CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 74782

ADMINISTRATIVE DOCUMENTS

ANDA **74-782** APPROVAL SUMMARY

DRUG PRODUCT: Ibuprofen Capsules, 200 mg

FIRM: Private Formulations, Inc.

DOSAGE FORM: Capsule

STRENGTH: 200 mg

cGMP STATEMENT/EIR UPDATE STATUS: EER Acceptable Date February 19, 1998.

BIO STUDY: APPROVE, Per Bio Review Dated February 26, 1998.

VALIDATION: Method Validation for DP is Pending; (DS is compendial).

STABILITY: Three months accelerated, 40°C/75% (RH), data in the market package size, bottles of 24 in both CRC and non-CRC, bottles of 1000 in both CRC and non-CRC containers, and blister pack with CR foil, provided. The container/closure system used for the stability study is equivalent to the system proposed for commercial use. All reported data are within specifications as listed. Thus, a 24 month expiration date is justified.

Tests and specifications for the drug product on stability include: assay (b)(4)(CC) [redacted]

LABELING: APPROVE, Review Date May 1, 1997.

STERILIZATION VALIDATION: (IF APPLICABLE): N/A

SIZE OF BIO BATCH:The bio batch, #G49136 is also the test batch. The drug substance source, (b)(4)(CC) [redacted] (lot #IB1C240), Firm's lot #95535; Batch size (b)(4)(CC) [redacted] caplets.

SIZE OF STABILITY BATCHES:Stability batch is the same as test batch, lot #G49136.

PROPOSED PRODUCTION BATCHES: The proposed production batch size remains the same as the test batch, i.e., (b)(4)(CC) [redacted] caplets. The manufacturing process for production batches is also the same as that for test batch.

CHEMIST: /S/ [redacted] **DATE:** 5/18/98

SUPERVISOR: **DATE:**

NTWAL HFD-623 JWil

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service
Food and Drug Administration

Memorandum

Date JUN 19 1997

From Consumer Safety Officer, Investigations & Preapproval Compliance Branch/DMPQ (HFD-324)

Subject Concurrence with District Withhold Recommendation, ANDA 74-782 Ibuprofen Gelatin Capsules, 200 mg

To

Gordon Johnston, Chief
Regulatory Support Staff, HFD-632

Applicant: Pharmaceutical Formulations, Inc.
460 Plainfield Ave.
Edison, NJ 08818

DMPQ has completed a review of an EIR covering an ANDA preapproval inspection conducted March 24-26, 31 and April 4, 1997 by NWJ-DO at the above applicant, Pharmaceutical Formulations, Inc. This EI covered the subject ANDA 74-782 (Ibuprofen Gelatin Capsules, 200mg) The EI covered the finished product manufacture and testing performed at this site.

The Division of Manufacturing and Product Quality (HFD-320) concurs with the District's recommendation to withhold approval of this ANDA. Our concurrence with NWJ-DO's withhold recommendation is based on the following significant GMP observations:

- Incomplete development data in support of 200 mg Ibuprofen Gelatin Capsule manufacture in that the following information was absent:

(b)(4)(TS)

[redacted]

(b)(4)(TS)

[redacted]

- There was no investigation into the out-of-specification conditions in the stability chamber or evaluation of the effects on the samples in the chamber. Additionally, the alarm did not warn of the out-of-specification condition on 3/26/97.

- There is [redacted]

(b)(4)(TS)

[redacted]

(b)(4)(TS) [redacted]

- Functions assigned to lab managers and the quality control unit were sometimes not carried out. Some examples cited on FDA-483 include but were not limited to:

a. An incident of failing to review and approve test results.

b. No record of calibration of the (b)(4)(TS) [redacted]

c. Failure to record in the batch records the actual amounts of raw materials weighed out for use

We also call to your attention the remaining observation (FDA-483 #2) that is a chemistry observation.

