CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 78-682

Name: Ibuprofen Capsules, 500 mg

Sponsor: Banner Pharmacaps Inc.

Approval Date: March 24, 2009

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 78-682

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 78-682

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-682

Banner Pharmacaps Inc.
Attention: Vandana Garikipati
Manager, Regulatory Affairs
4125 Premier Drive
High Point, NC 27265

Dear Sir:

This is in reference to your abbreviated new drug application (ANDA) dated December 15, 2006, submitted pursuant to section 505(j) of the Federal Food, Drug, and Cosmetic Act (the Act), for Ibuprofen Capsules, 200 mg.

Reference is also made to your amendments dated January 16, July 25, September 4, December 5, and December 23, 2008; and January 19, February 27, March 6, March 18, and March 20, 2009.

We have completed the review of this ANDA and have concluded that adequate information has been presented to demonstrate that the drug is safe and effective for Over-the Counter (OTC) use as recommended in the submitted labeling. Accordingly, the ANDA is approved effective on the date of this letter. The Division of Bioequivalence has determined your Ibuprofen Capsules, 200 mg, to be bioequivalent and, therefore, therapeutically equivalent to the reference listed drug, Advil Liqui-Gels® Capsules, 200 mg, of Wyeth Consumer Healthcare. 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 ANDA require an approved supplemental application before the change may be made.

We note that if FDA requires a Risk Evaluation & Mitigation Strategy (REMS) for a listed drug, an ANDA citing that listed drug also will be required to have a REMS, See 505-1(i).

Postmarketing reporting requirements for this ANDA 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,

{See appended electronic signature page}

Gary Buehler
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Robert L. West
3/24/2009 09:10:34 AM
Deputy Director, for Gary Buehler

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 78-682

LABELING

(b) (4)

(b) (4)

Drug Facts (continued)

directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Directions

- **do not take more than directed**
- **the smallest effective dose should be used**
- do not take longer than 10 days, unless directed by a doctor (see Warnings)
- adults and children 12 years and over:
  - take 1 capsule every 4 to 6 hours while symptoms persist
  - if pain or fever does not respond to 1 capsule, 2 capsules may be used
  - do not exceed 6 capsules in 24 hours, unless directed by a doctor
- children under 12 years: ask a doctor

Drug Facts (continued)

Other information

each capsule contains: potassium 20 mg

- read all warnings and directions before use. Keep carton.
- store at 20°-25°C (68°-77°F)
- avoid excessive heat above 40° C (104° F). Protect from light
- do not use if Tamper-Evident seal under bottle cap imprinted with "Sealed for Your Protection" is broken or missing
- †This product is not manufactured or distributed by Wyeth Consumer Healthcare, owner of the registered trademark Advil®.

Inactive ingredients

FD&C Blue #1, gelatin, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitan and sorbitol

Questions or comments?

Call toll free: **1-877-753-3935**

20 SOFTGELS**
(Liquid Filled Capsules**)

Pain Reliever/
Fever Reducer (NSAID)*

IBUPROFEN
CAPSULES, 200 mg

†Compare to the active ingredient in Advil®

NDC 59726-120-20

KEEP OUTER CARTON FOR COMPLETE WARNINGS AND PRODUCT INFORMATION

20 SOFTGELS**
(Liquid Filled Capsules**)

Pain Reliever/
Fever Reducer (NSAID)*

IBUPROFEN
CAPSULES, 200 mg

Drug Facts

Active ingredient (in each capsule) — Purpose

Solubilized ibuprofen equal to 200 mg ibuprofen (NSAID)*... Pain reliever/fever reducer (present as the free acid and potassium salt)

*nonsteroidal anti-inflammatory drug

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, especially in people allergic to aspirin.

Drug Facts (continued)

Symptoms may include:

- hives
- facial swelling
- asthma (wheezing)
- shock
- skin reddening
- rash
- blisters

If an allergic reaction occurs, stop use and seek medical help right away.

Stomach bleeding warning: This product contains a nonsteroidal anti-inflammatory drug (NSAID), which may cause stomach bleeding. The chance is higher if you:

- are age 60 or older
- have had stomach ulcers or bleeding problems
- take a blood thinning (anticoagulant) or steroid drug
- take other drugs containing an NSAID [aspirin, ibuprofen, naproxen, or others]
- have 3 or more alcoholic drinks every day while using this product
- take more or for a longer time than directed

Drug Facts (continued)

Do not use

- if you have ever had an allergic reaction to any other pain reliever/fever reducer
- right before or after heart surgery

Ask a doctor before use if you have

- problems or serious side effects from taking pain relievers or fever reducers
- stomach problems that last or come back, such as heartburn, upset stomach, or stomach pain
- ulcers
- bleeding problems
- high blood pressure
- heart or kidney disease
- asthma
- taken a diuretic
- reached age 60 or older

Ask a doctor or pharmacist before use if you are

- taking any other drug containing an NSAID (prescription or nonprescription)
- taking a blood thinning (anticoagulant) or steroid drug
- under a doctor's care for any serious condition

Drug Facts (continued)

- taking aspirin for heart attack or stroke, because ibuprofen may decrease this benefit of aspirin
- taking any other drug

When using this product

- take with food or milk if stomach upset occurs
- the risk of heart attack or stroke may increase if you use more than directed or for longer than directed

Stop use and ask a doctor if

- you feel faint, vomit blood, or have bloody or black stools. These are signs of stomach bleeding.
- 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

PLD-A
F120PLD20CL
Lot No.:
Exp. Date:

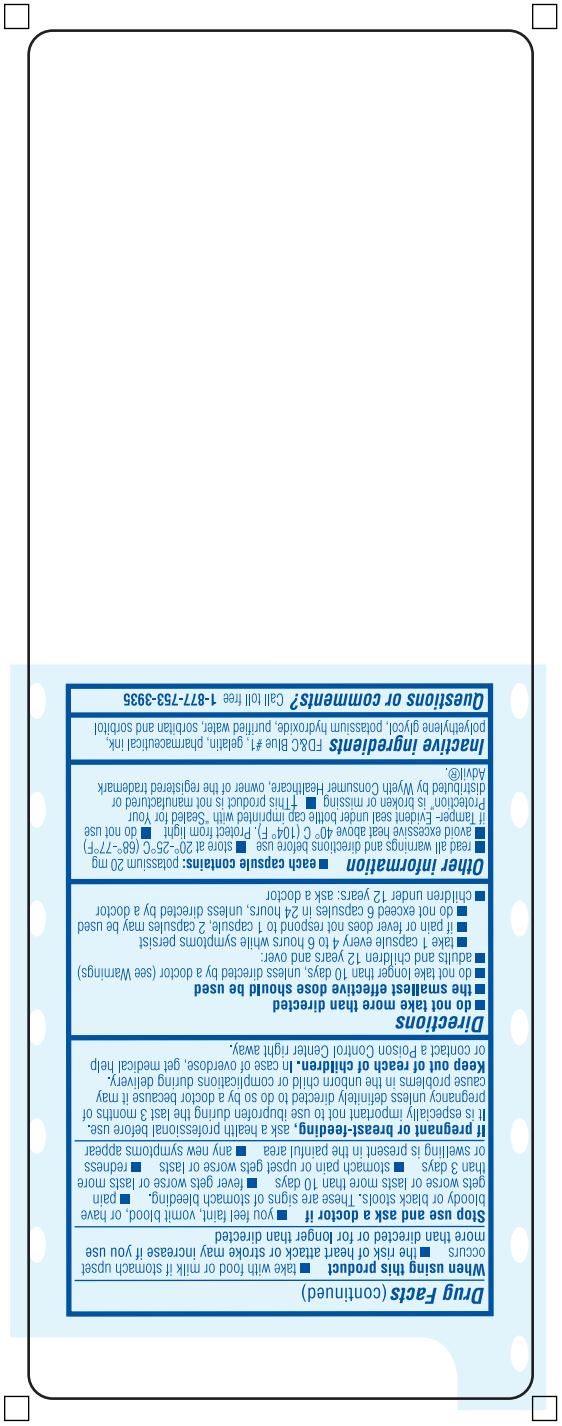
KEEP OUTER CARTON FOR COMPLETE WARNINGS AND PRODUCT INFORMATION

3 59726 12140 8

Distributed by:
PL Developments
Westbury, NY 11590 USA

Manufactured by:
Banner Pharmacaps Inc.
4125 Premier Drive
High Point, NC 27265

12of5
PP#



Drug Facts (continued)

When using this product
- take with food or milk if stomach upset occurs
- the risk of heart attack or stroke may increase if you use more than directed or for longer than directed

Stop use and ask a doctor if
- you feel faint, vomit blood, or have bloody or black stools. These are signs of stomach bleeding.
- 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 reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.

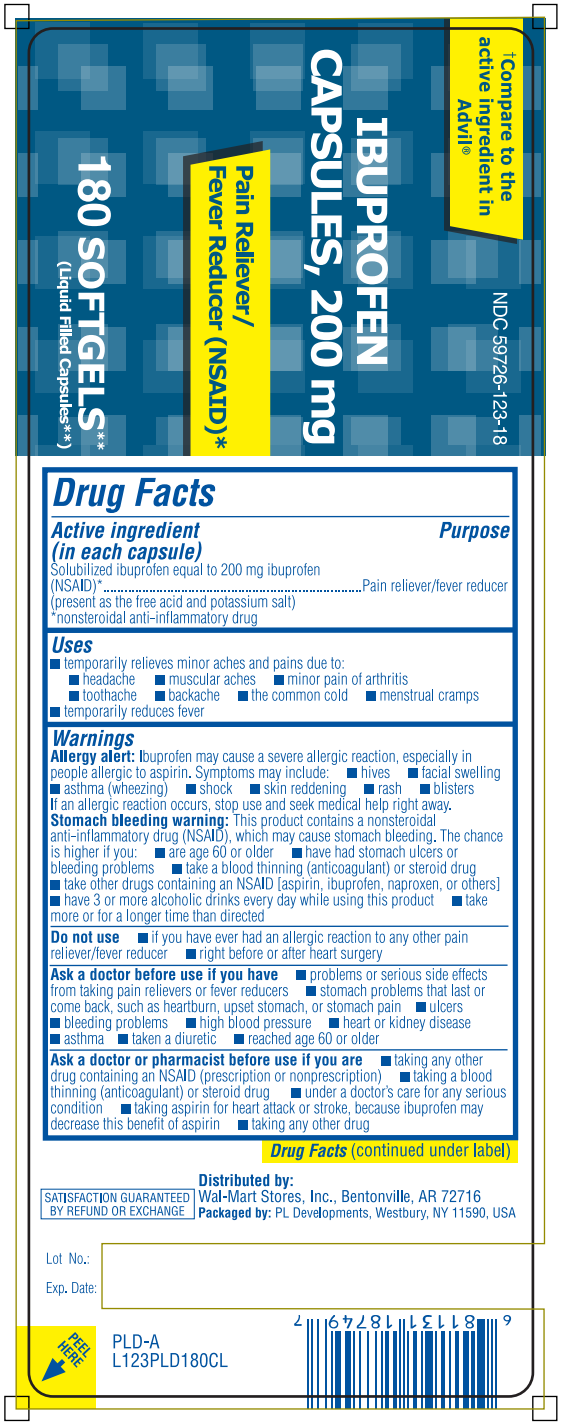
Directions
- **do not take more than directed**
- **the smallest effective dose should be used**
- do not take longer than 10 days, unless directed by a doctor (see Warnings)
- adults and children 12 years and over:
  - take 1 capsule every 4 to 6 hours while symptoms persist
  - if pain or fever does not respond to 1 capsule, 2 capsules may be used
  - do not exceed 6 capsules in 24 hours, unless directed by a doctor
- children under 12 years: ask a doctor

Other information
- **each capsule contains:** potassium 20 mg
- read all warnings and directions before use
- store at 20°-25°C (68°-77°F)
- avoid excessive heat above 40° C (104° F). Protect from light
- do not use if Tamper- Evident seal under bottle cap imprinted with "Sealed for Your Protection" is broken or missing
- †This product is not manufactured or distributed by Wyeth Consumer Healthcare, owner of the registered trademark Advil®.

Inactive ingredients
FD&C Blue #1, gelatin, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitan and sorbitol

Questions or comments?
Call toll free **1-877-753-3935**

(b) (4)



Drug Facts

Active ingredient (in each capsule) — Purpose

Solubilized ibuprofen equal to 200 mg ibuprofen (NSAID)*.....Pain reliever/fever reducer
(present as the free acid and potassium salt)
*nonsteroidal anti-inflammatory drug

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, especially in people allergic to aspirin. Symptoms may include:
- hives
- facial swelling
- asthma (wheezing)
- shock
- skin reddening
- rash
- blisters

If an allergic reaction occurs, stop use and seek medical help right away.

Stomach bleeding warning: This product contains a nonsteroidal anti-inflammatory drug (NSAID), which may cause stomach bleeding. The chance is higher if you:
- are age 60 or older
- have had stomach ulcers or bleeding problems
- take a blood thinning (anticoagulant) or steroid drug
- take other drugs containing an NSAID [aspirin, ibuprofen, naproxen, or others]
- have 3 or more alcoholic drinks every day while using this product
- take more or for a longer time than directed

Do not use
- if you have ever had an allergic reaction to any other pain reliever/fever reducer
- right before or after heart surgery

Ask a doctor before use if you have
- problems or serious side effects from taking pain relievers or fever reducers
- stomach problems that last or come back, such as heartburn, upset stomach, or stomach pain
- ulcers
- bleeding problems
- high blood pressure
- heart or kidney disease
- asthma
- taken a diuretic
- reached age 60 or older

Ask a doctor or pharmacist before use if you are
- taking any other drug containing an NSAID (prescription or nonprescription)
- taking a blood thinning (anticoagulant) or steroid drug
- under a doctor's care for any serious condition
- taking aspirin for heart attack or stroke, because ibuprofen may decrease this benefit of aspirin
- taking any other drug

Drug Facts (continued under label)

SATISFACTION GUARANTEED BY REFUND OR EXCHANGE

Distributed by:
Wal-Mart Stores, Inc., Bentonville, AR 72716
Packaged by: PL Developments, Westbury, NY 11590, USA

Lot No.:

Exp. Date:

PEEL HERE

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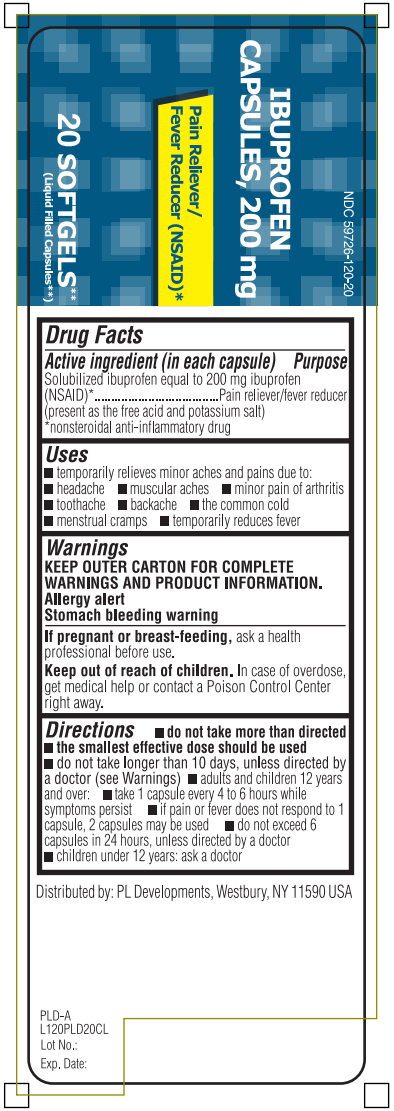
IBUPROFEN
CAPSULES, 200 mg
NDC 69726-120-20
Pain Reliever/
Fever Reducer (NSAID)*
20 SOFTGELS**
(Liquid Filled Capsules**)
Drug Facts
Active ingredient (in each capsule) Purpose
Solubilized ibuprofen equal to 200 mg ibuprofen (NSAID)*.....Pain reliever/fever reducer
(present as the free acid and potassium salt)
*nonsteroidal anti-inflammatory drug
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
KEEP OUTER CARTON FOR COMPLETE WARNINGS AND PRODUCT INFORMATION.
Allergy alert
Stomach bleeding warning
If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.
Directions ■ do not take more than directed ■ the smallest effective dose should be used
■ do not take longer than 10 days, unless directed by a doctor (see Warnings) ■ adults and children 12 years and over: ■ take 1 capsule every 4 to 6 hours while symptoms persist ■ if pain or fever does not respond to 1 capsule, 2 capsules may be used ■ do not exceed 6 capsules in 24 hours, unless directed by a doctor
■ children under 12 years: ask a doctor
Distributed by: PL Developments, Westbury, NY 11590 USA
PLD-A
L120PLD20CL
Lot No.:
Exp. Date:

(b) (4)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 78-682

LABELING REVIEWS

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

ANDA Number: 78-682
Dates of Submission: **January 19, 2009**
Applicant's Name: Banner Pharmacaps Inc.
Established Name: Ibuprofen Capsules, 200 mg

Approval Summary:

1. **Do you have copies of final printed labels and labeling? Yes**

2. **CONTAINER - 20s and 180s**
   Satisfactory in **final print** as of the January 19, 2009 electronic submission

3. **CARTONs – 20s**
   Satisfactory in **final print** as of the January 19, 2009 electronic submission

4. **Revisions needed post-approval:** None

BASIS OF APPROVAL:

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Advil Liqui-Gels®
NDA Number: N 20-402
NDA Drug Name: Advil Liqui-Gels®
NDA Firm: Wyeth Consumer Healthcare; Approved June 11, 2008. (NDA-20-402/S-024)
Date of Approval of NDA Insert and supplement: Approved June 11, 2008; NDA N 20-402/S-024
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, Advil Liqui-Gels®

FOR THE RECORD:

1. **MODEL LABELING**
   Wyeth Consumer Healthcare. (ANDA 20-402/S-024, Approved June 11, 2008).

2. **INACTIVE INGREDIENTS**
   COMPONENTS AND COMPOSITION: *Satisfactory per chemistry review #1*

The proposed drug product is a clear, light blue, oblong, solution-filled, immediate-release soft gelatin capsule containing 200 mg ibuprofen.

The quantitative composition and function of each component in the drug product is listed below:

Fill Ingredient	Function	Weight / Capsule	% w/w
Ibuprofen, USP	Active	200.00 mg	(b) (4)
			(b) (4)

(b) (4)

3. **Patent Data – NDA 20-402**

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 20-402

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

4. **STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON**
   USP: Preserve in tight, light-resistant container.
   RLD: Store at 20 to 25°C(68 to 77°F) avoid excessive heat above 40°C (104°F).
   ANDA: store at 20-25°C (68-77°F) avoid and excessive heat above 40°C (104°F).

5. **PACKAGING CONFIGURATIONS**
   NDA – 2, 4, 20, 80, 135, 180 and 240 count bottles.
   ANDA: Bottles of 20 and 180 **count**
   Tamper evident device is ((b) (4)
   (b) (4) as described in chemistry review.

6. The tablet/capsule imprintings have been accurately described as required by 21 CFR 206,et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).
   -- Clear, light blue, oblong, soft gelatin capsule with white print

7. **Manufacturing will be done by**
   Name: Banner Pharmacaps Inc.
   Address: 4125 Premier Drive
   High Point, NC 27265

8. **CONTAINER/CLOSURE**
   CONTAINER: Satisfactory per chemistry review –
   (b) (4) bottles with child resistant closure for the 20 and 180 count bottles.

9. The following question regarding potassium content being equivalent to the RLD holder was asked to bioequivalence and here is the response.
   Good afternoon Doctor Qing,
   Just wanted to ask you a question. This is the question I asked the firm manufacturing this drug product.

   (b) (4)

   Mr. Barlow,
   After consulting with my team leader in DBE1, we conclude that the potassium content is unlikely to have significant impact on the bioavailability results. Based on the BE study data (ANDA #78682), 90% confidence interval for lnAUCT, lnAUCI and lnCmax of ibuprofen are within the acceptable BE limits of 80-125%.

   If you have further questions, please let us know.

   Thank you!
   Qing

10. Bioequivalence is acceptable as of 11/25/08 sign-off.

11. Please note that the statement (b) (4) was included as a voluntary update to the oral OTC Childrens cough and Cold Medicines. Confirmed as of the 12/23/08 submission. It has been removed as of the 1/19/09 submission per OGD request to be the same as the RLD.

Date of Review: 1/28/09 Date of Submission: 1/19/09

Primary Reviewer: Jim Barlow Date:

Team Leader: Koung Lee Date:

(b) (4)

(b) (4)

Drug Facts (continued)

directed to do so by a doctor because it may cause problems in the unborn child or complications during delivery.

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

Directions

- **do not take more than directed**
- **the smallest effective dose should be used**
- do not take longer than 10 days, unless directed by a doctor (see Warnings)
- adults and children 12 years and over:
  - take 1 capsule every 4 to 6 hours while symptoms persist
  - if pain or fever does not respond to 1 capsule, 2 capsules may be used
  - do not exceed 6 capsules in 24 hours, unless directed by a doctor
- children under 12 years: ask a doctor

Drug Facts (continued)

Other information

each capsule contains: potassium 20 mg

- read all warnings and directions before use. Keep carton.
- store at 20°-25°C (68°-77°F)
- avoid excessive heat above 40° C (104° F). Protect from light
- do not use if Tamper-Evident seal under bottle cap imprinted with "Sealed for Your Protection" is broken or missing
- †This product is not manufactured or distributed by Wyeth Consumer Healthcare, owner of the registered trademark Advil®.

Inactive ingredients

FD&C Blue #1, gelatin, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitan and sorbitol

Questions or comments?

Call toll free: **1-877-753-3935**

20 SOFTGELS**
(Liquid Filled Capsules**)

Pain Reliever/
Fever Reducer (NSAID)*

IBUPROFEN
CAPSULES, 200 mg

†Compare to the active ingredient in Advil®

NDC 59726-120-20

20 SOFTGELS**
(Liquid Filled Capsules**)

Pain Reliever/
Fever Reducer (NSAID)*

IBUPROFEN
CAPSULES, 200 mg

KEEP OUTER CARTON FOR COMPLETE WARNINGS AND PRODUCT INFORMATION

Drug Facts

Active ingredient (in each capsule) — Purpose

Solubilized ibuprofen equal to 200 mg ibuprofen (NSAID)*... Pain reliever/fever reducer (present as the free acid and potassium salt)

*nonsteroidal anti-inflammatory drug

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, especially in people allergic to aspirin.

Drug Facts (continued)

Symptoms may include:

- hives
- facial swelling
- asthma (wheezing)
- shock
- skin reddening
- rash
- blisters

If an allergic reaction occurs, stop use and seek medical help right away.

