CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 76-460

Name: Ibuprofen Tablets USP, 200 mg

Sponsor: Neil Laboratories, Inc.

Approval Date: November 26, 2003

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-460

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-460

APPROVAL LETTER

ANDA 76-460

NOV 26 2003

Neil Laboratories, Inc.
Attention: Bharat Patel
55 Lake Drive
P.O. Box 1088
East Windsor, NJ 08520

Dear Sir:

This is in reference to your abbreviated new drug application dated July 12, 2002, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ibuprofen Tablets USP, 200 mg.

Reference is also made to your amendments dated March 12, May 16, May 20, August 11, and August 12, 2003.

We have completed the review of this abbreviated application and have concluded that the drug is safe and effective for use as recommended in the submitted Over-The-Counter (OTC) labeling. Accordingly the application is approved. The Division of Bioequivalence has determined your Ibuprofen Tablets USP, 200 mg to be bioequivalent to the listed drug (Motrin IB® 200 mg Tablets of McNeil Consumer Products Company, Division of McNeilab, Inc.). Your dissolution testing should be incorporated into the stability and quality control program using the same method proposed in your application.

Under Section 506A of the Act, certain changes in the conditions described in this abbreviated application require an approved supplemental application before the change may be made.

Post-marketing reporting requirements for this abbreviated application are set forth in 21 CFR 314.80-81 and 314.98.

The Office of Generic Drugs should be advised of any change in the marketing status of this drug.

Sincerely yours,

Gary Buehler 11/26/03
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 76-460
Division File
Field Copy
HFD-610/R. West
HFD-330
HFD-205
HFD-610/Orange Book Staff

Endorsements:
HFD-620/S.Dhanesar/
HFD-623/A.Mueller/
HFD-617/C.Kiester/
HFD-613/J.Barlow/
HFD-613/J.Grace/

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F/T by:ard/11/7/03

APPROVAL

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-460

LABELING

76-460

Drug Facts (continued)

Directions

■ do not take more than directed

adults and children 12 years and older	■ take 1 tablet every 4 to 6 hours while symptoms persist ■ if pain or fever does not respond to 1 tablet, 2 tablets may be used, but do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ the smallest effective dose should be used
children under 12 years	■ ask a doctor

Other Information do not use if the imprinted foil seal under cap is broken or missing. ■ store at room temperature. ■ avoid excessive heat above 40°C (104°F).

Inactive ingredients black iron oxide, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, red iron oxide, stearic acid, titanium dioxide, yellow iron oxide.

NDC 60242-327-01

NL

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

100 Brown Coated Tablets **200 mg Each**

NL

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

100 Brown Coated Tablets 200 mg Each

Manufactured By:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520

APPROVED

Made in US

3 60242 32701 4

Lot No.

Exp Date

Drug Facts

Active Ingredient (in each tablet) — **Purposes**

Ibuprofen USP, 200 mg ..... Pain Reliever/Fever Reducer

Uses temporarily relieves minor aches and pains due to:

- headache
- minor pain of arthritis
- backache
- menstrual cramps
- muscular aches
- toothache
- the common cold
- reduces fever

Warnings

Allergy alert: Ibuprofen may cause a severe allergic reaction which may include:

- hives
- facial swelling
- asthma (wheezing)
- shock

Alcohol Warning If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer

Ask a doctor before use if you have

■ stomach pain ■ problems or serious side effects from taking pain relievers or fever reducers

▼

*This product is not manufactured or distributed by McNeil Consumer Healthcare, owner of the registered trademark MOTRIN®.

NOV 26 2009

Drug Facts (continued)

Ask a doctor or pharmacist before use if you are

- under a doctor's care for any serious condition
- taking any other drug
- taking any other product that contains Ibuprofen, or any other pain reliever/fever reducer

When using this product give with food or milk if stomach upset occurs

Stop use and see a doctor if

- an allergic reaction occurs. Seek medical help right away.
- pain gets worse or lasts more than 10 days
- fever gets worse or lasts more than 3 days
- stomach pain or upset gets worse or lasts
- redness or swelling is present in the painful area
- any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

▼

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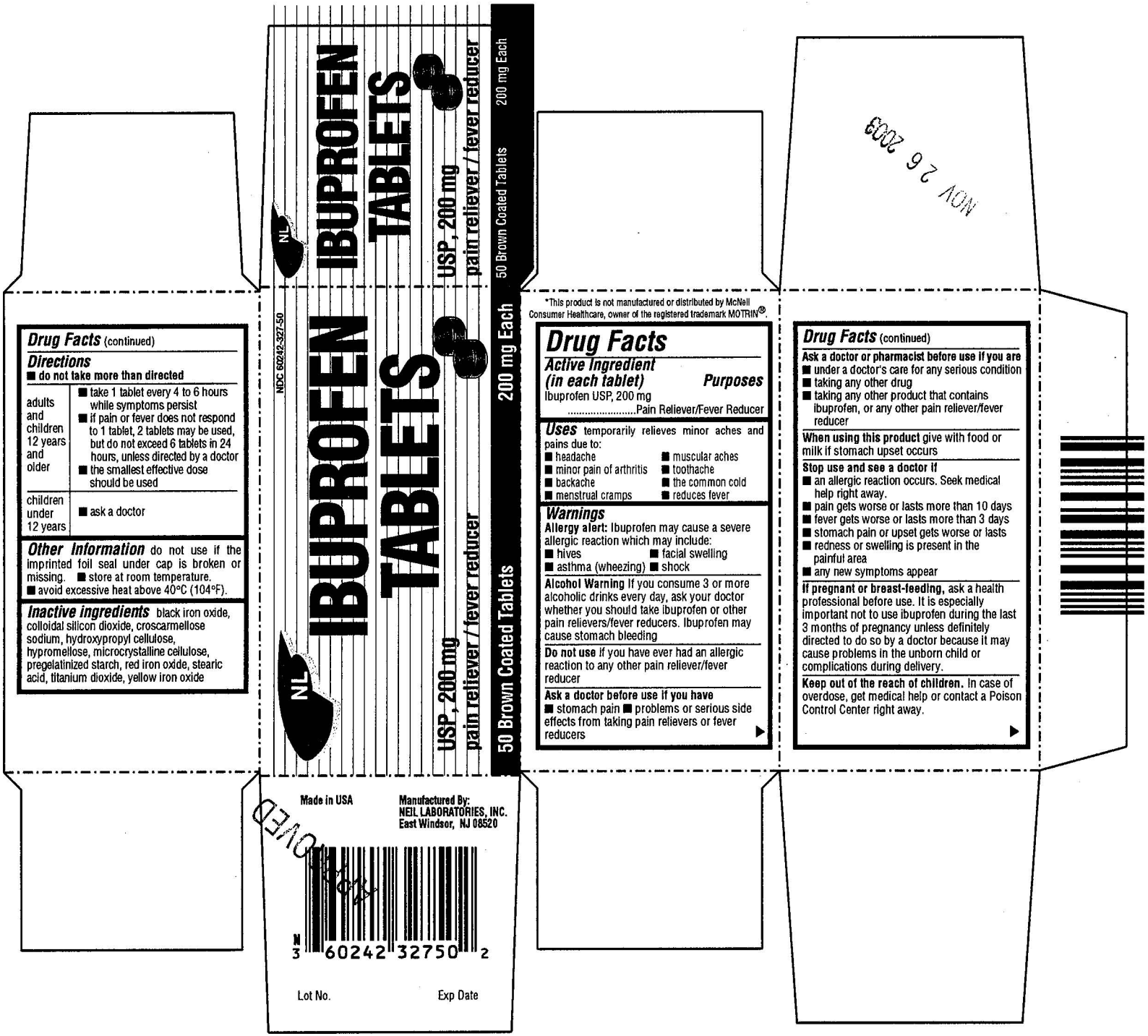
IBUPROFEN TABLETS
USP, 200 mg
pain reliever / fever reducer
50 Brown Coated Tablets
200 mg Each
NDC 60242-327-50
NL
Drug Facts (continued)
Directions
■ do not take more than directed
adults and children 12 years and older
■ take 1 tablet every 4 to 6 hours while symptoms persist
■ if pain or fever does not respond to 1 tablet, 2 tablets may be used, but do not exceed 6 tablets in 24 hours, unless directed by a doctor
■ the smallest effective dose should be used
children under 12 years
■ ask a doctor
Other Information do not use if the imprinted foil seal under cap is broken or missing. ■ store at room temperature. ■ avoid excessive heat above 40°C (104°F).
Inactive ingredients black iron oxide, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, red iron oxide, stearic acid, titanium dioxide, yellow iron oxide
Made in USA
Manufactured By:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520
3 60242 32750 2
Lot No.
Exp Date
*This product is not manufactured or distributed by McNeil Consumer Healthcare, owner of the registered trademark MOTRIN®.
Drug Facts
Active Ingredient (in each tablet)
Purposes
Ibuprofen USP, 200 mg
.....Pain Reliever/Fever Reducer
Uses temporarily relieves minor aches and pains due to:
■ headache
■ minor pain of arthritis
■ backache
■ menstrual cramps
■ muscular aches
■ toothache
■ the common cold
■ reduces fever
Warnings
Allergy alert: Ibuprofen may cause a severe allergic reaction which may include:
■ hives
■ facial swelling
■ asthma (wheezing)
■ shock
Alcohol Warning If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding
Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer
Ask a doctor before use if you have
■ stomach pain ■ problems or serious side effects from taking pain relievers or fever reducers
Drug Facts (continued)
Ask a doctor or pharmacist before use if you are
■ under a doctor's care for any serious condition
■ taking any other drug
■ taking any other product that contains ibuprofen, or any other pain reliever/fever reducer
When using this product give with food or milk if stomach upset occurs
Stop use and see a doctor if
■ an allergic reaction occurs. Seek medical help right away.
■ pain gets worse or lasts more than 10 days
■ fever gets worse or lasts more than 3 days
■ stomach pain or upset gets worse or lasts
■ redness or swelling is present in the painful area
■ any new symptoms appear
If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.
Keep out of the reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.
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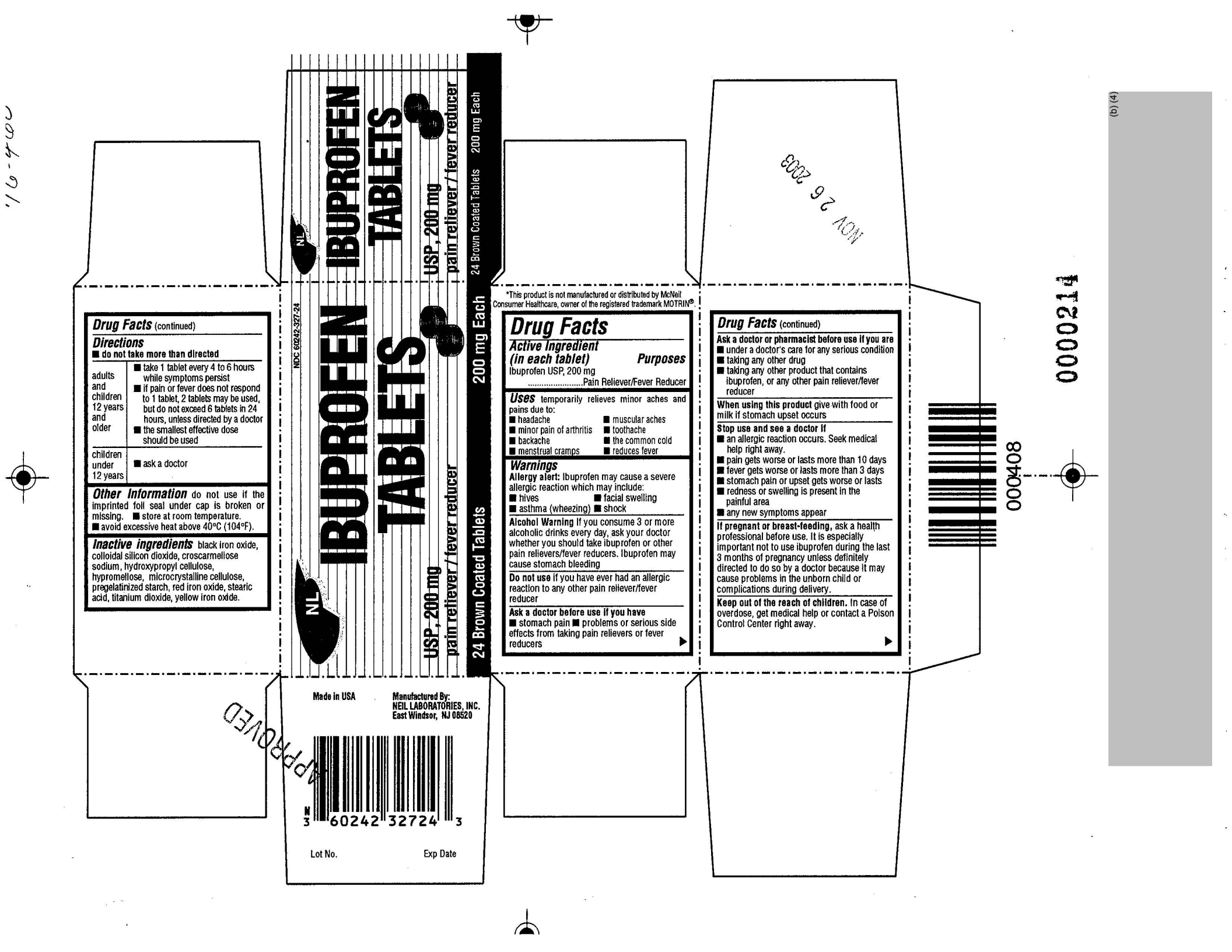
76-460



Drug Facts (continued)

Directions

■ do not take more than directed

adults and children 12 years and older	■ take 1 tablet every 4 to 6 hours while symptoms persist ■ if pain or fever does not respond to 1 tablet, 2 tablets may be used, but do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ the smallest effective dose should be used
children under 12 years	■ ask a doctor

Other Information do not use if the imprinted foil seal under cap is broken or missing. ■ store at room temperature. ■ avoid excessive heat above 40°C (104°F).

Inactive ingredients black iron oxide, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, red iron oxide, stearic acid, titanium dioxide, yellow iron oxide.

NDC 60242-327-24

NL

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

24 Brown Coated Tablets

200 mg Each

Made in USA

Manufactured By:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520

N 3 60242 32724 3

Lot No.

Exp Date

APPROVED

*This product is not manufactured or distributed by McNeil Consumer Healthcare, owner of the registered trademark MOTRIN®.

Drug Facts

Active Ingredient (in each tablet) — **Purposes**

Ibuprofen USP, 200 mg ..... Pain Reliever/Fever Reducer

Uses temporarily relieves minor aches and pains due to:

- ■ headache
- ■ minor pain of arthritis
- ■ backache
- ■ menstrual cramps
- ■ muscular aches
- ■ toothache
- ■ the common cold
- ■ reduces fever

Warnings

Allergy alert: Ibuprofen may cause a severe allergic reaction which may include:

- ■ hives
- ■ facial swelling
- ■ asthma (wheezing)
- ■ shock

Alcohol Warning If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer

Ask a doctor before use if you have

■ stomach pain ■ problems or serious side effects from taking pain relievers or fever reducers ▶

Drug Facts (continued)

Ask a doctor or pharmacist before use if you are

- ■ under a doctor's care for any serious condition
- ■ taking any other drug
- ■ taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product give with food or milk if stomach upset occurs

Stop use and see a doctor if

- ■ an allergic reaction occurs. Seek medical help right away.
- ■ pain gets worse or lasts more than 10 days
- ■ fever gets worse or lasts more than 3 days
- ■ stomach pain or upset gets worse or lasts
- ■ redness or swelling is present in the painful area
- ■ any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

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APPROVED

NDC 60242-325-01

NL

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reduced

100 White Coated Tablets 200 mg Each

NL

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

100 White Coated Tablets 200 mg Each

*This product is not manufactured or distributed by McNeil Consumer Healthcare, owner of the registered trademark MOTRIN®

Drug Facts

Active Ingredient (in each tablet) — **Purposes**

Ibuprofen USP, 200 mg ..... Pain Reliever/Fever Reducer

Uses temporarily relieves minor aches and pains due to:

- headache
- minor pain of arthritis
- backache
- menstrual cramps
- muscular aches
- toothache
- the common cold
- reduces fever

Warnings

Allergy alert: Ibuprofen may cause a severe allergic reaction which may include:

- hives
- asthma (wheezing)
- facial swelling
- shock

Alcohol Warning If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer

Ask a doctor before use if you have

- stomach pain
- problems or serious side effects from taking pain relievers or fever reducers

Drug Facts (continued)

Ask a doctor or pharmacist before use if you are

- under a doctor's care for any serious condition
- taking any other drug
- taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product give with food or milk if stomach upset occurs

Stop use and see a doctor if

- an allergic reaction occurs. Seek medical help right away.
- pain gets worse or lasts more than 10 days
- fever gets worse or lasts more than 3 days
- stomach pain or upset gets worse or lasts
- redness or swelling is present in the painful area
- any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Drug Facts (continued)

Directions

do not take more than directed

adults and children 12 years and older	■ take 1 tablet every 4 to 6 hours while symptoms persist ■ if pain or fever does not respond to 1 tablet, 2 tablets may be used, but do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ the smallest effective dose should be used
children under 12 years	■ ask a doctor

Other Information do not use if the imprinted foil seal under cap is broken or missing. ■ store at room temperature. ■ avoid excessive heat above 40°C (104°F).

Inactive ingredients colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, stearic acid, titanium dioxide

Made in USA

Manufactured By:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520

Lot No.