Management has promised to make all necessary corrections and to respond in writing. NWJ-DO should verify correction prior to any approval recommendation. A copy of the EIR and exhibits are attached for your review. If you have questions, please contact me at (301)-827-0065.

/S/ [redacted]

Randall L. Woods

Attachments - EIR and Exhibits

March 4, 1996

To: Peter Rickman
Team Leader
Regulatory Support

From: Keith Chan, Ph.D. /S/ [redacted] 3/5/96
Director, Division of Bioequivalence

Concur: Jason Gros /S/ [redacted] 96

re: 74-782
Private Formulations
Ibuprofen Capsules, 200 mg

Background:

Private Formulations would like to market an ibuprofen capsule. The RLD Midol Capsules (Sterling) was approved for marketing through a suitability petition in which Nuprin Tablets (Bristol Myers) was used as the reference listed drug. Sterling subsequently submitted an application and it was approved, but the product was never marketed. Private Formulations through written correspondence (Bio 95-021) letter dated 2/13/95 requested that the Agency designate a new RLD since Midol was not being marketed. In subsequent communication to the firm Agency letter dated 4/4/95, the firm was given permission to use Nuprin Tablets (Bristol Myers) as the RLD for BE-comparison since Midol Capsules was not marketed. Sterling subsequently submitted to the Agency an application which compared Nuprin Tablets with Private Formulations Ibuprofen Capsule. The application was received by the Agency 11/16/95, and was considered to be a refuse to file (reason: failure to cite the appropriate RLD). Sandoz had received approval of Provel Capsules NDA 20-402 on 4/20/95, and Provel was now considered the appropriate RLD. Private Formulations agreed to the terms of the Agency and agreed to conduct another BE-study using Provel. However based on communication with Sandoz (letter from Sandoz date 2/23/96), Private Formulations was informed that Provel is not available in the market place.

Requested Action by Private Formulations:

Private formulations would like to submit an application for Ibuprofen Capsules and wants the Agency to designate a RLD since both Midol (Sterling) and Provel (Sandoz) are unavailable.

Recommendations:

The Division is not opposed to accepting Private Formulations application which compares there test product to Nuprin Tablets (Bristol).

I called Sandoz & verified that Provel is not being marketed pending reformulation

/S/ [redacted] 96

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER 74782

CORRESPONDENCE

PRIVATE FORMULATIONS

Division of PHARMACEUTICAL FORMULATIONS, INC.

Middleton
Chase
12/7/95
RTF

November 10, 1995

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

Dear Sir:

Pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act, enclosed is our abbreviated new drug application for Ibuprofen Capsules 200 mg (solid-filled). Also enclosed are two additional copies of the analytical methods used in the testing of the product.

Information is provided in the application to demonstrate that our product is the same as the listed drug, Nuprin, in conditions for use, active ingredient, route of administration, strength and labeling.

We certify pursuant to 21 CFR 314.70(a) that a complete and accurate copy of the chemistry, manufacturing and control sections of this application has been provided to the FDA New Jersey District.

Thank you for your attention to this application.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V.P. of Quality &
Regulatory Affairs

BB/lk

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NOV 16 1995

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Please note RTF response was not forwarded to Reg Support for initially.

PRIVATE FORMULATIONS

Division of PHARMACEUTICAL FORMULATIONS, INC.

10/1/96 [redacted]

September 16, 1996

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

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SEP 17 1996
GENERIC DRUGS

Re: ANDA 74-782, Ibuprofen Capsules 200 mg.