Stomach bleeding warning: This product contains a nonsteroidal anti-inflammatory drug (NSAID), which may cause stomach bleeding. The chance is higher if you:

- are age 60 or older
- have had stomach ulcers or bleeding problems
- take a blood thinning (anticoagulant) or steroid drug
- take other drugs containing an NSAID [aspirin, ibuprofen, naproxen, or others]
- have 3 or more alcoholic drinks every day while using this product
- take more or for a longer time than directed

Drug Facts (continued)

Do not use

- if you have ever had an allergic reaction to any other pain reliever/fever reducer
- right before or after heart surgery

Ask a doctor before use if you have

- problems or serious side effects from taking pain relievers or fever reducers
- stomach problems that last or come back, such as heartburn, upset stomach, or stomach pain
- ulcers
- bleeding problems
- high blood pressure
- heart or kidney disease
- asthma
- taken a diuretic
- reached age 60 or older

Ask a doctor or pharmacist before use if you are

- taking any other drug containing an NSAID (prescription or nonprescription)
- taking a blood thinning (anticoagulant) or steroid drug
- under a doctor's care for any serious condition

Drug Facts (continued)

- taking aspirin for heart attack or stroke, because ibuprofen may decrease this benefit of aspirin
- taking any other drug

When using this product

- take with food or milk if stomach upset occurs
- the risk of heart attack or stroke may increase if you use more than directed or for longer than directed

Stop use and ask a doctor if

- you feel faint, vomit blood, or have bloody or black stools. These are signs of stomach bleeding.
- 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

PLD-A
F120PLD20CL
Lot No.:
Exp. Date:

KEEP OUTER CARTON FOR COMPLETE WARNINGS AND PRODUCT INFORMATION

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Distributed by:
PL Developments
Westbury, NY 11590 USA

Manufactured by:
Banner Pharmacaps Inc.
4125 Premier Drive
High Point, NC 27265

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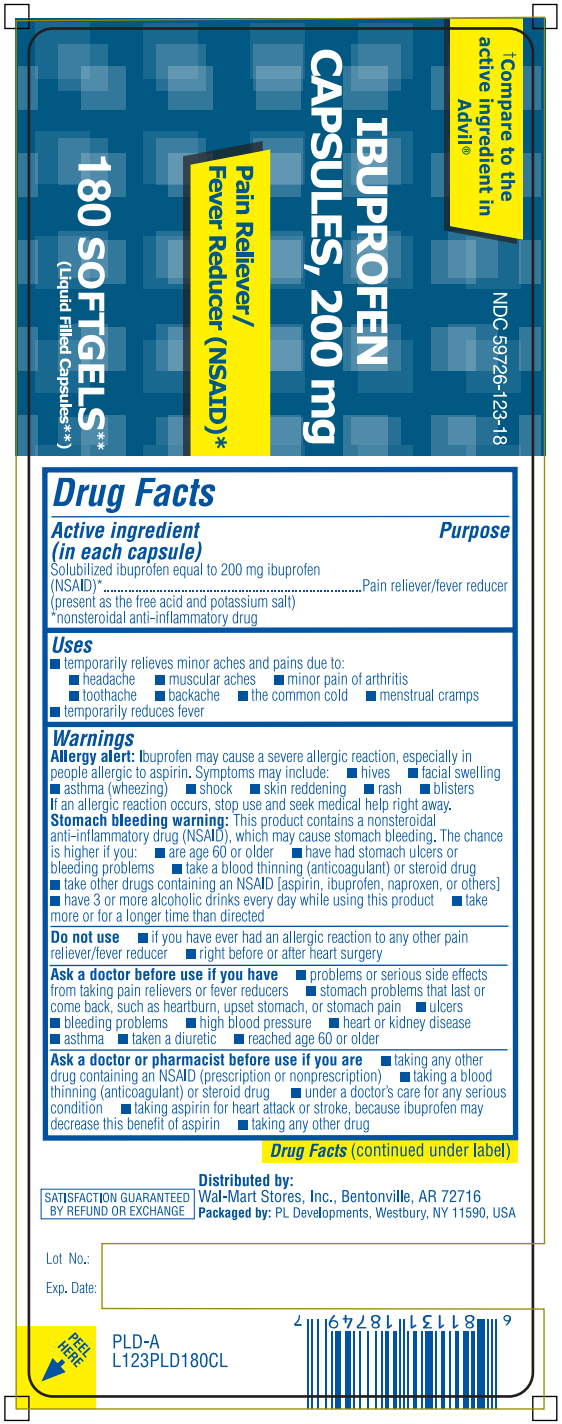
PP#


†Compare to the active ingredient in Advil®
IBUPROFEN CAPSULES, 200 mg
Pain Reliever/ Fever Reducer (NSAID) *
180 SOFTGELS**
(Liquid Filled Capsules**)
NDC 59726-123-18
Drug Facts
Active ingredient (in each capsule)
Purpose
Solubilized ibuprofen equal to 200 mg ibuprofen (NSAID)*
Pain reliever/fever reducer
(present as the free acid and potassium salt)
*nonsteroidal anti-inflammatory drug
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, especially in people allergic to aspirin. Symptoms may include: ■ hives ■ facial swelling ■ asthma (wheezing) ■ shock ■ skin reddening ■ rash ■ blisters
If an allergic reaction occurs, stop use and seek medical help right away.
Stomach bleeding warning: This product contains a nonsteroidal anti-inflammatory drug (NSAID), which may cause stomach bleeding. The chance is higher if you: ■ are age 60 or older ■ have had stomach ulcers or bleeding problems ■ take a blood thinning (anticoagulant) or steroid drug ■ take other drugs containing an NSAID [aspirin, ibuprofen, naproxen, or others] ■ have 3 or more alcoholic drinks every day while using this product ■ take more or for a longer time than directed
Do not use ■ if you have ever had an allergic reaction to any other pain reliever/fever reducer ■ right before or after heart surgery
Ask a doctor before use if you have ■ problems or serious side effects from taking pain relievers or fever reducers ■ stomach problems that last or come back, such as heartburn, upset stomach, or stomach pain ■ ulcers ■ bleeding problems ■ high blood pressure ■ heart or kidney disease ■ asthma ■ taken a diuretic ■ reached age 60 or older
Ask a doctor or pharmacist before use if you are ■ taking any other drug containing an NSAID (prescription or nonprescription) ■ taking a blood thinning (anticoagulant) or steroid drug ■ under a doctor's care for any serious condition ■ taking aspirin for heart attack or stroke, because ibuprofen may decrease this benefit of aspirin ■ taking any other drug
Drug Facts (continued under label)
SATISFACTION GUARANTEED BY REFUND OR EXCHANGE
Distributed by:
Wal-Mart Stores, Inc., Bentonville, AR 72716
Packaged by: PL Developments, Westbury, NY 11590, USA
Lot No.:
Exp. Date:
PEEL HERE
PLD-A
L123PLD180CL
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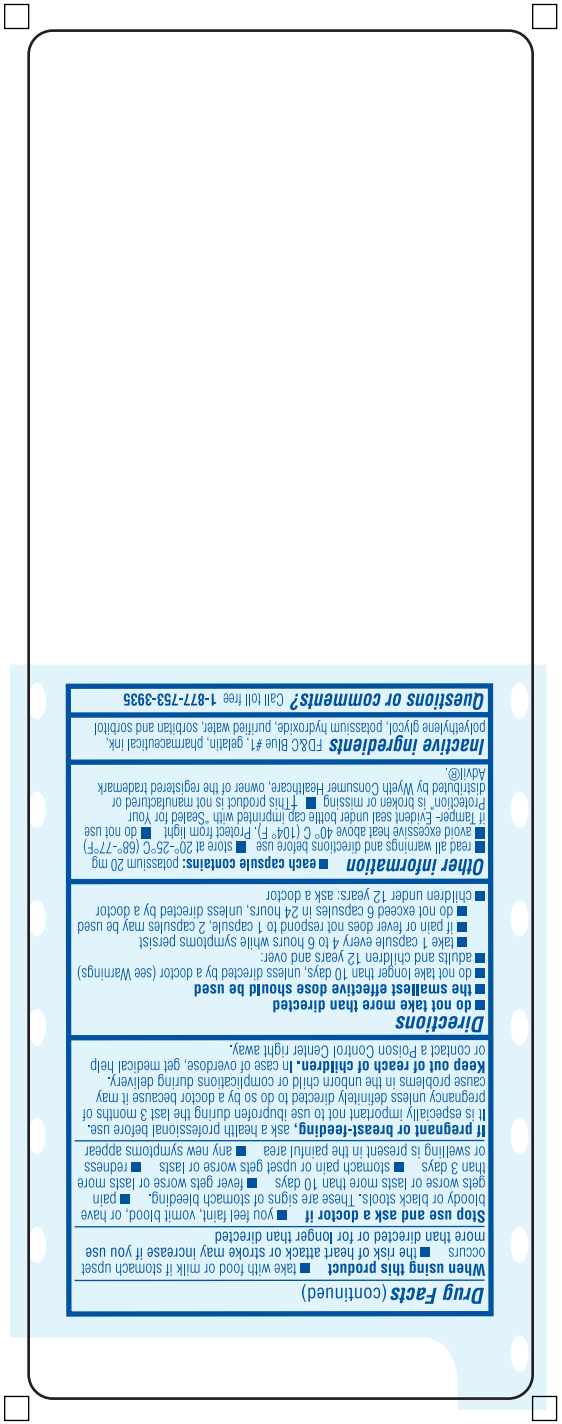
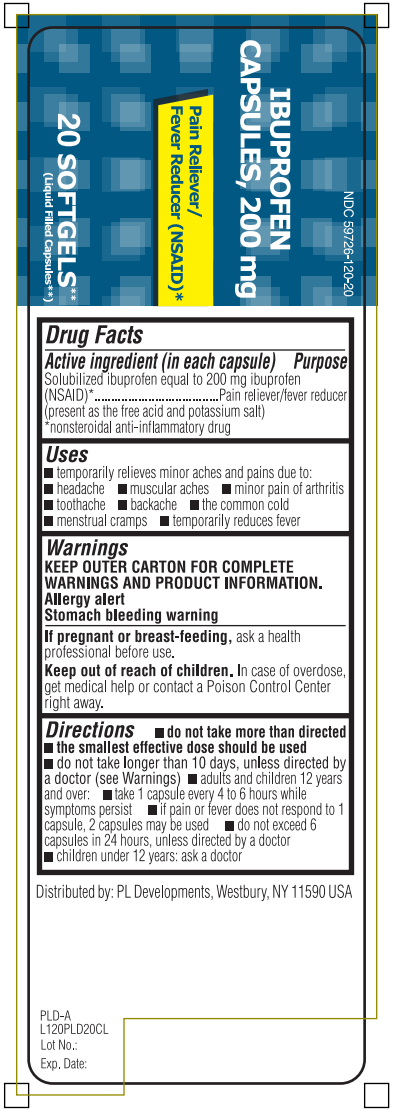

Drug Facts (continued)
When using this product ■ take with food or milk if stomach upset occurs ■ the risk of heart attack or stroke may increase if you use more than directed or for longer than directed
Stop use and ask a doctor if ■ you feel faint, vomit blood, or have bloody or black stools. These are signs of stomach bleeding. ■ 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 reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.
Directions
■ do not take more than directed
■ the smallest effective dose should be used
■ do not take longer than 10 days, unless directed by a doctor (see Warnings)
■ adults and children 12 years and over:
■ take 1 capsule every 4 to 6 hours while symptoms persist
■ if pain or fever does not respond to 1 capsule, 2 capsules may be used
■ do not exceed 6 capsules in 24 hours, unless directed by a doctor
■ children under 12 years: ask a doctor
Other information ■ each capsule contains: potassium 20 mg
■ read all warnings and directions before use ■ store at 20°-25°C (68°-77°F)
■ avoid excessive heat above 40° C (104° F). Protect from light ■ do not use if Tamper- Evident seal under bottle cap imprinted with "Sealed for Your Protection" is broken or missing ■ †This product is not manufactured or distributed by Wyeth Consumer Healthcare, owner of the registered trademark Advil®.
Inactive ingredients FD&C Blue #1, gelatin, pharmaceutical ink, polyethylene glycol, potassium hydroxide, purified water, sorbitan and sorbitol
Questions or comments? Call toll free 1-877-753-3935

(b) (4)


IBUPROFEN
CAPSULES, 200 mg
NDC 69726-120-20
Pain Reliever/
Fever Reducer (NSAID)*
20 SOFTGELS**
(Liquid Filled Capsules**)
Drug Facts
Active ingredient (in each capsule) Purpose
Solubilized ibuprofen equal to 200 mg ibuprofen (NSAID)*.....Pain reliever/fever reducer
(present as the free acid and potassium salt)
*nonsteroidal anti-inflammatory drug
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
KEEP OUTER CARTON FOR COMPLETE WARNINGS AND PRODUCT INFORMATION.
Allergy alert
Stomach bleeding warning
If pregnant or breast-feeding, ask a health professional before use.
Keep out of reach of children. In case of overdose, get medical help or contact a Poison Control Center right away.
Directions ■ do not take more than directed
■ the smallest effective dose should be used
■ do not take longer than 10 days, unless directed by a doctor (see Warnings) ■ adults and children 12 years and over: ■ take 1 capsule every 4 to 6 hours while symptoms persist ■ if pain or fever does not respond to 1 capsule, 2 capsules may be used ■ do not exceed 6 capsules in 24 hours, unless directed by a doctor
■ children under 12 years: ask a doctor
Distributed by: PL Developments, Westbury, NY 11590 USA
PLD-A
L120PLD20CL
Lot No.:
Exp. Date:

(b) (4)

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

James Barlow
1/30/2009 01:55:36 PM
LABELING REVIEWER

Koung Lee
1/30/2009 02:37:10 PM
LABELING REVIEWER
For Wm Peter Rickman

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

ANDA Number: 78-682
Dates of Submission: **December 5, 2008**
Applicant's Name: Banner Pharmacaps Inc.
Established Name: Ibuprofen Capsules, 200 mg

Labeling Deficiencies:

1. **CONTAINER - 20s and 180s**
   We note that you include the statement " [redacted] (b) (4) **" in the text of your labeling. This statement is NOT found in the reference listed drugs labeling. Please revise and/or comment.**

2. **CARTONs – 20s**
   See comment above.

Revise your labels and labeling as requested above and submit final printed labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - 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 the enclosed copy of the reference listed drug's labeling with all differences annotated and explained.

3. Patent Data – NDA 20-402

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 20-402

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

5. Revisions needed post-approval: None

BASIS OF APPROVAL:

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Advil Liqui-Gels®
NDA Number: N 20-402
NDA Drug Name: Advil Liqui-Gels®
NDA Firm: Wyeth Consumer Healthcare; Approved June 11, 2008. (NDA-20-402/S-024)
Date of Approval of NDA Insert and supplement: Approved June 11, 2008; NDA N 20-402/S-024
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, Advil Liqui-Gels®

FOR THE RECORD:

1. MODEL LABELING
   Wyeth Consumer Healthcare. (ANDA 20-402/S-024, Approved June 11, 2008).

2. INACTIVE INGREDIENTS
   COMPONENTS AND COMPOSITION: **Not Satisfactory per Chemistry review- Description of Dosage Form The proposed drug product is a clear, light blue, oblong, solution-filled, immediate-release soft gelatin capsule containing 200 mg ibuprofen.**

(b) (4)

3. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON
   USP: Preserve in tight, light-resistant container.
   RLD: Store at 20 to 25°C(68 to 77°F) avoid excessive heat above 40°C (104°F).
   ANDA: store at 20-25°C (68-77°F) avoid and excessive heat above 40°C (104°F).

4. PACKAGING CONFIGURATIONS
   NDA – 2, 4, 20, 80, 135, 180 and 240 count bottles.
   ANDA: Bottles of 20 and 180 **count**

5. The tablet/capsule imprintings have been accurately described as required by 21 CFR 206,et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).
   -- Clear, light blue, oblong, soft gelatin capsule with white print

6. Manufacturing will be done by
   Name: Banner Pharmacaps Inc.

Address: 4125 Premier Drive
High Point, NC 27265

7. CONTAINER/CLOSURE
   CONTAINER: Satisfactory per chemistry review –
   (b) (4) bottles with child resistant closure for the 20 and 180 count bottles.

8. The following question regarding potassium content being equivalent to the RLD holder was asked to bioequivalence and here is the response.
   Good afternoon Doctor Qing,
   Just wanted to ask you a question. This is the question I asked the firm manufacturing this drug product.

   (b) (4)

   Mr. Barlow,
   After consulting with my team leader in DBE1, we conclude that the potassium content is unlikely to have significant impact on the bioavailability results. Based on the BE study data (ANDA #78682), 90% confidence interval for lnAUCT, lnAUCI and lnCmax of ibuprofen are within the acceptable BE limits of 80-125%.

   If you have further questions, please let us know.

   Thank you!
   Qing

   Bioequivalence is acceptable as of 11/25/08 sign-off.

Date of Review: 12/22/08 Date of Submission: 12/5/08

Primary Reviewer: Jim Barlow Date:

Team Leader: Koung Lee Date:

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

James Barlow
12/22/2008 01:18:14 PM
LABELING REVIEWER

James Barlow
12/22/2008 01:18:23 PM
LABELING REVIEWER

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

ANDA Number: 78-682
Dates of Submission: **July 25, 2008**
Applicant's Name: Banner Pharmacaps Inc.
Established Name: Ibuprofen Potassium Capsules, 200 mg

Labeling Deficiencies:

1. CONTAINER/CARTONs – 20s and (b) (4)s

a. After further review, please revise to read as follows throughout the text –

Ibuprofen Potassium Capsules, 200 mg
(liquid-filled, solubilized, soft gelatin capsules)
Pain Reliever/Fever Reducer (NSAID)*
*nonsteroidal anti-inflammatory drug

xx Liquid Filled Capsules

b. Delete the large font **ibuprofen** **following your trademark. It looks as if it is a proposed proprietary name.**

c. Delete the "Compare to the active ingredient in Advil®" statement from the text.

d. After further review, please confirm that the correct font size was utilized in the text of your labels and labeling. We refer you to 21 CFR 201.66(d) for guidance referencing OTC format requirements.

e. We note that you have included "(b) (4)" in your storage statement. Please revise and/or comment.

Revise your labels and labeling as requested above and submit final printed labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - 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 the enclosed copy of the reference listed drug's labeling with all differences annotated and explained.

Patent Data – NDA 20-402

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 20-402

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

Revisions needed post-approval: None

BASIS OF APPROVAL:

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Advil Liqui-Gels®
NDA Number: N 20-402
NDA Drug Name: Advil Liqui-Gels®
NDA Firm: Wyeth Consumer Healthcare; Approved June 11, 2008. (NDA-20-402/S-024)
Date of Approval of NDA Insert and supplement: Approved June 11, 2008; NDA N 20-402/S-024
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, Advil Liqui-Gels®

FOR THE RECORD:

1. MODEL LABELING
   Wyeth Consumer Healthcare. (ANDA 20-402/S-024, Approved June 11, 2008).

2. INACTIVE INGREDIENTS
   COMPONENTS AND COMPOSITION: **Not Satisfactory per Chemistry review- Description of Dosage Form The proposed drug product is a clear, light blue, oblong, solution-filled, immediate-release soft gelatin capsule containing 200 mg ibuprofen**

(b) (4)

3. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON
   USP: Preserve in tight, light-resistant container.
   RLD: Store at 20 to 25°C(68 to 77°F) avoid excessive heat above 40°C (104°F).
   ANDA: store at 20-25°C (68-77°F) avoic (b) (4) excessive heat above 40°C (104°F).

4. PACKAGING CONFIGURATIONS
   NDA – 2, 4, 20, 80, 135, 180 and 240 count bottles.
   ANDA: Bottles of 20 anc (b) (4) **count**

5. The tablet/capsule imprintings have been accurately described as required by 21 CFR 206,et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).
   -- Clear, light blue, oblong, soft gelatin capsule with white print

6. Manufacturing will be done by
   Name: Banner Pharmacaps Inc.

Address: 4125 Premier Drive
High Point, NC 27265

7. CONTAINER/CLOSURE
   CONTAINER: Satisfactory per chemistry review –
   (b) (4) bottles with child resistant closure for the 20 and (b) (4) count bottles.

8. The following question regarding potassium content being equivalent to the RLD holder was asked to bioequivalence and here is the response.

   Good afternoon Doctor Qing,
   Just wanted to ask you a question. This is the question I asked the firm manufacturing this drug product.

   (b) (4)

   Mr. Barlow,
   After consulting with my team leader in DBE1, we conclude that the potassium content is unlikely to have significant impact on the bioavailability results. Based on the BE study data (ANDA #78682), 90% confidence interval for lnAUCT, lnAUCI and lnCmax of ibuprofen are within the acceptable BE limits of 80-125%.

   If you have further questions, please let us know.

   Thank you!

   Qing

Date of Review: 11/17/08 Date of Submission: 7/25/08

Primary Reviewer: Jim Barlow Date:

Team Leader: John Grace Date:

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

James Barlow
11/17/2008 04:06:37 PM
LABELING REVIEWER

James Barlow
11/17/2008 04:10:14 PM
LABELING REVIEWER

Telephone Fax

ANDA 78-682

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8979

TO: Banner Pharmacaps Inc.

TEL: 336-812-8700

ATTN: Dana S. Toops

FAX: 336-812-9091

FROM: Jim Barlow (Labeling Reviewer)

:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for (Ibuprofen Potassium Capsules).

Pages (including cover): 4

SPECIAL INSTRUCTIONS:

Labeling Comments or questions -

james.barlow@fda.hhs.gov

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

ANDA Number: 78-682
Dates of Submission: **July 25, 2008**
Applicant's Name: Banner Pharmacaps Inc.
Established Name: Ibuprofen Potassium Capsules, 200 mg

Labeling Deficiencies:

1. CONTAINER/CARTONs – 20s and (b) (4)s

a. After further review, please revise to read as follows throughout the text –

Ibuprofen Potassium Capsules, 200 mg
(liquid-filled, solubilized, soft gelatin capsules)
Pain Reliever/Fever Reducer (NSAID)*
*nonsteroidal anti-inflammatory drug

xx Liquid Filled Capsules

b. Delete the large font **ibuprofen** **following your trademark. It looks as if it is a proposed proprietary name.**

c. Delete the "Compare to the active ingredient in Advil®" statement from the text.

d. After further review, please confirm that the correct font size was utilized in the text of your labels and labeling. We refer you to 21 CFR 201.66(d) for guidance referencing OTC format requirements.

e. We note that you have included (b) (4)" in your storage statement. Please revise and/or comment.

Revise your labels and labeling as requested above and submit final printed labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - 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 the enclosed copy of the reference listed drug's labeling with all differences annotated and explained.

{See appended electronic signature page}

_____

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

James Barlow

11/17/2008 04:09:28 PM

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

ANDA Number: 78-682
Dates of Submission: **July 5, 2007**
Applicant's Name: Banner Pharmacaps Inc.
Established Name: Ibuprofen Capsules, 200 mg

Labeling Deficiencies:

1. **GENERAL COMMENTS -**
   a. **Please revise your labels and labeling to be in accord with the most recently approved labeling for the reference listed drug, ADVIL LIQUI-GELS® (NDA 20-402/S-024; approved June 12, 2008)**

   b. **We see that you have proposed a 20 count bottle, but did not supply us with your proposed carton for this package size. Please submit and/or comment.**

2. **CONTAINER** – Bottles of 20 and (b) (4) **count (for the 200 mg strength capsules)**
   a. **Revise to read as follows -**
   Front Panel - Revise to read as follows -

   xx Softgels**
   Liquid Filled Capsules**

   b. **Front Panel – Revise to read as follows -**

   Drug Facts
   Active Ingredient (in each capsule) Purpose

   Solubilized Ibuprofen equal to
   200 mg ibuprofen (NSAID)*…….Pain reliever/Fever reducer
   (present as the free acid and potassium salt)
   ***nonsteroidal anti-inflammatory drug**

   c **Other Information –**

(b) (4)

Revise your labels and labeling as requested above and submit final printed labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - 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 the enclosed copy of the reference listed drug's labeling with all differences annotated and explained.

Patent Data – NDA 20-402

Patent No.	Patent Expiration	Use Code	Description	How Filed	Labeling Impact
None	None	None	There are no unexpired patents for this product in the Orange Book Database.	N/A	None

Exclusivity Data– NDA 20-402

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

Revisions needed post-approval: None

BASIS OF APPROVAL:

Was this approval based upon a petition? No
What is the RLD on the 356(h) form: Advil Liqui-Gels®
NDA Number: N 20-402
NDA Drug Name: Advil Liqui-Gels®
NDA Firm: Wyeth Consumer Healthcare; Approved June 12, 2008. (NDA-20-402/S-024)
Date of Approval of NDA Insert and supplement: Approved June 12, 2008; NDA N 20-402/S-024
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, Advil Liqui-Gels®

FOR THE RECORD:

1. MODEL LABELING
   Wyeth Consumer Healthcare. (ANDA 20-402/S-024), Approved June 12, 2008).

2. INACTIVE INGREDIENTS
   COMPONENTS AND COMPOSITION: Not Satisfactory per Chemistry review- Description of Dosage Form The proposed drug product is a clear, light blue, oblong, solution-filled, immediate-release soft gelatin capsule containing 200 mg ibuprofen.

(b) (4)

3. STORAGE TEMPERATURE RECOMMENDATIONS COMPARISON
   USP: Preserve in tight, light-resistant container.
   RLD: Store at 20 to 25°C(68 to 77°F) avoid excessive heat above 40°C (104°F).
   ANDA: Same as RLD

4. PACKAGING CONFIGURATIONS
   NDA – 2, 4, 20, 80, 135, 180 and 240 count bottles.
   ANDA: Bottles of 20 and (b) (4) **count**

5. The tablet/capsule imprintings have been accurately described as required by 21 CFR 206,et al. (Imprinting of Solid Oral Dosage Form Products for Human Use; Final Rule, effective 9/13/95).
   -- Clear, light blue, oblong, soft gelatin capsule with white print

6. Manufacturing will be done by
   Name: Banner Pharmacaps Inc.
   Address: 4125 Premier Drive
   High Point, NC 27265

7. CONTAINER/CLOSURE
   CONTAINER: Satisfactory per chemistry review –
   (b) (4) bottles with child resistant closure for the 20 and (b) (4) count bottles.

Date of Review: 7/14/08 Date of Submission: July 5, 2007

Primary Reviewer: Jim Barlow Date:

Team Leader: John Grace Date:

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

James Barlow
7/14/2008 12:12:36 PM
LABELING REVIEWER

John Grace
7/16/2008 11:02:09 AM
LABELING REVIEWER

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 78-682

CHEMISTRY REVIEWS

ANDA 78-682

Ibuprofen Capsules, 200 mg

Banner Pharmacaps Inc.

Subhash C. Dhanesar, Ph.D.
Chemistry Division I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 78-682

2. REVIEW # 3

3. REVIEW DATE: June 9, 2008

4. REVIEWER: Subhash C. Dhanesar, Ph.D.

5. PREVIOUS DOCUMENTS: None

Original Submission December 15, 2006
Amendment (CMC) July 5, 2007
Amendment (Labeling) July 25, 2008; December 5, 2008; January 19, 2009
Amendment (Bio) January 16, 2008; September 4, 2008
Amendment (CMC) May 16, 2008
Amendment November 3, 2008
Amendment January 16, 2009

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	February 27, 2009
Telephone Amendment	March 5, 2009
Telephone Amendment	March 6, 2009
Telephone Amendment	March 18, 2009
Telephone Amendment	March 20, 2009

7. NAME & ADDRESS OF APPLICANT:

Name: Banner Pharmacaps Inc.

Address: 4125 Premier Drive
High Point, NC 27265

Representative: Vandana Garikipati

Telephone: 336-812-8700 X23988
Fax: 336-812-9091

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Ibuprofen Capsules

9. LEGAL BASIS FOR SUBMISSION: Advil® Liqui-Gels® from Wyeth

There are no patents listed for the RLD, which is not entitled to a period of marketing exclusivity. However, the product is distributed under U.S. Patent Nos. 5,071,643 and 5,360,615 which will expire December 10, 2008.

10. PHARMACOL. CATEGORY: NSAID

11. DOSAGE FORM: Solid (Capsules)

12. STRENGTH/POTENCY: 200 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: __Rx __X_OTC

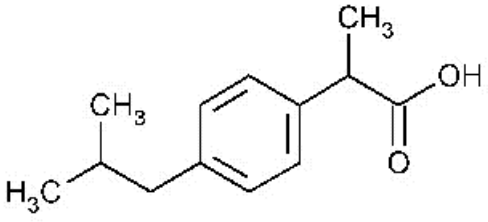
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____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
[redacted] (b) (4)			Ibuprofen	1	Adequate	02-28-2009	S. Dhanesar
			[redacted] (b) (4)	4			
				4			
				4			
				4			
				4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application

[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: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	11-09-2007	
Methods Validation	Not required		S. Dhanesar
Labeling	Acceptable	01-29-2009	J. Barlow
Bioequivalence	Acceptable	11-25-2008	S. Mazzella
EA	Granted		
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 78-682

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is approvable.

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 light blue gelatin capsules containing 200 mg Ibuprofen. The drug substance is Ibuprofen USP. The maximum daily dose is 1200 mg.

(b) (4)

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

The drug product is to be used as directed in the package insert or as directed by a physician.

C. Basis for Approval Recommendation

The ANDA is approvable.

12 PAGES HAVE BEEN WITHHELD IN FULL AS B4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Rosario DCosta
3/24/2009 10:14:13 AM
CHEMIST

Albert Mueller
3/24/2009 10:17:34 AM
CHEMIST
Rosario D'Costa entered this Review #3 for Subhash Dhanesar who's out of the office at this time.

Dat Doan
3/24/2009 10:22:38 AM
CSO

ANDA 78-682

Ibuprofen Capsules, 200 mg

Banner Pharmacaps Inc.