Exp Date

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NOV 26 2003

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(b) (4)

76-460

APPROVED

NDC 60242-325-50

NL

IBUPROFEN TABLETS

USP, 200 mg
pain reliever / fever reducer

50 White Coated Tablets 200 mg Each

NL

IBUPROFEN TABLETS

USP, 200 mg
pain reliever / fever reducer

50 White Coated Tablets 200 mg Each

Made in USA

Manufactured By:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520

Lot No.

Exp Date

3 60242 32550 8

*This product is not manufactured or distributed by McNeil Consumer Healthcare, owner of the registered trademark MOTRIN®

Drug Facts

Active Ingredient (in each tablet) — **Purposes**

Ibuprofen USP, 200 mg ..... Pain Reliever/Fever Reducer

Uses temporarily relieves minor aches and pains due to:

- headache
- minor pain of arthritis
- backache
- menstrual cramps
- muscular aches
- toothache
- the common cold
- reduces fever

Warnings

Allergy alert: Ibuprofen may cause a severe allergic reaction which may include:

- hives
- asthma (wheezing)
- facial swelling
- shock

Alcohol Warning If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer

Ask a doctor before use if you have

- stomach pain
- problems or serious side effects from taking pain relievers or fever reducers

Drug Facts (continued)

Ask a doctor or pharmacist before use if you are

- under a doctor's care for any serious condition
- taking any other drug
- taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product give with food or milk if stomach upset occurs

Stop use and see a doctor if

- an allergic reaction occurs. Seek medical help right away.
- pain gets worse or lasts more than 10 days
- fever gets worse or lasts more than 3 days
- stomach pain or upset gets worse or lasts
- redness or swelling is present in the painful area
- any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Drug Facts (continued)

Directions

do not take more than directed	
adults and children 12 years and older	■ take 1 tablet every 4 to 6 hours while symptoms persist ■ if pain or fever does not respond to 1 tablet, 2 tablets may be used, but do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ the smallest effective dose should be used
children under 12 years	■ ask a doctor

Other Information do not use if the imprinted foil seal under cap is broken or missing. ■ store at room temperature. ■ avoid excessive heat above 40°C (104°F).

Inactive ingredients colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, stearic acid, titanium dioxide

NOV 26 2003

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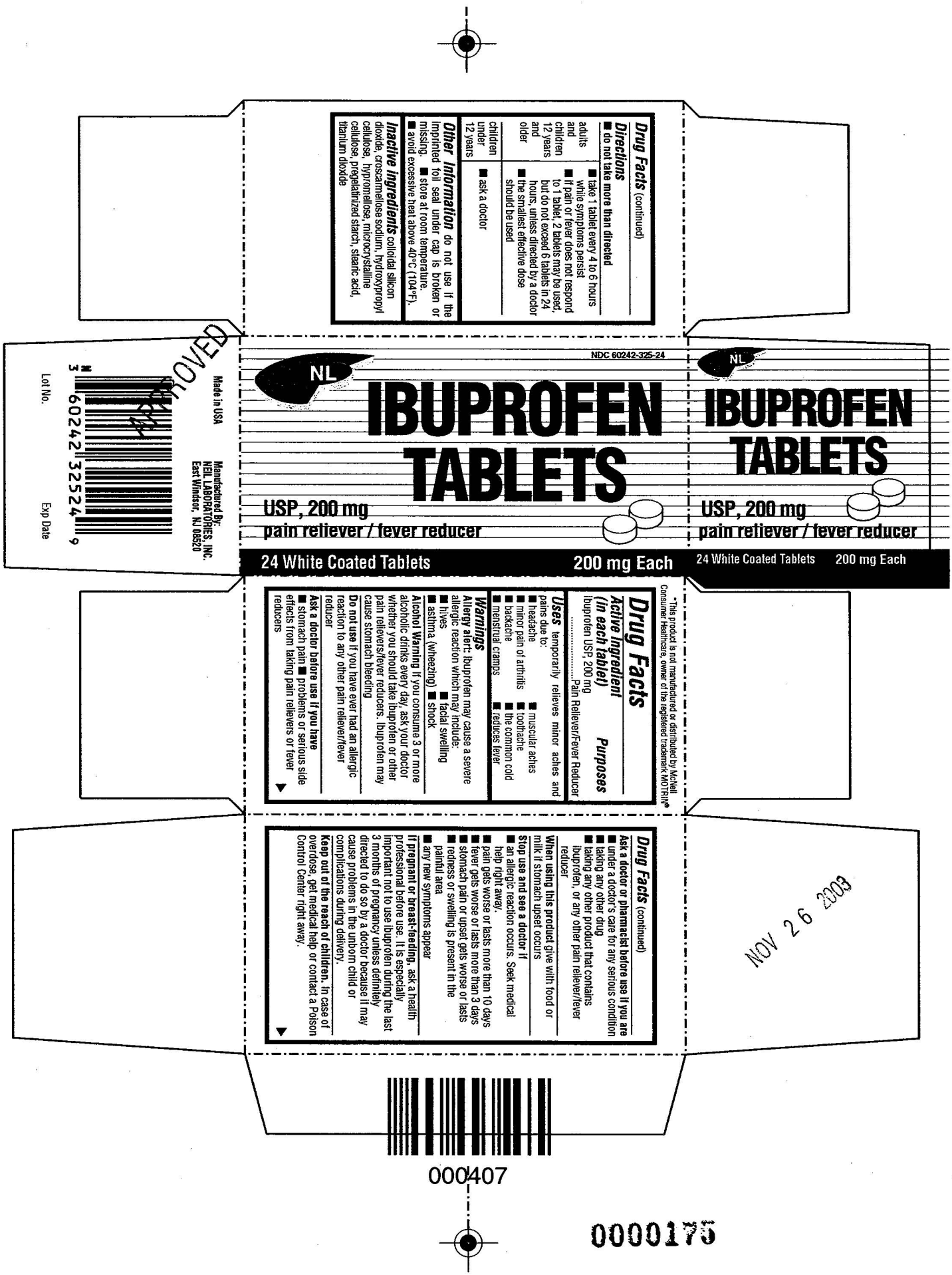
76-460



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(b) (4)

76-460

(b) (4)

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

1000 BROWN COATED TABLETS
200 mg Each

NL

NDC 60242-327-10

(b) (4)

NOV 26 2003

Drug Facts

Active Ingredient *(in each tablet)* — **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings **Allergy alert:** Ibuprofen may cause a severe allergic reaction which may include:
■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take Ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

Ask a doctor before use if you have ■ stomach pain ■ problems or serious side effects from taking pain relievers/fever reducers.

Ask a doctor or pharmacist before use if you are ■ under doctor's care for any serious condition ■ taking any other drug ■ taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product take with food or milk if stomach upset occurs

Stop use and ask a doctor if ■ an allergic reaction occurs. Seek medical help right away. ■ pain gets worse or lasts more than 10 days ■ fever gets worse or lasts more than 3 days ■ stomach pain or upset gets worse or lasts ■ redness or swelling is present in the painful area ■ any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use Ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. **Keep out of the reach of children.** In case of accidental overdose, get medical help or contact a Poison Control Center right away.

Directions ■ **do not take more than directed**
■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist ■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing ■ store at room temperature ■ avoid excessive heat 40°C (104°F)

Inactive Ingredients: black iron oxide, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, red iron oxide, stearic acid, titanium dioxide, yellow iron oxide.

Manufactured by:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

APPROVED

N 60242-327-10 6
3

Lot No. Exp. Date

(b) (4)

SIZE: 3" X 7.25"

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76-460

(b) (4)

SIZE: 2.5" X 6"

NL NDC 60242-327-05

NOV 26 2003

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

500 BROWN COATED TABLETS
200 mg Each

Drug Facts

Active Ingredient (in each tablet)	Purpose
Ibuprofen 200 mg	Pain Reliever/Fever Reducer

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

Warnings Allergy alert: ibuprofen may cause a severe allergic reaction which may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

Ask a doctor before use if you have ■ stomach pain ■ problems or serious side effects from taking pain relievers/fever reducers.

Ask a doctor or pharmacist before use if you are ■ under doctor's care for any serious condition ■ taking any other drug ■ taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product take with food or milk if stomach upset occurs

Stop use and ask a doctor if ■ an allergic reaction occurs. Seek medical help right away. ■ pain gets worse or lasts more than 10 days ■ fever gets worse or lasts more than 3 days ■ stomach pain or upset gets worse or lasts ■ redness or swelling is present in the painful area ■ any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. Keep out of the reach of children. In case of accidental overdose, get medical help or contact a Poison Control Center right away.

Directions ■ do not take more than directed. ■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist ■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing. ■ store at room temperature ■ avoid excessive heat 40°C (104°F)

Inactive Ingredients: carnauba wax, colloidal silicon dioxide, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, pigment, pregelatinized starch, red iron oxide, stearic acid, titanium dioxide, yellow iron oxide

APPROVED

Manufactured by:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

N 60242-327-05 2 3

Lot No. Exp. Date

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IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

250 BROWN COATED TABLETS
200 mg Each

NDC 60242-327-03

NOV 26 2003

Drug Facts

Active Ingredient *(in each tablet)* — **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings Allergy alert: Ibuprofen may cause a severe allergic reaction which may include:
■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

Ask a doctor before use if you have
■ stomach pain ■ problems or serious side effects from taking pain relievers/fever reducers.

Ask a doctor or pharmacist before use if you are
■ under doctor's care for any serious condition ■ taking any other drug ■ taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product take with food or milk if stomach upset occurs

Stop use and ask a doctor if
■ an allergic reaction occurs. Seek medical help right away. ■ pain gets worse or lasts more than 10 days ■ fever gets worse or lasts more than 3 days ■ stomach pain or upset gets worse or lasts ■ redness or swelling is present in the painful area ■ any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. Keep out of the reach of children. In case of accidental overdose, get medical help or contact a Poison Control Center right away.

Directions ■ do not take more than directed.
■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist
■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing. ■ store at room temperature ■ avoid excessive heat 40°C (104°F).

Inactive Ingredients: black iron oxide, colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, red iron oxide, stearic acid, titanium dioxide, yellow iron oxide.

APPROVED

Manufactured by:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

N 3 60242-327-03 8

Lot No. Exp. Date

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(b) (4)

SIZE: 2.5" X 6"

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FY 6-40 (b) (4)

00001121

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(b) (4)

NDC 60242-327-01

NOV 26 2009

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

100 BROWN COATED TABLETS
200 mg Each

Drug Facts

Active Ingredient *(in each tablet)* **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings **Allergy alert:** Ibuprofen may cause a severe allergic reaction which may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use Ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Save carton for complete WARNINGS. Save carton for future reference.

Directions ■ **do not take more than directed.**
■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours if the symptoms persist ■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing ■ store at room temperature ■ avoid excessive heat 40°C (104°F)

Manufactured by:
NEI LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

N 3 60242-327-01 4

Lot No. Exp. Date

SIZE: 1.625" X 5"

(b) (4)

(b) (4)

D6-460

(b) (4)

NDC 60242-327-50

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

50 BROWN COATED TABLETS
200 mg Each

NOV 26 2003

Drug Facts

Active Ingredient *(in each tablet)* — **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings **Allergy alert:** Ibuprofen may cause a severe allergic reaction which may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take Ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

If **pregnant or breast-feeding,** ask a health professional before use. It is especially important not to use Ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Save carton for complete WARNINGS. Save carton for future reference.

Directions ■ **do not take more than directed.** ■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist ■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing. ■ store at room temperature ■ avoid excessive heat 40°C (104°F).

Manufactured by:
NCK LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

N 3 60242-327-50 2

Lot No. Exp. Date

APPROVED

(b) (4)

(b) (4)

SIZE: 1.625" X 5"

(b) (4)

00001108

76-460

(b) (4)

NDC 60242-327-24

NOV 26 2003

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

24 BROWN COATED TABLETS
200 mg Each

Drug Facts

Active Ingredient *(in each tablet)* **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings **Allergy alert:** Ibuprofen may cause a severe allergic reaction which may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take Ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use Ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Save carton for complete WARNINGS. Save carton for future reference.

Directions ■ **do not take more than directed.** ■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist ■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing. ■ store at room temperature ■ avoid excessive heat 40°C (104°F).

Manufactured by:
NCL LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

N 60242-327-24 3

APPROVED

Lot No. Exp. Date

(b) (4)

(b) (4)

SIZE: 1.625" X 5"

(b) (4)

96-960

00000095

2800000

(b) (4)

(b) (4)

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

1000 WHITE COATED TABLETS
200 mg Each

NL

NDC 60242-325-10

NOV 26 2003

Drug Facts

Active Ingredient *(in each tablet)* — **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings **Allergy alert:** Ibuprofen may cause a severe allergic reaction which may include:
■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take Ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

Ask a doctor before use if you have ■ stomach pain ■ problems or serious side effects from taking pain relievers/fever reducers.

Ask a doctor or pharmacist before use if you are ■ under doctor's care for any serious condition ■ taking any other drug ■ taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product take with food or milk if stomach upset occurs

Stop use and ask a doctor if ■ an allergic reaction occurs. Seek medical help right away. ■ pain gets worse or lasts more than 10 days ■ fever gets worse or lasts more than 3 days ■ stomach pain or upset gets worse or lasts ■ redness or swelling is present in the painful area ■ any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use Ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. **Keep out of the reach of children.** In case of accidental overdose, get medical help or contact a Poison Control Center right away.

Directions ■ do not take more than directed
■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist
■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing ■ store at room temperature ■ avoid excessive heat 40°C (104°F)

Inactive Ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, stearic acid, titanium dioxide.

Manufactured by:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

APPROVED

N 3 60242-325-10 2

Lot No. Exp. Date

SIZE: 3" X 7.25"

(b) (4)

004-96

6300000

(b) (4)

NDC 60242-325-05

NOV 26 2003

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

500 WHITE COATED TABLETS
200 mg Each

Drug Facts

Active Ingredient *(in each tablet)* **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings Allergy alert: ibuprofen may cause a severe allergic reaction which may include:
■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

Ask a doctor before use if you have
■ stomach pain ■ problems or serious side effects from taking pain relievers/fever reducers.

Ask a doctor or pharmacist before use if you are
■ under doctor's care for any serious condition ■ taking any other drug ■ taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product take with food or milk if stomach upset occurs

Stop use and ask a doctor if
■ an allergic reaction occurs. Seek medical help right away. ■ pain gets worse or lasts more than 10 days
■ fever gets worse or lasts more than 3 days ■ stomach pain or upset gets worse or lasts
■ redness or swelling is present in the painful area ■ any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. **Keep out of the reach of children.** In case of accidental overdose, get medical help or contact a Poison Control Center right away.

Directions ■ do not take more than directed.
■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist
■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing. ■ store at room temperature ■ avoid excessive heat 40°C (104°F).

Inactive Ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, stearic acid, titanium dioxide.

Manufactured by:
NEIL LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

APPROVED

60242-325-05 8

Lot No. Exp. Date

(b) (4)

(b) (4)

SIZE: 2.5" X 6"

(b) (4)

NDC 60242-325-03

NOV 26 2003

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

250 WHITE COATED TABLETS
200 mg Each

Drug Facts

Active Ingredient *(in each tablet)* **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings **Allergy alert:** Ibuprofen may cause a severe allergic reaction which may include:
■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

Ask a doctor before use if you have
■ stomach pain ■ problems or serious side effects from taking pain relievers/fever reducers.

Ask a doctor or pharmacist before use if you are
■ under doctor's care for any serious condition ■ taking any other drug ■ taking any other product that contains ibuprofen, or any other pain reliever/fever reducer

When using this product take with food or milk if stomach upset occurs

Stop use and ask a doctor if
■ an allergic reaction occurs. Seek medical help right away. ■ pain gets worse or lasts more than 10 days ■ fever gets worse or lasts more than 3 days ■ stomach pain or upset gets worse or lasts ■ redness or swelling is present in the painful area ■ any new symptoms appear

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery. **Keep out of the reach of children.** In case of accidental overdose, get medical help or contact a Poison Control Center right away.

Directions ■ **do not take more than directed.**
■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist ■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing. ■ store at room temperature ■ avoid excessive heat 40°C (104°F).

Inactive Ingredients: colloidal silicon dioxide, croscarmellose sodium, hydroxypropyl cellulose, hypromellose, microcrystalline cellulose, pregelatinized starch, stearic acid, titanium dioxide.

APPROVED N3

Manufactured By:
NEIL LABORATORIES INC.
East Windsor, NJ 08520
Made in USA

60242-325-03 4

Lot No. Exp. Date

(b) (4)

(b) (4)

(b) (4)

SIZE: 2.5" X 6"

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76-460

(b) (4)

(b) (4)

IBUPROFEN TABLETS

USP 200 mg

pain reliever / fever reducer

100 WHITE COATED TABLETS
200 mg Each

NDC 60242-325-01

Drug Facts

Active Ingredient *(in each tablet)* **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings **Allergy alert:** Ibuprofen may cause a severe allergic reaction which may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take Ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use Ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Save carton for complete WARNINGS. Save carton for future reference.

Directions ■ do not take more than directed.
■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist ■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing. ■ store at room temperature ■ avoid excessive heat 40°C (104°F).

APPROVED

Manufactured by:
MCK LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

N 3 60242-325-01 0

Lot No. Exp. Date

NOV 26 2003

(b) (4)

SIZE: 1.625" X 5"

0000043

116-400

76-460

(b) (4)

SIZE: 1.265" X 5"

(b) (4)

NL NDC 60242-325-50

NOV 26 2003

IBUPROFEN TABLETS

USP, 200 mg

pain reliever / fever reducer

50 WHITE COATED TABLETS
200 mg Each

Drug Facts

Active Ingredient *(in each tablet)* — **Purpose**

Ibuprofen 200 mg ..... Pain Reliever/Fever Reducer

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

Warnings Allergy alert: Ibuprofen may cause a severe allergic reaction which may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock

Alcohol Warning: If you consume 3 or more alcoholic drinks every day, ask your doctor whether you should take Ibuprofen or other pain relievers/fever reducers. Ibuprofen may cause stomach bleeding.