Gentlemen:

Reference is made to Jerry Phillip's letter of May 31, 1996 concerning our abbreviated new drug application for the above product. This letter explains the Agency's refusal to file our application of November 10, 1995. The basis for this refusal is as follows:

> In our refuse to file letter dated February 6, 1996, you were informed that the reference listed drug was Provel® (Ibuprofen) Capsules 200 mg. However, the Office of Generic Drugs was unaware that the active ingredient in Provel® was not identical to the active ingredient in your proposed product. The correct reference listed drug is Midol® (Ibuprofen) Capsules 200 mg., a discontinued drug product manufactured by Winthrop Pharmaceuticals, Division of Sterling Drug. In order to submit an abbreviated application that relies on a listed drug that is no longer marketed, you must submit a petition seeking a determination whether the listed drug was withdrawn for safety or effectiveness reasons [21 CFR 314.122(a)]. Please submit the required citizens petition, following procedures outlined under 21 CFR 10.25(a) and 10.30.
>
> In addition, please amend your form FDA 356h, 505(j)(2)(A) information, and labeling comparison to reflect Midol as the reference listed drug.

In mid-July, 1996 we received the Summary Basis of Approval for Midol capsules from the Freedom of Information Staff. The Midol product was labeled as a premenstrual drug. This caused a dilemma since PFI wishes to submit this application as a conventional pain reliever/fever reducer similar to Advil, Nuprin, and Motrin.

On July 24, 1996 I had a telephone conversation with Adolph Vezza, Labeling Division, Office of Generic Drugs, in regards to the Midol® Ibuprofen capsule labeling. Mr. Vezza advised me that since Midol capsules are not marketed and that they were approved under a suitability

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petition with Nuprin® Ibuprofen Tablets, that we should use the Nuprin labeling in our side-by-side comparison as well as our intended packaging.

Pursuant to 21CFR314.101(b)(3)(ii), please amend our application . Enclosed please find:

- Form 356h referencing Midol® Capsules
- Amended 505(j) (2) (A) information
- Acknowledgement letter for our Citizen's Petition
- Copies of Midol Capsule labeling
- A side-by-side comparison of labeling referencing Nuprin®
- Draft copies of container labeling

We trust that we have satisfactorily answered all deficiencies mentioned in your letter.

We certify pursuant to 21CFR314.96(b), that a complete and accurate copy of this response has been provided to the FDA New Jersey District.

Sincerely,

Gregory R. Okrasinski

Gregory R. Okrasinski,
Regulatory Affairs Assistant

GRO/mc

enc.

70-676
70-122

PFI Pharmaceutical Formulations, Inc.

May 15,1997

Liz Sanchez
Food and Drug Administration
Division of Bioequivalence
Center for Drug Evaluation and Research
Office of Generic Drugs
Metro Park North II
7500 Standish Place
Rockville, MD 20855-2773

RE: Bioequivalence Study for Ibuprofen Capsules 200 mg., ANDA 74-782

Dear Ms. Sanchez:

This is a follow-up to our conversation regarding the bioequivalence study for ANDA 74-782, Ibuprofen Capsules 200 mg. Since the fasting study failed and the food study was acceptable, we will repeat the fasting study, but not the food study. The reference listed drug has since been changed to Motrin IB, ANDA #N73019 001, manufactured by McNeil Consumer Products, which is a gelatin-coated capsule-shaped tablet. We will do the new bioequivalence study against the new reference listed drug. At the time the food study was done, Nuprin was the reference listed drug, and this study is still acceptable.

If you have any questions, or if I have misinterpreted any of our conversation, please call me at (908) 819-3325.

Sincerely,

Michael J. Theil

Michael J. Theil
Regulatory Affairs Supervisor

MJT/lk

460 Plainfield Avenue, Edison, NJ 08818 Tel:908-985-7100 Fax:908-819-3330

MAJOR AMENDMENT

JUN 12 1997

ANDA/~~CADA~~ 74-782

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 [redacted]

TO: APPLICANT Private Formulations, Inc. PHONE 908-819-3325
ATTN: ~~Ann Barber~~ Michael Theil FAX 908-819-3330

FROM: Jim Wilson PROJECT MANAGER (301-827-5848)

Dear Sir/~~Madam~~:

This facsimile is in reference to your abbreviated new drug/antibiotic application 74-782 dated 11/10/95, submitted pursuant to Section 505(j)/507 of the Federal Food, Drug, and Cosmetic Act for IBUPROFEN GELATIN ~~CAPSULE~~ CAPLETS 200 mg

Reference is also made to your amendments dated MARCH 24, 1997.