Subhash C. Dhanesar, Ph.D.
Chemistry Division I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 78-682

2. REVIEW # 2A

3. REVIEW DATE: June 9, 2008

4. REVIEWER: Subhash C. Dhanesar, Ph.D.

5. PREVIOUS DOCUMENTS: None

   Original Submission December 15, 2006
   Amendment (CMC) July 5, 2007
   Amendment (Labeling) July 25, 2008; December 5, 2008; January 19, 2009
   Amendment (Bio) January 16, 2008; September 4, 2008
   Amendment (CMC) May 16, 2008

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Amendment	November 3, 2008
Amendment	January 16, 2009

7. NAME & ADDRESS OF APPLICANT:

Name:	Banner Pharmacaps Inc.
Address:	4125 Premier Drive High Point, NC 27265
Representative:	Vandana Garikipati
Telephone:	336-812-8700 X23988
Fax:	336-812-9091

8. DRUG PRODUCT NAME/CODE/TYPE:

   a) Proprietary Name: N/A
   b) Non-Proprietary Name (USAN): Ibuprofen Capsules

9. LEGAL BASIS FOR SUBMISSION: Advil® Liqui-Gels® from Wyeth

There are no patents listed for the RLD, which is not entitled to a period of marketing exclusivity. However, the product is distributed under U.S. Patent Nos. 5,071,643 and 5,360,615 which will expire December 10, 2008.

10. PHARMACOL. CATEGORY: NSAID

11. DOSAGE FORM: Solid (Capsules)

12. STRENGTH/POTENCY: 200 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: __Rx __X_OTC

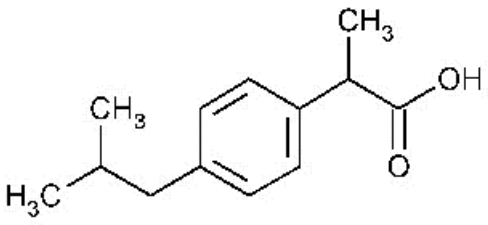
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____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
[redacted]	[redacted]	(b) (4)	Ibuprofen	1	Adequate	02-28-2009	S. Dhanesar
[redacted]	[redacted]	[redacted]	(b) (4)	4			
[redacted]	[redacted]	[redacted]	[redacted]	4			
[redacted]	[redacted]	[redacted]	[redacted]	4			
[redacted]	[redacted]	[redacted]	[redacted]	4			
[redacted]	[redacted]	[redacted]	[redacted]	4			

[1] Action codes for DMF Table:
1 – DMF Reviewed.
2 –Type 1 DMF
3 – Reviewed previously and no revision since last review
4 – Sufficient information in application

[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: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	11-09-2007	
Methods Validation	Not required		S. Dhanesar
Labeling	Acceptable	01-29-2009	J. Barlow
Bioequivalence	Acceptable	11-25-2008	S. Mazzella
EA	Granted		
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 78-682

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is not approvable. CMC is deficient.

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 light blue gelatin capsules containing 200 mg Ibuprofen.
The drug substance is Ibuprofen USP. The maximum daily dose is 1200 mg.

(b) (4)

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

The drug product is to be used as directed in the package insert or as directed by a physician.

C. Basis for Non-Approval Recommendation

The ANDA is not approvable. CMC is deficient.

11 PAGES HAVE BEEN WITHHELD IN FULL AS B4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

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/s/

Subhash Dhanesar
2/20/2009 09:33:15 AM
CHEMIST

Albert Mueller
2/20/2009 05:45:34 PM
CHEMIST

Dat Doan
2/23/2009 11:17:47 AM
CSO

ANDA 78-682

Ibuprofen Capsules, 200 mg

Banner Pharmacaps Inc.

Subhash C. Dhanesar, Ph.D.
Chemistry Division I

Table of Contents

Chemistry Review Data Sheet

1. ANDA 78-682

2. REVIEW # 1B

3. REVIEW DATE: December 13, 2007

4. REVIEWER: Subhash C. Dhanesar, Ph.D.

5. PREVIOUS DOCUMENTS: None

6. SUBMISSION(S) BEING REVIEWED:

Submission(s) Reviewed	Document Date
Original Submission	December 15, 2006
Amendment (CMC)	July 5, 2007
Amendment (Bio)	January 16, 2008

7. NAME & ADDRESS OF APPLICANT:

Name: Banner Pharmacaps Inc.

Address: 4125 Premier Drive
High Point, NC 27265

Representative: Dale Kruep

Telephone: 336-812-8700
Fax: 336-812-9091

8. DRUG PRODUCT NAME/CODE/TYPE:

a) Proprietary Name: N/A
b) Non-Proprietary Name (USAN): Ibuprofen Capsules

9. LEGAL BASIS FOR SUBMISSION: Advil® Liqui-Gels® from Wyeth

There are no patents listed for the RLD, which is not entitled to a period of marketing exclusivity. However, the product is distributed under U.S. Patent Nos. 5,071,643 and 5,360,615 which will expire December 10, 2008.

10. PHARMACOL. CATEGORY: NSAID

11. DOSAGE FORM: Solid (Capsules)

12. STRENGTH/POTENCY: 200 mg

13. ROUTE OF ADMINISTRATION: Oral

14. Rx/OTC DISPENSED: __Rx __X_OTC

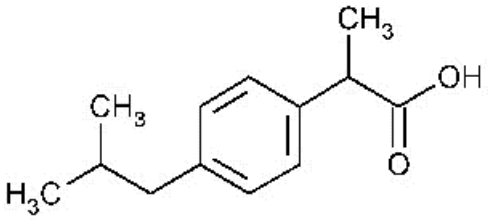
15. SPOTS (SPECIAL PRODUCTS ON-LINE TRACKING SYSTEM):

_____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:

Chemistry Review Data Sheet

A. DMFs:

DMF #	TYPE	HOLDER	ITEM REFERENCED	CODE[1]	STATUS[2]	DATE REVIEW COMPLETED	COMMENTS
[redacted]		(b) (4)	Ibuprofen	1	Adequate	01-28-2008	S. Dhanesar
			(b) (4)	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 N/A (There is enough data in the application, therefore the DMF did not need to be reviewed)

B. Other Documents: None

18. STATUS:

CONSULTS/ CMC RELATED REVIEWS	RECOMMENDATION	DATE	REVIEWER
Microbiology	N/A		
EES	Acceptable	11-09-2007	
Methods Validation	Not required		S. Dhanesar
Labeling	Pending		
Bioequivalence	Pending		
EA	Granted		
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 78-682

The Executive Summary

I. Recommendations

A. Recommendation and Conclusion on Approvability

The ANDA is not approvable due to pending Labeling and Bioequivalence reviews and deficient CMC review. EER is 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 light blue gelatin capsules containing 200 mg Ibuprofen. The drug substance is Ibuprofen USP. The maximum daily dose is 1200 mg.

(b) (4)

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

The drug product is to be used as directed in the package insert or as directed by a physician.

C. Basis for Not-Approval Recommendation

The ANDA is not approvable due to pending Labeling and Bioequivalence reviews and deficient CMC review. EER is acceptable.

28 PAGES HAVE BEEN WITHHELD IN FULL AS B4 (CCI/TS) IMMEDIATELY FOLLOWING THIS PAGE

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/s/

Subhash Dhanesar
4/2/2008 03:17:22 PM
CHEMIST

Albert Mueller
4/2/2008 03:44:11 PM
CHEMIST

Dat Doan
4/3/2008 11:00:08 AM
CSO

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 78-682

BIOEQUIVALENCE REVIEWS

DIVISION OF BIOEQUIVALENCE DISSOLUTION ACKNOWLEDGEMENT REVIEW

ANDA No.	78-682
Drug Product Name	Ibuprofen Capsules
Strength	200 mg
Applicant Name	Banner Pharmacaps, Inc.
Submission Date	September 4, 2008
Reviewer	Steven Mazzella,R.Ph.

EXECUTIVE SUMMARY

This is a review of the dissolution specification acknowledgement from the firm.

The firm has accepted the FDA-recommended dissolution method and specification.

The bioequivalence section of the application is complete.

COMMENTS:

None

DEFICIENCY COMMENTS:

None

RECOMMENDATIONS:

From a bioequivalence point of view, the firm has met the requirements for *in-vivo* bioequivalence and *in-vitro* dissolution testing. The bioequivalence section of the application is acceptable.

I. Completed Assignment for 78682 ID: 6913

Back to Main Menu

Reviewer: Mazzella, Steven **Date Completed:**

Verifier: , **Date Verified:**

Division: Division of Bioequivalence

Description:

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
6913	9/4/2008	Dissolution Data	Dissolution Acknowledgement	0	0
				Bean Total:	0

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/s/

Steven Mazzella
11/25/2008 02:08:35 PM
BIOPHARMACEUTICS

Lizzie Sanchez
11/25/2008 02:20:54 PM
BIOPHARMACEUTICS

DIVISION OF BIOEQUIVALENCE REVIEW

ANDA No.	78-682		
Drug Product Name	Ibuprofen Liquid-Filled Capsules (OTC)		
Strength(s)	200 mg		
Applicant Name	Banner Pharmacaps Inc.		
Address	4125 Premier Drive, High point, NC 27265		
Applicant's Point of Contact	Dale A. Kruep		
Contact's Telephone Number	(336) 812-8700 (ext. 3303)		
Contact's Fax Number	(336) 812-9091		
Original Submission Date(s)	December 15, 2006		
Submission Date(s) of Amendment(s) Under Review	January 16, 2008 (Bio-summary tables); July 5, 2007 (Non-fasting study)		
Reviewer	Qing Liu, Ph.D.		
Study Number (s)	R06-0364	R07-0362	
Study Type (s)	Fasting	Non-fasting	
Strength (s)	200 mg single dose	200 mg single dose	
Clinical Site	PRACS Institute, Ltd.		
Clinical Site Address	625 DeMers Avenue, East Grand Forks, MN 56721, USA		
Analytical Site	(b) (4)		
Analytical Site Address	(b) (4)		
OUTCOME DECISION	**INCOMPLETE**		

1 EXECUTIVE SUMMARY

This application contains the results of fasting and non-fasting bioequivalence (BE) studies comparing the test product, Ibuprofen Liquid-Filled Capsules, 200 mg (OTC), to the corresponding reference product, Advil® Liqui-Gels®, 200 mg (OTC) (Wyeth Consumer Healthcare). Each of the BE studies was designed as a single center, randomized, single-dose, two-way crossover study in healthy, adult subjects. The firm's fasting and non-fasting studies are acceptable. The results are summarized in the tables below (NOTE: The analytical assay used in the two studies was conducted in two different laboratories. The concentration units are "ng/mL" for the fasting study and "µg/mL" for the non-fasting study):

Ibuprofen Dose (1 x 200 mg) Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data				
Fasting Bioequivalence Study (R06-0364) N=24				
Parameter	**Test**	**Reference**	**% Ratio**	**90% CI**
AUC_{0-t} (hr * ng/ml)	76076.87	73731.10	103	100.44 - 106.00
$AUC_{0-\infty}$ (hr * ng/ml)	78431.49	76063.79	103	100.29 - 106.01
C_{max} (ng/ml)	25351.96	24925.57	102	94.27 - 109.74

Ibuprofen Dose (1 x 200 mg) Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data				
Non-Fasting Bioequivalence Study (R07-0362) N=24				
Parameter	**Test**	**Reference**	**% Ratio**	**90% C.I.**
AUC_{0-t} (hr * µg/ml)	58.18	57.41	101	98.90 - 103.84
$AUC_{0-\infty}$ (hr * µg/ml)	60.42	59.25	102	99.57 - 104.42
C_{max} (µg/ml)	15.14	16.52	92	83.71 - 100.33

The firm has conducted acceptable comparative dissolution testing of its test product using the FDA-recommended dissolution method (See dissolution reviews in DFS N 078682 N000 AB 16-Jan-2008 and N 078682 N000 AC 05-Jul-2007). The firm was advised to acknowledge its acceptance of the FDA-recommended dissolution method (900 mL of pH 7.2 phosphate buffer with basket at 150 rpm) and specification of NLT (b)(4)% (Q) in 20 minutes.

The application is incomplete pending the firm's acknowledgement of its acceptance of the FDA-recommended dissolution method and specification.

No Division of Scientific Investigations (DSI) inspection is pending or necessary.

2 TABLE OF CONTENTS

3 SUBMISSION SUMMARY

3.1 Drug Product Information

Test Product	Ibuprofen Capsules, 200 mg (OTC)
Reference Product	Advil® Liqid Gels®, 200 mg (OTC)
RLD Manufacturer	Wyeth Consumer Healthcare
NDA No.	20-402
RLD Approval Date	April 20, 1995
Indication	• Temporarily relieves minor aches and pains due to the common cold, headache, toothache, muscular aches, backache, minor pain of arthritis, menstrual cramps • Temporarily reduces fever.

3.2 PK/PD Information[1]

Bioavailability	The orally administered drug is approximately 80% absorbed from the gut. A linear dose-response is noted for single ibuprofen doses up to 800 mg. There is also a correlation between the reduction of fever and drug concentration over time.
Food Effect	Although the peak concentration is lower and time to peak concentration is slower if the drug is taken with food, the extent of ibuprofen absorption is not affected.
Tmax	1.15 hour (non-fasting); 0.7 hour (fasting) [2]
Metabolism	Ibuprofen is metabolized via hepatic oxidation by cytochrome P450 2C9 to two inactive metabolites.
Excretion	Ibuprofen is excreted in the urine, 50—60% as metabolites and approximately 10% as unchanged drug. Some biliary excretion may occur. Excretion is usually complete within 24 hours of oral administration.
Half-life	2.526 hour (single oral dose)
Drug Specific Issues (if any)	The FDA pregnancy category is B during the first and second trimesters and D during the third trimester of pregnancy.

[1] http://www.clinicalpharmacology-p.com/Forms/Monograph/monograph.aspx?cpnum=303&sec=monphar
[2] Enterprisesearch- NDA 20-402; 200 mg (Ibuprofen) Liquigel Capsules. Submission Date: December 11, 1996

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3.3 OGD Recommendations for Drug Product

Number of studies recommended:	2: fasting and non-fasting

1.	**Type of study:**	Fasting
	Design:	Single-dose, two-treatment, two-period crossover *in vivo*
	Strength:	200 mg
	Subjects:	Healthy, non-smoking subjects
	Additional Comments:	Female subjects that are pregnant, lactating or have the child bearing potential should be excluded from the study.

2.	**Type of study:**	Non-fasting
	Design:	Single-dose, two-treatment, two-period crossover *in vivo*
	Strength:	200 mg
	Subjects:	Healthy, non-smoking subjects
	Additional Comments:	Female subjects that are pregnant, lactating or have childbearing potential should be excluded from the study.

Analytes to measure (in plasma/serum/blood):	Parent drug (ibuprofen) in human plasma
Bioequivalence based on:	90% CI: $\ln AUC_{0-t}$, $\ln AUC_{0-\infty}$, $\ln C_{max}$ of ibuprofen
Waiver request of *in vivo* testing:	N/A
Source of most recent recommendations:	OGD 07-0327 (Perrigo)
Summary of OGD or DBE History (for details, see Appendix 4.4):	To date, no ANDAs have been approved for Advil® Liqid Gels® capsules (OTC) according to Orange Book. The following ANDA applications are currently pending per OGD Master Que:

ANDA#	Firm	Strength
77-338	Dr. Reddys	200 mg
78-682	Banner	200 mg
79-205	Marksans	200 mg

3.4 Contents of Submission

Study Types	Yes/No?	How many?
Single-dose fasting	Yes	1
Single-dose fasting (sprinkle)	No	--
Single-dose fed	Yes	1
Steady-state	No	--
In vitro dissolution	Yes	1
Waiver requests	No	--
BCS Waivers	No	--

Clinical Endpoints	No	--
Failed Studies	No	--
Amendments	Yes	2

3.5 Pre-Study Bioanalytical Method Validation

For the fasting study (R06-0364) - PRACS:

Information Requested	Data
Bioanalytical method validation report location	Volume 4 (original ANDA), Page 1327
Analyte	Ibuprofen
Internal standard (IS)	Ibuprofen-d3
Method description	Solid Phase Extraction with LC/MS/MS method
Limit of quantitation	100.00 ng/mL
Average recovery of drug (%)	74.46%
Average recovery of IS (%)	72.85%
Standard curve concentrations (ng/mL)	100.00, 500.00, 1000.00, 5000.00, 10000.00, 20000.00, 30000.00, 40000.00
QC concentrations (ng/mL)	300.00, 15000.00, 35000.00
QC Intraday precision range (%)	0.73% - 2.06%
QC Intraday accuracy range (%)	92.68% - 105.26%
QC Interday precision range (%)	1.67% - 3.59%
QC Interday accuracy range (%)	102.21% - 108.74%
Bench-top stability (hrs)	25:29 hours-minutes @ room temperature
Stock stability (hrs)	168:18 hours-minutes @ 4°C, 19:49 @ room temperature
Processed stability (hrs)	96:00 @ 4°C
Freeze-thaw stability (cycles)	4 cycles
Long-term storage stability (days)	63 days @ -20ºC
Dilution integrity	50000.00 ng/mL, diluted 3 and 10-fold. Accuracy: 97.00% and 99.00%
Selectivity	No interfering peaks noted in blank plasma samples for 6 out of 6 lots

Note: Blank human plasma used in preparation of calibration standards and QCs contained K_3EDTA in the pre-study. The blood samples from study subjects were collected in 6 mL K_2EDTA vacutainers. The firm also conducted cross validation of K_2EDTA vs. K_3EDTA as anti-coagulant and demonstrated that that either K_3EDTA plasma or K_2EDTA plasma may be used in this method.

SOP submitted	Yes	
SOP No.	**Effective Date of SOP**	**SOP Title**
L1100.100	01/27/2006	Sample Reanalysis And Reporting Criteria
Bioanalytical method is acceptable	Yes	

For the non-fasting study (R07-0362) –BA Research:

Information Requested	Data
Bioanalytical method validation report location	Volume 2.2, Appendix 16.5
Analyte	Ibuprofen
Internal standard (IS)	(b) (4)
Method description	Protein precipitation extraction with LC/MS/MS method
Limit of quantitation (µg/mL)	0.2000 µg/mL
Average recovery of drug (%)	93.7%
Average recovery of IS (%)	88.8%
Standard curve concentrations (µg/mL)	0.2000, 0.4000, 1.000, 2.000, 5.000, 10.00, 20.00, 34.00 and 40.00 µg/mL
QC concentrations (µg/mL)	0.6000, 4.000 and 30.00 µg/mL
QC Intraday precision range (%)	2.0 to 11.3%
QC Intraday accuracy range (%)	96.4 to 110%
QC Interday precision range (%)	6.8 to 9.7%
QC Interday accuracy range (%)	99.7 to 104%
Bench-top stability (hrs)	24 hours in human plasma @ room temperature
Stock stability (days/hours)	23 days @ 4°C for drug and 14 days @ 4°C for internal standard 6 hours at room temperature for drug and internal standard
Processed stability (hrs)	70 hours @ room temperature; 70 hours @ 4°C
Freeze-thaw stability (cycles)	6 freeze-thaw cycles
Long-term storage stability (days)	65 days @ -20°C
Dilution integrity	200.0 and 30 µg/mL diluted 10-fold. Accuracy: 101 and 102%
Selectivity	No interfering peaks noted in blank plasma samples

Note: Blank human plasma used in preparation of calibration standards, and QCs contained K_2EDTA. The blood samples from study subjects were collected in 6 mL K_2EDTA vacutainers.

SOP submitted	Yes	
SOP No.	**Effective Date of SOP**	**SOP Title**
L100.115	06/30/2005	Sample Analysis Chromatographic (for sample analysis)
L1100.100	01/27/2006	Sample Reanalysis And Reporting Criteria (for re-assay samples)
Bioanalytical method is acceptable	Yes	

Comments on the Pre-Study Method Validation:

- The pre-study method validation is acceptable.

3.6 In Vivo Studies

Table 1. Summary of all *in vivo* Bioequivalence Studies

Study Ref. No.	Study Objective	Study Design	Treatment (Dose, Dosage Form, Route) [Product ID]	Subjects (No. (M/F) Type Age: mean (range)	Arithmetic Mean (± SD) Pharmacokinetic Parameters Median (Range) for Tmax						Study Report Location
					Cmax (ng/mL)	Tmax (hrs)	AUCt (ng/mL x hr)	AUCi (ng/mL x hr)	tHalf (hrs)	Kel (1/hr)	
Study # R06-0364	A relative bioavailability Study of 200 mg ibuprofen liquid solution in soft gelatin capsules under fasting conditions	Open, randomized, two-way crossover, single 200 mg dose.	Test: ibuprofen 200 mg soft gelatin capsules, Oral [Lot No. P060508-B2]	24 (9/15) healthy volunteers 37.00 yr (19 – 59 yr).	25971 ± 5503	0.81 (0.33-3.0)	77995 ± 18945	80791 ± 21889	2.31 ± 0.43	0.3085 ± 0.0506	5.3.1.2
			Reference: Advil® LIQUI-GELS 200 mg capsules, oral [Lot No. B44305]		25654 ± 5709	0.82 (0.33-4.0)	75646 ± 18101	78271 ± 19962	2.32 ± 0.38	0.3062 ± 0.05	
Study # R07-0362	A relative bioavailability study of 200 mg ibuprofen liquid solution in soft gelatin capsules under non-fasting conditions	Open, randomized, two-way crossover, single 200 mg dose conditions.	Test: ibuprofen 200 mg soft gelatin capsules, Oral [Lot No. P060508-B2]	24 (13/11) healthy volunteers 33.83 yr (18 - 52 yr)	15510 ± 3394	1.88 (0.67 – 4.00)	59090 ± 11322	61530 ± 12829	2.34 ± 0.40	0.3052 ± 0.0575	Volumes 1 & 2
			Reference: Advil® LIQUI-GELS 200 mg capsules, oral [Lot No. B44305]		17090 ± 4399	1.50 (0.67 – 4.00)	58380 ± 11577	60400 ± 12962	2.20 ± 0.38	0.3242 ± 0.0579	

Table 2. Statistical Summary of the Comparative Bioavailability Data Calculated by the Reviewer

Ibuprofen Dose (1 x 200 mg) Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data Fasting Bioequivalence Study (R06-0364) N=24				
Parameter	**Test**	**Reference**	**% Ratio**	**90% CI**
AUC_{0-t} (hr * ng/ml)	76076.87	73731.10	103	100.44 - 106.00
$AUC_{0-\infty}$ (hr * ng/ml)	78431.49	76063.79	103	100.29 - 106.01
C_{max} (ng/ml)	25351.96	24925.57	102	94.27 - 109.74

Ibuprofen Dose (1 x 200 mg) Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data Non-Fasting Bioequivalence Study (R07-0362) N=24				
Parameter	**Test**	**Reference**	**% Ratio**	**90% C.I.**
AUC_{0-t} (hr * µg/ml)	58.18	57.41	101	98.90 - 103.84
$AUC_{0-\infty}$ (hr * µg/ml)	60.42	59.25	102	99.57 - 104.42
C_{max} (µg/ml)	15.14	16.52	92	83.71- 100.33

Table 3. Reanalysis of Study Samples

Fasting Study, Study No: R06-0364:

Fasting Bioequivalence Study R06-0364								
Reason for Reanalysis	**Number of Samples Reanalyzed**				**Number of Recalculated Values Used After Reanalysis[5]**			
	Actual Number		**% of Total Assays**		**Actual Number**		**% of Total Assays**	
	Test N=429[2]	**Reference N=432[2]**	**Test N=429[2]**	**Reference N=432[2]**	**Test N=429[2]**	**Reference N=432[2]**	**Test N=429[2]**	**Reference N=432[2]**
	n[3]	**n[3]**	**%[4]**	**%[4]**	**n[3]**	**n[3]**	**%[4]**	**%[4]**
Pharmacokinetic[1]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Adjusted lower limit of quantitation	5	8	1.17	1.85	0.0	0.0	0.0	0.0
Total Number of Samples Reanalyzed	5	8	1.17	1.85	0.0	0.0	0.0	0.0

[1] If no repeats were performed for pharmacokinetic reasons, insert "0.0" throughout the table
[2] N = Number of samples analyzed for each treatment
[3] n = Number of samples repeated
[4] % = percentage of assays repeated (i.e. 100*(n/N)%)
[5] Reported values that are different from the original value

Did use of recalculated plasma concentration data change study outcome? No

No re-calculated values were used after reanalysis (all 13 samples were below LOQ in the original and repeat assays).

Non-fasting Study, Study No: R07-0362:

Study No. R07-0362 Ibuprofen Additional information in Volume(s) 2, Page(s) 13 and 20 to 21								
Reason why assay was repeated	**Number of samples reanalyzed**				**Number of recalculated values used after reanalysis**			
	Actual number		**% of total assays**		**Actual number**		**% of total assays**	
	T	**R**	**T**	**R**	**T**	**R**	**T**	**R**
Pharmacokinetic[1]	0.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Low internal standard	6	6	0.69	0.69	6	6	0.69	0.69
Low standard eliminated	5	3	0.58	0.35	5	3	0.58	0.35
High internal standard	1	0	0.12	0.00	1	0	0.12	0.00
Extraction error (transferring error)	1	0	0.12	0.00	1	0	0.12	0.00
Total	13	9	1.50	1.04	13	9	1.50	1.04

[1] - If no repeats were performed for pharmacokinetic reasons, insert "0.0."

Did use of recalculated plasma concentration data change study outcome? No

Comments from the Reviewer:

Reanalysis in both studies is acceptable.

3.7 Formulation

Location in appendix	Section 4.2, Page 30
If a tablet, is the RLD scored?	N/A
If a tablet, is the test product biobatch scored	N/A
Is the formulation acceptable?	**ACCEPTABLE**
If not acceptable, why?	

3.8 In Vitro Dissolution

Location of DBE Dissolution Review	DFS N 078682 N 000 16-Jan-2008 DFS, N 078682 N 000 05-Jul-2007
Source of Method (USP, FDA or Firm)	FDA
Medium	Phosphate buffer, pH 7.2
Volume (mL)	900 ml
USP Apparatus type	I (Basket)
Rotation (rpm)	150
DBE-recommended specifications	NLT (b)(4)% (Q) in 20 minutes
If a modified-release tablet, was testing done on ½ tablets?	N/A
F2 metric calculated?	No
If no, reason why F2 not calculated	Single strength and more than (b)(4) dissolved in 20 minutes
Is method acceptable?	**INCOMPLETE**
If not then why?	Pending the firm's acknowledgement of the FDA-recommended dissolution method and specification.

3.9 Waiver Request(s)

N/A

3.10 Deficiency Comments

None

Both BE studies are acceptable. However, the dissolution testing is incomplete pending the firm's acknowledgement of the FDA-recommended dissolution method and specification.

3.11 Recommendations

1. The Division of Bioequivalence accepts the fasting BE study # R06-0364 conducted by Banner Pharmacaps, Inc., on its Ibuprofen Capsules, 200 mg, lot # P060508-B2 comparing it to Advil® Liqid Gels®, 200 mg, lot # P060508-B2 of Wyeth Consumer Healthcare.