Do not use if you have ever had an allergic reaction to any other pain reliever/fever reducer.

If pregnant or breast-feeding, ask a health professional before use. It is especially important not to use Ibuprofen during the last 3 months of pregnancy unless definitely directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Save carton for complete WARNINGS. Save carton for future reference.

Directions ■ do not take more than directed. ■ adults and children 12 years and older: take 1-2 tablets every 4 to 6 hours while symptoms persist ■ do not exceed 6 tablets in 24 hours, unless directed by a doctor ■ children under 12 years: ask a doctor

Other Information ■ do not use if the imprinted foil seal is broken or missing. ■ store at room temperature ■ avoid excessive heat 40°C (104°F).

Manufactured by:
NEL LABORATORIES, INC.
East Windsor, NJ 08520
Made in USA

3 60242-325-50 8

Lot No. Exp. Date

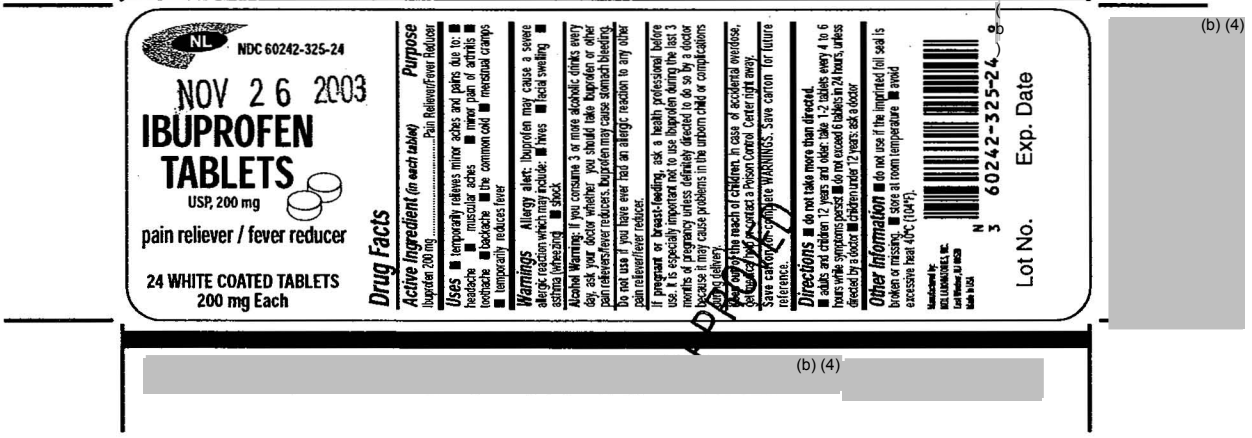
(b) (4)

0000030

76-460

(b) (4)

SIZE: 1.625" X 5"



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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-460

LABELING REVIEWS

APPROVAL SUMMARY
REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number: 76-460
Date of Submission: August 12, 2003
Applicant's Name: Neil Laboratories, Inc..
Established Name: Ibuprofen tablets USP, 200 mg

APPROVAL SUMMARY

1. **Do you have 12 Final Printed Labels and Labeling? Yes**

2. **CONTAINER – Bottles of 24, 50, 100, 250, 500 and 1000 tablets**
   Satisfactory in **final print** as of the August 12, 2003
   (See blue jacket volume 4.1)

3. **CARTON – 24's 50's and 100's**
   Satisfactory in **final print** as of the August 12, 2003
   (See blue jacket volume 4.1)

4. Revisions needed post-approval; None

5. **Patent Information:**
   Patent Data – NDA 19-012

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	***None***	None		None	None

Exclusivity Data– NDA 19-012

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

BASIS OF APPROVAL:
Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Motrin IB
NDA Number: N 19-012
NDA Drug Name: Motrin IB
NDA Firm: McNeil; N 19-012/S-028; Approved September 7, 2001.
Date of Approval of NDA Insert and supplement: September 7, 2001; NDA 19-012/S-028
Has this been verified by the MIS system for the NDA? Yes
Was this approval based upon an OGD labeling guidance? No
Basis of Approval for the Container Labels: Most recently approved labeling of the reference listed drug, and Motrin IB®.
Basis of Approval for the Carton Labeling: Most recently approved labeling of the reference listed drug, and Motrin IB®

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24	X		

Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		X	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			X
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			X
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	Yes	No	N.A.
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	
Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		X	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		X	

Has the firm failed to describe the scoring in the HOW SUPPLIED section?		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			X
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		X	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?			
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values; insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. The labeling submitted by the firm was based on the most recently approved labeling for this drug product. (Approved September 7, 2001/Supplement 28). We requested some additional revisions above

2. Patent Data – NDA 19-012

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	***None***	None		None	None

Exclusivity Data– NDA 19-012

Code	Reference	Expiration	Labeling Impact
None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

3. Storage/Dispensing Conditions:
   NDA: Store at room temperature. Avoid excessive heat 40°C(104°F).
   ANDA: Store at room temperature. Avoid excessive heat 40°C(104°F).

4. Product Line:
   The applicant proposes to market their product as 200 mg strength tablets available in bottles of 24, 50,100, 250, 500 and 1000.

The tablet imprinting have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206, et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95. (See **pg. 0002921 vol. B. 1.3)**

5. Inactive Ingredients:
   The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the **statement of components appearing on page** 0002514, Vol B. 1.1.

6. Container/Closure(See page 0002849 in Vol. B.. 1.2)
   Containers: HDPE
   Closure: non-CRC closures for bottles of 500 and 1000 tablets. CRC closures for bottles of 24, 50, 100 and 250 tablets.

7. All manufacturing will be done by Neil Laboratories, Inc. (See pg. 2649 in vol. B. 1.2)

Date of Review: 9/5/03 Date of Submission: 8/12/03
Primary Reviewer: Jim Barlow Date: 9/5/03

Team Leader: John Grace Date: 9/8/2003

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cc:

ANDA: 76-460
DUP/DIVISION FILE
HFD-613/JBarlow/JGrace (no cc)
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Review

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number:	76-460
Date of Submission:	May 20, 2003
Applicant's Name:	Neil Laboratories, Inc..
Established Name:	Ibuprofen tablets USP, 200 mg

Labeling Deficiencies:

1. **CONTAINER – Bottles of 24, 50, 100, 250, 500 and 1000 tablets**
   Satisfactory in **draft** as of the May 20, 2003

2. **CARTON – 24's 50's and 100's**
   Satisfactory in **draft** as of the May 20, 2003

Please prepare and submit 12 copies of final printed labels and labeling.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-

http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

REVIEW OF PROFESSIONAL LABELING CHECKLIST

Established Name	Yes	No	N.A.
Different name than on acceptance to file letter?		X	
Is this product a USP item? If so, USP supplement in which verification was assured. USP 24	X		
Is this name different than that used in the Orange Book?		X	
If not USP, has the product name been proposed in the PF?			X
Error Prevention Analysis			
Has the firm proposed a proprietary name? If yes, complete this subsection.		X	
Do you find the name objectionable? List reasons in FTR, if so. Consider: Misleading? Sounds or looks like another name? USAN stem present? Prefix or Suffix present?			X
Has the name been forwarded to the Labeling and Nomenclature Committee? If so, what were the recommendations? If the name was unacceptable, has the firm been notified?			X
Packaging			
Is this a new packaging configuration, never been approved by an ANDA or NDA? If yes, describe in FTR.		X	
Is this package size mismatched with the recommended dosage? If yes, the Poison Prevention Act may require a CRC.		X	
Does the package proposed have any safety and/or regulatory concerns?		X	
If IV product packaged in syringe, could there be adverse patient outcome if given by direct IV injection?			X
Conflict between the DOSAGE AND ADMINISTRATION and INDICATIONS sections and the packaging configuration?		X	
Is the strength and/or concentration of the product unsupported by the insert labeling?		X	
Is the color of the container (i.e. the color of the cap of a mydriatic ophthalmic) or cap incorrect?			X
Individual cartons required? Issues for FTR: Innovator individually cartoned? Light sensitive product which might require cartoning? Must the package insert accompany the product?		X	
Are there any other safety concerns?		X	
Labeling			
Is the name of the drug unclear in print or lacking in prominence? (Name should be the most prominent information on the label).		X	
Has applicant failed to clearly differentiate multiple product strengths?			X
Is the corporate logo larger than 1/3 container label? (No regulation - see ASHP guidelines)		X	
Labeling(continued)	**Yes**	**No**	**N.A.**
Does RLD make special differentiation for this label? (i.e., Pediatric strength vs Adult; Oral Solution vs Concentrate, Warning Statements that might be in red for the NDA)		X	
Is the Manufactured by/Distributor statement incorrect or falsely inconsistent between labels and labeling? Is "Jointly Manufactured by...", statement needed?		X	

Failure to describe solid oral dosage form identifying markings in HOW SUPPLIED?		X	
Has the firm failed to adequately support compatibility or stability claims which appear in the insert labeling? Note: Chemist should confirm the data has been adequately supported.			
Scoring: Describe scoring configuration of RLD and applicant (page #) in the FTR			
Is the scoring configuration different than the RLD?		X	
Has the firm failed to describe the scoring in the HOW SUPPLIED section?		X	
Inactive Ingredients: (FTR: List page # in application where inactives are listed)			
Does the product contain alcohol? If so, has the accuracy of the statement been confirmed?			X
Do any of the inactives differ in concentration for this route of administration?		X	
Any adverse effects anticipated from inactives (i.e., benzyl alcohol in neonates)?		X	
Is there a discrepancy in inactives between DESCRIPTION and the composition statement?		X	
Has the term "other ingredients" been used to protect a trade secret? If so, is claim supported?		X	
Failure to list the coloring agents if the composition statement lists e.g., Opacode, Opaspray?		X	
Failure to list gelatin, coloring agents, antimicrobials for capsules in DESCRIPTION?			X
Failure to list dyes in imprinting inks? (Coloring agents e.g., iron oxides need not be listed)		X	
USP Issues: (FTR: List USP/NDA/ANDA dispensing/storage recommendations)			
Do container recommendations fail to meet or exceed USP/NDA recommendations? If so, are the recommendations supported and is the difference acceptable?			
Does USP have labeling recommendations? If any, does ANDA meet them?		X	
Is the product light sensitive? If so, is NDA and/or ANDA in a light resistant container?		X	
Failure of DESCRIPTION to meet USP Description and Solubility information? If so, USP information should be used. However, only include solvents appearing in innovator labeling.			
Bioequivalence Issues: (Compare bioequivalency values: insert to study. List Cmax, Tmax, T 1/2 and date study acceptable)			
Insert labeling references a food effect or a no-effect? If so, was a food study done?		X	
Has CLINICAL PHARMACOLOGY been modified? If so, briefly detail where/why.		X	
Patent/Exclusivity Issues?: FTR: Check the Orange Book edition or cumulative supplement for verification of the latest Patent or Exclusivity. List expiration date for all patents, exclusivities, etc. or if none, please state.			

FOR THE RECORD:

1. The labeling submitted by the firm was based on the most recently approved labeling for this drug product. (Approved September 7, 2001/Supplement 28). We requested some additional revisions above

2. Patent Data – NDA 19-012

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	***None***	None		None	None

Exclusivity Data– NDA 19-012

Code	Reference	Expiration	Labeling Impact

None	There is no unexpired exclusivity for this product in the Orange Book Database.	N/A	None

3. Storage/Dispensing Conditions:
   NDA: Store at room temperature. Avoid excessive heat 40°C(104°F).
   ANDA: Store at room temperature. Avoid excessive heat 40°C(104°F).

4. Product Line:
   The applicant proposes to market their product as 200 mg strength tablets available in bottles of 24, 50,100, 250, 500 and 1000.

   The tablet imprinting have been accurately described in the HOW SUPPLIED section as required by 21 CFR 206, et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95. (See **pg. 0002921 vol. B. 1.3)**

5. Inactive Ingredients:
   The listing of inactive ingredients in the DESCRIPTION section of the package insert appears to be consistent with the listing of inactive ingredients found in the **statement of components appearing on page** 0002514, Vol B. 1.1.

6. Container/Closure(See page 0002849 in Vol. B.. 1.2)
   Containers: HDPE
   Closure: non-CRC closures for bottles of 500 and 1000 tablets. CRC closures for bottles of 24, 50, 100 and 250 tablets.

7. All manufacturing will be done by Neil Laboratories, Inc. (See pg. 2649 in vol. B. 1.2)

Date of Review: 7/24/03 Date of Submission: 5/20/03

Primary Reviewer: Jim Barlow Date: 7/24/03

Team Leader: John Grace Date: John J Grace 7/24/2003

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cc:

ANDA: 76-460
DUP/DIVISION FILE
HFD-613/JBarlow/JGrace (no cc)
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Review

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-460

CHEMISTRY REVIEWS

SUMMARY PACKAGE

A. ANDA NUMBER: 76-460

B. FIRM: Neil Laboratories Inc.
55 Lake Drive
East Windsor, NJ 08520

C. DOSAGE FORM: Solid

D. STRENGTH: 200 mg

E. DRUG: Ibuprofen Tablets USP (White Film Coated and Brown Film Coated)

F. cGMP STATEMENT/EIR UPDATE STATUS: Acceptable (J. D'Ambrogio, 16-JUN-2003)

G. BIO STUDY: Acceptable (K. Dhariwal, 26-JUN-2003)

H. METHOD VALIDATION – (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S): The drug substance and the drug product have USP monographs. Analytical methods follow the USP monograph. No methods were sent out for methods validation.

I. STABILITY – ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION? Containers used in the stability studies are identical to those listed in container section. The same as proposed in the application.

J. LABELING: Acceptable (J. Barlow, 24-JULY-2003)

K. STERILIZATION VALIDATION (IF APPLICABLE): N/A

L. SIZE OF BIO BATCH – (FIRM'S SOURCE OF NDS O.K.?): (b) (4) tablets (Brown Film Coated Tablets) and (b) (4) tablets (White Film Coated Tablets)

M. SIZE OF STABILITY BATCHES – (IF DIFFERENT FROM BIO BATCH WERE THEY MANUFACTURED VIA THE SAME PROCESS?): The Bio Batch and the Stability Batches were the same batch.

N. PROPOSED PRODUCTION BATCH – MANUFACTURING PROCESS THE SAME AS BIO/STABILITY? Yes, for (b) (4) tablets (both White and Brown Film Coated Tablets)

CHEMIST: SCDhanesar, Ph.D. DATE: 9/24/03

SUPERVISOR: AMueller, Ph.D. DATE: 11-19-03

V:\FIRMSNZ\NEIL\LTRS&REV\76460APS.DOC
F/T

ANDA 76-460

Ibuprofen Tablets USP, 200 mg

Neil Laboratories, Inc.

Subhash C. Dhanesar
Chemistry Division I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 76-460

2. REVIEW #: 2

3. REVIEW DATE: 20-June-2003

4. REVIEWER: Subhash C. Dhanesar

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date
Original	July 12, 2002
Refusal to Receive Letter	September 25, 2002
Amendment	November 8, 2002
Telephone Amendment	December 2, 2002
Acceptable for Filing Letter	December 30, 2002

6. SUBMISSION (S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
New Correspondence	March 14, 2003
Amendment (CMC)	May 16, 2003
Amendment (Labeling)	May 20, 2003
Telephone Amendment	August 11, 2003
Labeling Amendment	August 12, 2003

7. NAME & ADDRESS OF APPLICANT:

Name: Neil Laboratories Inc.

Address: 55 Lake Drive, P.O. Box 1088
East Windsor, NJ 08520

Representative: Bharat Patel

Telephone: 609-448-5500
Fax: 609-443-9316
e-mail: neillabs@aol.com

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: None

b) Non-Proprietary Name (USAN): Ibuprofen

9. LEGAL BASIS FOR SUBMISSION:
Motrin IB Tablets, 200 mg manufactured by McNeil (ANDA #19012)

10. PHARMACOL. CATEGORY: NSAID

11. DOSAGE FORM: Tablets

12. STRENGTH/POTENCY: 200 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___Rx _X__OTC

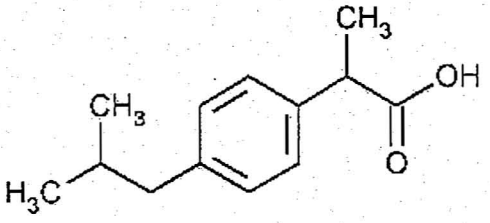
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X____Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: (±)-2-(p-Isobutylphenyl) propionic acid [15687-27-1]
Or Benzeneacetic acid, a-methyl-4-(2-methylpropyl), (±)-.
Molecular Formula: $C_{13}H_{18}O_2$
Molecular Weight: 206.28
Structural Formula:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
		(b) (4)	Ibuprofen USP	1	Adequate	04-25-03	S.Dhanesar
			Ibuprofen USP	3	Adequate	11-07-03	S.Dhanesar
		(b) (4)		4			
				4			
				4			
				4			
				4			
				4			
				4			
				4			
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				4			
				4			
				4			
				4			
				4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or there is enough data in the application, therefore the DMF did not need to be reviewed

B. Other Documents: None

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	16-JUN-03	J. D'Ambrogio
Methods Validation	N/A (USP product)		
Labeling	Acceptable	09-05-03	J. Barlow
Bioequivalence	Acceptable	6-26-03	K. Dhariwal
EA	Acceptable		
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt.
___ Yes __x__ No If no, explain reason(s) below: Minor Amendment

The Chemistry Review for ANDA 76-460

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is approvable. CMC, Labeling, EA and EES, and Bioequivalency are acceptable. Analytical methods are USP monograph methods and are acceptable.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if approvable: N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug product is White Film Coated and Brown Film Coated Ibuprofen Tablets USP, 200 mg based on McNeil's RLD Motrin IB. (b) (4) . (b) (4) . The drug product will be packaged in 24, 50, 100, 250, 500, and 1000 (bulk) tablet count sizes. CRC closure will be used for the 24, 50 and 100 tablet counts.