The application is deficient and, therefore not approvable under Section 505/507 of the Act for the reasons provided in the 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 MAJOR AMENDMENT and will be reviewed according to current OGD policies and procedures. The designation as a MAJOR 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 this represents a second or greater occasion upon which significant (MAJOR) deficiencies have been identified, please contact the Project Manager within 30 days for further clarification or assistance.

SPECIAL INSTRUCTIONS:

REVERTED TO A MAJOR STATUS BASED ON BIO ISSUES

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.
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JUN 12 1997

38. Chemistry Comments to be Provided to the Applicant

ANDA: #74-782 APPLICANT: Private Formulations, Inc.

DRUG PRODUCT: Ibuprofen Capsules 200 mg

The deficiencies presented below represent Major deficiencies.

Deficiencies:

1. Please refer to the deficiency letter dated April 14, 1997 from the Division of Bioequivalence. Please do not respond to this letter until all the deficiencies in the letter dated April 14, 1997 have been addressed.

2. Please revise your stability protocol to include a test and specification for (b)(4)(CC) [redacted] We recommend (b)(4)(CC) [redacted] limits identical to the limits established in the drug substance specification.

Sincerely yours,

/S/ [redacted]

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

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

ANDA 74-782

Private Formulations, Inc.
Attention: Brian Barbee
460 Plainfield Avenue
Edison NJ 08818

APR 14 1997

Dear Sir:

Reference is made to the bioequivalence study data submitted on November 10, 1996, for Ibuprofen Capsules, 200 mg.

The Office of Generic Drugs has reviewed the submitted bioequivalence data and the following comments are provided for your consideration:

1. For the single-dose bioequivalence study under fasting conditions, the 90% confidence interval for LnC_{max} is 79.1-90.5%, which is outside the acceptable range of 80-125%.

2. The potency and content uniformity for the test and reference products should be submitted. The size of the bioequivalence batch also is needed.

3. Comparative dissolution testing should be submitted. This should include raw data from 12 dosage units each of the test and reference products, as well as, the mean, range, and %CV at each time point.

As described under 21 CFR 314.96 an action which will amend this application is required, should you have any questions, please call Lizzie Sanchez, Pharm.D., Project Manager, at (301) 594-2290. In future correspondence regarding this issue, please include a copy of this letter.

Sincerely yours,

/S/ [redacted]

for Nicholas Fleischer, Ph.D.
Director
Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

PFI Pharmaceutical Formulations, Inc.

ORIG AMENDMENT

N/A

MAJOR AMENDMENT

September 8, 1997

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: **ANDA 74-782 Ibuprofen Capsules 200 mg**

Gentlemen:

Reference is made to Jim Wilson's facsimile of June 12, 1997 containing comments from Rashmikant M. Patel and referencing Nicholas Fleischer's letter of April 14, 1997. This letter listed deficiencies in our bioequivalence study submitted November 10, 1996.

Pursuant to 21CFR314.101(b)(3), please amend our application to correct these deficiencies. The deficiencies are listed below and are followed by our response.

1. Please refer to the deficiency letter dated April 14, 1997 from the Division of Bioequivalence. Please do not respond to this letter until all the deficiencies in the letter dated April 14, 1997 have been addressed.

Division of Bioequivalence Letter of April 14, 1997

1. For the single-dose bioequivalence study under fasting conditions, the 90% confidence interval for LnC_{max} is 79.1-90.5%, which is outside the acceptable range of 80-125%.