2. The Division of Bioequivalence accepts the non-fasting BE study # R07-0362 conducted by Banner Pharmacaps, Inc., on its Ibuprofen Capsules, 200 mg, lot # P060508-B2 comparing it to Advil® Liqid Gels®, 200 mg, lot # B44305 of Wyeth Consumer Healthcare.

3. The firm's in vitro dissolution testing is incomplete. The firm is asked to acknowledge the following FDA-recommended dissolution method and specification.

The dissolution testing should be conducted in 900 ml of Phosphate buffer, pH7.2 using USP Apparatus I (basket) at 150 rpm. The test product should meet the following specification:

NLT(b) (4)% (Q) of labeled amount of ibuprofen in the dosage form is dissolved in 20 min

4. The Division of Bioequivalence deems the test product, Ibuprofen Capsules, 200 mg, manufactured by Banner Pharmacaps, Inc., to be bioequivalent to the reference product, Advil® Liqid Gels®, 200 mg, manufactured by Wyeth Consumer Healthcare.

5. The application is incomplete. The firm has not yet acknowledged its acceptance of the FDA-recommended dissolution method and specification.

3.12 Comments for Other OGD Disciplines

None

4 APPENDIX

4.1 Individual Study Reviews

4.1.1 Single-dose Fasting Bioequivalence Study

4.1.1.1 Study Design

Table 4. Study Information

Study Number	R06-0364
Study Title	A Relative Bioavailability Study of 200 mg Ibuprofen Liquid Solution in Soft Gelatin Capsules under Fasting Conditions
Clinical Site (Name, Address, Phone #)	PRACS Institute, Ltd. 625 DeMers Avenue, East Grand Forks, MN 56721, USA 218-773-5560
Principal Investigator	Alan K. Copa
Dosing Dates	Period I: 25 August 2006 Period II: 01 September 2006
Analytical Site (Name, Address, Phone #)	(b) (4)
Analysis Dates	11 September 06 to 21 September 06
Analytical Director	(b) (4)
Storage Period of Biostudy Samples (no. of days from the first day of sample collection to the last day of sample analysis)	27 days

Table 5. Product information

Product	Test	Reference
Treatment ID	A	B
Product Name	Ibuprofen	Advil® Liqui-Gels®
Manufacturer	Banner™	Wyeth Consumer Healthcare
Batch/Lot No.	P060508-B2	B44305
Manufacture Date	06/2006	N/A
Expiration Date	N/A	01/08
Strength	200 mg	200 mg
Dosage Form	Capsules	Liquid-Gels®
Bio-batch Size	(b) (4)	N/A
Production Batch Size	(b) (4)	N/A
Potency	(b) (4)%	(b) (4)%
Content Uniformity (mean, %CV)	102.3%	N/A
Dose Administered	200 mg	200 mg
Route of Administration	Oral	Oral

Table 6. Study Design, Single-Dose Fasting Bioequivalence Study

Number of Subjects	Number of Subjects enrolled: 24 Number of Subjects completed: 24 Number of Subjects analyzed statistically: 24
No. of Sequences	2
No. of Periods	2
No. of Treatments	2
No. of Groups	1
Washout Period	7 days
Randomization Scheme	AB: 1, 4, 8, 9, 11, 12, 13, 17, 18, 19, 20, 24 BA: 2, 3,5, 6, 7, 9,10, 14, 15, 16, 21, 22, 23
Blood Sampling Times	Pre-dose (within 1 hour before the scheduled dosing time), 0.167, 0.33, 0.5, 0.67, 0.83, 1, 1.25, 1.5, 1.75, 2, 2.5, 3, 4, 6, 8, 10, and 12 hours post dose.
Blood Volume Collected/Sample	A total of 216 ml (6 ml x 18 x2) blood samples were collected during each period in vacutainers containing K_2 EDTA.
Blood Sample Processing/Storage	Samples were collected by direct venipuncture and centrifuged at approximately 3000 RPM and 4˚C for 10 minutes. The plasma was then pipetted into polypropylene tubes, and frozen and stored at approximately -20˚C or colder until transfer for analysis.
IRB Approval	16 August 2006
Informed Consent	28 June 2006.
Length of Fasting	Subjects fasted overnight before dosing and for 4.25 hours following dose administration**.**
Length of Confinement	12 h prior to dosing until 12 h post-dose blood draw
Safety Monitoring	The following assessments were completed during screening, within 28 days prior to Period I dose administration: medical and medication history, physical examination, sitting blood pressure and heart rate, oral temperature, respiratory rate, electrocardiogram, clinical laboratory evaluations, screens for HIV antibody, hepatitis B surface antigen, hepatitis C antibody, drugs of abuse and pregnancy (females only). All subjects were briefly evaluated before each confinement period to assess whether they continued to meet the study inclusion/exclusion criteria. In addition, a blood sample was collected for a pregnancy screen (females only). Sitting blood pressure and radial heart rate were measured prior to dosing and at 12 hours after each dose. A 12-lead ECG was recorded during the screening visit. Study exit procedures were completed within 14 days after the last blood sample collection. The exit procedures included general observations, clinical laboratory assessments, a physical examination, blood pressure, heart rate and temperature evaluations.

Comments on Study Design:

The study design is acceptable.

4.1.1.2 Clinical Results

Table 7. Demographics Profile of Subjects Completing the Bioequivalence Study

Fasting Bioequivalence Study R06-0364		
	Treatment Groups	
	Test Product N=24[1]	Reference Product N=24[1]
Age (years)		
Mean ± SD	37.00 ± 12.05	37.00 ± 12.05
Range	19 - 59	19 - 59
Groups		
<18	-	-
18-39	12 (50.00%)	12 (50.00%)
40-64	12 (50.00%)	12 (50.00%)
65-75	-	-
>75	-	-
Sex		
Female	15 (62.50%)	15 (62.50%)
Male	9 (37.50%)	9 (37.50%)
Hispanic or Latino		
Race		
N	-	-
A	-	-
B	-	-
I	-	-
W	-	-
Not Hispanic or Latino		
Race		
N	-	-
A	-	-
B	-	-
I	-	-
W	23 (95.83%)	23 (95.83%)
WN	1 (4.17%)	1 (4.17%)

RACE:

American Indian or Alaskan Native	N	Native Hawaiian or Other Pacific Islander	I	
Asian	A	White	W	[1]Subjects Used in Final Statistical Report
Black or African American	B			

Table 8. Dropout Information, Fasting Bioequivalence Study

None of the study subjects were dropped out.

Table 9. Study Adverse Events, Fasting Bioequivalence Study

Body System/Adverse Event[1]	Reported Incidence by Treatment Groups	
	Fasting Bioequivalence Study R06-0364	
	Test N=24[2]	Reference N=24[2]
	n (%)[3]	n (%)[3]
Gastrointestinal disorders		
Nausea	-	1 (4.17%)
Nervous system disorders		
Headache	1 (4.17%)	-
Total Subjects Reporting at Least One Adverse Event	1 (4.17%)	1 (4.17%)

[1] MedDRA Version 9.1
[2] N = Number of subjects dosed for each treatment
[3] n = Number of subjects reporting at least one incidence of respective adverse event; (%) = percentage of subjects reporting at least one incidence of respective adverse event (i.e. 100*(n/N)%)

Table 10. Protocol Deviations, Fasting Bioequivalence Study
None was reported.

4.1.1.3 Bioanalytical Results

Table 11. Assay Validation – Within the Fasting Bioequivalence Study

R06-0364 Ibuprofen									
Parameter	**Standard Curve Samples**								
Concentration (ng/mL)	100	200	500	1000	5000	10000	20000	30000	40000
Interday Precision (%CV)	3.73	4.18	3.00	3.01	3.22	3.24	2.83	4.56	4.22
Interday Accuracy (% Deviation)	-3.60	1.50	8.60	10.00	5.60	-0.90	-4.50	-5.67	-8.75
Linearity	0.9915 – 0.9960								
Linearity Range (ng/mL)	100 – 40000								
Sensitivity/LOQ (ng/mL)	100								

R06-0364 Ibuprofen				
Parameter	**Quality Control Samples**			
Concentration (ng/mL)	300	3000	18000	28000
Interday Precision (%CV)	5.63	2.77	3.38	2.31
Interday Accuracy (%Deviation)	6.00	9.00	-2.22	-6.43

Comments on Study Assay Validation: Acceptable.

- The standard curve used in the fasting bioequivalence (BE) study included an additional concentration of 200 ng/mL, which was not used in the pre-study validation. In addition, the BE study used 300, 3000, 18000 and 28000 ng/ml as QCs while 300, 15,000 and 35,000 ng/ml were used as QCs in the pre-study validation.

Any interfering peaks in chromatograms?	No
Were 20% of chromatograms included?	Yes
Were chromatograms serially or randomly selected?	Serially (Subjects 0009-0016)

Comments on Chromatograms: Acceptable.

Table 12. SOP's Dealing with Bioanalytical Repeats of Study Samples

SOP No.	Effective Date of SOP	SOP Title
405_07 version: 01	15 August, 2005	Sample Repeats, Re-injections and Re-integrations

Table 13. Additional Comments on Repeat Assays

Were all SOPs followed?	Yes
Did recalculation of PK parameters change the study outcome?	No
Does the reviewer agree with the outcome of the repeat assays?	Yes
If no, reason for disagreement	

Summary/Conclusions, Study Assays: Acceptable.

4.1.1.4 Pharmacokinetic Results

Table 14. Arithmetic Mean Pharmacokinetic Parameters

Fasting Bioequivalence Study, Study No. R06-0364									
Parameter (units)	Test				Reference				T/R
	Mean	%CV	Min	Max	Mean	% CV	Min	Max	
AUC0-t (hr *ng/ml)	77994.51	24.29	46737.21	139362.74	75645.77	23.93	45479.47	127276.76	1.310
AUC∞ (hr *ng/ml)	80790.88	27.09	47468.03	155910.10	78270.55	25.5	46312.13	137584.98	1.032
Cmax (ng/ml)	25970.83	21.19	15200	37200	25654.17	22.25	12200	34800	1.0123
Tmax* (hr)	0.81		0.33	3.00	0.82		0.33	4.00	0.9863
Kel (hr^{-1})	0.3085	16.34	0.1813	0.4168	0.3062	16.32	0.2222	0.3935	1.0075
T1/2 (hr)	2.31	18.66	1.66	3.82	2.32	16.40	1.76	3.12	0.9952

* Tmax values are presented as median, range

Table 15. Geometric Means and 90% Confidence Intervals - Firm Calculated

Ibuprofen Dose (1 x 200 mg) Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data				
Fasting Bioequivalence Study (R06-0364) N=24				
Parameter	Test	Reference	% Ratio	90% CI
AUC_{0-t} (hr * ng/ml)	76076.87	73731.10	103.18	100.44 - 106.00
$AUC_{0-\infty}$ (hr * ng/ml)	78431.49	76063.79	103.11	100.29 - 106.01
C_{max} (ng/ml)	25351.96	24925.57	101.71	94.27 - 109.74

Table 16. Geometric Means and 90% Confidence Intervals - Reviewer Calculated

Ibuprofen Dose (1 x 200 mg) Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data				
Fasting Bioequivalence Study (R06-0364) N=24				
Parameter	Test	Reference	% Ratio	90% CI
AUC_{0-t} (hr * ng/ml)	76076.87	73731.10	103	100.44 - 106.00
$AUC_{0-\infty}$ (hr * ng/ml)	78431.49	76063.79	103	100.29 - 106.01
C_{max} (ng/ml)	25351.96	24925.57	102	94.27 - 109.74

Table 17. Additional Study Information, Fasting Study No. R06-0364

Root mean square error, AUC0-t	0.0543	
Root mean square error, AUC∞	0.0559	
Root mean square error, Cmax	0.1532	
	Test	**Reference**
Kel and AUC∞ determined for how many subjects?	24	24
Do you agree or disagree with firm's decision?	Yes	Yes
Indicate the number of subjects with the following:		
measurable drug concentrations at 0 hr	None	None
first measurable drug concentration as Cmax	None	None
Were the subjects dosed as more than one group?	No	No

Ratio of AUC0-t/AUC∞				
Treatment	**n**	**Mean**	**Minimum**	**Maximum**
Test	24	0.97	0.89	0.99
Reference	24	0.97	0.93	0.99

Comments on Pharmacokinetic and Statistical Analysis:

- The reviewer agrees with the firm's calculation of the pharmacokinetic parameters and 90% confidence intervals.

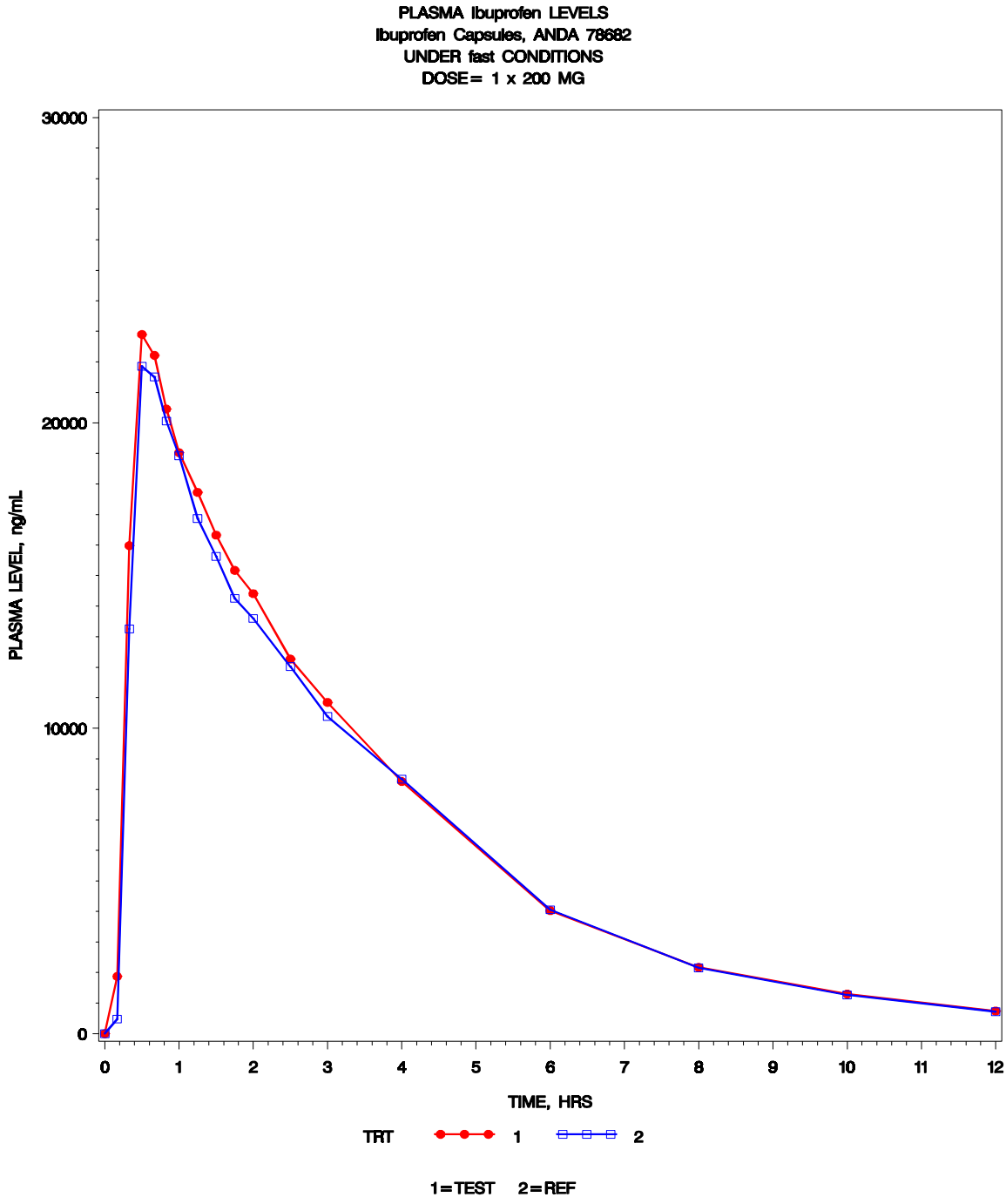
- The 90% confidence intervals for lnAUCT, lnAUCI, and lnC_{max} of ibuprofen are within the acceptable BE limits of 80.00-125.00%.

Summary and Conclusions, Single-Dose Fasting Bioequivalence Study: Acceptable.

Table 18. Mean Plasma Concentrations, Single-Dose Fasting Bioequivalence Study

	Test (n=24)		Reference (n=24)		Ratio
Time (hr)	Mean (ng/mL)	CV%	Mean (ng/mL)	CV%	(T/R)
0.00	0.00	.	0.00	.	.
0.17	1874.67	247.97	481.08	303.52	3.90
0.33	15980.52	75.93	13254.58	84.53	1.21
0.50	22895.65	36.77	21855.71	42.87	1.05
0.67	22211.67	29.93	21504.58	32.25	1.03
0.83	20455.42	26.32	20061.67	29.67	1.02
1.00	19025.83	24.53	18922.08	28.20	1.01
1.25	17725.00	20.45	16863.75	27.46	1.05
1.50	16325.00	22.00	15626.25	24.68	1.04
1.75	15170.83	21.01	14254.58	27.49	1.06
2.00	14408.70	21.53	13595.83	27.78	1.06
2.50	12267.92	23.36	12019.17	28.44	1.02
3.00	10846.67	27.87	10387.92	31.68	1.04
4.00	8257.08	32.98	8334.17	32.14	0.99
6.00	4030.42	42.20	4057.92	41.85	0.99
8.00	2171.75	56.72	2154.00	51.46	1.01
10.00	1296.96	66.46	1267.54	57.94	1.02
12.00	739.29	81.00	718.58	66.91	1.03

Figure 1. Mean Plasma Concentrations, Single-Dose Fasting Bioequivalence Study



4.1.2 Single-dose Nonfasting Bioequivalence Study

4.1.2.1 Study Design

Table 19. Study Information

Study Number	R07-0362
Study Title	A Relative Bioavailability study of 200 mg Ibuprofen Liquid Solution in Soft Gelatin Capsules Under Non-Fasting Conditions
Clinical Site (Name, Address, Phone #)	PRACS Institute, Ltd. 625 DeMers Avenue, East Grand Forks, MN 56721, USA 701-239-4750
Principal Investigator	Alan K. Copa
Dosing Dates	Period I: 27 April 2007 Period II: 04 May 2007
Analytical Site (Name, Address, Phone #)	(b) (4)
Analysis Dates	May 24, 2007 to June 01, 2007
Analytical Director	(b) (4)
Storage Period of Biostudy Samples (no. of days from the first day of sample collection to the last day of sample analysis)	35 days (April 27, 2007 to June 01, 2007)

Table 20. Product Information

Product	Test	Reference
Treatment ID	A	B
Product Name	Ibuprofen	Advil® LIQUI-GELS®
Manufacturer	Banner™, A Sobel Company	Distributed by Wyeth Consumer Healthcare
Batch/Lot No.	P060508-B2	B44305
Manufacture Date	06/2006	N/A
Expiration Date	N/A	01/08
Strength	200 mg	200 mg
Dosage Form	Soft gelatin capsule	Capsule
Bio-batch Size	(b) (4) capsules	N/A
Production Batch Size	(b) (4) capsules	N/A
Potency	(b) (4) %	(b) (4) %
Content Uniformity (mean, %CV)	N/A	N/A
Dose Administered	1 X 200 mg	1 X 200 mg
Route of Administration	Oral	Oral

Table 21. Study Design, Single-Dose Non-fasting Bioequivalence Study

No. of Subjects	Number of Subjects enrolled: 24 Number of Subjects completed: 24 Number of Subjects analyzed statistically: 24
No. of Sequences	2
No. of Periods	2
No. of Treatments	2
No. of Groups	1
Washout Period	7 days
Randomization Scheme	TR: 1, 3, 7, 9, 10, 11, 14, 15, 16, 19, 23, 24 RT: 2, 4, 5, 6, 8, 12, 13, 17, 18, 20, 21, 22
Blood Sampling Times	In each study period, blood samples were collected at pre-dose (0 hour) and post-dose at study hours 0.167, 0.33, 0.5, 0.67, 0.83, 1, 1.25, 1.5, 1.75, 2, 2.5, 3, 4, 6, 8, 10, and 12. The subjects were allowed to leave the clinical facility after the 12 hour blood sample collection.
Blood Volume Collected/Sample	A total of 216 ml (6 ml x 18 x 2) blood samples were collected during each period in vacutainers containing K_2 EDTA.
Blood Sample Processing/Storage	Samples were collected by direct venipuncture, placed on ice, and centrifuged at approximately 3000 RPM and 4°C for 10 minutes. The plasma was then pipetted into duplicate polypropylene tubes, frozen, and stored at –20°C or colder pending sample shipment for sample analysis.
IRB Approval	April 04 2007
Informed Consent	April 04 2007
Length of Fasting Before Meal	Following an overnight fast, the subjects were served an FDA standardized high fat breakfast 30 minutes prior to dose administration. A fast was maintained for 4.25 hours after dosing. At 4.25 and 10.5 hours after dose administration, standardized meals and beverages were provided to each subject.
Length of Confinement	Evening prior to dosing until 12 h post-dose blood draw
Safety Monitoring	Individual vital signs were monitored. Blood pressure and heart rate were measured prior to dosing and at 12 hours after each dose.
Standard FDA Meal Used?	Yes

Comments on Study Design:

The study design is acceptable.

4.1.2.2 Clinical Results

Table 22. Demographics Profile of Subjects Completing the Bioequivalence Study

R07-0362			
		Treatment Groups	
		Test Product N=241	Reference Product N=241
Age (years)	Mean ± SD	33.83 ± 12.85	33.83 ± 12.85
	Range	18 - 52	18 - 52
Age Groups	< 18	-	-
	18 – 39	13 (54.17%)	13 (54.17%)
	40 – 64 65 – 75	11 (45.83%) -	11 (45.83%) -
	> 75	-	-
Sex	Male Female	13 (54.17%) 11 (45.83%)	13 (54.17%) 11 (45.83%)
Hispanic or Latino Race	N A	--	--
	B	-	-
	I	-	-
	W	-	-
Not Hispanic or Latino Race	N A	--	--
	B	-	-
	I	-	-
	W	24 (100.00%)	24 (100.00%)
BMI	Mean ± SD	26.06 ± 2.68	26.06 ± 2.68
	Range	21 - 31.7	21 - 31.7
Other Factors			

Table 23. Dropout Information, Non-fasting Bioequivalence Study

None

Table 24. Study Adverse Events, Non-fasting Bioequivalence Study

Body System/Adverse Event[1]	Reported Incidence by Treatment Groups	
	R07-0362	
	Test	Reference
	N=24[2]	N=24[2]
	n (%)[3]	n (%)[3]
Gastrointestinal disorders		
Aphthous stomatitis	-	1 (4.17%)
Total Subjects Reporting at Least One Adverse Event	-	1 (4.17%)

[1] MedDRA Version 9.12
[2] N = number of subjects dosed for each treatment
[3] n = number of subjects reporting at least one incidence of respective adverse events;
(%) = percentage of subjects reporting at least one incidence of respective adverse event (i.e. 100* (n/N)%)

Table 25. Protocol Deviations, Non-fasting Bioequivalence Study
None

4.1.2.3 Bioanalytical Results

Table 26. Assay Validation – Within the Non-fasting Bioequivalence Study

Bioequivalence Study No. R07-0362 Ibuprofen									
Parameter	**Standard Curve Samples**								
Concentration (µg/mL)	0.20	0.40	1.00	2.00	5.00	10.0	20.0	34.0	40.0
Inter day Precision (%CV)	7.7	4.8	3.8	5.2	2.3	3.8	3.8	2.9	3.1
Inter day Accuracy (% Deviation)	2.8	2.3	-3.3	-5.6	-0.5	4.5	-0.2	-1.1	0.3
Linearity	0.997094 to 0.999636								
Linearity Range (µg/mL)	0.2000 to 40.00								
Sensitivity/LOQ (µg/mL)	0.2000								

Bioequivalence Study No. R07-0362 Ibuprofen			
Parameter	**Quality Control Samples**		
Concentration (µg/mL)	0.6000	4.000	30.00
Inter day Precision (%CV)	9.0	5.5	7.4
Inter day Accuracy (%Deviation)	-3.4	-4.2	-9.0

Comments on Study Assay Validation: Acceptable.

Any interfering peaks in chromatograms?	No
Were 20% of chromatograms included?	Yes
Were chromatograms serially or randomly selected?	Serially (Subjects 0001-0006)

Comments on Chromatograms: Acceptable.

Table 27. SOP's Dealing with Bioanalytical Repeats of Study Samples

SOP No.	Effective Date of SOP	SOP Title
L1100.100	01/27/06	Sample Reanalysis and Reporting Criteria

Table 28. Additional Comments on Repeat Assays

Were all SOPs followed?	Yes
Did recalculation of PK parameters change the study outcome?	No
Does the reviewer agree with the outcome of the repeat assays?	Yes
If no, reason for disagreement	

Summary/Conclusions, Study Assays: Acceptable.