The ANDA/BIO batch size of the White Film Coated tablets is (b) (4) tablets and the proposed commercial batch size is (b) (4) tablets. The ANDA batch size for the Brown Film Coated Tablets is (b) (4) tablets and the proposed commercial batch size is (b) (4) tablets. In both cases the pilot batch sizes are greater than 10% of the commercial batch size making them representative of the manufacturing process.

Originally, the firm provided incomplete Exhibit Batches and incomplete packaging comments. These deficiencies are now resolved and specifications are acceptable

The drug substance is Ibuprofen USP obtained either from (b) (4) . The DMF's for these companies are adequate.

B. Description of How the Drug Product is Intended to be Used

The drug product is a tablet and will be taken orally or as prescribed by a doctor.

C. Basis for Approvability or Not-Approval Recommendation

The drug product ANDA meets all requirements for approval.

16 PAGES WITHHELD IN FULL AS B4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

S. Dhanesar, Ph.D./06-20-03/11-07-03
A. Mueller, Ph.D./06-20-03/11-07-03
C. Kiester, R.Ph./06-20-03/11-07-03

11/7/03
11-7-03
11/7/03

C. CC Block

cc: ANDA 76-460
ANDA DUP
DIV FILE
Field Copy

Endorsements:

HFD-623/SDhanesar, Ph.D./06-20-03/11-07-03 11/7/03

HFD-623/AMueller, Ph.D./06-20-03/11-07-03 11-17-03

HFD-615/Ckiester, R.Ph./06-20-03/11-07-03 11/17/03

F/T by
File: v:\firmsnz\neil\ltrs&rev\76460r02.doc

TYPE OF LETTER: APPROVABLE

ANDA 76-460

Ibuprofen Tablets USP, 200 mg

Neil Laboratories, Inc.

Subhash C. Dhanesar
Chemistry Division I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 76-460

2. REVIEW #: 1

3. REVIEW DATE: 04-FEB-03

4. REVIEWER: Subhash C. Dhanesar

5. PREVIOUS DOCUMENTS:

Previous Documents	Document Date

6. SUBMISSION (S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original	July 12, 2002
Refusal to Receive Letter	September 25, 2002
Amendment	November 8, 2002
Telephone Amendment	December 2, 2002
Acceptable for Filing Letter	December 30, 2002

7. NAME & ADDRESS OF APPLICANT:

Name: Neil Laboratories Inc.
Address: 55 Lake Drive, P.O. Box 1088
East Windsor, NJ 08520
Representative: Bharat Patel
Telephone: 609-448-5500
Fax: 609-443-9316
e-mail: neillabs@aol.com

8. DRUG PRODUCT NAME/CODE/TYPE:
a) Proprietary Name: None
b) Non-Proprietary Name (USAN): Ibuprofen

9. LEGAL BASIS FOR SUBMISSION:
Motrin IB Tablets, 200 mg manufactured by McNeil (ANDA #19012)

10. PHARMACOL. CATEGORY: Anti-inflammatory

11. DOSAGE FORM: Tablets

12. STRENGTH/POTENCY: 200 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: ___Rx _X__OTC

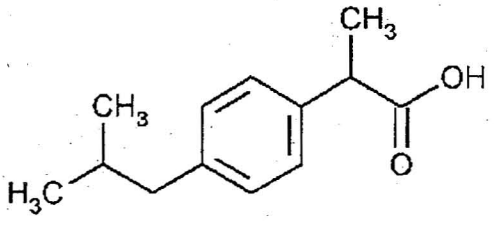
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____SPOTS product – Form Completed

__X____Not a SPOTS product

16. CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA, MOLECULAR WEIGHT:

Chemical Name: (±)-2-(p-Isobutylphenyl) propionic acid [15687-27-1]
Or Benzeneacetic acid, a-methyl-4-(2-methylpropyl), (±)-.
Molecular Formula: $C_{13}H_{18}O_2$
Molecular Weight: 206.28
Structural Formula:



17. RELATED/SUPPORTING DOCUMENTS:

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
(b) (4)			Ibuprofen USP	1	Adequate	04-25-03	S.Dhanesar
			Ibuprofen USP	3	Adequate	11-19-02	R. Bykadi
(b) (4)				4			
				4			
				4			
				4			
				4			
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[1] Action codes for DMF Table:
1 – DMF Reviewed.
Other codes indicate why the DMF was not reviewed, as follows:
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application
5 – Authority to reference not granted
6 – DMF not available
7 – Other (explain under "Comments")

[2] Adequate, Inadequate, or N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents:

DOCUMENT	APPLICATION NUMBER	DESCRIPTION

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Pending		
Methods Validation	N/A		
Labeling	Pending		
Bioequivalence	Pending		
EA	Acceptable	2/4/03	S. Dhanesar
Radiopharmaceutical	N/A		

19. ORDER OF REVIEW

The application submission(s) covered by this review was taken in the date order of receipt. __x__ Yes _____ No If no, explain reason(s) below:

The Chemistry Review for ANDA 76-460

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is not approvable due to major deficiencies in analytical chemistry, manufacturing, and in documentation.

B. Recommendation on Phase 4 (Post-Marketing) Commitments, Agreements, and/or Risk Management Steps, if approvable

N/A

II. Summary of Chemistry Assessments

A. Description of the Drug Product(s) and Drug Substance(s)

The drug product is White Film Coated and Brown Film Coated Ibuprofen Tablets USP, 200 mg based on McNeil's RLD Motrin IB. (b) (4) (b) (4) . The drug product will be packaged in 24, 50, 100, 250, 500, and 1000 (bulk) tablet count sizes. CRC closure will be used for the 24, 50 and 100 tablet counts.

The ANDA/BIO batch size of the White Film Coated tablets is (b) (4) tablets and the proposed commercial batch size is (b) (4) tablets. The ANDA batch size for the Brown Film Coated Tablets is (b) (4) tablets and the proposed commercial batch size is (b) (4) tablets. In both cases the pilot batch sizes are greater than 10% of the commercial batch size making them representative of the manufacturing process.

However, the firm has provided incomplete Exhibit Batches and incomplete packaging comments.

The drug substance is Ibuprofen USP obtained from (b) (4)

B. Description of How the Drug Product is Intended to be Used

The drug product is a tablet and will be taken orally.

C. Basis for Approvability or Not-Approval Recommendation

There are no effective patents for NDA 19-012, Ibuprofen IB from McNeil. There is no exclusivity associated with NDA 19-012.

III. Administrative

A. Reviewer's Signature

B. Endorsement Block

S. Dhanesar, Ph.D./02-04-03 5/2/03
A. Mueller, Ph.D./02-04-03 5-2-03
C. Kiester, R.Ph./02-04-03

C. CC Block

cc: ANDA 76-460
ANDA DUP
DIV FILE
Field Copy

Endorsements:

HFD-623/SDhanesar, Ph.D./02-25-03

HFD-623/AMueller, Ph.D./02-04-03

HFD-615/Ckiester, R.Ph./02-04-03

F/T by gp/03-28-03

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TYPE OF LETTER: NOT APPROVABLE - MINOR

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-460

BIOEQUIVALENCE REVIEWS

Dhariwal

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	76-460
Drug Product Name	Ibuprofen tablets, USP
Strength	200 mg (round white and round brown)
Applicant Name	Neil Laboratories
Address	55 Lake Drive, P.O. Box 1088, East Windsor, NJ 08520
Submission Date(s)	November 8, 2002
Reviewer	Kuldeep R. Dhariwal, Ph.D.
First Generic	No
File Location	V:\firmsnz\Neil\ltrs&rev\764601102.doc

I. Executive Summary

This is an OTC drug product. This application references McNeil's (NDA 19012) Motrin® IB 200 mg tablets and includes one fasting and one fed study. The fasting study is a single-dose two-way crossover study using 26 male and female healthy volunteers given a dose of 200 mg (white tablets). The results (point estimate, 90% CI) of the fasting BE study are LAUCt of 95, 91.79-97.89%; LAUCi of 95, 92.00-97.89%; and LCmax of 93, 86.38-100.96%. The fed BE study is a single-dose two-way crossover study using 18 male and female normal healthy volunteers given a dose of 200 mg (white tablets). The results of the fed BE study are LAUCt of 100, 95.58-103.98%; LAUCi of 100, 95.37-104.38%; and LCmax of 90, 82.52-97.31%. These studies are acceptable. The dissolution (900 mL pH 7.2 phosphate buffer, paddle at 50 rpm) testing is acceptable. The waiver of in vivo bioequivalence study requirements for the test brown 200 mg ibuprofen tablets is granted. The waiver of in vivo bioequivalence study requirements for additional source (b) (4)) of active ingredient is also granted. McNeil's 200 mg Nuprin® tablet (NDA 19012) was listed as RLD in the Orange Book when the BE studies were conducted and therefore the test drug was compared with 200 mg Nuprin® tablet in the BE studies. The current RLD is Motrin®; however, Motrin® and Nuprin® are linked by bioequivalence studies conducted by the innovator. Therefore, the use of Nuprin® as the RLD in this application is acceptable.

II. Table of Contents

III. Submission Summary

A. Drug Product Information

Test Product	Ibuprofen tablets
Reference Product	Motrin® IB (NDA #19012 by McNeil, Approval Date: Dec. 17, 1990). The firm used Nuprin® (NDA #19012) as RLD because Nuprin® was the RLD at the time the bio-studies were conducted. Lot # 902578
Indication	For temporary relief of headache, muscular aches, the minor pain of arthritis, toothache, backache, minor aches and pains associated with the common cold, the pain of menstrual cramps, and for reduction of fever.
Half Life	2 hours
Tmax	1-2 hours
Excretion	About 1% is excreted in urine as unchanged ibuprofen and about 14% as conjugated ibuprofen.

Relevant DBE History:

July 12, 2002	Original submission
Sep 25, 2002	Refuse to receive letter sent to the firm. One of the several reasons for refusing to file was the choice of RLD used for the bioequivalence study. The firm used Nuprin® as RLD but Motrin® IB was listed as RLD in the 2002 Orange Book.
November 8, 2002	Response to refuse to receive letter. The firm replied that Nuprin® was the RLD at the time bioequivalence studies were conducted. The firm also attached OGD letter dated September 29, 2000 stating that Nuprin® should be used as the RLD. The fasting and fed studies were conducted in April 2001. The 2001 Orange Book listed Nuprin® 200 mg tablets as the RLD. Firm's response was accepted by the Agency. The ANDA was accepted for filing on December 30, 2002.
Motrin®/Nuprin® history:	See page 14

B. Contents of Submission

		How many?
Single-dose fasting study	x	1
Single-dose fed study	x	1
Steady-state study	☐	
In vitro dissolution testing	x	2
Waiver requests	x	For round brown tablets
Waiver requests	x	For additional source of active ingredient

C. Bioanalytical Method Validation (Pre-Study, Vol. C1.2, Pages 266-287)

Number of analytes	1		
	Parent	Metabolite	Metabolite2
Analyte name	Ibuprofen		
Internal Standard	Diclofenac sodium		
Method description	HPLC		
QC samples, ng/mL	165, 3935, 18993, 30307		
Standard curve range, ng/mL	100 to 40,000		
Limit of quantitation, ng/mL	100		
Average recovery of Drug (%)	80.1		
Average Recovery of Int. Std (%)	89.4		
Intraday precision range (%)	0.7 to 2.4		
Intraday accuracy range (%)	94.0 to 108.9		
Interday precision range (%)	4.5 to 6.8		
Interday accuracy range (%)	100 to 100		
Bench-top stability (hrs)	21 at RT		
Stock stability (days)	21 at 4^0C		
Processed stability (hrs)	43 h in autosampler at RT		
Freeze-thaw stability (cycles)	4		
Long-term storage stability (days)	179 at -20^0C		
Dilution integrity	No, not needed because study samples were not diluted		
Specificity	Yes		
SOPs submitted	No, not needed		
Bioanalytical method is acceptable	Yes		
20% Chromatograms included	Yes	Serially Selected?	Yes

D. In Vivo Studies

1. Single-dose Fasting Bioequivalence Study

Study No.	R00-739
Study Design	Two-way crossover
No. of subjects enrolled	26
No. of subjects completing	26
No. of subjects analyzed	26
Subjects	Normal
Sex(es) included	Male: 19 Female: 7
Test product	Ibuprofen tablets
Reference product	Nuprin® Tablets
Strength tested	200 mg
Dose	1x200 mg

Summary of Statistical Analysis

Parameter	Point Estimate	90% Confidence Interval
LAUCt	0.95	91.79-97.89
LAUCi	0.95	92.00-97.89
LCmax	0.93	86.38-100.96

The study is acceptable.

2. Single-dose Fed Bioequivalence Study

Study No.	R00-740	
Study Design	Two-way crossover	
No. of subjects enrolled	18	
No. of subjects completing	18	
No. of subjects analyzed	18	
Subjects	Normal	
Sex(es) included:	Male: 14	Female: 4
Test product	Ibuprofen tablets	
Reference product	Nuprin® Tablets	
Strength tested	200 mg	
Dose	1x200 mg	

Summary of Statistical Analysis

Parameter	Point Estimate	90% Confidence Interval
LAUCt	1.00	95.58-103.98
LAUCi	1.00	95.37-104.38
LCmax	0.90	82.52-97.31

The study is acceptable.

E. Formulation

The test product formulations are shown in Table 1 of the Appendix.
Inactive Ingredients are within IIG limits.
Dosage form information
Test drug product
Round, white film coated biconvex tablets embossed with "NL/325" on one side plain on the other.
Reference drug product
Nuprin®: Yellow coated tablets.
Motrin® IB: Round, orange film coated biconvex tablets printed "Motrin IB" on one side and plain on other side.
The formulation is acceptable: Yes

F. In Vitro Dissolution

Methods Submitted	USP 26
Recommended Method based on the data submitted: USP 26	
Medium	Phosphate buffer, pH 7.2
Volume (mL)	900 mL
USP Apparatus Type	2 (paddle)
Rotation (rpm)	50
Firm's proposed specifications	NLT 80% (Q) in 60 minutes
FDA-recommended specifications	NLT 80% (Q) in 60 minutes

F2- value (s) not relevant, rapidly dissolving
In vitro dissolution is acceptable Yes

G. **Waiver Request** Yes

The firm proposes to make tablets of two different colors: white and brown. The white tablets were used in the bio-studies. The applicant requests a waiver of in vivo bioequivalence testing for the brown tablets. (b) (4) l. The DBE may grant the waiver based on the comparative dissolution data on brown tablets, white tablets and the RLD.

The applicant also requests use of an additional source of the active ingredient. The white tablets used in the bio-studies were manufactured using the active ingredient from (b) (4). The firm also wants to manufacture the tablets using active ingredient from (b) (4). For this request, the firm should submit the dissolution data on white and brown tablets manufactured using the additional source (b) (4)) and compare them with the dissolution data on white and brown tablets manufactured using active ingredient from (b) (4). The firm submitted dissolution data on white tablets manufactured using active ingredient from (b) (4), brown tablets manufactured using active ingredient from (b) (4), and the RLD. The firm did not provide dissolution data on the:

a. white tablets manufactured using active ingredient from (b) (4).
b. brown tablets manufactured using active ingredient form (b) (4)

This reviewer will grant waiver of in vivo bioequivalence study requirements for brown tablets and will accept additional source of active ingredient in the absence of the above data because:

a. it is an immediate release drug product
b. it dissolves nearly 90% in 10 minutes
c. (b) (4), and
d. the dissolution profile of the white tablets manufactured using active ingredient from (b) (4) is similar to that of the brown tablets manufactured using active ingredient from (b) (4).

The firm should however be asked to commit to submit the dissolution data on the brown tablets manufactured using active ingredient from (b) (4) and white tablets manufactured using active ingredient from (b) (4) at a later date.

H. **Deficiency Comments** No

I. Recommendations

1. The bioequivalence study conducted under fasting conditions by Neil Laboratories on its ibuprofen 200 mg white tablets, lot #RD-0325-03/01 comparing it to Nuprin® 200 mg tablets, lot #902578 manufactured by McNeil is acceptable to the Division of Bioequivalence. The study demonstrates that ibuprofen 200 mg white tablet manufactured by Neil Laboratories is bioequivalent to the reference product, Nuprin® 200 mg tablet manufactured by McNeil.

2. The bioequivalence study conducted under non-fasting conditions by Neil Laboratories on its ibuprofen 200 mg white tablets, lot #RD-0325-03/01 comparing it to Nuprin® 200 mg tablets, lot #902578 manufactured by McNeil is acceptable to the Division of Bioequivalence. The study demonstrates that under non-fasting conditions, the bioavailability of ibuprofen 200 mg white tablet manufactured by Neil Laboratories is similar to the reference product, Nuprin® manufactured by McNeil.
3. The dissolution testing conducted by the firm on its test tablets is acceptable. (b) (4) , which underwent bioequivalence testing. The waiver of in vivo bioequivalence study requirements for the round brown tablets is granted. The dissolution testing should be conducted in 900 mL of pH 7.2 phosphate buffer at 37^0C using apparatus 2 (paddle) at 50 rpm. The test product should meet the following specifications:
   Not less than 80% (Q) of the labeled amount of ibuprofen in the dosage form is dissolved in 60 minutes.
4. The waiver of in vivo bioequivalence study requirements for an additional source (b) (4)) of active ingredient is granted for white and brown ibuprofen 200 mg tablets.
5. The Division of Chemistry should ask the firm to commit to submit the dissolution data on brown tablets manufactured using active ingredient from (b) (4) and white tablets manufactured using active ingredient from (b) (4).