Since the original Bioequivalence studies were performed, the Reference Listed Drug changed from Nuprin Tablets to Motrin IB Gelcaps (Gelatin-Coated Capsule-Shaped Tablets). Micheal Theil confirmed orally with Liz Sanchez that the food study versus Nuprin Tablets is acceptable and that the fasting study should be repeated using the new Reference Listed Drug (Motrin IB Gelcaps). A copy of Michael Theil's letter summarizing this conversation can be found following this letter. A new bioequivalence study under fasting conditions was performed using the new Reference Listed Drug and this can be found on pages 3 - 244.

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2. The potency and content uniformity for the test and reference products should be submitted. The size of the bioequivalence batch also is needed.

Certificates of analysis and content uniformity data for the test and reference products can be found on pages 245 - 250. The size of the bioquivalence batch is (b)(4)(CC) capsules.

3. Comparative dissolution testing should be submitted. This should include raw data from 12 dosage units each of the test and reference products, as well as, the mean, range, and %CV (RSD) at each time point.

Comparative dissolution data for the test and reference products can be found on pages 251 - 254.

End of Division of Bioequivalence Letter

2. Please revise your stability protocol to include a test and specification for (b)(4)(CC) (b)(4)(CC) We recommend (b)(4)(CC) limits identical to the limits established in the drug substance specification.

The stability protocol has been revised to include a test for (b)(4)(CC) y. The specification has been set as "Not more than (b)(4)(CC) Sum of all (b)(4)(CC) which is identical to the drug substance specification. Please see the stability protocol on pages 255 - 258.

We trust that we have satisfactorily answered all deficiencies mentioned in your letter.

We certify, pursuant to 21CFR314.96(b), that a complete and accurate copy of the CMC section of this response has been provided to the FDA New Jersey District Office.

Sincerely,

/S/

Brian W. Barbee
V. P. Scientific Affairs

PRIVATE FORMULATIONS
Division of PHARMACEUTICAL FORMULATIONS, INC.

FACSIMILE AMENDMENT

NEW CORRESP

March 24, 1997

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: **ANDA 74-782 Ibuprofen Capsules 200 mg**

Gentlemen:

Reference is made to Jim Wilson's facsimile of February 26, 1997 containing letters from Rashmikant M. Patel and Jerry Phillips listing chemistry and labeling deficiencies in the above abbreviated new drug application dated September 16, 1996.

Pursuant to 21CFR314.101(b)(3), please amend our application to correct these deficiencies. The deficiencies are summarized below and are followed by our response.

A) Chemistry Deficiencies

1. Please revise your specifications for the drug substance and drug product to meet the current requirements established in the USP.

Since the original ANDA was filed, three raw material specifications have been updated (Ibuprofen USP, Microcrystalline Cellulose NF, and Sodium Starch Glycolate NF). These revised specifications can be found on pages 03 - 07.

2. Please revise specifications for Core Caplets to include a specification for identification by (b)(4)(CC and a specification for dissolution to meet current USP requirements.

The specifications for (b)(4)(TS) have been updated to include the (b)(4)(CC) and dissolution specifications. These tests will be performed on the finished capsule (b)(4)(CC) The updated specifications can be found on pages 08 - 09.

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MAR 25 1997
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3. Please revise the specification for stearic acid NF to include testing for (b)(4)(CC) as required by USP 23.

This test is included in the current specification sheet found on page 675 of the original application. This is listed under "Identification - (b)(4)(CC) and is performed on every batch of Stearic Acid NF received at Private Formulations, Inc.

(b)(4)(TS)

B) In addition to responding to these deficiencies, please note and acknowledge the following in your response:

1. Please provide the pharmaceutical function of each ingredient used in the formulation.

A table describing the pharmaceutical function of each excipient in the formulation can be found on page 17.

2. Please commit to update the specifications for all ingredients to meet current requirements established in the USP/NF.

Private Formulations, Inc. commits to updating the specifications for all ingredients to meet current USP/NF requirements.