4.1.2.4 Pharmacokinetic Results

Table 29. Arithmetic Mean Pharmacokinetic Parameters

Non-fasting Bioequivalence Study, Study R									
Parameter (units)	Test				Reference				T/R
	Mean	%CV	Min	Max	Mean	% CV	Min	Max	
AUC0-t (hr *µg/ml)	59.09	19.16	46.53	89.09	58.38	19.83	45.52	88.92	1.0122
AUC∞ (hr *µg/ml)	61.53	20.85	47.38	96.16	60.4	21.46	46.28	97.65	1.0188
Cmax (µg/ml)	15.51	21.88	9	23	17.09	25.74	9	25	0.9074
Tmax* (hr)	1.88		0.67	4.0	1.58		0.67	4.0	1.1921
Kel (hr^{-1})	0.3052	18.83	0.2214	0.4531	0.3242	17.87	0.212	0.4459	0.9415
T1/2 (hr)	2.34	17.25	1.53	3.13	2.20	17.48	1.55	3.27	1.0632

* Tmax values are presented as median, range

Table 30. Geometric Means and 90% Confidence Intervals - Firm Calculated

Ibuprofen Dose (1 x 200 mg) Geometric Means1, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data				
Non-Fasting Bioequivalence Study (R07-0362) N=24				
Parameter	**Test**	**Reference**	**% Ratio**	**90% C.I.**
AUC_{0-t} (hr * µg/ml)	58.18	57.41	101.34	98.90 - 103.84
$AUC_{0-\infty}$ (hr * µg/ml)	60.42	59.25	101.97	99.57 - 104.42
C_{max} (µg/ml)	15.14	16.52	91.65	83.71 - 100.33

Table 31. Geometric Means and 90% Confidence Intervals - Reviewer Calculated

Ibuprofen Dose (1 x 200 mg) Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data				
Non-Fasting Bioequivalence Study (R07-0362) N=24				
Parameter	**Test**	**Reference**	**% Ratio**	**90% C.I.**
AUC_{0-t} (hr * µg/ml)	58.18	57.41	101	98.90 - 103.84
$AUC_{0-\infty}$ (hr * µg/ml)	60.42	59.25	102	99.57 - 104.42
C_{max} (µg/ml)	15.14	16.52	92	83.71 - 100.33

Table 32. Additional Study Information, Non-fasting Bioequivalence Study No. BA0686054

Root mean square error, AUC0-t	0.0491	
Root mean square error, AUC∞	0.0480	
Root mean square error, Cmax	0.1827	
	Test	**Reference**
Kel and AUC∞ determined for how many subjects?	24	24
Do you agree or disagree with firm's decision?	Agree	Agree
Indicate the number of subjects with the following:		
measurable drug concentrations at 0 hr	None	None
first measurable drug concentration as Cmax	None	None
Were the subjects dosed as more than one group?	No	No

Ratio of AUC0-t/AUC∞				
Treatment	**n**	**Mean**	**Minimum**	**Maximum**
Test	24	0.96	0.91	0.99
Reference	24	0.97	0.91	0.99

Comments on Pharmacokinetic and Statistical Analysis:

- The reviewer agrees with the firm's calculation of the pharmacokinetic parameters and 90% confidence intervals.

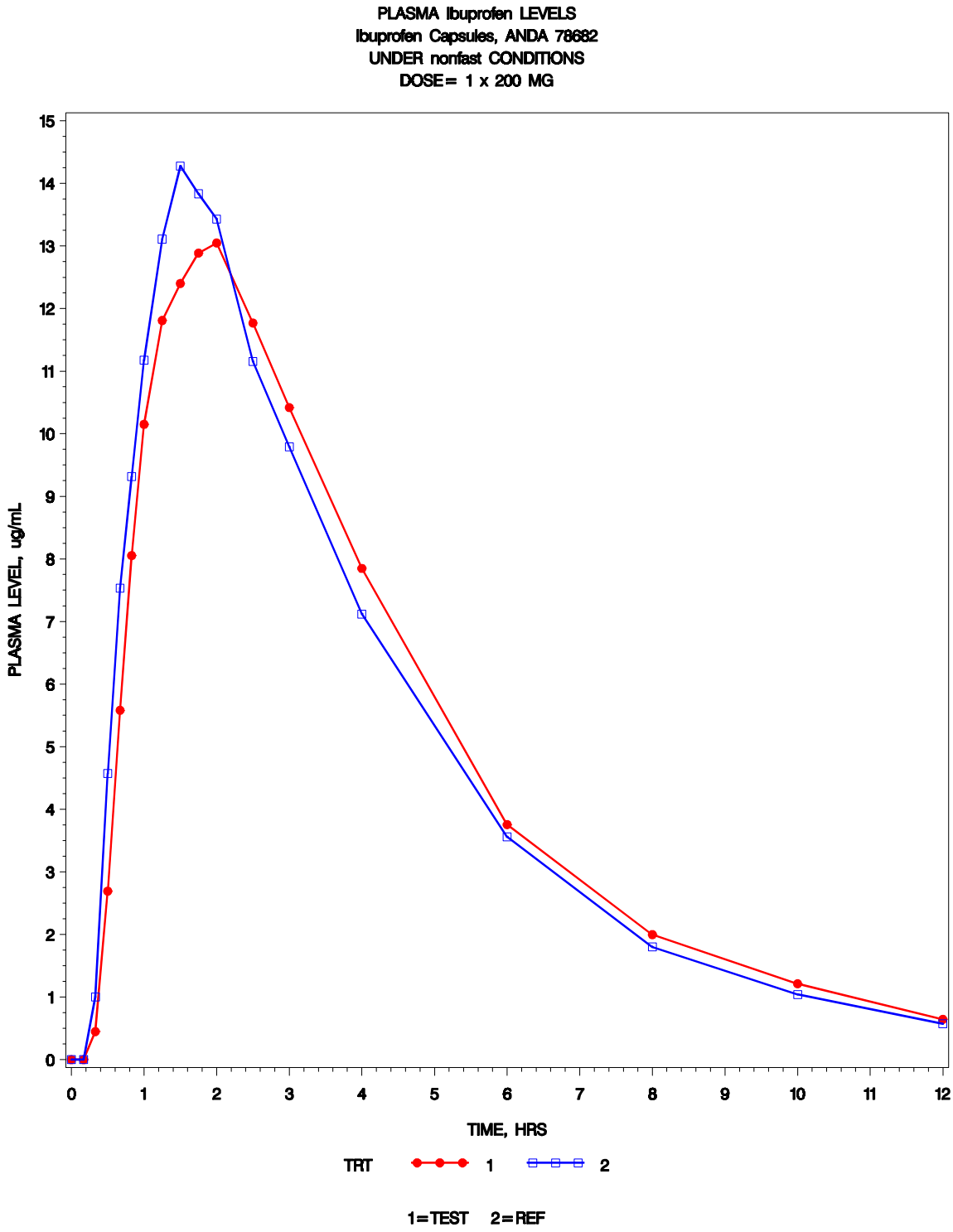
- The 90% confidence intervals for lnAUCT, lnAUCI, and lnC_{max} of ibuprofen are within the acceptable BE limits of 80.00-125.00%.

Summary/Conclusions, Single-Dose Non-fasting Bioequivalence Study: Acceptable.

Table 33. Mean Plasma Concentrations, Single-Dose Non-fasting Bioequivalence Study

	Test (n=24)		Reference (n=24)		Ratio
Time (hr)	Mean (µg/mL)	CV%	Mean (µg/mL)	CV%	(T/R)
0.00	0.00	.	0.00	.	.
0.17	0.00	.	0.00	.	.
0.33	0.45	143.42	1.00	185.91	0.45
0.50	2.69	104.76	4.57	138.41	0.59
0.67	5.58	97.55	7.53	99.35	0.74
0.83	8.05	71.00	9.31	78.36	0.86
1.00	10.15	57.80	11.17	60.97	0.91
1.25	11.81	40.20	13.11	43.36	0.90
1.50	12.40	34.11	14.28	35.45	0.87
1.75	12.89	22.51	13.83	29.18	0.93
2.00	13.05	19.91	13.43	29.42	0.97
2.50	11.77	21.64	11.15	29.96	1.06
3.00	10.42	26.75	9.79	26.14	1.06
4.00	7.85	27.64	7.12	29.97	1.10
6.00	3.76	37.05	3.56	41.93	1.06
8.00	2.00	51.82	1.80	48.18	1.11
10.00	1.21	56.32	1.04	55.77	1.16
12.00	0.64	68.34	0.57	68.97	1.12

Figure 2. Mean Plasma Concentrations, Single-Dose Non-fasting Bioequivalence Study



4.2 Formulation Data

Ingredient	Amount (mg) / Capsule	Amount (%) / Capsule
	200 mg strength	**200 mg strength**
Fill		
Ibuprofen, USP	200.00 mg	(b) (4)
(b) (4)		

Is there an overage of the active pharmaceutical ingredient (API)?	No
If the answer is yes, has the appropriate chemistry division been notified?	N/A
If it is necessary to reformulate to reduce the overage, will bioequivalence be impacted?	N/A
Comments on the drug product formulation:	The inactive ingredients are within the IIG limits. The level of the color additive, FD&C Blue #1 is (b) (4) and therefore, considered not significant.

4.3 Dissolution Data

Dissolution Review Path	DFS, Bioequivalence Dissolution, N 078682 N 000 AB (16-Jan-2008). DFS, Bioequivalence Dissolution, N 078682 N 000 AC (05-Jul-2007).

Table 34. Dissolution Data

Dissolution Conditions	**Apparatus:**	Apparatus I (baskets)
	Speed of Rotation:	150 RPM
	Medium:	Phosphate Buffer, pH 7.2
	Volume:	900 mL
	Temperature:	37°C ±0.5°C
Firm's Proposed Specifications	Q(b) (4)% at (b) (4) min.	
Dissolution Testing Site (Name, Address)	Banner Pharmacaps Inc. High Point, NC 27265	

Study Ref No.	**Testing Date**	**Product ID \ Batch No. (Test - Manufacture Date) (Reference – Expiration Date)**	**Dosage Strength & Form**	**No. of Dosage Units**		**Collection Times (minutes or hours)**				**Study Report Location**
						5 min	**10 min**	**20 min**	**30 min**	
PD08-012	1/08	Test Product Banner/P060508-B2 DOM 6/21/06	200 mg Capsule	12	Mean	1	87	101	101	5.3.1.3 (BE Amendment)
					Range	1-2	60-95	99-103	99-102	
					%CV	19.3	13.0	1.1	1.1	
	1/08	Reference Product Advil/B44305 Exp. 01/2008	200 mg Capsule	12	Mean	0	13	98	99	
					Range	0-1	2-37	97-98	98-99	
					%CV	38.2	87.1	0.6	0.3	

Comments by the Reviewer: The DBE previously reviewed the dissolution data submitted in the firm's original application. Based on the dissolution data obtained using the FDA-recommended method, the test product meets the FDA-recommended specification of NLT (b) (4)% (Q) in 20 minutes at the S1 level. The firm's dissolution data are acceptable; however, the firm is requested to acknowledge its acceptance of the FDA-recommended method and specification.

4.4 Detailed Regulatory History

ANDAs: There is no approved ANDA for Advil® Liqui-Gels® 200 mg listed on Orange Book (OTC section).

Controlled Document:

Current DBE recommendations for demonstration of bioequivalence of Advil® Liqui-Gels® 200 mg are as follows (OGD #07-0327 Perrigo):

1. The following studies are recommended to establish bioequivalence of Ibuprofen Potassium Capsules:
a. A single-dose fasting in-vivo bioequivalence study comparing Ibuprofen Potassium Capsules, 200 mg to the reference listed drug (RLD), Advil Liqui-Gels® (Ibuprofen Potassium), 200mg.
b. A single-dose fed in-vivo bioequivalence study comparing Ibuprofen Potassium Capsules, 200 mg, to the RLD.

2. Please measure ibuprofen in plasma.

3. Please note that a new Dissolution Methods Database is available to the public at the OGD website at http://www.fda.gov/cder/ogd/index.htm. Please find the dissolution information for this product at this website.

4.5 Consult Reviews

None.

4.6 SAS Output

4.6.1 Fasting Study SAS Code

```
/*=============================================================================
====
/ Program   : BE02dp7.SAS (Updated: 27 March 2007)
/ SubMacros : macrolib.sas, continu2.sas, continu.sas, calcke.sas
/ Purpose   : To analyze two-way crossover bioequivalence studies.
/ Notes     :
/
/=============================================================================
===
/ PARAMETERS:
/-------name------- ------------------------description---------------------
---

/=============================================================================
===
```

BIOEQUIVALENCE DEFICIENCIES

ANDA:	78-682
APPLICANT:	Banner Pharmacaps Inc.
DRUG PRODUCT:	Ibuprofen Liquid-Filled Capsules, 200mg (OTC)

The Division of Bioequivalence has completed its review of your submission acknowledged on the cover sheet. The following deficiency has been identified.

As previously communicated to you, your dissolution testing data are acceptable. However, your proposed dissolution specification of NLT (b) (4)% (Q) in (b) (4) minutes is unacceptable.

Please acknowledge the following FDA-recommended dissolution method and specification:

The dissolution testing should be conducted in 900 mL of Phosphate buffer, pH 7.2, using the USP apparatus I (basket) at 150 rpm. The test product should meet the following specification:

> Not less than (b) (4)% (Q) of the labeled amount of the ibuprofen in the dosage form is dissolved in 20 minutes.

Please note that the bioequivalence 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 bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

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

4.8 Outcome Page

COMPLETED ASSIGNMENT FOR 78682 ID: 6006

Reviewer: Liu, Qing **Date Completed:**
Verifier: **Date Verified:**
Division: Division of Bioequivalence
Description: Ibuprofen Capsule, 200mg

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
6006	12/15/2006	Bioequivalence Study	Fasting Study	1	1
6006	7/5/2007	Bioequivalence Study	Fed Study	1	1
				Bean Total:	2

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Qing Liu
8/18/2008 03:36:17 PM
BIOPHARMACEUTICS

Yih Chain Huang
8/18/2008 04:00:38 PM
BIOPHARMACEUTICS

Hoainhon T. Nguyen
8/18/2008 04:06:43 PM
BIOPHARMACEUTICS
For Dale P. Conner, Pharm. D., Director, Division of Bioequivalence I

DIVISION OF BIOEQUIVALENCE DISSOLUTION REVIEW

ANDA No.	78682	
Drug Product Name	Ibuprofen Liquid – Filled Capsules	
Strength (s)	200 mg	
Applicant Name	Banner Pharmacaps, Inc.	
Address	4125 Premier Drive High Point, NC 27265	
Applicant's Point of Contact	Rosanne Sylvia-Heeter	
Contact's Phone Number	336-812-8700 ext. 3885	
Contact's Fax Number	336-812-9091	
Submission Date(s)	05 July 2007	
Submission Date(s) of Amendment(s) Under Review	16 January 2008 (Current Amendment)	
First Generic	No	
Reviewer	Johnetta L. Farrar, Ph.D.	
Study Number (s)	R06-0364	R07-0362
Study Type (s)	Fasting	Fed
Strength(s)	200 mg	200 mg
Clinical Site	PRACS Institute, Ltd.	
Clinical Site Address	4801 Amber Valley Parkway Fargo, ND 58104	
Analytical Site	(b) (4)	
Analytical Address		
OUTCOME DECISION	**Incomplete**	

Review of a Dissolution Amendment

I. Executive Summary

This dissolution amendment was submitted in response to a request from the Division of Bioequivalence (DBE) requesting further dissolution testing using the FDA-recommended method. The firm conducted dissolution testing using the FDA method and the test product meets the FDA-recommended dissolution specification of NLT (b) (4)% (Q) in 20 minutes at the S1 level. The dissolution testing is incomplete pending the firm's acceptance of the FDA-recommended specification.

The DBE will review the fasted and fed BE studies at a later date.

II. RESPONSE TO DEFICIENCIES

DBE's Previous Dissolution Deficiency Comment No. 1:

Please also conduct dissolution testing on the test and reference products (12 units each) using the following FDA-recommended method:

Medium:	*Phosphate buffer, pH 7.2*
Volume:	*900 mL*
Apparatus:	*I (basket)*
Speed:	*150 rpm*
Sampling Times:	*5, 10, 20, and 30 minutes or until at least* (b)(4)*% of the labeled amount of ibuprofen is dissolved.*

The data from your proposed method and the FDA-recommended method will be compared. Specifications will be established based on the dissolution data submitted.

Firm's Response No. 1:

The requested dissolution data is provided in **Module 5.3.1.3** (see below) of this amendment.

Reviewer's Comment:

Based on the dissolution data obtained using the FDA-recommended method, submitted currently, the test product meets the FDA-recommended dissolution specification of NLT (b)(4)% (Q) in 20 minutes at the S1 level[1]. The firm's dissolution testing is acceptable; however, the firm should acknowledge their acceptance of the FDA-recommended method and specification.

[1]Source: ANDA #78-082 Dissolution Amendment Review; Amendment Date – 10 July 2006.

Dissolution Conditions	**Apparatus:**	Apparatus I (baskets)
	Speed of Rotation:	150 RPM
	Medium:	Phosphate Buffer, pH 7.2
	Volume:	900 mL
	Temperature:	37°C ±0.5°C
Firm's Proposed Specifications	Q (b)(4)% at (b)(4)min.	
Dissolution Testing Site (Name, Address)	Banner Pharmacaps Inc. High Point, NC 27265	

Study Ref No.	Testing Date	Product ID \ Batch No. (Test - Manufacture Date) (Reference – Expiration Date)	Dosage Strength & Form	No. of Dosage Units		Collection Times (minutes or hours) 5 min	10 min	20 min	30 min	Study Report Location
PD08-012	1/08	Test Product Banner/P060508-B2 DOM 6/21/06	200 mg Capsule	12	Mean	1	87	101	101	5.3.1.3 (BE Amendment)
					Range	1-2	60-95	99-103	99-102	
					%CV	19.3	13.0	1.1	1.1	
	1/08	Reference Product Advil/B44305 Exp. 01/2008	200 mg Capsule	12	Mean	0	13	98	99	
					Range	0-1	2-37	97-98	98-99	
					%CV	38.2	87.1	0.6	0.3	

It should be noted that in the ANDA 78-082 Dissolution Amendment, the dissolution data for the RLD showed high variability at 10 minutes (CV%=60%). Similarly high variability at 10 minutes is also observed for the test and RLD products in the current amendment (CV% equals 13% and 87% respectively). However, at 20 minutes, both products had acceptable CV% of 1.1% and 0.6%, respectively.

DBE's Previous Deficiency Comment No. 2:

You have submitted incomplete number of bioequivalence summary tables. The Division of Bioequivalence has recently developed new data summary tables in a concise format consistent with the Common Technical Document (CTD). Please provide complete 16 tables and send them with the rest of the bioequivalence submission. The tables are available in Word and PDF format under the title "Model Bioequivalence Data Summary Tables" in our website at http://www.fda.gov/ cder/ogd/index.htm. To improve the efficiency of the Division, please provide these tables in the ANDA submission amendment.

Firm's Response No. 2:

> Reference is made to Module 2, Section 2.7 of our 7/5/07 refuse-to-file amendment which provided the new BE CTD tables for the non-fasting BE study (R07 – 0362). For ease of review, these tables are provided in **Module 5.3.1.2** of this amendment.
>
> The requested Bioequivalence Summary Tables for the fasting study (R06 – 0362) are provided in Module 5.3.1.2 of this amendment.

Reviewer's Comment:

This amendment contains one Archival Copy (paper and electronic copies) and one Review copy (paper only). The Summary Tables for the fasting and fed studies as submitted in the current amendment are adequate and acceptable.

> This application is **incomplete**, pending the firm's acceptance of the FDA-recommended dissolution method and specification.

III. RECOMMENDATIONS

1. The *in vitro* dissolution testing conducted by Banner Pharmacaps, Inc. on its test product, Ibuprofen Liquid-Filled Capsules, 200 mg (lot# P060508-B2) comparing it to Wyeth Consumer Healthcare's Advil® (ibuprofen liquid-filled capsules) Capsules, 200 mg (lot# B44305), is incomplete pending the firm's acceptance of the DBE-recommended dissolution method and specification.

2. The dissolution testing should be conducted in 900 mL Phosphate buffer, pH 7.2 (37°C) using Apparatus I (basket) at 150 rpm. The test product should meet the following specification:

   NLT (b)(4)% (Q) of labeled amount of the drug in the dosage form is dissolved in 20 minutes.

   The firm should be informed of the deficiency comment and recommendations.

BIOEQUIVALENCE DEFICIENCIES

ANDA: 78-682

APPLICANT: Banner Pharmacaps, Inc.

DRUG PRODUCT: Ibuprofen liquid-filled capsules, 200 mg

The Division of Bioequivalence (DBE) has completed its review of the dissolution testing portion of your submission acknowledged on the cover sheet. The review of the bioequivalence studies will be conducted later. The following deficiency has been identified:

Your dissolution testing is acceptable. Please acknowledge your acceptance of the following FDA-recommended dissolution method and specification:

Medium:	Phosphate buffer, pH 7.2
Volume:	900 mL
Apparatus:	USP apparatus 1 (basket)
Speed:	150 rpm
Sampling times:	5, 10, 20, and 30 minutes
Specification:	Not less than (b)(4)% (Q) of the labeled amount of the drug in the dosage form is dissolved in 20 minutes.

Sincerely yours,

{See appended electronic signature page}

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

VII. OUTCOME

ANDA: 78682

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
4797	1/16/2008	Dissolution Data	Dissolution Amendment	1	1
				Bean Total:	1

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Johnetta Farrar
2/25/2008 03:43:44 PM
BIOPHARMACEUTICS

Hoainhon T. Nguyen
2/25/2008 03:50:15 PM
BIOPHARMACEUTICS

Barbara Davit
2/28/2008 01:54:19 PM
BIOPHARMACEUTICS

DIVISION OF BIOEQUIVALENCE DISSOLUTION CHECKLIST

ANDA No.	78-682	
Drug Product Name	Ibuprofen Liquid-Filled Capsule	
Strength (s)	200 mg	
Applicant Name	Banner Pharmacaps, Inc.	
Address	4125 Premier Drive High Point, NC 27265	
Applicant's Point of Contact	Rosanne Sylvia-Heeter	
Contact's Phone Number	336-812-8700 ext. 3885	
Contact's Fax Number	336-812-9091	
Submission Date(s)	05 July 2007	
First Generic	No	
Reviewer	Johnetta L. Farrar, Ph.D.	
Study Number (s)	R06-0364	R07-0362
Study Type (s)	Fasting	Fed
Strength(s)	200 mg	200 mg
Clinical Site	PRACS Institute, Ltd.	
Clinical Site Address	4801 Amber Valley Parkway Fargo, ND 58104	
Analytical Site	(b) (4)	
Analytical Address		
OUTCOME DECISION	**INCOMPLETE**	

I. EXECUTIVE SUMMARY

This is a review of the dissolution testing data only.

There is no USP or FDA-recommended method for this product. The firm's dissolution testing should be conducted using the following method[1]:

Medium:	Phosphate buffer, pH 7.2
Volume:	900 mL
Apparatus:	I (basket)
Speed:	150 rpm
Sampling Times:	5, 10, 20, and 30 minutes or until at least (b)(4)% of the labeled amount of ibuprofen is dissolved.

The firm should submit the following DBE summary tables for both the fasting and non-fasting studies:

- Summary Table 1 – Submission Summary
- Table 6 – Formulation Data
- Table 10 – Study Information
- Table 11 – Product Information
- Table 12 – Dropout Information
- Table 13 Protocol Deviations
- Table 14 – Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses
- Table 15 – SOPs Dealing with Bioanalytical Repeats of Study Samples
- Table 16 – Composition of Meal Used in Fed Bioequivalence Study

The tables should be submitted in the formats specified in the FDA website http://www.fda.gov/cder/ogd/index.htm.

The long-term stability data are acceptable.

The DBE will review the fasted and fed BE studies at a later date.

[1] ANDA 78-082; V:\firmsnz\Ranbaxy\ltrs&rev\78082A0706.doc and OCPB Review of NDA 20-402 (SE1-005) submission dated 05/14/1999. The recommended NDA specification was (b)(4)%(Q) in 20 minutes.

Table 1. Submission Content Checklist

Information			YES	NO	N/A
Did the firm use the FDA-recommended dissolution method			☐	☒	☐
Did the firm use the USP dissolution method			☐	☐	☒
Did the firm use 12 units of both test and reference in dissolution testing			☒	☐	☐
Did the firm provide complete dissolution data (all raw data, range, mean, % CV)			☒	☐	☐
Did the firm conduct dissolution testing with its own proposed method			☒	☐	☐
Is FDA method in the public dissolution database (on the web)			☐	☒	☐
SAS datasets submitted to the electronic document room (edr)	Fasting BE study	PK parameters	☒	☐	☐
		Plasma concentrations	☒	☐	☐
	Fed BE study	PK parameters	☒	☐	☐
		Plasma concentrations	☒	☐	☐
	Other study	PK parameters	☐	☐	☒
		Plasma concentrations	☐	☐	☒
Are the (16) DBE summary tables present in either PDF and/or MS Word format?			☐	☒	☐
Is the Long Term Storage Stability (LTSS) sufficient to cover the maximum storage time of the study samples?			☒	☐	☐

If the answer to either of the last two questions is no, indicate which summary biotables are

- Not present: Summary Table 1 – Submission Summary, Table 6 – Formulation Data, Table 10 – Study Information, Table 11 – Product Information, Table 12 – Dropout Information, Table 13 Protocol Deviations, Table 14 – Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses, Table 15 – SOPs Dealing with Bioanalytical Repeats of Study Samples, Table 16 – Composition of Meal Used in Fed Bioequivalence Study

- Not in pdf format: See above

Table 2. Summary of *In Vitro* Dissolution Data

Summary of In Vitro dissolution studies

Study Ref. No.	Product ID/Lot No.	Dosage Form	Conditions	No. of Dosage Units	Collection Times Mean% Dissolved (Range) 10 min.	20 min.	30 min.	45 min.	60 min.	Study Report Location
PD06-373	Banner/ P060508-B2	200 mg capsules	Dissolution: Apparatus 1 Speed of Rotation: 100 rpm Medium: Buffer Volume: 900 mL Temperature: 37 °C ± 0.5 °C	12	21 (3-82)	99 (92-101)	102 (101-102)	103 (101-104)	103 (101-104)	5.3.1.3
PD06-373	Advil/ B44305	200 mg capsules		12	3 (1-9)	98 (97-99)	100 (100-100)	100 (100-100)	100 (100-101)	5.3.1.3

II. COMMENTS:

1. The firm conducted dissolution testing on the test and reference products using the following method:

Medium:	pH 7.5 buffer[2]
Volume:	900 mL
Apparatus:	I (basket)
Speed:	100 rpm
Sampling Times:	10, 20, 30, 45, and 60 minutes

The firm proposed the following specification:

NLT (Q) = (b) (4)% in (b) (4) minutes.

The data are presented in **Table 2. Summary of *In Vitro* Dissolution Data**.

The firm has proposed to use a more acceptable basket speed of (b) (4) rpm, compared with the basket speed of 150 rpm recommended for the RLD product. However, the firm should submit dissolution data using both methods for comparison.

2. The long-term stability data are acceptable.

III. DEFICIENCY COMMENTS

1. The firm should also conduct dissolution testing using the following FDA-recommended method:

Medium:	Phosphate buffer, pH 7.2
Volume:	900 mL
Apparatus:	I (basket)
Speed:	150 rpm
Sampling Times:	5, 10, 20, and 30 minutes or until at least (b) (4)% of the labeled amount of ibuprofen is dissolved.

2. The firm should submit the following DBE summary tables for both the fasting and non-fasting studies:

- Summary Table 1 – Submission Summary
- Table 6 – Formulation Data
- Table 10 – Study Information
- Table 11 – Product Information
- Table 12 – Dropout Information

[2] ANDA 78-682; Volume 1.1; Section 2.3 – Quality Overall Summary; p. 19 of 22

- Table 13 Protocol Deviations
- Table 14 – Summary of Standard Curve and QC Data for Bioequivalence Sample Analyses
- Table 15 – SOPs Dealing with Bioanalytical Repeats of Study Samples
- Table 16 – Composition of Meal Used in Fed Bioequivalence Study

The tables should be submitted in the formats specified in the FDA website http://www.fda.gov/cder/ogd/index.htm.