Dhariwal 6/26/03

Kuldeep R. Dhariwal, Ph.D.
Review Branch II

6/26/2003

S. Nerurkar, Ph.D.
Review Branch II

for Barbara M Saint 6/26/03

Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs

IV. Appendix

A. Individual Study Reviews

1. Single-dose Fasting Bioequivalence Study

Study Information

Study Number	R00-739
Clinical Site	PRACS Institute, Fargo, ND 58102
Principal Investigator	James Carlson, Pharm.D.
Study/Dosing Dates	Period 1 April 19, 2001 Period 2 April 26, 2001
Analytical Site	(b) (4)
Analytical Director	
Analysis Dates	May 1-8, 2001
Storage Period	20 days

Treatment ID	A	B
Test or Reference	Test	Reference
Product Name	Ibuprofen (white tablets)	Nuprin®
Manufacturer	Neil Labs	Bristol-Myers
Batch/Lot No.	RD-0325-03/01	902578
Manufacture Date	March 2001	N/A
Expiration Date	N/A	02/02
Strength	200 mg	200 mg
Dosage Form	Tablet	Tablet
Batch Size	(b) (4) tablets	N/A
Production Batch Size	(b) (4) tablets	N/A
Potency	99.7%	98.76%
Content Uniformity	99.7%	98.8%
Formulation	See Table #1	
Dose Administered	1x200 mg	1x200 mg
Route of Administration	Oral	

No. of Sequences	2		
No. of Periods	2		
No. of Treatments	2	**Balanced**	Yes
No. of Groups	1	**Washout Period**	7 days
Randomization Scheme		AB: 1,2,4,5,6,8,9,11,13,17,18,23,25 BA: 3,7,10,12,14,15,16,19,20,21,22,24,26	
Blood Sampling Times		0,0.25,0.50,0.75,1,1.25,1.5,2,2.5,3,4,6,8,10 and 12 h	
Blood Volume Collected/Sample		7 mL	

Blood Sample Processing/Storage	Blood samples were centrifuged at 2400 rpm and 4^0C for 15 minutes and the plasma was separated and stored at -20^0C.
IRB Approval	Yes
Informed Consent	Yes
Length of Fasting	Overnight
Length of Confinement	10 h prior to dosing until 12 h after dosing
Safety Monitoring	Blood pressure and heart rate were measured prior to dosing and at 12 hours after dose administration.

Subjects Demographics

Race:	Caucasian 23, African American 1, Asian 1, Hispanic 1
Height:	Mean 175.2 cm, range 160.0-190.5 cm
Weight:	Mean 75.4 kg, range 53.0-89.2 kg
Sex:	Male 19, Female 7
Age group:	<18 0 18-40 26 41-64 0 65-74 0 >75 0 Mean age 21.0 years, range 18-30

Study Results

Clinical: The firm's clinical summary is provided on Page 920, Vol. C1.2)

Dropout Information: none	
Adverse Events	5 Total events (dizziness and syncope secondary to phlebotomy and headache) 4 received Treatment A 1 received Treatment B For additional information see Vol. C1.3 page # 999

Protocol Deviations	Deviations in blood sampling times: Some, actual times were used. Other Deviations: nothing major

Assay Validation – Within Study (Vol. C1.1, pages 289-309)								
	Parent				**Metabolite**			
QC Conc. (ng/mL)	250	2000	32000	10000				
Inter day Precision (%CV)	7.7	6.4	6.4	7.3				
Inter day Accuracy (% Accuracy)	95.5	93.8	95.4	98.5				
Cal. Standards Conc. (ng/mL)	100,500,1000,5000,10000,20000, 30000, 40000							

Inter day Precision (%CV)	0.76-4.10				
Inter day Accuracy (% Accuracy)	96.0-104.6				
Linearity Range (range of R^2 values)	0.9960-0.9996				

Repeat Assays: Six samples for possible interference.

Chromatograms: Look O.K.

Conclusion: Analytical method is acceptable.

Pharmacokinetic/Statistical Analysis

Mean Plasma Concentrations	Table 2, Figure 1	
Mean Pharmacokinetic Parameters	Table 2	
90% Confidence Intervals	LnAUCt LnAUCi LnCmax Details in Table 2	91.79-97.89% 92.00-97.89% 86.38-100.96%
AUCt/AUCi ratio	Test 0.97 (0.89-0.99) Ref 0.97 (0.89-0.99)	
Root MSE	LnAUCt LnAUCi LnCmax	0.06772 0.06545 0.16433

Comments: (on pharmacokinetic analysis)

1. Ke and AUCi were determined for all subjects.
2. Indicate the number of subjects with the following:
   a. measurable drug concentrations at 0 hr: subject #20 had measurable concentrations (142.01 ng/mL and 148.56 ng/mL) in both the periods. These concentrations are well below 5% of Cmax.
   b. first scheduled post-dose sampling time as Tmax: none
   c. first measurable drug concentration as Cmax: none
3. The pharmacokinetic parameters and 90% confidence intervals calculated by the reviewer agree with firm's calculations.
4. There was statistically significant treatment and period effects for LAUCt and LAUCi.
5. The 90% confidence intervals for AUCt, AUCi, and Cmax are within the acceptable limits of 80-125%.

Conclusion: The single-dose fasting bioequivalence study is acceptable.

2. Single-dose Fed Bioequivalence Study

Study Information

Study Number	R00-740
Clinical Site	PRACS Institute, Fargo, ND 58102
Principal Investigator	James Carlson, Pharm.D.
Study/Dosing Dates	Period 1 April 20, 2001 Period 2 April 27, 2001
Analytical Site	(b) (4)
Analytical Director	
Analysis Dates	May 7-11, 2001
Storage Period	22 days

Treatment ID	A	B
Test or Reference	Test	Reference
Product Name	Ibuprofen (white tablets)	Nuprin®
Manufacturer	Neil Labs	Bristol-Myers
Batch/Lot No.	RD-0325-03/01	902578
Manufacture Date	March 2001	N/A
Expiration Date	N/A	02/02
Strength	200 mg	200 mg
Dosage Form	Tablet	Tablet
Batch Size	(b) (4) tablets	N/A
Production Batch Size	(b) (4) tablets	N/A
Potency	99.7%	98.76%
Content Uniformity	99.7%	98.8%
Formulation	See Table #1	
Dose Administered	1x200 mg	1x200 mg
Route of Administration	Oral	
Standard Breakfast	Yes, 30 minutes before dosing	

No. of Sequences	2		
No. of Periods	2		
No. of Treatments	2	**Balanced**	Yes
No. of Groups	1	**Washout Period**	7 days
Randomization Scheme		AB: 1,3,5,6,8,9,16,17,18 BA: 2,4,7,10,11,12,13,14,15	
Blood Sampling Times		0,0.25,0.50,0.75,1,1.25,1.5,2,2.5,3,4,6,8,10 and 12 h	
Blood Volume Collected/Sample		7 mL	
Blood Sample Processing/Storage		Blood samples were centrifuged at 2400 rpm and 4^0C for 15 minutes and the plasma was separated and stored at -20^0C.	
IRB Approval		Yes	
Informed Consent		Yes	

Length of Fasting	Overnight
Length of Confinement	10 h prior to dosing until 12 h after dosing
Safety Monitoring	Blood pressure and heart rate were measured prior to dosing and at 12 hours after dose administration.

Subjects Demographics

Race:	Caucasian 16, African American 1, Hispanic 1
Height:	Mean 172 cm, range 154.9-185.4 cm
Weight:	Mean 78.5 kg, range 60.2-87.9 kg
Sex:	Male 14, Female 4
Age group:	<18 0 18-40 16 41-64 2 65-74 0 >75 0 Mean age 27.6 years, range 18-53

Study Results

Clinical: The firm's clinical summary is provided on Pages 2072-2084, Vol. C1.5.

Dropout Information: None	
Adverse Events	One subject experienced headache during the study. For additional information see Vol. C1.5 page #2082.

Protocol Deviations	Deviations in blood sampling times: Some, actual times were used. Other Deviations: none reported.

Assay Validation – Within Study (Vol. C1.4, pages 1640-1659)								
	Parent				**Metabolite**			
QC Conc. (ng/mL)	250	20000	32000	10000				
Inter day Precision (%CV)	12.5	7.3	6.7	7.9				
Inter day Accuracy (% Accuracy)	98.9	101.7	102.2	102.7				
Cal. Standards Conc. (ng/mL)	100,500,1000,5000,10000,20000, 30000,40000							
Inter day Precision (%CV)	0.44-6.62							
Inter day Accuracy (% Accuracy)	97.8-106.0							
Linearity Range (range of R^2 values)	0.9948-0.9986							

Repeat Assays: Total seven samples. Four due to possible interference, one due to missed vial, and two due to low internal standard.

Chromatograms: Look O.K.

Conclusion: Analytical method is acceptable.

Pharmacokinetic/Statistical Analysis

Mean Plasma Concentrations	Table 3, Figure 2
Mean Pharmacokinetic Parameters	Table 3
90% Confidence Intervals	LnAUCt 95.58-103.98% LnAUCi 95.37-104.38% LnCmax 82.52-97.31% Details in Table 3
Ratios of Means	LnAUCt 1.00 LnAUCi 1.00 LnCmax 0.90
AUCt/AUCi ratio	Test 0.96 (0.87-0.98) Ref 0.96 (0.84-0.99)
Root MSE	LnAUCt 0.0724 LnAUCi 0.0775 LnCmax 0.1415

Comments: (on pharmacokinetic analysis)

1. Ke and AUCi were determined for all subjects.
2. Indicate the number of subjects with the following:
   a. measurable drug concentrations at 0 hr: Two subjects in period 2. The concentrations were well below 5% of Cmax.
   b. first scheduled post-dose sampling time as Tmax: none
   c. first measurable drug concentration as Cmax: none
3. The pharmacokinetic parameters and 90% confidence intervals calculated by the reviewer agree with firm's calculations.
4. There was statistically significant treatment effect for LCmax.
5. The 90% confidence intervals for AUCt, AUCi, and are Cmax within the acceptable limits of 80-125%. The ratios of means are also within the acceptable limits.

Conclusion: The single-dose fed bioequivalence study is acceptable.

Dissolution Data

Method: USP 26
Dissolution Medium: 900 mL of phosphate buffer, pH 7.2
Dissolution Apparatus: 2 (Paddle) at 50 rpm

Mean Dissolution Data:

Test (Round white tablets)*				Reference (Nuprin®)		
Lot No.: RD-0325-03/01, used in bio-studies				Lot No.: 902578, used in bio-studies		
Strength: 200 mg				Strength: 200 mg		
No. of Units: 12				No. of Units: 12		
Time(min)	Mean	Range	%CV	Mean	Range	%CV
10	95.06	89.3-99.3	3.18	67.25	36.2-82.6	19.6
20	94.86	89.4-97.6	2.81	92.93	87.1-95.8	3.03
30	94.02	87.8-96.1	2.85	95.79	92.0-98.3	1.95
45	95.15	87.3-97.9	3.05	96.52	93.2-101	2.47
60	94.96	87.7-99.6	3.03	96.14	93-99.0	1.91

*active ingredient from (b) (4)

Mean Dissolution Data:

Test (Round brown tablets)*				Reference (Motrin® IB)		
Lot No.: RD-0325-03/04				Lot No.: FDA 129		
Strength: 200 mg				Strength: 200 mg		
No. of Units: 12				No. of Units: 12		
Time(min)	Mean	Range	%CV	Mean	Range	%CV
10	93.77	92.54-95.1	0.84	88.24	81.51-93.5	4.9
20	96.54	95.94-97.4	0.48	96.35	94.5-98.9	1.24
30	97.43	94.1-100	1.73	98.38	96.39-101.15	1.25
45	97.63	95.34-99.0	1.05	98.90	96.36-101.51	1.64
60	97.76	96.91-98.8	0.64	99.35	97.72-102.69	1.91

* active ingredient from (b) (4)

Comments:

1. The dissolution testing was conducted using the USP 26 method.
2. The test products dissolve more than 90% in 10 minutes and therefore f2 tests are irrelevant.
3. The test products meet USP specifications of NLT 80% (Q) in 60 minutes.

B. **Attachments**

Motrin® /Nuprin® History: Not to be released under FOI

The following summary is provided based on reviewer's study of DFS, RetrievalWare, NDA 19-012 jackets, and NDA 19-012 division files:

1. Prescription Motrin® ibuprofen 300 mg, 400 mg, 600 mg and 800 mg tablets were approved on 9/19/74 under NDA #17-463.
2. In May 1984, the FDA approved OTC Nuprin® 200 mg tablets under NDA #19-012. The Nuprin® 200 mg tablets were recommended for approval based on results of a bioequivalence study comparing 4x100 mg Nuprin® tablets, 2x200 mg Nuprin® tablets and already marketed 1x400 mg Motrin® tablets. Approval for a new 100 mg formulation was not requested by the firm. The 200 mg Nuprin® tablet core formulation was proportionally similar to the 400 mg Motrin® tablet core formulation (NDA 19-012 file D1 and blue jacket 11.1).
3. The formulations of Nuprin® 200 mg core tablets and Motrin® IB 200 mg core tablets are identical (Nuprin® formulation as per NDA 19-012 file D2; Motrin® formulation as per NDA 19-012 jacket 61.1).
4. On 8/6/1999, McNeil submitted a supplement (SCM-019) for use of an additional manufacturing site and a different color for the Motrin® IB 200 mg tablets. While the core tablet formulation was unchanged, the tablet color was changed from white to orange. The supplement was approved (NCA 19-012 jacket 61.1) on 2/4/2000.

Table 1.

Composition of the White Coated Tablets (Bio batch RD-0325-03/01, p. 2512/3):

Component / grade/ function	Amount per tablet (mg)	% w/w	Amount (kg) per batch of (b) (4) tablets	Amount (kg) per batch of (b) (4) tablets
(b) (4)				

Composition of the Brown Coated Tablets (Batch No. RD-0325-03/04)

Component / function	Amount per tablet (mg)	% w/w	Amount (kg) per batch of (b) (4) tablets (p. 2809):	Amount (kg) per batch of (b) (4) tablets
(b) (4)				

Table 2

MEAN PLASMA IBUPROFEN LEVELS FOR TEST (1) AND REFERENCE (2) PRODUCTS IN FASTING STUDY, N=26

	MEAN1	SD1	MEAN2	SD2	RMEAN12
TIME HR					
0	5.46	27.85	5.71	29.14	0.96
0.25	2876.51	3662.63	2340.29	4341.02	1.23
0.5	6210.40	5566.02	6465.03	7208.34	0.96
0.75	8900.01	6799.36	8558.88	6996.31	1.04
1	11384.81	6823.72	10914.07	6463.94	1.04
1.25	13560.11	7321.53	12708.13	7169.09	1.07
1.5	13830.30	6204.03	12991.64	6492.49	1.06
2	13197.37	3955.57	14580.69	4637.31	0.91
2.5	12736.18	3224.94	13419.73	3924.98	0.95
3	10511.08	3098.25	11385.62	2657.10	0.92
4	8264.45	2656.00	9061.50	2570.18	0.91
6	4048.74	1950.68	4239.86	1622.30	0.95
8	2119.10	1187.10	2286.38	1153.13	0.93
10	1184.99	794.96	1244.82	670.02	0.95
12	681.09	587.66	710.07	523.07	0.96

UNIT: PLASMA LEVEL=NG/ML TIME=HRS

ARITHMETIC MEANS AND RATIOS

	MEAN1	SD1	MEAN2	SD2	RMEAN12
PARAMETER					
AUCI	67020.038	20768.695	70022.500	18443.581	0.957
AUCT	64528.577	18191.575	67511.962	16032.687	0.956
CMAX	17507.268	4001.432	18661.763	3809.905	0.938
KE	0.314	0.045	0.316	0.038	0.993
LAUCI	64756.862	0.252	68237.576	0.219	0.949
LAUCT	62592.814	0.241	66033.293	0.206	0.948
LCMAX	17060.835	0.235	18269.584	0.215	0.934
THALF	2.262	0.385	2.232	0.337	1.013
TMAX	1.780	1.054	1.788	0.921	0.995

UNIT: AUC=NG HR/ML CMAX=NG/ML TMAX=HR
LOG-TRANSFORMED DATA WERE CONVERTED TO ANTI-LOG IN THE TABLE

LSMEANS AND 90% CONFIDENCE INTERVALS

	LSM1	LSM2	RLSM12	LOWCI12	UPPCI12
PARAMETER					
AUCI	67020.04	70022.50	0.96	92.76	98.67
AUCT	64528.58	67511.96	0.96	92.64	98.52
CMAX	17507.27	18661.76	0.94	87.31	100.32
LAUCI	64756.86	68237.58	0.95	92.00	97.89
LAUCT	62592.81	66033.29	0.95	91.79	97.89
LCMAX	17060.83	18269.58	0.93	86.38	100.96