3. The facilities referenced in the application relative to the manufacturing and testing of the product must be in compliance with cGMPs at the time of approval. We have requested an evaluation from the Division of Manufacturing and Product Quality.

We understand that all facilities referenced in this application relative to the manufacturing and testing of the product must be in compliance with cGMPs at the time of approval.

Labeling Deficiencies

1. GENERAL COMMENTS:

a. On your application form (Form FDA 356h) it appears that your proposed established name "Ibuprofen Gelatin Caplets" is inadvertently listed as the proprietary name. The correct established name of your drug product name is "Ibuprofen Capsules, 200 mg". Please revise all labels and labeling accordingly.

All labels and labeling has been revised to use "Ibuprofen Capsules, 200 mg" as both the established and proprietary name.

b. We note that you have defined "gelatin caplets" as "solid-filled capsules" in the net quantity statement. Please note that "caplet" is not an officially recognized dosage form, however, we have approved labeling which has defined "caplet" as a "capsule-shaped tablet" in the net quantity statement. Since this product is a capsule, not a tablet, delete "caplet" from all labels and labeling.

We have revised the net quantity statement to read "___ gel caplets* *solid-filled capsules". We are defining "gel caplet", not "caplet", as a "solid-filled capsule". Our intended targets for this application are Motrin Gelcaps and Advil Gel Caplets (see label copies on page 18). In order for us to successfully market our product, it is necessary to distinguish our product from a conventional powder filled two piece capsule.

2. CONTAINER - 24's and 1000's

a. GENERAL

i. Regarding "Health Cross Brand" - Per 21 CFR 201.1(h), no person other than the manufacturer, packer, or distributor may be identified on the label. The appearance of a drug product label of a person's name without qualification is a representation that the named person is the sole manufacturer of the product. You have identified "Private Formulations, Inc." as the manufacturer of this proposed drug product. Therefore, the appearance of "Health Cross" on the label without qualification is misleading. If "Health Cross" is not the name of a manufacturer, packer or distributor, it must be deleted from the labels. Please revise and/or comment.

"Health Cross Brand" is a registered trademark of Private Formulations, Inc. "Health Cross Brand" products are manufactured by Private Formulations, Inc.

ii. We note that you have proposed both Child-resistant Closure (CRC) and Non-CRC configurations for both package sizes of 24's and 1000's. Please assure that the closure for your package sizes complies with the "Poison Prevention Packaging" standard. We refer you to the CFR 1700.14 and 1700.15 for your guidance.

Not all of our customers prefer the same package size as their non-complying size. Some prefer small sizes - 24's, while others prefer larger sizes - 500's or 1000's. We guarantee that only one size per customer will use a non-CRC configuration and that we will be in compliance with the Poison Prevention Act.

b. 24's

Include the storage statement as appears in the carton labeling.

The storage statement can be found in the bottle label text after the "ACTIVE INGREDIENT" and it is identical to the storage statement on the carton labeling.

c. 1000's

i. DIRECTIONS

We encourage you to print "Adults:" and "Children:" in bold type.

The labels and cartons have been revised accordingly.

ii. WARNINGS

We note that the container labels and insert labeling of your reference listed drug do not contain an "Alcohol Warning" statement. However, on September 8, 1993, in conjunction with the Arthritis Drugs Advisory committee, the Agency's Nonprescription Drugs Advisory Committee concluded that an "Alcohol Warning" statement should be required for OTC drug products containing aspirin, ibuprofen, and naproxen sodium. Thus, the Agency is currently developing a proposed regulation to require an "Alcohol Warning" statement for OTC analgesic drug products. The Agency has been encouraging manufacturers of OTC drug products containing analgesic active ingredients to voluntarily implement an "Alcohol Warning" statement. Please include the following "Alcohol Warning" statement immediately following the "WARNINGS" section.