RECOMMENDATIONS

1. The in vitro dissolution testing conducted by the firm on the test and reference products is not complete. The dissolution testing should also be conducted using the following FDA-recommended method[3]:

Medium:	Phosphate buffer, pH 7.2
Volume:	900 mL
Apparatus:	I (basket)
Speed:	150 rpm
Sampling Times:	5, 10, 20, and 30 minutes or until at least (b)(4)% of the labeled amount of ibuprofen is dissolved.

The data from the firm's proposed method and the FDA-recommended method will be compared. Specifications will be given at the time of ANDA review and based on the dissolution data submitted.

2. The Division of Bioequivalence has developed new data summary tables in a concise format consistent with the Common Technical Document (CTD). Please provide complete tables and send them with the rest of the bioequivalence submission. The tables are available in Word and PDF format under the title "Model Bioequivalence Data Summary Tables" in our website at http://www.fda.gov/cder/ogd/index.htm. To improve the efficiency of the Division, these tables should be provided in the ANDA submission.

[3] ANDA 78-082; V:\firmsnz\Ranbaxy\ltrs&rev\78082A0706.doc

BIOEQUIVALENCE DEFICIENCIES

ANDA: 78-682 APPLICANT: Banner Pharmacaps, Inc.

DRUG PRODUCT: Ibuprofen Liquid-Filled Capsule, 200 mg

The Division of Bioequivalence (DBE) has completed its review of the dissolution testing portion of your submission acknowledged on the cover sheet. The review of the bioequivalence studies will be conducted later. The following deficiencies have been identified:

1. Please also conduct dissolution testing on the test and reference products (12 units each) using the following FDA-recommended method:

Medium:	Phosphate buffer, pH 7.2
Volume:	900 mL
Apparatus:	I (basket)
Speed:	150 rpm
Sampling Times:	5, 10, 20, and 30 minutes or until at least (b)(4)% of the labeled amount of ibuprofen is dissolved.

The data from your proposed method and the FDA-recommended method will be compared. Specifications will be established based on the dissolution data submitted.

2. You have submitted incomplete number of bioequivalence summary tables. The Division of Bioequivalence has recently developed new data summary tables in a concise format consistent with the Common Technical Document (CTD). Please provide complete 16 tables and send them with the rest of the bioequivalence submission. The tables are available in Word and PDF format under the title "Model Bioequivalence Data Summary Tables" in our website at http://www.fda.gov/cder/ogd/index.htm. To improve the efficiency of the Division, please provide these tables in the ANDA submission amendment.

Sincerely yours,

{See appended electronic signature page}

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

BIOEQUIVALENCE - INCOMPLETE Submission date: 05 July 2007

[NOTE: The *in vitro* testing is incomplete. The fasting and fed BE studies are pending review]

ANDA: 78-682

Enter Review Productivity and Generate Report

Productivity:

ID	*Letter Date*	*Productivity Category*	*Sub Category*	*Productivity*	*Subtotal*
1084	7/5/2007	Dissolution Data	Dissolution Review	1	1
				Bean Total:	1

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Johnetta Farrar
12/17/2007 03:03:25 PM
BIOPHARMACEUTICS

Hoainhon T. Nguyen
12/17/2007 03:09:38 PM
BIOPHARMACEUTICS

Barbara Davit
12/17/2007 03:12:40 PM
BIOPHARMACEUTICS

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 78-682

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

OGD APPROVAL ROUTING SUMMARY

ANDA # 78-682 Applicant Banner Pharmacaps Inc.
Drug Ibuprofen Capsules (Liquid Filled), 200 mg Strength(s)

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

REVIEWER:	**DRAFT Package**	**FINAL Package**
1. **Martin Shimer** Chief, Reg. Support Branch	Date14 January 2009 InitialsMHS	Date 3/23/09 Initialsrlw

Contains GDEA certification: Yes ☒ No ☐ Determ. of Involvement? Yes ☐ No ☒
(required if sub after 6/1/92)
Pediatric Exclusivity System
RLD =Advil Liqui NDA#20-402
Patent/Exclusivity Certification: Yes ☒ No ☐ Date Checked N/A
If Para. IV Certification- did applicant Nothing Submitted ☐
Notify patent holder/NDA holder Yes ☐ No ☐ Written request issued ☐
Was applicant sued w/in 45 days:Yes ☐ No ☐ Study Submitted ☐
Has case been settled: Yes ☐ No ☐ Date settled:
Is applicant eligible for 180 day
Generic Drugs Exclusivity for each strength: Yes ☐ No ☒
Date of latest Labeling Review/Approval Summary _____
Any filing status changes requiring addition Labeling Review Yes ☐ No ☒
Type of Letter:Full Approval.
Comments:ANDA submitted on 12/18/2006, BOS=Advil Liquid Gels NDA 20-402, no relevant patent cert provided. RTR issued on 3/16/2007. ANDA determined to be ACK for filing on 7/6/2007. There are no remaining patents or exclusivities which protect the RLD. This ANDA is eligible for Full Approval.

2. Project Manager, Dat Doan Team1 Review Support Branch	Date1/14/09 Initialsdd	Date_____ Initials_____

Original Rec'd date12/15/06
Date Acceptable for Filing12/18/06
Patent Certification (type)PI
Date Patent/Exclus.expires
Citizens' Petition/Legal Case Yes☐ No ☒
(If YES, attach email from PM to CP coord)
First Generic Yes ☐ No ☒
Priority Approval Yes ☐ No ☒
(If yes, prepare Draft Press Release, Email it to Cecelia Parise)
Acceptable Bio review tabbed Yes ☐ No ☒
Bio Review Filed in DFS: Yes ☒ No ☐
Suitability Petition/Pediatric Waiver
Pediatric Waiver Request Accepted ☐ Rejected ☐ Pending ☐

EER Status Pending ☐ Acceptable ☒ OAI ☐
Date of EER Status 11/19/07
Date of Office Bio Review 11/25/08
Date of Labeling Approv. Sum
Date of Sterility Assur. App.
Methods Val. Samples Pending Yes ☐ No ☒
MV 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. /NA Minor issued ☐ Date _____
Comments:

3. Labeling Endorsement
Reviewer: Labeling Team Leader:
Date_____ Date3/23/09
Name/Initials_____ Name/Initials rlw/for
Comments:

From: Lee, Koung U
Sent: Monday, February 02, 2009 3:26 PM
To: Doan, Dat; Barlow, James T
Subject: RE: 78-862/Ibuprofen/Banner Pharmacaps

Hi Doan,

I concur.

Koung

From: Doan, Dat
Sent: Monday, February 02, 2009 2:41 PM
To: Barlow, James T; Lee, Koung U
Subject: 78-862/Ibuprofen/Banner Pharmacaps

Hi Koung, Jim:

Can I please get your endorsement for ANDA 78-862/Ibuprofen/Banner Pharmacaps?

Thanks,

Dat

4. David Read **(PP IVs Only)** Pre-MMA Language included ☐ Date 3/23/09
OGD Regulatory Counsel, Post-MMA Language Included ☐ Initials rlw/for
Comments:N/A. There are no patents listed in the current "Orange Book" for this drug product.

5. Div. Dir./Deputy Dir. Date3/23/09
Chemistry Div. I II OR III Initials PS
Comments:CMC OK.
Same API as in their NDA.

6. Frank Holcombe **First Generics Only** Date3/23/09
Assoc. Dir. For Chemistry Initials rlw/for Comments: (First generic drug review)
N/A. Multiple ANDAs have been approved for various ibuprofen immediate-release dosage forms - both Rx and OTC.

7. Vacant Date_____ Deputy Dir., DLPS
Initials_____
RLD = Advil Liqui-Gels 200 mg
Wyeth Consumer Healthcare NDA 20-402

8. Peter Rickman Date 3/23/09
Director, DLPS Initialsrlw/for
Para.IV Patent Cert: Yes☐ No☐;Pending Legal Action: Yes ☐No ☐;Petition: Yes☐ No☐ Comments: Bioequivalence studies (fasting and non-fasting) found acceptable.
In-vitro dissolution testing also found acceptable. Bio study sites have acceptable DSI inspection histories. Office-level bio endorsed 8/18/08 and 11/25/08.

Final-printed labeling (FPL) found acceptable for approval 1/30/09.

CMC found acceptable for approval (Chemistry Review #3).

OR

8. Robert L. West Date 3/24/09
Deputy Director, OGD Initials RLWest
Para.IV Patent Cert: Yes☐ No☒; Pending Legal Action: Yes☐ No☒; Petition: Yes☐ No☒
Press Release Acceptable ☐
Comments: Acceptable EES dated 11/9/07 (Verified 3/23/09). No "OAI" Alerts noted.

There are no patents or exclusivity currently listed in the "Orange Book" for this drug product.

This ANDA is recommended for approval (OTC use).

9. Gary Buehler Date 3/24/09
Director, OGD Initials rlw/for
Comments:
First Generic Approval ☐ PD or Clinical for BE ☐ Special Scientific or Reg.Issue ☐
Press Release Acceptable ☐

10. Project Manager, Team Dat Doan — Date 3/24/09
Review Support Branch — Initials dd

_____ Date PETS checked for first generic drug (just prior to notification to firm)

Applicant notification:
9:21am Time notified of approval by phone
9:25am Time approval letter faxed

FDA Notification:
3/24/09 Date e-mail message sent to "CDER-OGDAPPROVALS" distribution list.
3/24/09 Date Approval letter copied to \\CDS014\DRUGAPP\ directory.

EER DATA:

EES Data for: 078682

*** Compliance Recommendations ***

App No	Doc Seq No	Date	OC Recommendation
078682	000	11/9/2007	ACCEPTABLE

*** EER Table ***

CFN	Name	Profile Code	Last Milestone Name	Last Milestone Date	Last Status	Last Status Date	OAI Alert/ Effective Date
(b) (4)		CSN	OC RECOMMENDATION	8/3/2007	AC	8/3/2007	None
1063522	BANNER PHARMACAPS INC	CSG	OC RECOMMENDATION	7/23/2007	AC	7/23/2007	None
	BANNER PHARMACAPS	CTL	OC RECOMMENDATION	7/23/2007	AC	7/23/2007	None

COMIS TABLE:

Comis Application Table Data for Application No: 078682

***** Note: For Enterprise Search Files you may have to click and close the new window on first use***

Back to Search Form | ***COMIS Pool Reviewers*** | **ES DFS Files Only** | **ES - All Files** | **EDR** | **Cycles**

Drug Name: IBUPROFEN

Potency: 200 MG Dosage Form: CAP APPL Type: N

Applicant: BANNER PHARMACAPS

Status Code: PN Status Date: 3/23/2009 Clock Date: 12/18/2006 USP: N Org: 600

Therapeutic Drug Class: ACUTE PAIN, NON-OPIOID

Patent Certification: 1 Patent Expiration Date: PEPFAR:

Incom Doc Type	Seq No	Supp Mod Type	Letter Date	Stamp Date	Decision Code	Decision_Date	Status code	Status Date	Priority Flag	Document ID-Click to see Assignment	Priority Date
N Volume Locator	000		12/15/2006	12/18/2006	RF	3/16/2007	PN	3/23/2009	1	3032036	3/2/2009
N Volume Locator	000	AC	7/5/2007	7/6/2007	NM	4/3/2008				3125136	
N Volume Locator	000	MC	8/22/2007	8/23/2007	CL	8/23/2007				3147375	
N Volume Locator	000	AB	1/16/2008	1/17/2008	OP	1/17/2008				3894708	
N Volume Locator	000	AM	5/16/2008	5/19/2008	NM	2/23/2009				3956513	

N ***Volume Locator***	000	AF	7/25/2008	7/28/2008	OP	7/28/2008				3990202	
N ***Volume Locator***	000	AB	9/4/2008	9/5/2008	OP	9/5/2008				4009639	
N ***Volume Locator***	000	AM	11/3/2008	11/4/2008	NM	2/23/2009				4039065	
N ***Volume Locator***	000	AF	12/5/2008	12/8/2008	OP	12/8/2008				4054620	
N ***Volume Locator***	000	AF	12/23/2008	12/24/2008	OP	12/24/2008				4064138	
N ***Volume Locator***	000	AA	1/16/2009	1/21/2009	NM	2/23/2009				4073336	
N ***Volume Locator***	000	AF	1/19/2009	1/21/2009	OP	1/21/2009				4073358	
N ***Volume Locator***	000	AM	2/27/2009	3/2/2009	OP	3/2/2009				4095054	
N ***Volume Locator***	000	AM	3/6/2009	3/9/2009	OP	3/9/2009				4098237	
N ***Volume Locator***	000	AM	3/18/2009	3/19/2009	OP	3/19/2009				4104665	
N ***Volume Locator***	000	AM	3/20/2009	3/23/2009	OP	3/23/2009				4106531	***Comis Document Table Data***

ORANGE BOOK PRINT OFF:

Patent and Exclusivity Search Results from query on Appl No 020402 Product 001 in the OB_OTC list.

Patent Data

There are no unexpired patents for this product in the Orange Book Database.

[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]

Exclusivity Data

There is no unexpired exclusivity for this product.

View a list of all patent use codes
View a list of all exclusivity codes

Return to Electronic Orange Book Home Page

FDA/Center for Drug Evaluation and Research
Office of Generic Drugs
Division of Labeling and Program Support
Update Frequency:
Orange Book Data - **Monthly**
Generic Drug Product Information & Patent Information - **Daily**
Orange Book Data Updated Through February, 2009
Patent and Generic Drug Product Data Last Updated: March 23, 2009

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Dat Doan

3/24/2009 09:40:50 AM

COMPLETE RESPONSE -- MINOR

ANDA 78-682

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Banner Pharmacaps Inc. TEL: 336-812-8700 X23988

ATTN: Vandana Garikipati FAX: 336-812-9091

FROM: Dat Doan FDA CONTACT PHONE: (240) 276-8573

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated December 15, 2006, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ibuprofen Liquid-Filled Capsules, 200 mg.

Reference is also made to your amendments dated May 16, and November 3, 2008; and January 16, 2009.

SPECIAL INSTRUCTIONS: **please see attached**

Please submit your response in electronic format. This will improve document availability to review staff.

We have completed the review of your ANDA and have determined that we cannot approve this application in its present form. We have described below our reasons for this action and, where possible, our recommendations to address these issues in the following attachments (1 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. Upon OGD's acceptance for filing of your ANDA, it was determined that an adequate amount of information was submitted to allow for review of your Bioequivalence and Microbiology data. You will be notified in a separate communication of any further deficiencies identified during our review of your Bioequivalence and Microbiology data If you have substantial disagreement with our reasons for not approving this application, you may request an opportunity for a hearing.

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-682 APPLICANT: Banner Pharmacaps Inc.

DRUG PRODUCT: Ibuprofen Capsules, 200 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please revise your API impurities limits to comply with ICH Q3A(R) guidelines for a maximum daily dose of 1200 mg and provide a validated analytical HPLC method for the revised impurities specifications.

2. Please provide a specification, including test procedure, for potassium in the drug product and update your drug product specification.

3. Please update the drug product specification to include the residual solvents specification as meeting USP<467> requirements.

4. Please provide updated stability data generated using the FDA recommended dissolution conditions and specification.

Sincerely yours,

{See appended electronic signature page}

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Albert Mueller

2/23/2009 11:36:46 AM

BANNER®

ORIG AMENDMENT
N-AF

Banner Pharmacaps Inc.
4125 Premier Drive
High Point, NC 27265

PHONE 336.812.8700
FAX 336.812.9004

December 23, 2008

Telephone Labeling Amendment

Asia/Pacific

Canada

Europe

Mexico/Latin America

➤ United States

FDA, CDER
Office of Generic Drugs
7500 Standish Place, E-150
Rockville, MD 20855

RECEIVED
DEC 24 2008
OGD

RE: ANDA 78-682
Ibuprofen Capsules, 200 mg

Dear Sir or Madam:

Banner Pharmacaps Inc. (BPI) is hereby submitting an amendment to ANDA 78-682 for Ibuprofen Capsules, 200 mg, submitted 12/15/06, and amended 7/5/07, 1/16/08, 5/16/08, 7/25/08, 9/4/08 and 12/05/08. The purpose of this amendment is to provide responses to the labeling deficiencies identified in the Agency's Telephone fax dated 12/22/08. For reference, a copy of the Agency's communications is provided in Section 1.2 of this amendment. Each FDA comment is provided below in boldface type, followed by BPI's response.

FDA Comment:
Labeling Deficiencies:

1. CONTAINER – 20s and 180s
We note that you include the statement [redacted] (b) (4) [redacted] (b) (4) in the text of your labeling. This statement is NOT found in the reference listed drugs labeling. Please revise and/or comment.

BPI Response:
This statement was included as a voluntary label update to the oral OTC Children's Cough and Cold Medicines. Please find the supporting Consumer Healthcare Products Association (CHPA) link and document (point # 5) attached for support.

http://www.chpa-info.org/10_07_08_PedCC.aspx

2. CARTONs – 20s
See comment above

BPI Response:
Please refer to the response above for deficiency 1.

FDA Comment:
Revise your labels and labeling as requested above and submit final printed labeling electronically.

BPI Response:
As explained/commented to deficiency 1, the labels and labeling have not been revised and remain the same as submitted on December 5, 2008.

FDA Comment:
Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://www.fda.gov/cder/cdernew/listserv.html

BPI Response:
We acknowledge the Agency's comment.

FDA Comment:
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 the enclosed copy of the reference listed drug's labeling with all differences annotated and explained.

BPI Response:
Since there has been no labeling revision, a side-by-side comparison is not applicable in this amendment.

This amendment contains one Archival copy and one Review copy (paper only).

In accordance with 21 CFR 314.96(b), a Field Copy is not required for labeling.

If you have any questions, comments or require any additional information in regard to this amendment, please feel free to contact me by telephone at (336) 812-8700, extension 23988, by fax at (336) 812-9091, or by email at vgarikipati@banpharm.com.

Sincerely,

G. Vandana

Vandana Garikipati, MS, RAC
Manager, Regulatory Affairs

Telephone Fax

ANDA 78-682

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8979

TO: Banner Pharmacaps Inc.

TEL: 336-812-8700

ATTN: Dale Kruep

FAX: 336-812-9091

FROM: Jim Barlow (Labeling Reviewer)

:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for (Ibuprofen Potassium Capsules).

Pages (including cover): 3

SPECIAL INSTRUCTIONS:

Labeling Comments or questions -

james.barlow@fda.hhs.gov

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

ANDA Number: 78-682
Dates of Submission: **December 5, 2008**
Applicant's Name: Banner Pharmacaps Inc.
Established Name: Ibuprofen Capsules, 200 mg

Labeling Deficiencies:

1. **CONTAINER - 20s and 180s**
   We note that you include the statement " [redacted] (b) (4) **" in the text of your labeling. This statement is NOT found in the reference listed drugs labeling. Please revise and/or comment.**

2. **CARTONs – 20s**
   See comment above.

Revise your labels and labeling as requested above and submit final printed labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - 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 the enclosed copy of the reference listed drug's labeling with all differences annotated and explained.

{See appended electronic signature page}

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

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/s/

James Barlow

12/22/2008 01:17:14 PM

BIOEQUIVALENCY AMENDMENT

ANDA 78-682

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Banner Pharmacaps Inc. TEL: 336-812-8700

ATTN: Dale Kruep FAX: 336-812-9091

FROM: Beth Fabian-Fritsch FDA CONTACT PHONE: (240) 276-8782

Dear Sir or Madam:

This facsimile is in reference to the bioequivalency data submitted on July 5, 2007, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ibuprofen Liquid-Filled Capsules, 200 mg.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached **1** page. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all 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. Your cover letter should clearly indicate that the response is a "Bioequivalency Amendment" and clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this communication with your response. Please submit a copy of your amendment in both an archival (blue) and a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

BIOEQUIVALENCE DEFICIENCIES

ANDA:	78-682
APPLICANT:	Banner Pharmacaps Inc.
DRUG PRODUCT:	Ibuprofen Liquid-Filled Capsules, 200mg (OTC)

The Division of Bioequivalence has completed its review of your submission acknowledged on the cover sheet. The following deficiency has been identified.

As previously communicated to you, your dissolution testing data are acceptable. However, your proposed dissolution specification of NLT (b)(4)% (Q) in (b)(4) minutes is unacceptable.

Please acknowledge the following FDA-recommended dissolution method and specification:

The dissolution testing should be conducted in 900 mL of Phosphate buffer, pH 7.2, using the USP apparatus I (basket) at 150 rpm. The test product should meet the following specification:

> Not less than (b)(4)% (Q) of the labeled amount of the ibuprofen in the dosage form is dissolved in 20 minutes.

Please note that the bioequivalence 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 bioequivalence information and/or studies, or may result in a conclusion that the proposed formulation is not approvable.

Sincerely yours,

{See appended electronic signature page}

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Dale Conner

8/20/2008 04:38:58 PM

Telephone Fax

ANDA 78-682

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North I
7520 Standish Place
Rockville, MD 20855-2773
240-276-8979

TO: Banner Pharmacaps Inc.

TEL: 336-812-8700

ATTN: Dale Kruep

FAX: 336-812-9091

FROM: Jim Barlow (Labeling Reviewer)

:

This facsimile is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for (Ibuprofen Capsules).

Pages (including cover): 4

SPECIAL INSTRUCTIONS:

Labeling Comments or questions -

james.barlow@fda.hhs.gov

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

ANDA Number: 78-682
Dates of Submission: **July 5, 2007**
Applicant's Name: Banner Pharmacaps Inc.
Established Name: Ibuprofen Capsules, 200 mg

Labeling Deficiencies:

1. **GENERAL COMMENTS -**
   a. **Please revise your labels and labeling to be in accord with the most recently approved labeling for the reference listed drug, ADVIL LIQUI-GELS® (NDA 20-402/S-024; approved June 12, 2008)**

   b. **We see that you have proposed a 20 count bottle, but did not supply us with your proposed carton for this package size. Please submit and/or comment.**

2. **CONTAINER** – Bottles of 20 and (b) (4) **count (for the 200 mg strength capsules)**
   a. **Revise to read as follows -**
   Front Panel - Revise to read as follows -

   xx Softgels**
   Liquid Filled Capsules**

   b. **Front Panel – Revise to read as follows -**

   Drug Facts
   Active Ingredient (in each capsule) Purpose

   Solubilized Ibuprofen equal to
   200 mg ibuprofen (NSAID)*…….Pain reliever/Fever reducer
   (present as the free acid and potassium salt)
   ***nonsteroidal anti-inflammatory drug**

   c. **Other Information –**

(b) (4)

Revise your labels and labeling as requested above and submit final printed labeling electronically.

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - http://service.govdelivery.com/service/subscribe.html?code=USFDA_17

Prior to approval, it may be necessary to revise your labeling subsequent to approved changes for the reference listed drug. In order to keep ANDA labeling current, we suggest that you subscribe to the daily or weekly updates of new documents posted on the CDER web site at the following address - 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 the enclosed copy of the reference listed drug's labeling with all differences annotated and explained.

{See appended electronic signature page}

_____

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

John Grace
7/16/2008 11:01:54 AM
for Wm Peter Rickman

BIOEQUIVALENCY AMENDMENT

ANDA 78-682

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Banner Pharmacaps Inc. TEL: 336-812-8700 x 3885

ATTN: Rosanne Sylvia-Heeter FAX: 336-812-9091

FROM: Nam Chun PROJECT MANAGER: (240) 276-8782

Dear Madam:

This facsimile is in reference to the bioequivalency data submitted on July 05, 2007, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ibuprofen Liquid-Filled Capsules, 200 mg.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached **one** page. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all 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. Your cover letter should clearly indicate that the response is a "Bioequivalency Amendment" and clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this communication with your response. Please submit a copy of your amendment in both an archival (blue) and a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

Please submit your response in electronic format. This will improve document availability to review staff.

BIOEQUIVALENCE DEFICIENCIES

ANDA: 78-682

APPLICANT: Banner Pharmacaps, Inc.

DRUG PRODUCT: Ibuprofen liquid-filled capsules, 200 mg

The Division of Bioequivalence (DBE) has completed its review of the dissolution testing portion of your submission acknowledged on the cover sheet. The review of the bioequivalence studies will be conducted later. The following deficiency has been identified:

Your dissolution testing is acceptable. Please acknowledge your acceptance of the following FDA-recommended dissolution method and specification:

Medium:	Phosphate buffer, pH 7.2
Volume:	900 mL
Apparatus:	USP apparatus 1 (basket)
Speed:	150 rpm
Sampling times:	5, 10, 20, and 30 minutes
Specification:	Not less than (b)(4)% (Q) of the labeled amount of the drug in the dosage form is dissolved in 20 minutes.

Sincerely yours,

{See appended electronic signature page}

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Barbara Davit
3/6/2008 05:17:55 PM
Signing for Dale P Conner

MINOR AMENDMENT

ANDA 78-682

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Banner Pharmacaps Inc. TEL: 336-812-8700

ATTN: Dale Kruep FAX: 336-812-9091

FROM: Dat Doan PROJECT MANAGER: (240) 276-8573

Dear Sir:

This facsimile is in reference to your abbreviated new drug application dated July 05, 2007, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ibuprofen Liquid-Filled Capsules, 200 mg.

SPECIAL INSTRUCTIONS: **please see attached**

Please submit your response in electronic format. This will improve document availability to review staff.

The application is deficient and, therefore, Not Approvable under Section 505 of the Act for the reasons provided in the attachments (2 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.

CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 78-682 APPLICANT: Banner Pharmacaps Inc.

DRUG PRODUCT: Ibuprofen Liquid-Filled Capsules, 200 mg

The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

1. Please revise the specification for Chromatographic Purity of the API to comply with the ICH Q3A(R) recommended limits for a maximum daily dose of 1200 mg. Note that each impurity must be separated, identified and quantified by a validated HPLC method.

2. The drug product release and stability degradation products and (b) (4) levels are much higher than the test results. Please reduce the levels of these degradants to reflect the test results or qualify them at the levels you propose.

3. In your QOS Degradation Section (2.3 – Degradation products) and in your Summary of Stability Test Results, you referred to your current marketed product as having the same degradation products and a 2 year expiry date as the ANDA drug. Please identify which marketed drug product you are referring to. At the same time, provide evidence as to the structural identity of the degradation products and (b) (4) in the ANDA drug product.