Table 3

MEAN PLASMA IBUPROFEN LEVELS FOR TEST (1) AND REFERENCE (2) PRODUCTS IN FED STUDY, N=18

	MEAN1	SD1	MEAN2	SD2	RMEAN12
TIME HR					
0	0.00	0.00	14.25	41.50	0.00
0.25	844.16	1650.26	352.10	1010.43	2.40
0.5	3491.25	5011.62	3307.21	6023.12	1.06
0.75	5794.02	5856.49	6604.04	7709.47	0.88
1	7820.27	6038.63	9640.77	6828.44	0.81
1.25	9144.53	5873.85	11747.08	6088.85	0.78
1.5	10141.74	5944.86	13106.59	4809.21	0.77
2	10766.87	4992.38	13154.64	4257.58	0.82
2.5	10473.08	3850.05	11630.24	2281.10	0.90
3	10050.91	2473.69	10110.16	1942.08	0.99
4	10009.23	3561.87	8592.33	2254.15	1.16
6	5142.37	1944.15	4404.96	1760.08	1.17
8	2549.06	982.65	2293.78	1180.28	1.11
10	1412.73	687.62	1327.29	866.60	1.06
12	803.46	496.36	766.50	652.78	1.05

UNIT: PLASMA LEVEL=NG/ML TIME=HRS

ARITHMETIC MEANS AND RATIOS

	MEAN1	SD1	MEAN2	SD2	RMEAN12
PARAMETER					
AUCI	65726.222	15578.570	65579.389	15158.725	1.002
AUCT	62760.444	13765.707	62511.667	12049.322	1.004
CMAX	14720.009	3525.119	16484.054	4135.628	0.893
KE	0.319	0.059	0.310	0.063	1.029
LAUCI	64052.908	0.233	64198.336	0.205	0.998
LAUCT	61334.027	0.222	61522.238	0.180	0.997
LCMAX	14319.586	0.243	15979.636	0.261	0.896
THALF	2.267	0.544	2.347	0.588	0.966
TMAX	2.278	1.233	1.819	0.954	1.252

UNIT: AUC=NG HR/ML CMAX=NG/ML TMAX=HR
LOG-TRANSFORMED DATA WERE CONVERTED TO ANTI-LOG IN THE TABLE

LSMEANS AND 90% CONFIDENCE INTERVALS

	LSM1	LSM2	RLSM12	LOWCI12	UPPCI12
PARAMETER					
AUCI	65726.22	65579.39	1.00	95.84	104.61
AUCT	62760.44	62511.67	1.00	96.31	104.48
CMAX	14720.01	16484.05	0.89	81.49	97.10
LAUCI	64052.91	64198.34	1.00	95.37	104.38
LAUCT	61334.03	61522.24	1.00	95.58	103.98
LCMAX	14319.59	15979.64	0.90	82.52	97.31

FIG 1. PLASMA IBUPROFEN LEVELS

IBUPROFEN TABLETS, 200 MG, ANDA #76-460
UNDER FASTING CONDITIONS
DOSE=1 X 200 MG

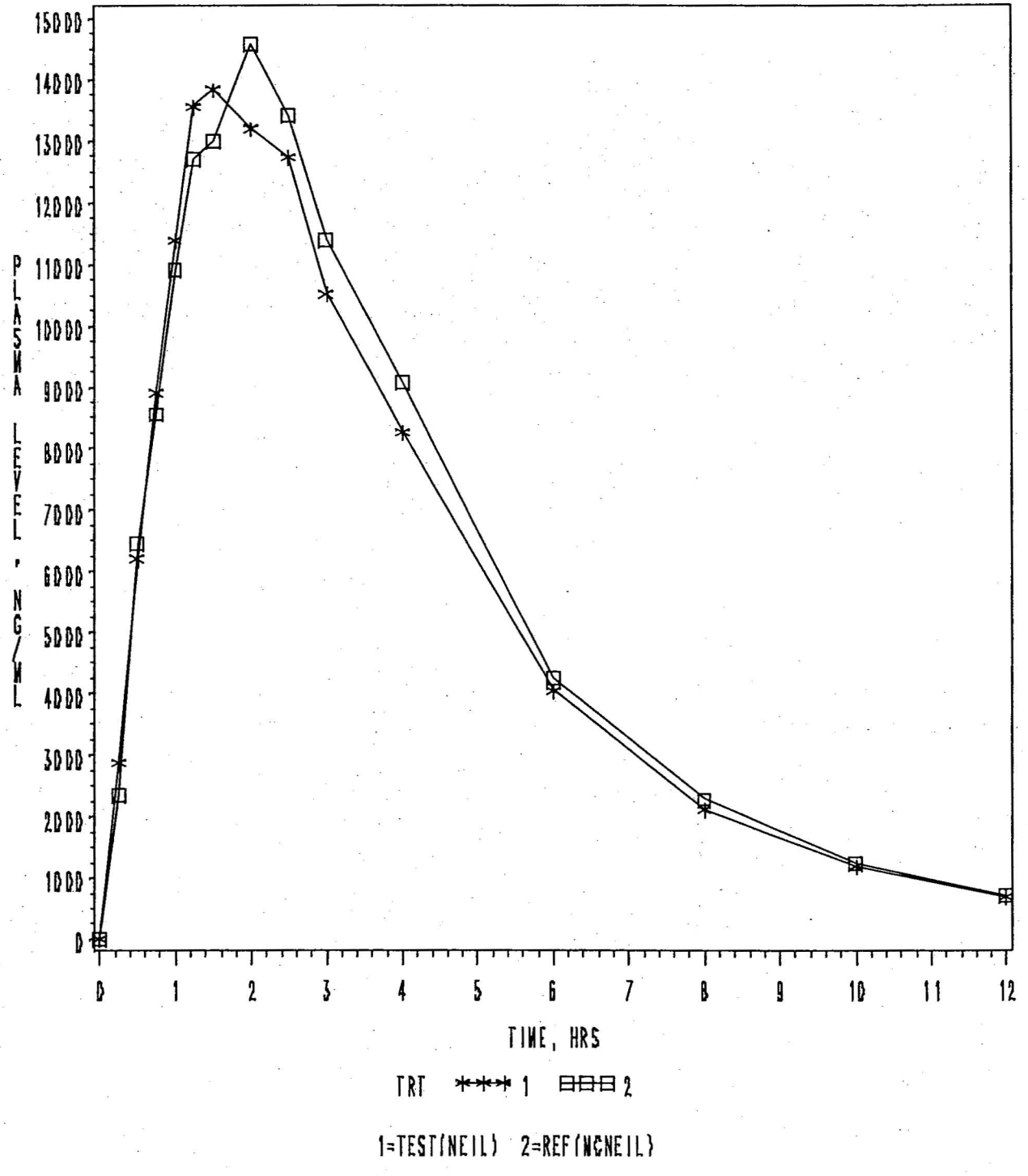
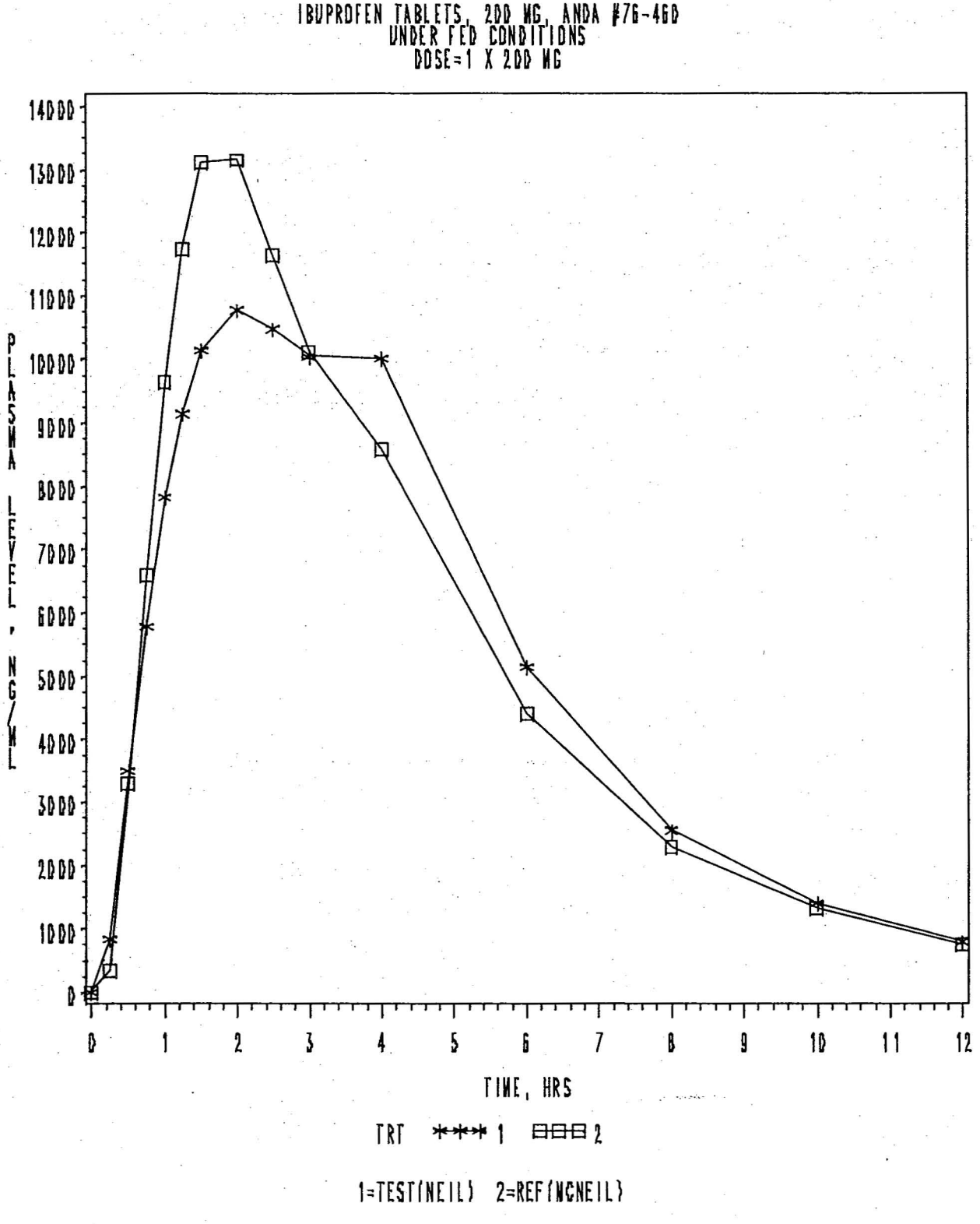


FIG 2. PLASMA IBUPROFEN LEVELS



BIOEQUIVALENCY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 76-460 APPLICANT: Neil Laboratories

DRUG PRODUCT: Ibuprofen Tablets USP, 200 mg
Round Tablets (white and brown)

The Division of Bioequivalence has completed its review and has no further questions at this time.

We acknowledge that the dissolution testing has been incorporated into your stability and quality control programs as specified in USP 26.

Please note that the bioequivalency comments provided in this communication are preliminary. These comments are subject to revision after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling, or other scientific or regulatory issues. Please be advised that these reviews may result in the need for additional bioequivalency information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

Barbara M. Davit

for Dale P. Conner, Pharm. D.
Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

CC: ANDA 76460
ANDA DUPLICATE
DIVISION FILE
HFD-651/ Bio Drug File
HFD-655/ Dhariwal

Printed in final on 6/26/03

6/26/03

Endorsements: (Final with Dates)
HFD-655/ Dhariwal 6/26/03
HFD-655/ Nerurkar
for HFD-650/ D. Conner 6/26/03

BIOEQUIVALENCY - ACCEPTABLE

Submission date: 11/8/02

1. **FASTING STUDY** (STF)
Clinical: PRACS Institute
Analytical (b) (4)

Strengths: 200 mg (white)
Outcome: AC

2. **FOOD STUDY** (STP)
Clinical: PRACS Institute
Analytical: (b) (4)

Strengths: 200 mg (white)
Outcome: AC

3. **DISSOLUTION WAIVER** (DIW)

Strengths: 200 mg (brown)
Outcome: AC

Outcome Decisions: **AC** - Acceptable

OFFICE OF GENERIC DRUGS
DIVISION OF BIOEQUIVALENCE

ANDA #: 76-460 SPONSOR: Neil Laboratories

DRUG AND DOSAGE FORM: Ibuprofen Tablets, USP (round white and brown)

STRENGTH(S): 200 mg

TYPES OF STUDIES: Fasting and fed

CLINICAL STUDY SITE(S): PRACS Institute

ANALYTICAL SITE(S): (b) (4)

STUDY SUMMARY: The fasting and fed studies are acceptable.

DISSOLUTION: The dissolution testing (as per USP 26) is acceptable. The waiver of in vivo bioequivalence study requirements for brown tablets is granted.

DSI INSPECTION STATUS

Inspection needed: No	Inspection status:	Inspection results:
First Generic _No__	Inspection requested: (date)	
New facility _____	Inspection completed: (date)	
For cause _____		
Other _____		

PRIMARY REVIEWER : Kuldeep R. Dhariwal, Ph.D. BRANCH: II

INITIAL : KRD DATE : 6/26/03

TEAM LEADER : S. Nerurkar, Ph.D. BRANCH: II

INITIAL : DATE : 6/26/2003

for DIRECTOR, DIVISION OF BIOEQUIVALENCE : DALE P. CONNER, Pharm.D.

INITIAL : Barbara M Davit DATE : 6/26/03

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 76-460

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

OGD APPROVAL ROUTING SUMMARY

ANDA # 76-460 Applicant Nail Laboratories
Drug Ibuprofen Tablets USP Strength 200 mg

APPROVAL ☒ TENTATIVE APPROVAL ☐ SUPPLEMENTAL APPROVAL (NEW STRENGTH) ☐ OTHER ☐

REVIEWER:	DRAFT Package	FINAL Package
1. Project Manager, Craig Kiester Review Support Br Team 1	Date 11/17/03 Initials CK	Date Initials

Application Summary:

Original Rec'd date 7/12/02
Date Acceptable for Filing 12/30/02
Patent Certification (type) I
Date Patent/Exclus.expires →
Citizens' Petition/Legal Case Yes ☐ No ☒
(If YES, attach email from PM to CP coord)
First Generic Yes ☐ No ☒
(If YES, Pediatric Exclusivity Tracking System (PETS)
RLD = Motrin IB
Date checked 11/17/03 NDA# 19012
Nothing Submitted ☒
Written request issued ☐
Study Submitted ☐

EER Status Pending ☐ Acceptable ☒ OAI ☐
Date of EER Status 6/16/03
Date of Office Bio Review 6/24/03
Date of Labeling Approv. Sum 9/8/03
Date of Sterility Assur. App.
Methods Val. Samples Pending Yes ☐ No ☒
Commitment Rcd. from Firm Yes ☐ No ☒
Modified-release dosage form: Yes ☐ No ☒
Interim Dissol. Specs in AP Ltr: Yes ☐

Previously reviewed and tentatively approved ☐ Date
Previously reviewed and CGMP def./N/A Minor issued ☐ Date
Comments:

2. Gregg Davis **PPIV ANDAs Only** Date 25 NOV 2003 Date 25 NOV 2003
Deputy Director, DLPS Initials Initials

Contains GDEA certification: Yes ☒ No ☐
(required if sub after 6/1/92)
Patent/Exclusivity Certification: Yes ☒ No ☐
If Para. IV Certification- did applicant
Notify patent holder/NDA holder Yes ☐ No ☐
Was applicant sued w/in 45 days: Yes ☐ No ☐
Has case been settled: Yes ☐ No ☐
Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes ☐ No ☐
Comments:

Determ. of Involvement? Yes ☐ No ☐
Pediatric Exclusivity System
Date Checked
Nothing Submitted ☐
Written request issued ☐
Study Submitted ☐

no patents or exclusivities
OK for full approval

3. Div. Dir./~~Deputy~~ Dir. Date 11/19/03 Date 11/19/03
Chemistry Div. I Initials RK Initials RK
Comments:

The Conc section is satisfactory

REVIEWER:	DRAFT Package	FINAL Package
4. Frank Holcombe Assoc. Dir. For Chemistry Comments: (First generic drug review)	Date_____ Initials_____	Date_____ Initials_____
5. Peter Rickman Director, DLPS	Date 11/25/03 Initials [illegible]	Date 11/26/03 Initials [illegible]

Para.IV Patent Cert: Yes☐ No☐; Pending Legal Action: Yes☐ No☐; Petition:Yes☐ No☐

Comments:

No patents or exclusivity issues
Office Level Pro acceptable 6/26/2003 (Facility & Field studies)
by DSI inspector medical
Labeling acceptable 9/8/2003
EER acceptable 6/16/2003

OR

5. Robert L. West Deputy Director, OGD	Date_____ Initials_____	Date_____ Initials_____

Para.IV Patent Cert: Yes☐ No☐; Pending Legal Action: Yes☐ No☐; Petition:Yes☐ No☐

Comments:

6. Gary Buehler Director, OGD Comments:	Date 11/26/03 Initials GJB	Date 11/26/03 Initials GJB

First Generic Approval ☐ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐

7. Project Manager, Craig Kiester Review Support Br Team 1	Date 11/26/— Initials [illegible]	Date_____ Initials_____

11/26/— Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
2 P— Time notified of approval by phone 2 05 PM Time approval letter faxed

FDA Notification:
11/26/03 Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
11/26/— Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

\rah\Templates\Approvrou2.doc

NEIL LABORATORIES INC.

ORIG AMENDMENT

N/AF

FPL

August 12, 2003

James Barlow
Division of Labeling and Program Support
Office of Generic Drugs-CDER
Food and Drug Administration (HFD-160)
7500 Standish Place
Rockville, MD 20855-2773

RE: Minor Amendment (Labels and Labeling) Ibuprofen Tablets USP, 200mg-ANDA #76-460

Dear Mr. Barlow:

This minor amendment response is in reference to your fax dated 7/28/03 of labeling deficiencies for our ANDA #76-460 (Ibuprofen Tablets USP, 200mg). We are submitting 12 true copies of the final printed labels and labeling with original color and size.

As per your suggestion, please find herewith the side-by-side comparison of our final printed labels and labeling with all the difference annotated and explained.

