pregelatinized starch, sodium starch glycolate, titanium dioxide, triacetin

Questions? Call 1-800-962-5357 (b)

What makes Tylenol® Arthritis Pain Extended Relief Caplets different?

- Uses a unique, patented bi-layer caplet. The first layer dissolves quickly to provide prompt relief while the second layer is time released to provide up to 8 hours of relief.
- For more information or questions, visit our website www.tylenol.com.
- The makers of Tylenol® do not manufacture store brands.

08717450

100 Caplets* - 650 mg EACH

Extended Relief Caplets

*Capsule-Shaped Tablets

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

100 Caplets* - 650 mg EACH

Extended Relief Caplets

*Capsule-Shaped Tablets

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

NDC 50580-112-10

McNeil Consumer Healthcare
 DIVISION OF MCNEIL - PPG, INC.
 FORT WASHINGTON, PA 19004 USA
www.tylenol.com



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 U.S. Pat. No. 4,820,822

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

Extended Relief Caplets

8717450

Drug Facts

Active ingredient (in each caplet) 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.

Active ingredient (in each caplet) 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.



NDC 50580-112-10

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

Extended Relief Caplets

Pain Reliever

100 Caplets* - 650 mg EACH *Capsule-Shaped Tablets

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 caplets every 8 hours with water
 ■ swallow whole - do not crush, chew or dissolve
 ■ do not take more than 6 caplets 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)

Inactive ingredients corn starch, hydroxyethyl cellulose, hydroxypropyl methylcellulose, magnesium stearate, microcrystalline cellulose, povidone, powdered cellulose, pregelatinized starch, sodium starch glycolate, titanium dioxide, triacetin

Questions? Call 1-800-962-5357

McNeil Consumer Healthcare
 DIVISION OF MCNEIL - PPG, INC.
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