4. From your drug product release and stability impurity profiles, there appears to be more than two (b) (4) degradants. Please identify and set specifications for these degradants separately based on test results.

5. Please establish a specification for pH of the fill solution for the drug product release and stability and provide test results in the COA for the drug product.

6. Please establish a specification for the relative amounts of ibuprofen potassium salt and free ibuprofen in your drug product. Please include the validated methods with data for these two new tests.

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

1. Your drug product dissolution conditions were found deficient by the Division of Bioequivalence. Your response dated January 16, 2008 is under review. The Division of Bioequivalence will respond to you under separate cover.

2. The labeling portion of your application is currently under review. The Division of Labeling and Program Support will notify you, under separate cover, of all labeling deficiencies.

3. To facilitate the review process, all changes (chemistry/manufacturing/ controls, labeling, bioequivalence, etc.) should be identified and itemized in your cover letter.

Sincerely yours,

{See appended electronic signature page}

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Albert Mueller

4/3/2008 02:34:47 PM

BIOEQUIVALENCY AMENDMENT

ANDA 78-682

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 (240-276-9327)

APPLICANT: Banner Pharmacaps Inc. TEL: 336-812-8700 x 3885

ATTN: Rosanne Sylvia-Heeter FAX: 336-812-9091

FROM: Aaron Sigler PROJECT MANAGER: (240) 276-8782

Dear Madam:

This facsimile is in reference to the bioequivalency data submitted on July 05, 2007, pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ibuprofen Liquid-Filled Capsules, 200 mg.

The Division of Bioequivalence has completed its review of the submission(s) referenced above and has identified deficiencies which are presented on the attached **2** pages. This facsimile is to be regarded as an official FDA communication and unless requested, a hard-copy will not be mailed.

You should submit a response to these deficiencies in accord with 21 CFR 314.96. Your amendment should respond to all 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. Your cover letter should clearly indicate that the response is a "Bioequivalency Amendment" and clearly identify any new studies (i.e., fasting, fed, multiple dose, dissolution data, waiver or dissolution waiver) that might be included for each strength. We also request that you include a copy of this communication with your response. Please submit a copy of your amendment in both an archival (blue) and a review (orange) jacket. Please direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

In an effort to improve document flow and availability to review staff, please submit your response in electronic PDF format, with a signed cover letter and 356h form.

BIOEQUIVALENCE DEFICIENCIES

ANDA: 78-682 APPLICANT: Banner Pharmacaps, Inc.

DRUG PRODUCT: Ibuprofen Liquid-Filled Capsule, 200 mg

The Division of Bioequivalence (DBE) has completed its review of the dissolution testing portion of your submission acknowledged on the cover sheet. The review of the bioequivalence studies will be conducted later. The following deficiencies have been identified:

1. Please also conduct dissolution testing on the test and reference products (12 units each) using the following FDA-recommended method:

Medium:	Phosphate buffer, pH 7.2
Volume:	900 mL
Apparatus:	I (basket)
Speed:	150 rpm
Sampling Times:	5, 10, 20, and 30 minutes or until at least (b) (4)% of the labeled amount of ibuprofen is dissolved.

The data from your proposed method and the FDA-recommended method will be compared. Specifications will be established based on the dissolution data submitted.

2. You have submitted incomplete number of bioequivalence summary tables. The Division of Bioequivalence has recently developed new data summary tables in a concise format consistent with the Common Technical Document (CTD). Please provide complete 16 tables and send them with the rest of the bioequivalence submission. The tables are available in Word and PDF format under the title "Model Bioequivalence Data Summary Tables" in our website at http://www.fda.gov/cder/ogd/index.htm. To improve the efficiency of the Division, please provide these tables in the ANDA submissior amendment.

Sincerely yours,

{See appended electronic signature page}

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

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Barbara Davit
12/21/2007 03:07:23 PM
Signing for Dale P Conner

BANNER®

Banner Pharmacaps Inc.
4125 Premier Drive
High Point, NC 27265

PHONE 336.812.8700
FAX 336.812.9004

Asia/Pacific

Canada

Europe

Mexico/Latin America

➤ United States

August 22, 2007

Office of Generic Drugs (HFD-600)
FDA, CDER
7500 Standish Place, Room 150
Rockville, MD 20855

General Correspondence

RE: ANDA 80-704 Ergocalciferol Capsules USP, 1.25 mg
ANDA 81-297 Benzonatate Capsules USP, 100 mg
ANDA 40-430 Ethosuximide Capsules USP, 100 mg
ANDA 73-484 Valproic Acid Capsules USP, 250 mg
ANDA 77-813 Zonisamide Capsules, 25, 50 & 100 mg
ANDA 78-682 Ibuprofen Capsules, 200 mg
ANDA 78-720 Amantadine HCl Capsules USP, 100 mg

Dear Sir or Madam:

Banner Pharmacaps Inc. (BPI) is hereby submitting general correspondence to the above referenced applications to provide formal notification that effective August 13, 2007, Mr. Dana S. Toops has assumed the role of Director, Regulatory Affairs and all future correspondence should be directed to his attention.

If you have any questions, comments or require any additional information in regard to this correspondence, please feel free to contact Dana by telephone at (336) 812-8700, extension 3312, by fax at (336) 812-9091, or by email at dstoops@banpharm.com.

Sincerely,

Dale A Kruep

Dale A. Kruep, Ph.D.
Director, Regulatory Affairs and Analytical Development

ANDA CHECKLIST FOR CTD or eCTD FORMAT
FOR COMPLETENESS and ACCEPTABILITY of an APPLICATION FOR FILING

For More Information on Submission of an ANDA in Electronic Common Technical Document (eCTD) Format please go to: http://www fda.gov/cder/regulatory/ersr/ectd.htm
***For a Comprehensive Table of Contents Headings and Hierarchy please go to:**
http://www fda.gov/cder/regulatory/ersr/5640CTOC-v1.2.pdf
** For more CTD and eCTD informational links see the final page of the ANDA Checklist**
*** A model Quality Overall Summary for an immediate release tablet and an extended release capsule can be found on the OGD webpage http://www.fda.gov/cder/ogd/ ***

ANDA #: 78-682 **FIRM NAME**: BANNER PHARMACAPS INC.

PIV: NO **Electronic or Paper Submission:** PAPER (CTD FORMAT)

RELATED APPLICATION(S): NA

First Generic Product Received? NO

DRUG NAME: IBUPROFEN

DOSAGE FORM: CAPSULES, 200 MG

Bio Assignments:		**Micro Review (No)**
☒ **BPH**	☐ **BCE**	☐
☐ **BST**	☒ **BDI**	

Random Queue: 1
Chem Team Leader: Mueller, Albert PM: Simon Eng Labeling Reviewer: James Barlow

Letter Date: DECEMBER 15, 2006 **Received Date**: DECEMBER 18, 2006

Comments: EC -1 YES **On Cards:** YES
Therapeutic Code: 5030300 NSAID

Archival copy: PAPER (CTD FORMAT) **Sections** I
Review copy: YES E-Media Disposition: YES SENT TO EDR
Not applicable to electronic sections

PART 3 Combination Product Category N Not a Part3 Combo Product
(Must be completed for ALL Original Applications) Refer to the Part 3 Combination Algorithm

Reviewing CSO/CST Iain Margand Date 7/20/07	**Recommendation:** ☒ **FILE** ☐ **REFUSE to RECEIVE**
Supervisory Concurrence/Date: _____	**Date:** _____

ADDITIONAL COMMENTS REGARDING THE ANDA:

Applicant has only provided a Fasting study comparing their proposed product to the RLD. Per DBE, a Non-Fasting study should also have been performed.

Additionally will need to provide:

A Field Copy Certification with original signature.

Revised Environmental Impact Statement stating applicant is compliance with all local, state and federal environmental laws.

A Methods of Validation Package for the archival (blue) copy of the ANDA.

Section 2.3, Quality Overall Summery, and section 2.7, Bioequivalence Clinical Summery, in both PDF and Word format.

3/15/07: S/W Dr. Mueller regarding applicant formulation. He stated the product would be acceptable for filing purposes, but chemistry would do a thorough review if/when the application is accepted by OGD.

7/20/07: Response to Refuse to Receive letter sent to OGD.

A non-fasting study has been performed by the applicant. AUC meets 80-125% CI (see attached).

Information is in both paper (two volumes) and electronic.

Remainder of requested information has been submitted with the response.

Contact: Dale Kruep, Ph.D. 336-812-8700

MODULE 1
ADMINISTRATIVE

		ACCEPTABLE
1.1	**1.1.2** **Signed and Completed Application Form (356h) (original signature)** (Check Rx/OTC Status) OTC YES	☒
1.2	**Cover Letter** Dated: DECEMBER 15, 2006	☒
*	**Table of Contents (paper submission only)** YES	☒
1.3.2	**Field Copy Certification (original signature)** YES **(N/A for E-Submissions)**	☐
1.3.3	**Debarment Certification-GDEA (Generic Drug Enforcement Act)/Other:** 1. Debarment Certification (original signature) YES 2. List of Convictions statement (original signature) YES	☒
1.3.4	**Financial Certifications** Bioavailability/Bioequivalence Financial Certification (Form FDA 3454) or Disclosure Statement (Form FDA 3455) YES	☒

1.3.5	**1.3.5.1** **Patent Information** Patents listed for the RLD in the Electronic Orange Book Approved Drug Products with Therapeutic Equivalence Evaluations No **1.3.5.2** **Patent Certification** 1. Patent number(s) N/A 2. Paragraph: (Check all certifications that apply) MOU ☐ PI ☒ PII ☐ PIII ☐ PIV ☐ No Relevant Patents ☐ 3. Expiration of Patent(s): NA a. Pediatric exclusivity submitted? b. Expiration of Pediatric Exclusivity? 4. Exclusivity Statement: YES no exclusivities	☒
1.4.1	**References** Letters of Authorization 1. DMF letters of authorization a. Type II DMF authorization letter(s) or synthesis for Active Pharmaceutical Ingredient Y b. Type III DMF authorization letter(s) for container closure Y 2. US Agent Letter of Authorization (U.S. Agent [if needed, countersignature on 356h]) N/A	☒
1.12.11	**Basis for Submission** NDA# : 20-402 Ref Listed Drug: ADVIL LIQUI-GELS Firm: WYETH CONSUMER HEALTHCARE ANDA suitability petition required? NA If Yes, then is change subject to PREA (change in dosage form, route or active ingredient) see section 1.9.1	☒

MODULE 1 (Continued)
ADMINISTRATIVE

ACCEPTABLE

1.12.12	**Comparison between Generic Drug and RLD-505(j)(2)(A)** 1. Conditions of use Same 2. Active ingredients Ibuprofen 3. Inactive ingredients 4. Route of administration Oral 5. Dosage Form Soft gel capsule 6. Strength 200mg	☒
1.12.14	**Environmental Impact Analysis Statement** YES - needs revision	☐
1.12.15	**Request for Waiver** Request for Waiver of In-Vivo BA/BE Study(ies): Paper, NA	☐

1.14.1	**Draft Labeling (Mult Copies N/A for E-Submissions)** **1.14.1.1** 4 copies of draft (each strength and container) Y **1.14.1.2** 1 side by side labeling comparison of containers and carton with all differences annotated and explained Y **1.14.1.3** 1 package insert (content of labeling) submitted electronically Y ***Was a proprietary name request submitted? No (If yes, send email to Labeling Reviewer indicating such.)	☒
1.14.3	**Listed Drug Labeling** **1.14.3.1** 1 side by side labeling (package and patient insert) comparison with all differences annotated and explained Y **1.14.3.3** 1 RLD label and 1 RLD container label Y	☒

MODULE 2
SUMMARIES

ACCEPTABLE

2.3	**Quality Overall Summary** **E-Submission: X___PDF (archive) X__ Word Processed e.g., MS Word** A model Quality Overall Summary for an immediate release table and an extended release capsule can be found on the OGD webpage http://www.fda.gov/cder/ogd/ **Question based Review (QbR) X__ YES _____ NO** **2.3.S** **Drug Substance (Active Pharmaceutical Ingredient)** **2.3.S.1** **General Information** **2.3.S.2** **Manufacture** **2.3.S.3** **Characterization** **2.3.S.4** **Control of Drug Substance** **2.3.S.5** **Reference Standards or Materials** **2.3.S.6** **Container Closure System** **2.3.S.7** **Stability** **2.3.P** **Drug Product** **2.3.P.1** **Description and Composition of the Drug Product** **2.3.P.2** **Pharmaceutical Development** **2.3.P.2.1** **Components of the Drug Product** **2.3.P.2.1.1** **Drug Substance** **2.3.P.2.1.2** **Excipients** **2.3.P.2.2** **Drug Product** **2.3.P.2.3** **Manufacturing Process Development** **2.3.P.2.4** **Container Closure System** **2.3.P.3** **Manufacture** **2.3.P.4** **Control of Excipients** **2.3.P.5** **Control of Drug Product** **2.3.P.6** **Reference Standards or Materials** **2.3.P.7** **Container Closure System** **2.3.P.8** **Stability**	☒

2.7	**Clinical Summary (Bioequivalence)** **E-Submission: _____PDF (archive) ____ Word Processed e.g., MS Word** **2.7.1** **Summary of Biopharmaceutic Studies and Associated Analytical Methods** **2.7.1.1** **Background and Overview** **2.7.1.2** **Summary of Results of Individual Studies** **2.7.1.3** **Comparison and Analyses of Results Across Studies** 1. Summary Bioequivalence tables: Table 1. Summary of Comparative Bioavailability (BA) Studies Table 2. Statistical Summary of the Comparative BA Data Table 4. Summary of In Vitro Dissolution Studies **2.7.1.4** **Appendix**	☒

MODULE 3

3.2.S DRUG SUBSTANCE

ACCEPTABLE

3.2.S.1	**General Information** **3.2.S.1.1** **Nomenclature** **3.2.S.1.2** **Structure** **3.2.S.1.3** **General Properties**	☒
3.2.S.2	**Manufacturer** **3.2.S.2.1** **Manufacturer(s) (This section includes contract manufacturers and testing labs)** **Drug Substance (Active Pharmaceutical Ingredient)** 1. Addresses of bulk manufacturers Y 2. Manufacturing Responsibilities Y 3. Type II DMF number for API DMF # (b) (4) 4. CFN or FEI numbers	☒
3.2.S.3	**Characterization**	☒

3.2.S.4	**Control of Drug Substance (Active Pharmaceutical Ingredient)** **3.2.S.4.1** **Specification** Testing specifications and data from drug substance manufacturer(s) Y **3.2.S.4.2** **Analytical Procedures** Y **3.2.S.4.3** **Validation of Analytical Procedures** **1.** Spectra and chromatograms for reference standards and test samples Y 2. Samples-Statement of Availability and Identification of: a. Drug Substance Y b. Same lot number(s) Y **3.2.S.4.4** **Batch Analysis** 1. COA(s) specifications and test results from drug substance mfgr(s) Y 2. Applicant certificate of analysis Y **3.2.S.4.5** **Justification of Specification** Y	☒
3.2.S.5	**Reference Standards or Materials**	☒
3.2.S.6	**Container Closure Systems**	☒
3.2.S.7	**Stability**	☒

MODULE 3

3.2.P DRUG PRODUCT ACCEPTABLE

3.2.P.1	**Description and Composition of the Drug Product** 1) Unit composition Y 2) Inactive ingredients are appropriate per IIG same inactive ingredients as RLD- see attached	☒
3.2.P.2	**Pharmaceutical Development** Pharmaceutical Development Report	☒
3.2.P.3	**Manufacture** **3.2.P.3.1** **Manufacture(s)** (Finished Dosage Manufacturer and Outside Contract Testing Laboratories) 1. Name and Full Address(es)of the Facility(ies) YES 2. CGMP Certification: YES 3. Function or Responsibility YES No testing of API or Drug Product 4. CFN or FEI numbers **3.2.P.3.2** **Batch Formula** Batch Formulation Y **3.2.P.3.3** **Description of Manufacturing Process and Process Controls** 1. Description of the Manufacturing Process Y 2. Master Production Batch Record(s) for largest intended production runs (no more than 10x pilot batch) with equipment specified (b) (4) capsules 3. If sterile product: Aseptic fill / Terminal sterilization N/A 4. Reprocessing Statement Y **3.2.P.3.4** **Controls of Critical Steps and Intermediates** Y **3.2.P.3.5** **Process Validation and/or Evaluation** 1. Microbiological sterilization validation N/A 2. Filter validation (if aseptic fill) N/A	☒
3.2.P.4	**Controls of Excipients (Inactive Ingredients)** Source of inactive ingredients identified **3.2.P.4.1** **Specifications** 1. Testing specifications (including identification and characterization) Y 2. Suppliers' COA (specifications and test results) Y **3.2.P.4.2** **Analytical Procedures** Y **3.2.P.4.3** **Validation of Analytical Procedures** Y **3.2.P.4.4** **Justification of Specifications** Applicant COA Y	☒

MODULE 3

3.2.P DRUG PRODUCT

ACCEPTABLE

3.2.P.5	**Controls of Drug Product** **3.2.P.5.1** **Specification(s)** Y **3.2.P.5.2** **Analytical Procedures** Y **3.2.P.5.3** **Validation of Analytical Procedures** Samples - Statement of Availability and Identification of: 1. Finished Dosage Form Y 2. Same lot numbers Y **3.2.P.5.4** **Batch Analysis** Certificate of Analysis for Finished Dosage Form Y P060508 **3.2.P.5.5** **Characterization of Impurities** Y **3.2.P.5.6** **Justification of Specifications** N/A	☒
3.2.P.7	**Container Closure System** 1. Summary of Container/Closure System (if new resin, provide data) Y 2. Components Specification and Test Data Y 3. Packaging Configuration and Sizes [redacted] (b) (4) bottles 4. Container/Closure Testing Y 5. Source of supply and suppliers address Y	☒
3.2.P.8	**3.2.P.8.1** **Stability (Finished Dosage Form)** 1. Stability Protocol submitted Y 2. Expiration Dating Period 24 months **3.2.P.8.2** **Post-approval Stability and Conclusion** Post Approval Stability Protocol and Commitments Y **3.2.P.8.3** **Stability Data** 1. 3 month accelerated stability data Y 2. Batch numbers on stability records the same as the test batch **P060508**	☒

MODULE 3

3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Substance)	**3.2.R.1.S** **Executed Batch Records for drug substance (if available)** **3.2.R.2.S** **Comparability Protocols** **3.2.R.3.S** **Methods Validation Package** YES Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☐

MODULE 3

3.2.R Regional Information

ACCEPTABLE

3.2.R (Drug Product)	**3.2.R.1.P.1** **Executed Batch Records** Copy of Executed Batch Record with Equipment Specified, including Packaging Records (Packaging and Labeling Procedures), Batch Reconciliation and Label Reconciliation Theoretical Yield (b) (4) Actual Yield (b) (4) Packaged Yield 20: (b) (4) (b) (4) **3.2.R.1.P.2** **Information on Components** N/A **3.2.R.2.P** **Comparability Protocols** N/A **3.2.R.3.P** **Methods Validation Package** Methods Validation Package (3 copies) (Mult Copies N/A for E-Submissions) (Required for Non-USP drugs)	☒

MODULE 5

CLINICAL STUDY REPORTS - Incomplete, requires a non-fasting study

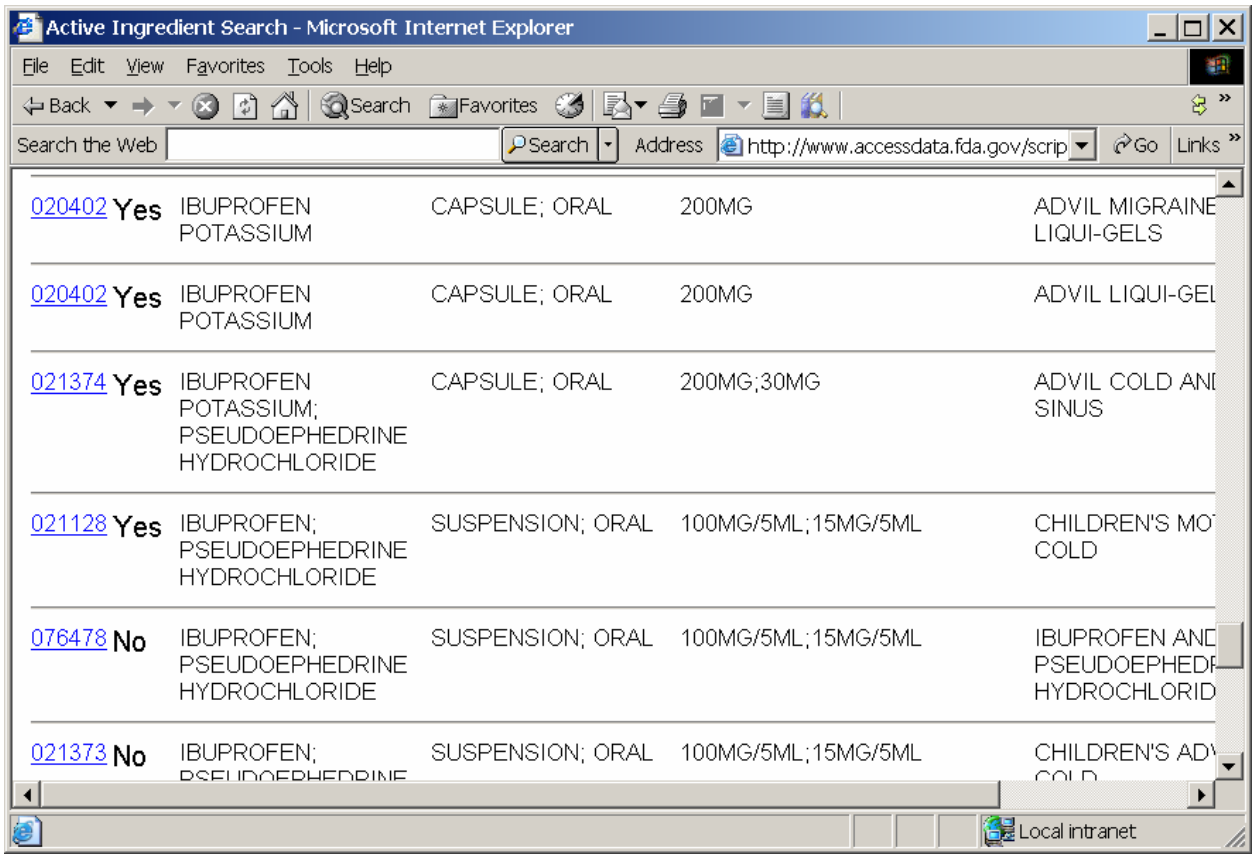
ACCEPTABLE

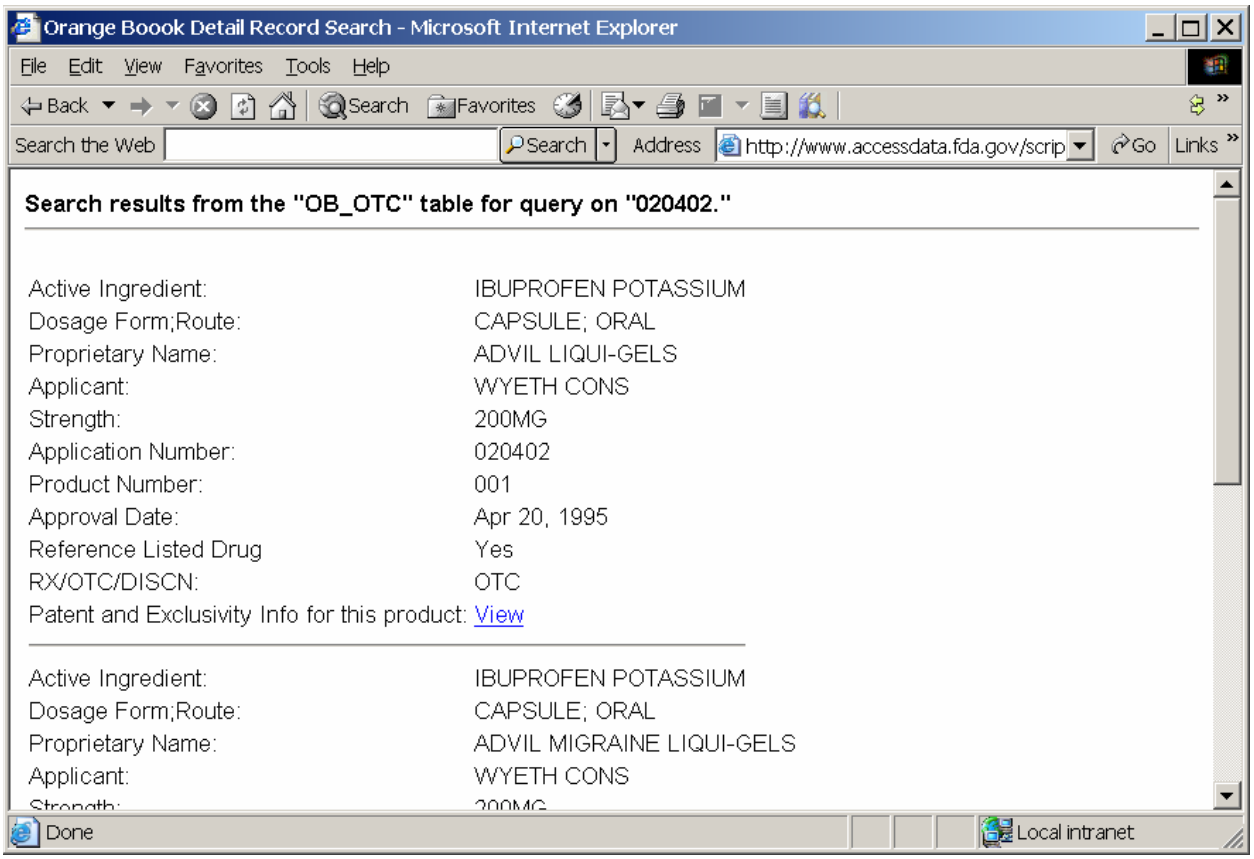
5.2	**Tabular Listing of Clinical Studies**	☒
5.3.1 (complete study data)	**Bioavailability/Bioequivalence** **1. Formulation data same?** a. Comparison of all Strengths (check proportionality of multiple strengths) N/A b. Parenterals, Ophthalmics, Otics and Topicals per 21 CFR 314.94 (a)(9)(iii)-(v) N/A **2. Lot Numbers of Products used in BE Study(ies):** P060508 **3. Study Type: IN-VIVO PK STUDY(IES)** (Continue with the appropriate study type box below)	☒
	5.3.1.2 **Comparative BA/BE Study Reports** Y 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) 2. Summary Bioequivalence tables: Table 6. Demographic Profile of Subjects Completing the Comparative BA Study Table 7. Incidence of Adverse Events in Individual Studies Table 8. Reanalysis of Study Samples **5.3.1.3** **In Vitro-In-Vivo Correlation Study Reports** Y 1. Summary Bioequivalence tables: Table 4. Summary of In Vitro Dissolution Studies Table 5. Formulation Data **5.3.1.4** **Reports of Bioanalytical and Analytical Methods for Human Studies** Y 1. Summary Bioequivalence table: Table 3. Bioanalytical Method Validation **5.3.7** **Case Report Forms and Individual Patient Listing** Y	☒