If you need any additional information please contact me at 609-448-5500 ext. 11.

Thank you very much.

Sincerely,

Bharat Patel
President/CEO

RECEIVED
AUG 13 2003
OGD/CDER

55 LAKE DRIVE, P.O. BOX 1088 • EAST WINDSOR, NEW JERSEY 08520
609-448-5500 • FAX: 609-443-9316 • EMAIL: neillabs@aol.com

NL

NEIL LABORATORIES INC.

Mr. Craig Kiester, Project Manager
Office of Generic Drugs, CDER, FDA
Metro Park North II
7500 Standish Place, Room 150
Food and Drug Administration
Rockville, MD 20855

August 7, 2003

Reference: Fax Amendment to Minor Deficiencies to Original ANDA 76-460 (Ibuprofen Tablets USP, 200 mg)

Dear Sir:

This fax amendment is in reference to the phone call received from Mr. Al Mueller and Mr. Subhash Dhanesar on August 6th 2003 requesting following correction and clarification.

1. ***Appropriately rounding of numbers, based on the specification where ever applicable in our Ibuprofen ANDA file.***

RESPONSE:

1. We have made the corrections based on the specification with reference to rounding of numbers to Water Content, Assay, Dissolution, Uniformity of Dosage Units, Heavy Metals and Impurity tests to our Original Ibuprofen ANDA file # 76-460. Following is the list of pages where we have made corrections and we will commit that we will make corrections on any other pages if it becomes necessary in the future.

Dissolution: 148, 149, 150, 151, 2947 and 3216
Raw Material Specification: 2542, 2589 and 2590
Impurity: 2543
Method Precision: 2977
Reproducibility: 2979, 3070 and 3073
Ruggedness: 2981, 3075 and 3187
Force Degradation: 2987, 3087 and 3316
Robustness: 3021 and 3028
Recovery: 3124 and 3200
Standard Precision & Method Precision: 3184
Stability data: 3417 to 3427

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2. ***Requiring further clarification for point #17 of Minor Amendment, dated May 5, 2003.***

RESPONSE:

2. In our "Induced Degradation" study we have stated "Ibuprofen is chemically very stable" which we have derived from Manufacturer's Technical Package. But in stress condition, Ibuprofen has degraded and result has been documented in Table 7, Page 3009 of our Original ANDA filing. The spectral scan of Ibuprofen from degradation samples showed no evidence of co-eluting peaks with Ibuprofen, thus Ibuprofen peak is pure and homogeneous. The observed degradation of 12% to 28% was due to extended 3 to 4 weeks (Page # 2087 of the Original ANDA filing) of harsh stress conditions employed. We believe that this condition has generated more degradation.

   We are correcting existing statement "Ibuprofen is chemically very stable" (Original ANDA file, Page # 2987) by adding that the Ibuprofen is not stable in extreme harsh condition. Thus the entire statement will read as "Ibuprofen is chemically very stable compound but it is not stable in extreme harsh condition."

We hope you find both the minor deficiencies addressed satisfactorily in our response.

If you need additional information you can contact me at (609) 448-5500.

Thank you,

Sincerely,

Bharat Patel
President/CEO
Neil Laboratories, Inc

Cc: Al Muller
Subhas Dhanesar

RECORD OF TELEPHONE CONVERSATION/MEETING

Called to clarify three items, prior to assembling an approval document. Talked with B. Patel who called in S. Daftary, a person knowledgeable in analytical chemistry, relating to our questions.

We requested that their API specifications/CoA reflect that their percentages be limited to two decimal places, except for Heavy metals which are normally reported as ppm values. Messrs. Patel/Daftary agreed and indicated no problems.

We also requested that uniformity of dosage values be reported as 85.0%-115.0%, not as 85%-115.0%. Messrs. Patel/Daftary indicated that this was a typographical error and will be corrected.

We then asked for a complete answer to Deficiency # 17 in our Review # 1. Neil did not offer a complete answer to mass balance differences observed in their stability indicating study. Their control sample assay indicated 98.0%, whereas their study values indicated 71.2% and 88.6%. We indicated that we needed a more complete answer. We asked a question regarding a time period for their response and they indicated that they could respond via a fax amendment to C. Kiester within a week's time.

(end of memo)

DATE:

August 6, 2003

ANDA NUMBER:

76-460

IND NUMBER:

N/A

TELECON

INITIATED BY:

- ☐ **APPLICANT/SPONSOR**
- ■ **FDA**

MADE:

- ■ **BY TELEPHONE**
- ☐ **IN PERSON**

PRODUCT NAME:

Ibuprofen Tablets USP

FIRM NAME:

Neil Laboratories, Inc.

NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD:

Bharat Patel, President

Satish Daftary, Analytical

TELEPHONE NUMBER:

(609) 448-5500

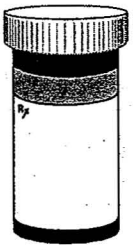
SIGNATURE:

A.J. Mueller

S.C. Dhanesar 8/6/03

V:\FIRMSNZ\NEIL\TELCONS\76460MEM.DOC

Fax Cover Sheet



Department of Health and Human Services
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research
Office of Generic Drugs
Rockville, Maryland

To: Neil Laboratories, Inc
Fax: 609-443-9316 **Phone 609-448-5500**

From: James Barlow
Fax: 301-443-3847 **Phone:** 301-827-5830

Number of Pages (including cover sheet): 2 **Date:** 7/28/03

Comments:

Dear Mr. Patel,
Attached you will find the labeling review for ANDA 76-460 (ibuprofen tablets) referencing the July 20, 2003 submission.

Sincerely,
LCDR James T. Barlow

REVIEW OF PROFESSIONAL LABELING
DIVISION OF LABELING AND PROGRAM SUPPORT
LABELING REVIEW BRANCH

ANDA Number:	76-460
Date of Submission:	May 20, 2003
Applicant's Name:	Neil Laboratories, Inc..
Established Name:	Ibuprofen tablets USP, 200 mg

Labeling Deficiencies:

1. **CONTAINER – Bottles of 24, 50, 100, 250, 500 and 1000 tablets**
   Satisfactory in **draft** as of the May 20, 2003

2. **CARTON – 24's 50's and 100's**
   Satisfactory in **draft** as of the May 20, 2003

Please prepare and submit 12 copies of final printed labels and labeling.

Prior to approval, it may be necessary to further revise your labeling subsequent to approved changes for the reference listed drug. We suggest that you routinely monitor the following website for any approved changes-

http://www.fda.gov/cder/cdernew/listserv.html

To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated and explained.

Wm. Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

NL

NEIL LABORATORIES INC.

May 20, 2003

Mr. James Barlow
Division of Labeling and Program Support
Office of Generic Drugs-CDER
Food and Drug Administration (HFD-160)
7500 Standish Place
Rockville, MD 20855-2773
Ph. 301-827-5846

RE: Minor Amendment (Labels and Labeling)
Ibuprofen Tablets USP, 200mg
ANDA #76-460

ORIG AMENDMENT
N/AH

Dear Mr. Barlow:

This minor amendment response is with reference to your fax dated May 12th, 2003 of labeling deficiencies for our ANDA #76-460 (Ibuprofen Tablets). We have revised our labels and labeling deficiencies as per your comments given in the deficiency letter.

We are submitting all revised labels and labeling for your review prior to approval. We hope you find all of the deficiencies addressed satisfactorily in our response.

If you need any additional information please contact me at 609-448-5500 ext. 11.

Thank you.

Sincerely,

Bharat Patel
President/CEO

cc: Wm Peter Rickman

RECEIVED
MAY 22 2003
OGD / CDER

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609-448-5500 • FAX: 609-443-9316 • EMAIL: neillabs@aol.com

Labeling Deficiencies:

1. *GENERAL COMMENTS*

   a. ***"We note that you submitted bulk labeling for review. We do not approve bulk labels and labeling, however your draft labels seem satisfactory in draft.***

   Response:

   We acknowledge your comments regarding bulk labels and labeling.

   b. ***"Note that the information leaflet is no longer utilized by the reference listed drug MOTRIN IB® since Drug Facts labeling has been in effect. The full text of the labeling is to be found on the carton of the smaller count bottles and/or the containers of the larger count bottles. Therefore, please delete this from your submission."***

   Response:

   Please note that we have incorporated your suggestion related to the information leaflet. We are deleting the leaflet information from the labeling section of our ANDA #76-460 (Ibuprofen Tablets USP, 200mg).

   c. ***"Inactive ingredients-revise 'hydroxypropyl methylcellulose' to read 'hypromellose' (compendial name).***

   Response:

   Please note that as per your comment we have revised all our labels and replaced the inactive ingredient Hydroxypropyl Methylcellulose to read 'hypromellose' (compendial name).

2. **CONTAINER-Bottles of 24, 50, 100, 250, 500, and 1000 tablets.**

   a. ***" Please delete "SUGAR FREE" from the text to be in accord with the reference listed drug."***

   Response:

   Please note that as per your suggestions, we are deleting 'SUGAR FREE' from all the container labels to be in accord with reference listed drug.

   b. ***" Revise to read-[delete information pertaining to leaflet]***
   Save carton for complete WARNINGS. Save carton for future reference.

   Response:

   Please note as per your comment related to our labels for White/Brown-Ibuprofen Tablets USP, 200mg, we have revised our labels on 24's, 50's & 100's to read 'Save carton for complete WARNINGS. Save carton for future reference.'

3. ***CARTON-24's, 50's and 100's***
See above comments under CONTAINER (a.) listed above

Response:

Please note that we have deleted 'SUGAR FREE' from the label on carton to be in accord with the reference listed drug.

4. ***"To facilitate review of your next submission, and in accordance with 21 CFR 314.94(a)(8)(iv), please provide a side-by-side comparison of your proposed labeling with your last submission with all differences annotated or explained.***

Response:

Please find herewith as per your suggestion, the side-by-side comparison of our proposed labeling for label and carton with all differences annotated & explained.

NEIL LABORATORIES INC.

May 16, 2003

DRUG AMENDMENT
N/Am

Mr. Craig Kiester
Office of Generic Drugs, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
(301-594-0320)

RE: Minor Amendment
Ibuprofen Tablets USP, 200mg
ANDA 76-460

Dear Mr. Kiester:

This minor amendment response is in reference to Dr. Rashmikant M. Patel's letter of May 5th, 2003 regarding the above mentioned Abbreviated New Drug Application.

We hope you find all of the deficiencies addressed satisfactorily in our response.

If you need any additional information please contact me at 609-448-5500 ext. 11.

Thank you.

Sincerely,

Bharat Patel
President/CEO

RECEIVED
MAY 19 2003
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5/22/03

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NEIL LABORATORIES INC.

NAI
11/26/03

Rashmikant M. Patel, Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
7500 Standish Place
Rockville, MD 20857

May 9, 2003

NEW CORRESP

NC

Reference: ANDA 76-460 (Ibuprofen Tablets, USP)

Dear Sir:

This is to acknowledge the receipt of your facsimile dated May 5, 2003 regarding MINOR AMENDMENT. We are reviewing the MINOR deficiencies presented in the letter. We are preparing all the necessary documents which will be properly filed with your office within ten days from the receipt of your letter.

Sincerely yours,

Satish R. Daftary
(Director, QC)

Cc: Garry Buehler, Director
Craig Kiester, Project Manager

RECEIVED
MAY 14 2003
OGD / CDER

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MINOR AMENDMENT

ANDA 76-460

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (301-594-0320)

MAY - 5 2003

APPLICANT: Neil Laboratories, Inc.

TEL: 609.448.5500

ATTN: Bharat Patel

FAX: 609.443.9316

FROM: Craig Kiester

PROJECT MANAGER: 301-827-5848

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated July 12, 2002, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ibuprofen Tablets USP, 200 mg.
Also reference is your amendment dated December 2, 2002 CK 5/7/03
The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (5 pages). This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed.

The file on this application is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Your amendment should respond to all of the deficiencies listed. Facsimiles or partial replies will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this facsimile will be considered to represent a MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MINOR AMENDMENT should appear prominently in your cover letter. You have been/will be notified in a separate communication from our Division of Bioequivalence of any deficiencies identified during our review of your bioequivalence data. If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

SPECIAL INSTRUCTIONS:

Chemistry comments provided.

CK 5/2/03

MAY - 5 2003

36. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 76-460 APPLICANT: Neil Laboratories Inc.

DRUG PRODUCT: Ibuprofen Tablets USP, 200 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. (b) (4)

2.

3.

4.

3 PAGES WITHHELD IN FULL AS B4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

B. In addition to responding to the deficiencies presented above, please note and acknowledge the following comments in your response:

1. We note that you have changed the drug product assay method from the USP method to an In-house method. Please be aware that in the event of a dispute, the USP method will be the prevailing method.

2. Your bioequivalence information is pending review. Deficiencies, if any, will be communicated separately.

3. Your labeling information is pending review. Deficiencies, if any, will be communicated separately.

4. The firms referenced in your ANDA application relative to the manufacturing and testing of the product must be in compliance with cGMP's at the time of approval.

Sincerely yours,

Rashmikant M. Patel, Ph.D.
Director
Division of Chemistry I
Office of Generic Drugs
Center for Drug Evaluation and Research

NEIL LABORATORIES INC.

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville, MD 20857

March 12, 2003
ORIG AMENDMENT
N/AC

Reference: Amendment to Original ANDA 76-460 (Ibuprofen Tablets USP, 200 mg)

Dear Sir:

Our facility, Neil Labs, Inc. has been audited for Ibuprofen Tablets USP 200 mg for ANDA pre-approval inspection. Ms. Marea K. Harmon, FDA Investigator, Voorhees Resident Post, NJ, was at this site between February 10 and February 26, 2003. During her investigation, she recommended to include in the analytical methods the preparation of a key impurity to its Limit of Quantitation (LOQ) concentration. We have incorporated her suggestion and revised our analytical finished product method; NLQC-FP024B. The revised method reflects the standard preparation for key impurities up to its LOQ levels to assure that the Chromatography system (HPLC) is capable of detecting to this concentration level at the time of performing impurity analysis.

This amendment consists of two volumes, a blue jacketed archival copy and red jacketed review copy. The volume contains the following document related to Volume 8 Section XV. The page number in the original filing begins from '0002921' to '0002943' where as the page number assigned to this method for this addendum begins from '1' and ends at '26'.

1. Method and Specification for Analysis:
   Ibuprofen Finished Product Testing. Method # NLQC – FP024B

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609-448-5500 • FAX: 609-443-9316 • EMAIL: neillabs@aol.com

Also, we certify that a maroon jacket field copy which is true identical copy of this amendment has been filed with the District Director, New Jersey District Office, FDA, in accordance with 21 CFR 314.94 (C) (d) (5).

If you have any question please feel free to call me at (609) 448 - 5500.

Sincerely,

Bharat Patel
President/CEO
Neil Laboratories, Inc.

Cc: Gary Buehler
Director, Office of Generic Drugs

Christine Bina
Project Manager

ANDA 76-460

DEC 30 2002

Neil Laboratories, Inc.
Attention: Bharat Patel
55 Lake Drive
P.O. Box 1088
East Windsor, NJ 08520

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is made to our "Refuse to Receive" letter dated September 25, 2002 and your amendment dated November 8, 2002.

Reference is also made to the telephone conversation dated November 20, 2002 and December 16, 2002 and your correspondence dated December 2, 2002 and December 18, 2002.

NAME OF DRUG: Ibuprofen Tablets USP, 200 mg

DATE OF APPLICATION: July 12, 2002

DATE (RECEIVED) ACCEPTABLE FOR FILING: November 13, 2002

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the ANDA number shown above.

Should you have questions concerning this application, contact:

Craig Keister
Project Manager
(301) 827-5848

Sincerely yours,

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 76-460
cc: DUP/Jacket
Division File
Field Copy
HFD-610/R.West
HFD-610/P.Rickman
HFD-92
HFD-615/M.Bennett
HFD-600/
Endorsement:
HFD-615/GDavis, Chief, RSB 30-Dec-2002 date
HFD-615/CBina, CSO 12-30-02 date
Word File V:\Firmsnz\neil\ltrs&rev\76460.ack
F/T
ANDA Acknowledgment Letter!

NL

NEIL LABORATORIES INC.

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville, MD 20857

December 18, 2002

NEW CORRESP

Reference: ANDA # 76-460 (Ibuprofen Tablets USP, 200 mg)

Dear Sir:

This is in reference to the phone call received from Ms Christine Bina on December 16th 2002 requesting Archival Copy, Volumes 2 to 6 submitted with original ANDA filling, consisting of the Relative Bioavailability study and missing pages, 420 to 448 from Volume 3.

With this letter we are submitting an Archival Copy of Relative Bioavailability Study of Ibuprofen 200 mg Tablets consists of five Volumes from No 2 to 6 submitted with original ANDA filing.

We are also including missing pages from '0000420' to '0000438' but due to machine error, page numbers from '0000439' to '0000448' were not printed during pagination process. However, no information concerning to the filling of this ANDA is missing between these pages. Thus, page # '0000449' becomes the next page after '0000439'. This information was attached with our original ANDA filling after page # 0000439.

If you have any question please feel free to call me at (609) 448 – 5500.

Sincerely,

Bharat Patel
President/CEO
Neil Laboratories, Inc.

Cc: Gary Buehler
Director, Office of Generic Drugs

Christine Bina
Project Manager

55 LAKE DRIVE, P.O. BOX 1088 • EAST WINDSOR, NEW JERSEY 08520
609-448-5500 • FAX: 609-443-9316 • EMAIL: neillabs@aol.com

76-460

Teleconference

TC

Neil Laboratories Inc.
Firm: Satish Daftary
55 Lake Drive
P.O.Box 1088
East Windsor, NJ 08520
(609) 448-5500 ext. 14

12/17/02

November 20, 2002:

I spoke with Satish Daftary from Neil Laboratories regarding the Response to Refuse to Receive submitted on November 13, 2002. I informed him we did receive the fax containing the breakdown of (b) (4) with a % of each ingredient. He had further questions of the missing parts of the Archival copy. I informed him it appears that pages 154-2510 are missing from the Archival copy. (Bio. vols.) Satish will send those pages. In regard to the Package and Reconciliation record for lot # RD-0325-03/04, I informed Satish we are looking for a minimum of 100,000 tablets to be packaged in containers proposed for marketing. He told me he would have all the information I requested to me with in 10 days.

December 16, 2002:

I spoke with Satish Daftary from Neil Laboratories regarding the documentation which was provided. I informed him the volumes which were submitted to FDA were in the Orange Jackets. Also it appeares that pages 420-448 are missing. I told Satish we need the information submitted in the BLUE ARCHIVAL jackets. He will supply that information.

Today:

I spoke with Satish Daftary from Neil Laboratories today. He requested I send back the incorrect ANDA volumes, which Neil submitted, at his expense. He was concerned if they created new volumes the copies may not be legible. Satish gave me Neil's FedEx account number. I then informed him I must receive the revised copies by December 26, 2002 or I will refuse the Response to Refuse to Receive.

76-460

Teleconference

Neil Laboratories Inc.
Firm: Satish Daftary
55 Lake Drive
P.O.Box 1088
East Windsor, NJ 08520
(609) 448-5500 ext. 14

12/16/02

November 20, 2002:

I spoke with Satish Daftary from Neil Laboratories regarding the Response to Refuse to Receive submitted on November 13, 2002. I informed him we did receive the fax containing the breakdown of [redacted] (b) (4) with a % of each ingredient. He had further questions of the missing parts of the Archival copy. I informed him it appears that pages 154-2510 are missing from the Archival copy. (Bio. vols.) Satish will send those pages. In regard to the Package and Reconciliation record for lot # RD-0325-03/04, I informed Satish we are looking for a minimum of 100,000 tablets to be packaged in containers proposed for marketing. He told me he would have all the information I requested to me with in 10 days.

Today:

I spoke with Satish Daftary from Neil Laboratories regarding the documentation which was provided. I informed him the volumes which were submitted to FDA were in the Orange Jackets. Also it appeares that pages 420-448 are missing. I told Satish we need the information submitted in the BLUE ARCHIVAL jackets. He will supply that information.

NEIL LABORATORIES INC.

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville, MD 20857

December 2, 2002

ORIG AMENDMENT
N/AC

505(j)(7)(A)(i) OK
30-DEC-2002
Gregory D. Davis

Reference: Amendment to Original ANDA 76-460 (Ibuprofen Tablets USP, 200 mg)

Dear Sir:

This amendment is in reference to the phone call received from Ms Christine Bina on November 14th 2002 requesting following information.

1. Composition of [redacted] (b) (4) coating Ibuprofen 200 mg Tablets (Brown).

2. Packaging Reconciliation of Ibuprofen 200 mg Tablets (Brown), ANDA Batch # RD-0325-03/04.

3. A Relative Bioavailability Study of Ibuprofen 200 mg Tablets. Consist of five Volumes, original Volume No 2 to 6 submitted with initial ANDA filing for archival copy.

This amendment (Our Reference # AMD120202) consists of six (6) volumes. Submitting Volume No.1, a blue jacketed archival copy and a red jacketed review copy with information related to Inactive Raw material and Packaging Order. This filing also includes five (5) original volumes, without any amendment, consisting of Pharmacokinetic Section. Each volume submitted with this filling contains following documents related to Volume 1 through 8 filed with original ANDA.

Volume 1 Ingredient breakdown statement for inactive ingredient [redacted] (b) (4) executed packaging order and reconciliation for ANDA batch of Ibuprofen 200 mg Tablets (Brown), Batch # RD-0325-03/04.

RECEIVED
DEC 0 4 2002
OGD / CDER

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Volume 2-6 Statistical Report for A Relative Bioavailability Study of 200 mg Ibuprofen Tablets (White) under Non-fasting Conditions, which includes, Introduction, Methodology, Pharmacokinetic Parameters, Statistical Analysis and Conclusion.

A 'Table of Contents' relating to the submitted information is attached at the beginning of the volume. The page numbers assigned to the pages of this amendment are sequential number starting from '0001'. The page number for pharmacokinetics volumes, 2 to 6, will have original page number as assigned earlier with initial ANDA.

This amended ANDA covers one shape (round tablets) and two colors (white and brown) tablet as per our correspondence with FDA (letter reference: OGD# 00-344, dated January 12, 2001).

We certify that Volume 1, a burgundy jacket field copy which is a true identical copy of this amendment has been filed with the District Director, New Jersey District Office, FDA, in accordance with 21 CFR 314.94 (C) (d) (5).

If you have any question please feel free to call me at (609) 448 – 5500.

Sincerely,

Bharat Patel
President/CEO
Neil Laboratories, Inc.

Cc: Gary Buehler
Director, Office of Generic Drugs

Christine Bina
Project Manager

76-460

Teleconference

Neil Laboratories Inc.
Firm: Satish Daftary
55 Lake Drive
P.O.Box 1088
East Windsor, NJ 08520

11/21/02

I spoke with Satish Daftary from Neil Laboratories regarding the Response to Refuse to Receive submitted on November 13, 2002. I informed him we did receive the fax containing the breakdown of [redacted] (b) (4) with a % of each ingredient. He had further questions of the missing parts of the Archival copy. I informed him it appears that pages 154-2510 are missing from the Archival copy. (Bio. vols.) Satish will send those pages. In regard to the Package and Reconciliation record for lot # RD-0325-03/04, I informed Satish we are looking for a minimum of 100,000 tablets to be packaged in containers proposed for marketing. He told me he would have all the information I requested to me with in 10 days.

Dec. 16, 2002:

Vol. which were requested for the Archival Copy were submitted in Orange Cover and missing pages 420-448.

2 PAGES WITHHELD IN FULL AS B4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

76-460

Teleconference

Neil Laboratories Inc.
Firm: Satish Daftary
55 Lake Drive
P.O.Box 1088
East Windsor, NJ 08520

11/20/02

I spoke with Satish Daftary from Neil Laboratories regarding the Response to Refuse to Receive submitted on November 13, 2002. I informed him we still need a complete breakdown [redacted] (b) (4) a % of each ingredient. Also we still need a complete Archival copy. We currently have only 3 volumes and there should be a total of 8 vol. (Include Bio. vol.) We need a Package and Reconciliation record for lot # RD-0325-03/04. The explanation provided on p. 289 of the Response is not sufficient.

NEIL LABORATORIES INC.

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Rockville, MD 20857

November 8, 2002

ORIG AMENDMENT
N/AC

Reference: Amendment to Original ANDA 76-460 (Ibuprofen Tablets USP, 200 mg)

Dear Sir:

Reference is made to the refusal to file letter regarding the original ANDA filing for Ibuprofen Tablets USP 200 mg. We now provide the requested documents in this amendment to complete our ANDA filing for Ibuprofen Tablets, USP. Attached with this letter are five pages showing restated FDA letter comments followed by a brief response.

This amendment consists of two (2) volumes, a blue jacketed archival copy and a red jacketed review copy. Each volume contains following documents related to Volume 1 through 7 filed with original ANDA.

Volume 1	Signed and completed application (Form 356h), Basis for ANDA submission, Patent and exclusitivity certification, 505(j)(2)(A) – information generic/reference comparison, labeling, "*in vitro*" data of bioavailability/bioequivalence (dissolution profiles for proposed drug product vs. reference listed drug).
Volume 5	Results and Conclusions for the Non-Fasting, single dose *in-vivo* bioequivalence study for Ibuprofen Tablets 200mg.
Volume 7	Components and composition, raw material controls, packaging data, container and closures, finished product controls.

RECEIVED
NOV 1 3 2002
OGD / CDER

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A 'Table of Contents' relating to the submitted information is attached at the beginning of the volume.

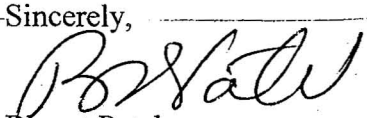
This Amendment ANDA covers one shape (round tablets) and two colors (White and brown) tablet as per our correspondence with FDA (letter reference: OGD# 00-344, dated January 12, 2001)(included in Section XXII). We have manufactured round white tablets (Lot # RD – 0325 – 03/01) and round brown tablets (Lot# RD – 0325 – 03/04). It may be noted that white round tablets were used for the comparative bioavailability/bioequivalence study. However, this ANDA includes comparative *in vitro* dissolution of the Reference Listed Drug MOTRIN® IB (McNeil Consumer Healthcare, a Division of McNeil-PPC, Inc.) with Neil Labs' white round tablets (Lot# RD – 0325 – 03/01) as well as brown round tablets (Lot# RD – 0325 – 03/04).

Also, we certify that a maroon jacket field copy which is true identical copy of this amendment has been filed with the District Director, New Jersey District Office, FDA, in accordance with 21 CFR 314.94 (C) (d) (5).

The page numbers assigned to the pages of this amendment are sequential number starting from '0001'. Some of the attached pages to this amendment are the copies from our original ANDA with original page number in the parenthesis and sequential number relating to this amendment are out side the parenthesis.

If you have any question please feel free to call me at (609) 448 - 5500.

Sincerely,



Bharat Patel
President/CEO
Neil Laboratories, Inc.

Cc: Gary Buehler
Director, Office of Generic Drugs

Christine Bina
Project Manager

ANDA 76-460

Neil Laboratories, Inc.
Attention: Bharat Patel
55 Lake Drive
P.O. Box 1088
East Windsor, NJ 08520

SEP 25 2002

Dear Sir:

Please refer to your abbreviated new drug application (ANDA) dated July 12, 2002, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Ibuprofen Tablets USP, 200 mg.

We have given your application a preliminary review, and we find that it is not sufficiently complete to merit a critical technical review.

We are refusing to file this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

> You have failed to properly identify the Agency's designated reference listed drug in your application. Reference listed drug means the listed drug identified by the FDA as the drug product upon which an applicant relies in seeking approval of its abbreviated application [21 CFR 314.3(b)]. Please note that the reference listed drug identified in the Approved Drug Products with Therapeutic Equivalence Evaluations, 22nd Edition is Motrin IB Tablets, 200mg, manufactured by McNeil, not Nuprin Tablets, 200mg manufactured by McNeil. Please provide a revised Form FDA 356h that cites the correct reference listed drug and application holder. In addition, please submit the information required under 21 CFR 314.94, including all 505(j)(2)(A) information. A basis for submission, a patent certification, and an exclusivity statement should be revised to make reference to Motrin IB by McNeil. New labeling comparisons to reflect the correct reference listed drug are required. You must submit four copies of draft labeling and a copy of the reference listed drug labeling. You must also provide a side-by-side comparison of the labeling of your proposed drug product with the approved

labeling of the reference listed drug with all differences annotated and explained.

You have failed to supply three required copies of the application. One complete archival copy, a review copy, and a field copy as per 21 CFR 314.94.

The comparative dissolution data, as presented, does not include all of the data necessary for a complete evaluation by the reviewer. You have failed to supply three way dissolution data within the bioequivalence section. You should provide complete dissolution data comparing [redacted] (b) (4) Lot # RD-0325-03/01, [redacted] (b) (4) Lot # RD-0325-03/04, and the RLD. A complete dissolution report should contain the individual data for twelve units, including means, range and relative standard deviation (RSD) at each time point, a description of the methodology being used, and the lot numbers being tested.

You have failed to provide any information to show that your finished product lot manufactured with active drug substance supplied by [redacted] (b) (4) is bioequivalent to the RLD.

It appears that your proposed formulation contains an inactive ingredient, [redacted] (b) (4) that has not been approved in a drug product for human use by the same route of administration [21 CFR 314.127(a)(8)(ii)]. According to the regulation, there is reasonable basis to conclude that the inactive ingredient in your proposed product may raise safety questions because of the lack of information that you have provided regarding its use. Therefore, the Office of Generic Drugs (OGD) will not file this application as an ANDA since new inactive ingredients must be the subject of a new drug application. Please provide additional information to support the safety of the use of this inactive ingredient in your proposed drug product. The information to demonstrate safety should include, but is not limited to, examples of approved drug products administered by the same route of administration which contain the same inactive ingredient within the same concentration range.

You have failed to provide data from the analysis of the bulk lot IBU0103137, supplied by [redacted] (b) (4) In addition, you have failed to provide COAs from Neil Laboratories and [redacted] (b) (4) for lot IBU0103137.

Your executed batch records are incomplete. You must supply packaging records for the test batch of Lot # RD-0325-03/04. These records should contain complete records for the packaging and labeling operations, including drug product and label reconciliation. Please note that the test batch must be completely packaged in the containers proposed for marketing. Please provide this information. We refer you to the Office of Generic Drugs, Policy and Procedure Guide #41-95 for guidance on the packaging of test batches.

You have failed to completely describe your container closure system. We refer you to the Office of Generic Drugs Policy and Procedure Guide #33-92 regarding Consistent Container Information in Abbreviated Applications.

You have failed to provide a certificate of analysis (COA) for the finished dosage form lot RD-0325-03/01.

In addition, you have failed to provide results and conclusions for the non-fasting, single dose *in vivo* bioequivalence study conducted to support approval of your application.

Please provide identification of which bulk lot numbers were used in manufacturing of the lots used to support approval of your application.

Thus, it will not be received as an abbreviated new drug application within the meaning of Section 505(j) of the Act.

Upon receipt of this communication, you may either amend your application to correct the deficiencies or withdraw your application under 21 CFR 314.99. If you have any questions please call:

Christine Bina
Project Manager
(301) 827-5862

Christine M. Bina

Sincerely yours,

Gregory D. Davis for

Wm Peter Rickman
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 76-460
cc: DUP/Jacket
Division File
HFD-92
Field Copy
HFD-610/R.West
HFD-610/P.Rickman
HFD-615/MBennett
Endorsement: HFD-615/GDavis, Chief, RSB 25-SEP-2002 date
HFD-615/CBina, CSO Sept. 25, 2002 date
Word File
V:/FIRMSnz/neil/ltrs&rev/76460.rtf.doc
F/T EEH 09/25/02 File
ANDA Refuse to Receive!

NEIL LABORATORIES INC.

August 11, 2002

ORIG AMENDMENT
N/AM

Craig Kiester
Project Manager
Office of Generic Drugs, CDER
Food and Drug Administration
7500 Standish Place, Room 150
Rockville, MD 20855

RE: Telephone Amendment to Minor Deficiencies to Original ANDA 76-460 (Ibuprofen Tablets USP, 200mg)

Dear Mr. Kiester:

On Thursday, August 7th, 2003 we faxed our response letter to the phone call we received from Mr. Al Mueller and Mr. Subhash Dhanesar with regard to a minor deficiency for a Telephone Amendment.

Enclosed please find the letter that was faxed last Thursday and the highlighted, amended archival and review copies (we are not sending a field copy) of our original ANDA 76-460, stamped with original page numbers.

If you have any questions please feel free to give us a call.

Thank you very much.

Sincerely,

Bharat Patel
President/CEO
Neil Laboratories, Inc.

RECEIVED
AUG 12 2003
OGD/CDER

cc: Mr. Al Mueller, Team Leader
Mr. Subhash Dhanesar, Chemistry Reveiwer

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609-448-5500 • FAX: 609-443-9316 • EMAIL: neillabs@aol.com

NL

NEIL LABORATORIES INC.

Refuse to receive 25-SEP-2002 Gregory S Davis

July 12, 2002

Mr. Gary Buehler
Director
Office Of Generic Drugs, HFD-600
Center For Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

RE: Original ANDA - Ibuprofen Tablets USP, 200 mg

Dear Mr. Buehler:

Pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, enclosed is an original Abbreviated New Drug Application for Ibuprofen Tablets USP, 200 mg. This application consists of the following volumes:

Volume 1	Signed and completed application (Form 356h), basis for ANDA submission, patent and exclusivity certification, 505(j)(2)(A)-information generic/reference comparison, labeling *"in vitro"* data of bioavailability/bioequivalence section (dissolution profiles etc. for proposed drug product vs. reference listed drug).
Volume 2-6	BIO study summary and test results including one CD each of raw data for fasting and non-fasting study (complete *"in vivo"* data and reports from PRACS Institute Ltd.).
Volume 7	Components and composition, raw material controls, manufacturing facility and outside firms, manufacturing and packaging data including executed batch record and in-process controls, container and closures, finished product controls.
Volumes 8	Methods validation stability data, control numbers, samples, environmental statement, GDEA including debarment/conviction and other.

A full table of contents precedes each appropriately paginated volume.

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In addition to the archival and review copies, we are submitting a certified true copy of the chemistry, manufacturing and controls data to the District Director, NJ District Office, Food and Drug Administration, Waterview Corporate Center 3rd Floor, 10 Waterview Boulevard, Parsippany, NJ 07054.

This ANDA covers one shape (round tablets) and two colors (white and brown) of tablets as per our correspondence with FDA (letter reference: OGD-344, attached in section XXII, under sub section "Previous Communications", of this ANDA). It may be noted that white round tablets (Batch No. RD-0325-03/01) were used for the comparative bioavailability/bioequivalence study. However, this ANDA includes comparative *in vitro* dissolution of the Reference Listed Drug NUPRIN® (McNeil Labs) with Neil Labs' white (Batch No. RD-0325-03/01) as well as brown round tablets (Batch No. RD-0325-03/04).

Please contact me at (609) 448-5500 for any comments/questions about this application.

Sincerely,

Bharat Patel
President/CEO
Neil Laboratories Inc.