5.4	**Literature References**	
	Possible Study Types:	
Study Type	**IN-VIVO PK STUDY(IES)** (i.e., fasting/fed/sprinkle) FASTING ONLY ON 200 MG 1. Study(ies) meets BE criteria (90% CI of 80-125, C max, AUC) see attached 2. EDR Email: Data Files Submitted: YES SENT TO EDR 3. In-Vitro Dissolution: YES	☐
Study Type	**IN-VIVO BE STUDY with CLINICAL ENDPOINTS** NO 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria: 90% CI of the proportional difference in success rate between test and reference must be within (-0.20, +0.20) for a binary/dichotomous endpoint. For a continuous endpoint, the test/reference ratio of the mean result must be within (0.80, 1.25). 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted	☐
Study Type	**IN-VITRO BE STUDY(IES)** (i.e., in vitro binding assays) NO 1. Study(ies) meets BE criteria (90% CI of 80-125) 2. EDR Email: Data Files Submitted: 3. In-Vitro Dissolution:	☐
Study Type	**NASALLY ADMINISTERED DRUG PRODUCTS** NO 1. Solutions (Q1/Q2 sameness): a. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile) 2. Suspensions (Q1/Q2 sameness): a. In-Vivo PK Study 1. Study(ies) meets BE Criteria (90% CI of 80-125, C max, AUC) 2. EDR Email: Data Files Submitted b. In-Vivo BE Study with Clinical End Points 1. Properly defined BE endpoints (eval. by Clinical Team) 2. Summary results meet BE criteria (90% CI within +/- 20% or 80-125) 3. Summary results indicate superiority of active treatments (test & reference) over vehicle/placebo ($p<0.05$) (eval. by Clinical Team) 4. EDR Email: Data Files Submitted c. In-Vitro Studies (Dose/Spray Content Uniformity, Droplet/Drug Particle Size Distrib., Spray Pattern, Plume Geometry, Priming & Repriming, Tail Off Profile)	☐
Study Type	**TOPICAL CORTICOSTEROIDS (VASOCONSTRICTOR STUDIES)** NO 1. Pilot Study (determination of ED50) 2. Pivotal Study (study meets BE criteria 90%CI of 80-125)	☐

Study Type	**TRANSDERMAL DELIVERY SYSTEMS** NO 1. In-Vivo PK Study 1. Study(ies) meet BE Criteria (90% CI of 80-125, C max, AUC) 2. In-Vitro Dissolution 3. EDR Email: Data Files Submitted 2. Adhesion Study 3. Skin Irritation/Sensitization Study	☐

Updated 10/10/2006 C. Bina

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Active Ingredient: IBUPROFEN POTASSIUM
Dosage Form;Route: CAPSULE; ORAL
Proprietary Name: ADVIL LIQUI-GELS
Applicant: WYETH CONS
Strength: 200MG
Application Number: 020402
Product Number: 001
Approval Date: Apr 20, 1995
Reference Listed Drug Yes
RX/OTC/DISCN: OTC
Patent and Exclusivity Info for this product: View
Active Ingredient: IBUPROFEN POTASSIUM
Dosage Form;Route: CAPSULE; ORAL
Proprietary Name: ADVIL MIGRAINE LIQUI-GELS
Applicant: WYETH CONS
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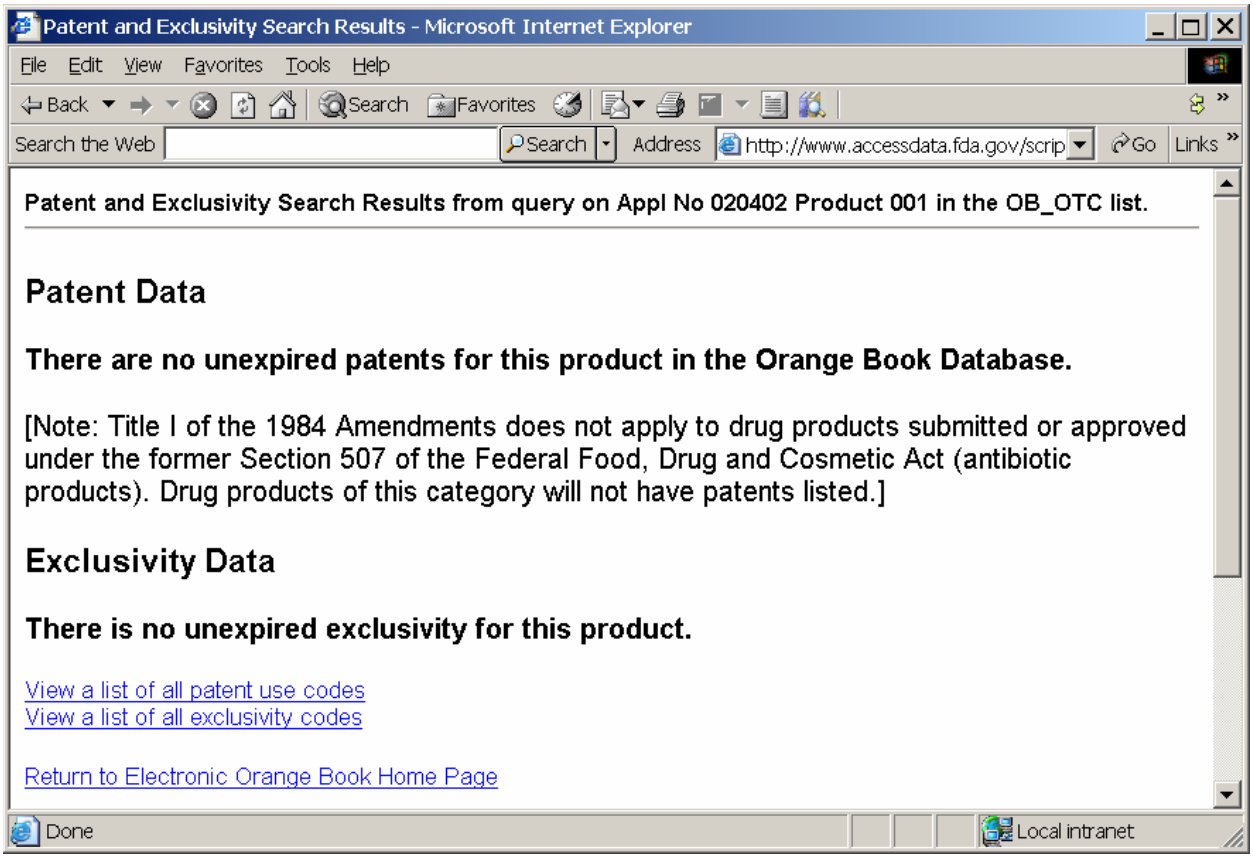
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Patent and Exclusivity Search Results from query on Appl No 020402 Product 001 in the OB_OTC list.
Patent Data
There are no unexpired patents for this product in the Orange Book Database.
[Note: Title I of the 1984 Amendments does not apply to drug products submitted or approved under the former Section 507 of the Federal Food, Drug and Cosmetic Act (antibiotic products). Drug products of this category will not have patents listed.]
Exclusivity Data
There is no unexpired exclusivity for this product.
View a list of all patent use codes
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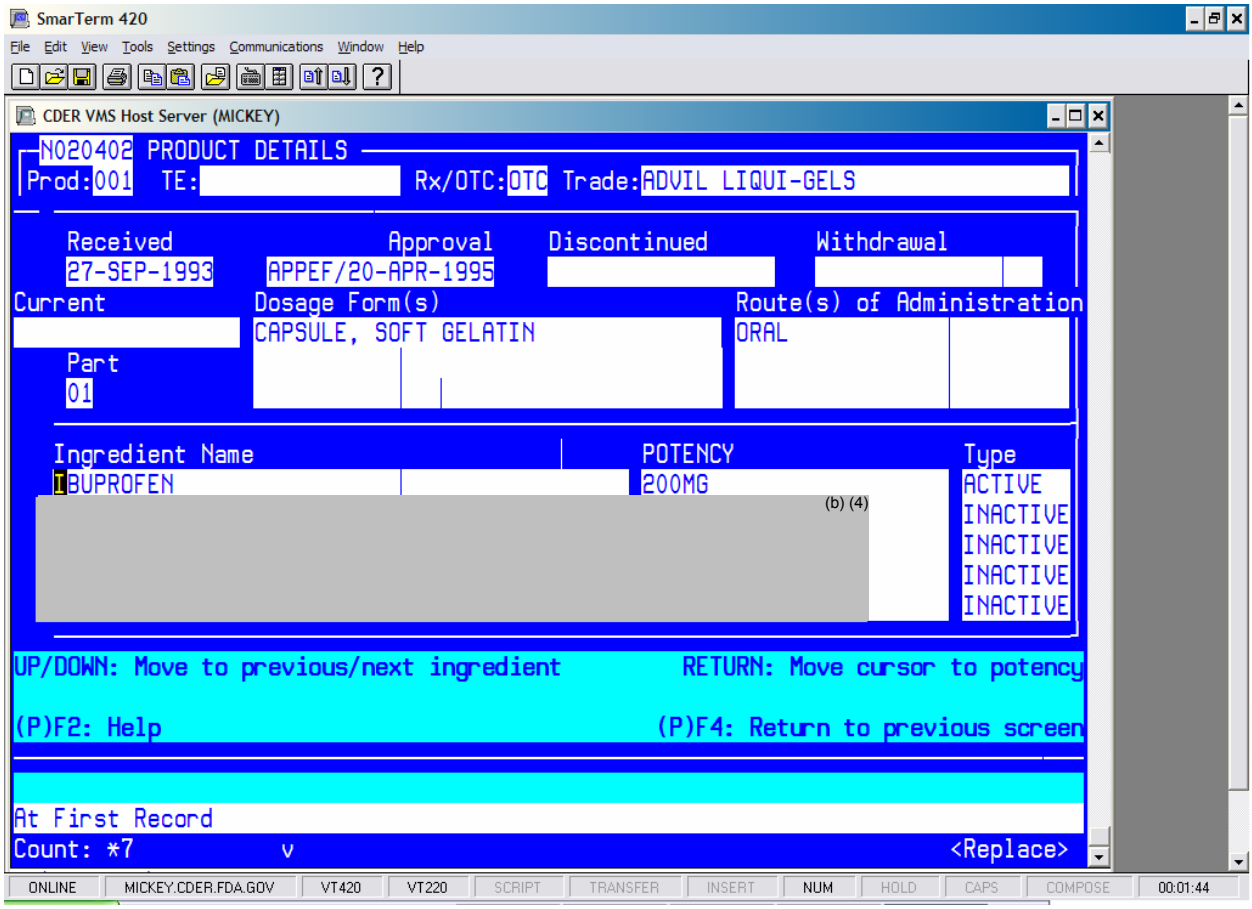
Done
Local intranet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CDER VMS Host Server (MICKEY)
N020402 PRODUCT DETAILS
Prod:001 TE: Rx/OTC:OTC Trade:ADVIL LIQUI-GELS
Received Approval Discontinued Withdrawal
27-SEP-1993 APPEF/20-APR-1995
Current Dosage Form(s) Route(s) of Administration
CAPSULE, SOFT GELATIN ORAL
Part
01
Ingredient Name POTENCY Type
IBUPROFEN 200MG ACTIVE
(b) (4)
INACTIVE
INACTIVE
INACTIVE
INACTIVE
UP/DOWN: Move to previous/next ingredient RETURN: Move cursor to potency
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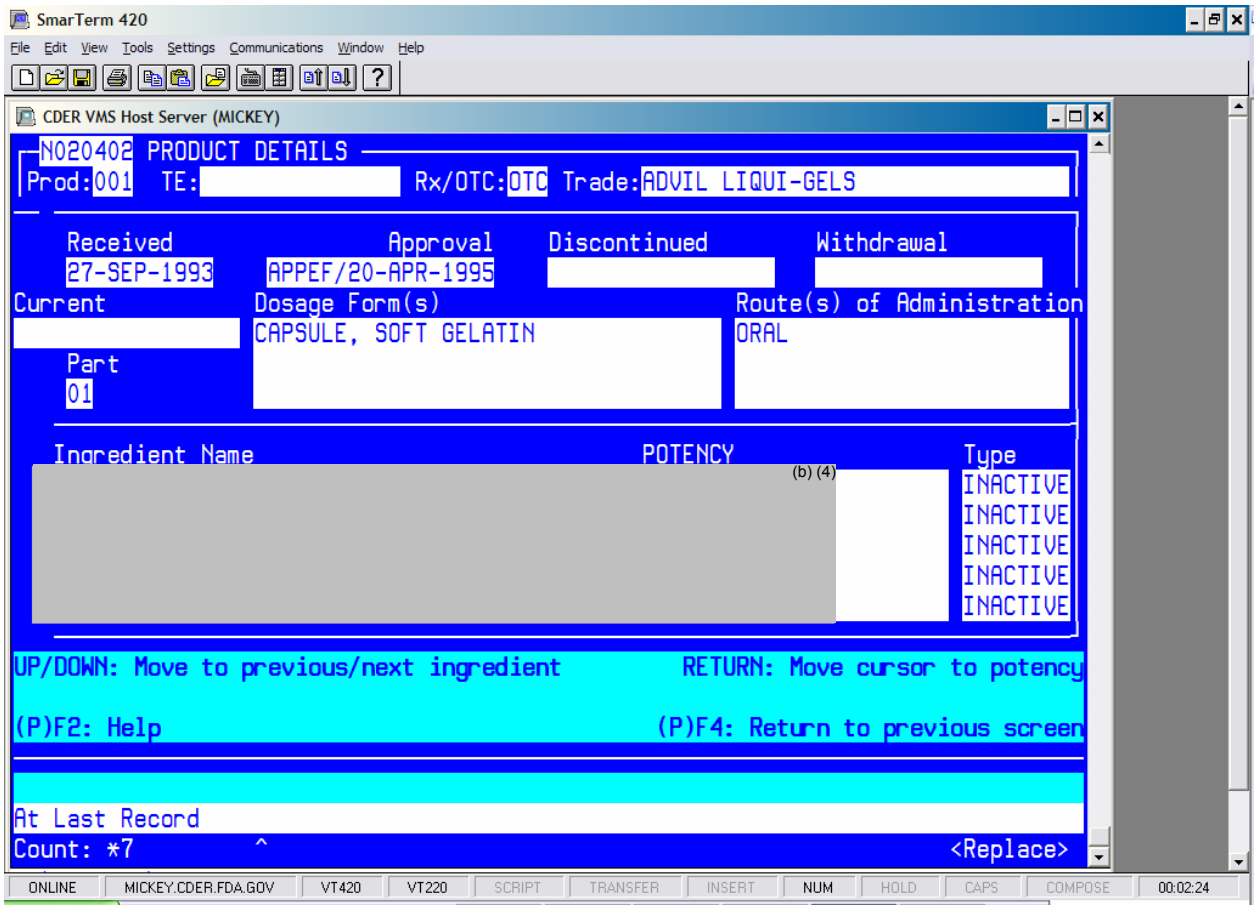
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Ingredient Name
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(b) (4)
Type
INACTIVE
INACTIVE
INACTIVE
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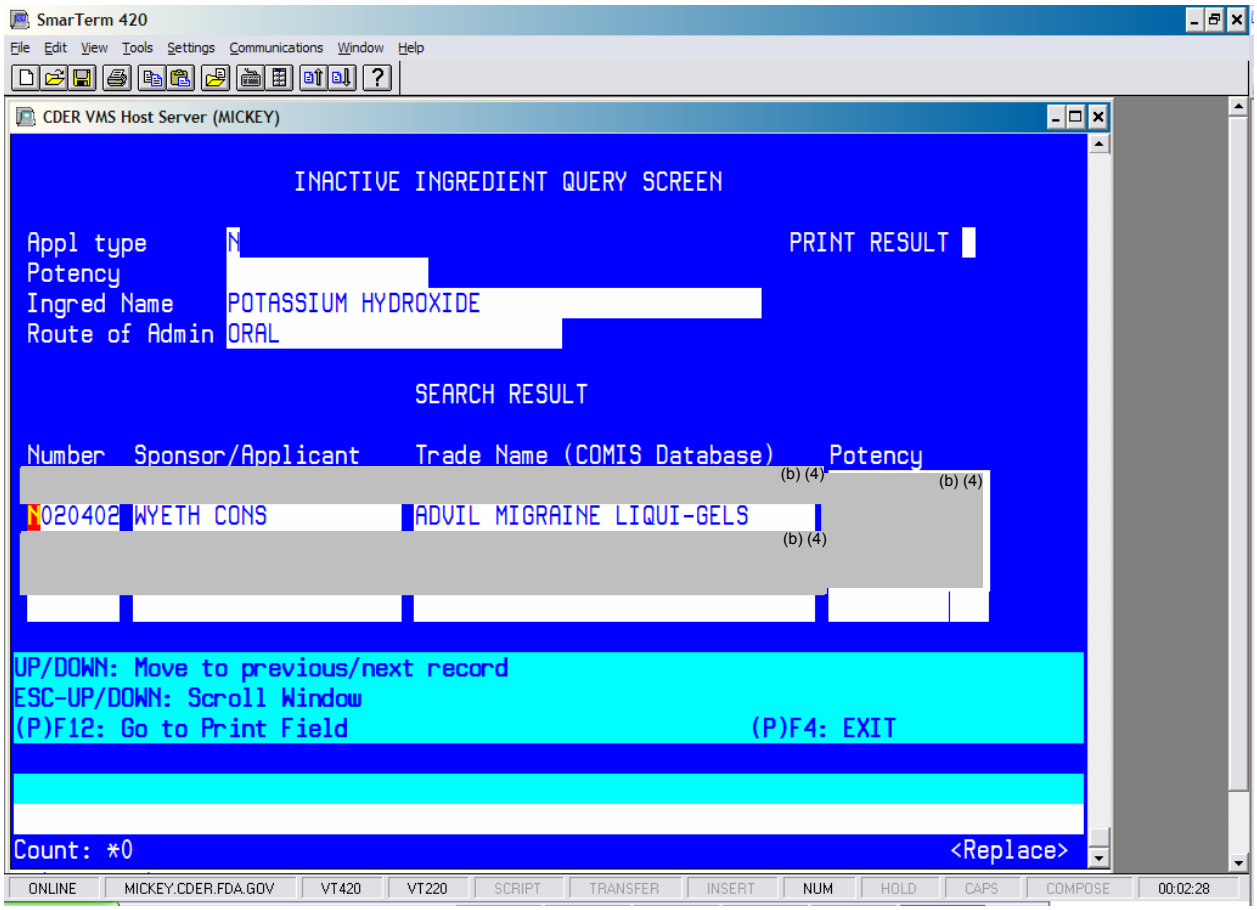
00:02:24

3.2.P.1.3 Composition Statement

Table 1: Target composition statement, capsule

Component	Quality Standard	Function	200 mg capsule
Capsule Fill:			
Ibuprofen 25	USP	Drug substance	200.00 mg
[redacted] (b) (4)			

[1] The quantitative composition of the ink is incorporated by reference to DMF [redacted] (b) (4) refer to section 1.4.1 for the letter of authorization. Refer to Table 4 for the qualitative composition.



FASTING:

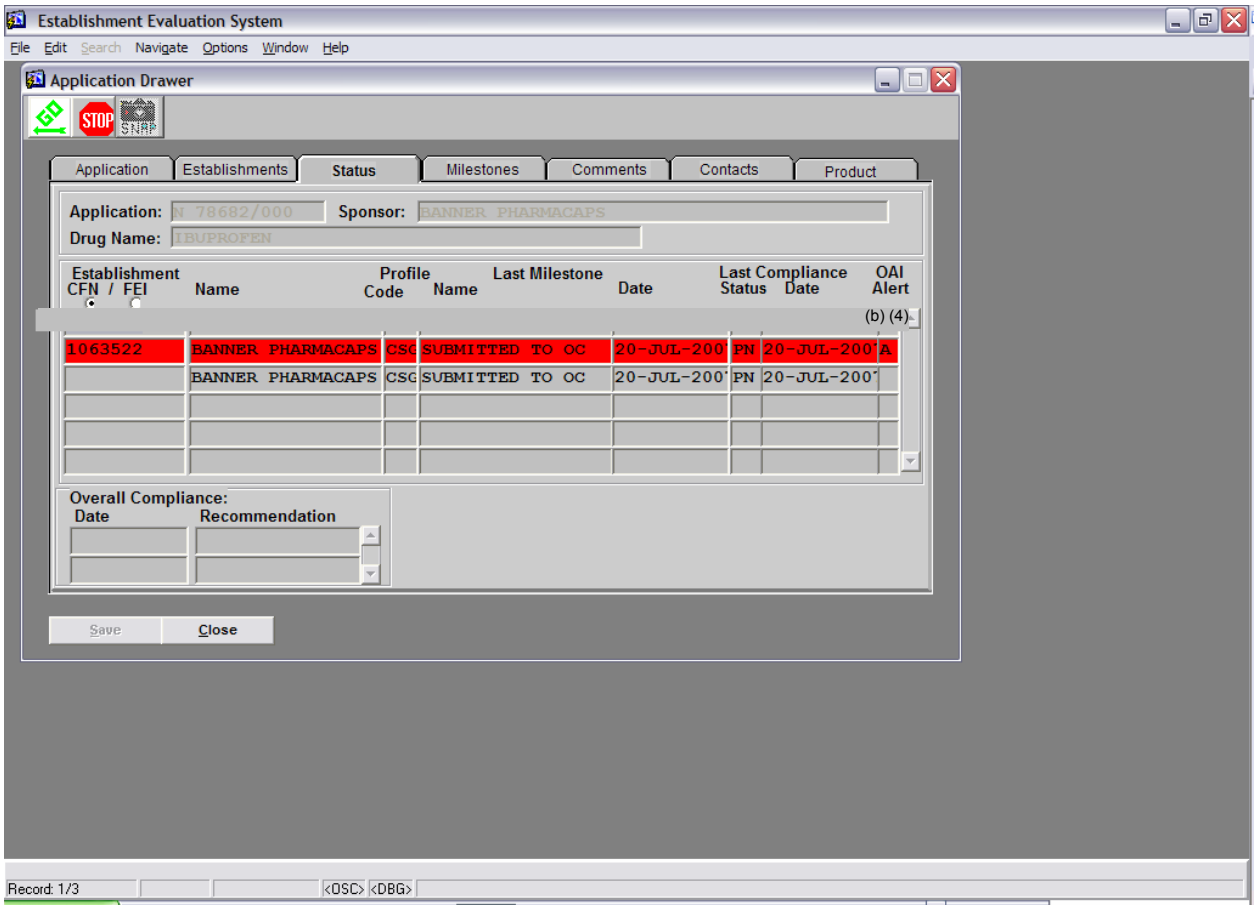
Table 11.2 – Summary of Ln-Transformed Pharmacokinetic Parameters

Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data Ibuprofen N=24				
Parameter	**Test**	**Reference**	**% Ratio**	**90% CI**
AUC_{0-t} (ng-hr/mL)	76076.87	73731.10	103.18	(100.44, 106)
$AUC_{0-\infty}$ (ng-hr/mL)	78431.49	76063.79	103.11	(100.29, 106.01)
C_{max} (ng/mL)	25351.96	24925.57	101.71	(94.27, 109.74)

NON-FASTING:

Study R07-0362

Geometric Means, Ratio of Means, and 90% Confidence Intervals Ln-Transformed Data Ibuprofen N=24				
Parameter	**Test**	**Reference**	**% Ratio**	**90% CI**
AUC_{0-t} (µg-hr/mL)	58.18	57.41	101.34	(98.9, 103.84)
$AUC_{0-\infty}$ (µg-hr/mL)	60.42	59.25	101.97	(99.57, 104.42)
C_{max} (µg/mL)	15.14	16.52	91.65	(83.71, 100.33)



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/s/

Martin Shimer

7/23/2007 01:52:33 PM

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-682

Banner Pharmacaps Inc.
Attention: Dale A. Kruep, Ph.D.
4125 Premier Drive
High Point, NC 27265

Dear Sir or Madam:

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 March 16, 2007 and your amendment dated July 5, 2007.

NAME OF DRUG: Ibuprofen Capsules, 200 mg

DATE OF APPLICATION: December 15, 2006

DATE (RECEIVED) ACCEPTABLE FOR FILING: July 6, 2007

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:

Dat Doan
Project Manager
301-827-5765

Sincerely yours,

{See appended electronic signature page}

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

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/s/

Martin Shimer
7/23/2007 01:50:13 PM
Signing for Wm Peter Rickman

DEPARTMENT OF HEALTH & HUMAN SERVICES

Food and Drug Administration
Rockville, MD 20857

ANDA 78-682

Banner Pharmacaps Inc.
Attention: Dale A. Kruep, Ph.D.
4125 Premier Drive
High Point, NC 27265

Dear Sir or Madam:

Please refer to your abbreviated new drug application (ANDA) dated December 15, 2006, submitted under Section 505(j) of the Federal Food, Drug and Cosmetic Act for Ibuprofen /Ibuprofen Potassium Capsules, 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 receive this ANDA under 21 CFR 314.101(d)(3) for the following reasons:

> The bioequivalence study submitted to support the approval of your application has been determined to be incomplete. You have failed to provide a nonfasting, *in vivo* bioequivalence study for your proposed drug product. If you have questions regarding your bioequivalence study, or bioequivalence requirements for this product, please contact Division of Bioequivalence, at (301) 827-5847 for further guidance.

In addition, please provide the following:

Please provide a Field Copy Certification with an original signature.

Please revise your Environmental Impact Statement to state you are in compliance with all local, state and federal environmental laws.

Please provide a copy of the Methods of Validation for the archival (blue) copy of the application.

Please provide the Quality Overall Summery, section 2.3, and the Clinical Summery, section 2.7, in both PDF and Word format.

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:

Iain Margand
Project Manager
(301) 827-5835

Sincerely yours,

{See appended electronic signature page}

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

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/s/

Martin Shimer
3/16/2007 07:38:20 AM
Signing for Wm Peter Rickman