ALCOHOL WARNING: If you generally consume 3 or more alcohol-containing drinks per day, you should consult your physician for advice on when and how you should take IBUPROFEN and other pain relievers.

This alcohol warning has been added to the 1000-count bottle label and was placed immediately following the warning for "Aspirin-Sensitive Patients".

iii. INACTIVE INGREDIENTS

A) Please alphabetize your list of inactive ingredients.

The labeling has been revised to alphabetize all inactive ingredients.

B) We note (b)(4)(CC) [redacted] is listed as one of the inactive ingredients. However, it is not found in your Components and Composition statement. Please revise and/or comment.

(b)(4)(CC) [redacted] is used as a manufacturing aid in the empty gelatin capsules. The gelatin and color additives likewise comprise a portion of the empty capsule. Please see the (b)(4)(CC) [redacted] sheet for the capsules (page 707 of the original application). The components and composition statement has been revised and can be found on page 16.

3. CARTON - 24's
See comments under CONTAINER.

Please see above comments concerning the "Health Cross Brand" and "Poison Prevention Packaging" standard. "Adults:" and "Children:" have been changed to bold type. The alcohol warning has been added to the 24-count bottle carton and was placed immediately following the warning for "Aspirin-Sensitive Patients". The inactive ingredients have been alphabetized.

4. BLISTER PACKAGING CARTON - 24's
See comments under CONTAINER.

Please see above comments concerning the "Health Cross Brand" and "Poison Prevention Packaging" standard. "Adults:" and "Children:" have been changed to bold type. The alcohol warning has been added to the 24-count blister packaging carton and was placed immediately following the warning for "Aspirin-Sensitive Patients". The inactive ingredients have been alphabetized.

5. BLISTER PACKAGE LABELING
Include the name and place of business of the manufacturer.

The name and place of business of the manufacturer has been added to the blister package labeling.

6. CONSUMER LABELING LEAFLET
See comments under CONTAINER.

Please see above comments concerning the "Health Cross Brand" and "Poison Prevention Packaging" standard. "Adults:" and "Children:" have been changed to bold type. The alcohol warning has been added to the consumer labeling leaflet and was placed immediately following the warning for "Aspirin-Sensitive Patients". The inactive ingredients have been alphabetized.

7. BULK PACKAGE LABELING
Although we do not review bulk package labeling for approval, we have reviewed the labeling for accuracy. Please refer to comments (c)(i) and (c)(ii) under CONTAINER.

"Adults:" and "Children:" have been changed to bold type. The alcohol warning has been added and was placed immediately following the warning for "Aspirin-Sensitive Patients".

Please revise your labels and labeling, as instructed above, and submit in final print, or draft if you prefer.

The final labeling can be found on pages 19 - 89. The final print for the blister package backing is a proof of the print mat used to stamp the back of the blister card. Because this is printed at the time of packaging the product, a final print is not available for this component. A side by side annotated comparison of the the original labeling (from the amendment dated September 16, 1996) with the revised labeling (included in this amendment) can be found on pages 90 - 115.

We trust that we have satisfactorily answered all deficiencies mentioned in your letter.

We certify, pursuant to 21CFR314.96, that a complete and accurate copy this response has been provided to the FDA New Jersey District Office.

Sincerely,

Michael J. Theil

Michael J. Theil
Regulatory Affairs Supervisor

FACSIMILE AMENDMENT

ANDA/~~AADA~~: 74-782

FEB 26 1997

Center for Drug Evaluation and Research · FDA ·

OFFICE OF GENERIC DRUGS, CDER, FDA
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773 [redacted]

TO: APPLICANT PRIVATE FORMULATIONS PHONE 908-985-7100
ATTN: BRIAN W. BARBEE FAX 908-819-3370

FROM: JIM WILSON PROJECT MANAGER (301-594-0310)

Dear Sir/~~Madam~~:

This facsimile is in reference to your abbreviated new drug/~~antibiotic~~ application 74-782 dated SEPT 16, 1996, submitted pursuant to Section 505(j)/507 of the Federal Food, Drug, and Cosmetic Act for IBUPROFEN GELATIN CAPLETS (Capsules)

Reference is also made to your amendment(s) dated SEPT 16, 1996

Attached are 6 pages of minor deficiencies and/or comments that should be responded to within 30 calendar days from the date of this document. This facsimile is to be regarded as an official FDA communication and unless requested, a hard copy will not be mailed. Your complete response should be (1) faxed directly to our document control room at 301-827-4337, (2) mailed directly to the above address, and (3) the cover sheet should be clearly marked a FACSIMILE AMENDMENT.

Please note that if you are unable to provide a complete response within 30 calendar days, the file on this application will be closed as a MINOR AMENDMENT and you will be required to take an action described under 21 CFR 314.120 which will either amend or withdraw the application. Accordingly, a response of greater than 30 days should be clearly marked MINOR AMENDMENT and will be reviewed according to current OGD policies and procedures. Facsimiles or incomplete responses received after 30 calendar days will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. 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. For further clarification or assistance please contact the Project Manager listed above.

SPECIAL INSTRUCTIONS:

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above addresee.

X:\new\ogdadmin\faxtrak\faxcov.fax

FEB 26 1997

38. Chemistry Comments to be Provided to the Applicant

ANDA: #74-782 APPLICANT: Private Formulations, Inc.

DRUG PRODUCT: Ibuprofen Capsules 200 mg

The deficiencies presented below represent FAXCIMILE deficiencies.

A. Deficiencies:

1. Please revise your specifications for the drug substance and drug product to meet the current requirements established in the USP.

2. Please revise specifications for Core Caplets to include a specification for identification by (b)(4)(and a specification for dissolution to meet current requirements.

3. Please revise the speci... include testing ... USP 23 ...

(b)(4)(TS) (b)(4)(CC)

[redacted]

6. [redacted]

addit... nowled...

1. [redacted] ...ponse: ...les, please note and ...ue the pharmaceutical function of each ...edient used in the formulation.

2. Please commit to update the specifications for all ingredients to meet current requirements established in the USP/NF.

3. The facilities referenced in the application relative to the manufacturing and testing of the product must be in compliance with cGMPs at the time of approval. We have requested an evalution from the Division of Manufacturing and Product Quality.

Sincerely yours,

/S/ [redacted]

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

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

ANDA Number: 74-782

Date of Submission: September 16, 1996

Applicant's Name: Private Formulations Inc.

Established Name: Ibuprofen Capsules, 200 mg

Labeling Deficiencies:

1. GENERAL COMMENTS:

   a. On your application from (Form FDA 356h) it appears that your proposed established name "Ibuprofen Gelatin Caplets" is inadvertently listed as a proprietary name. The correct established name of your drug product name is "Ibuprofen Capsules, 200 mg". Please revise all labels and labeling accordingly.

   b. We note that you have defined "gelatin caplets" as "solid-filled capsules" in the net quantity statement. Please note that "caplet" is not an officially recognized dosage form, however, we have approved labeling which has defined "caplet" as a "capsule-shaped tablet" in the net quantity statement. Since this product is a capsule, not a tablet, delete "caplet" from all labels and labeling.

2. CONTAINER - 24's and 1000's

   a. GENERAL

      i. Regarding "Health Cross Brand" - Per 21 CFR 201.1(h), no person other than the manufacturer, packer, or distributor may be identified on the label. The appearance on a drug product label of a person's name without qualification is a representation that the named person is the sole manufacturer of the product. You have identified "Private Formulations, Inc." as the manufacturer of this proposed drug product. Therefore, the appearance of "Health Cross" on the label without qualification is misleading. If "Health Cross" is not the name of a manufacturer, packer, or distributor, it must

be deleted from the labels. Please revise and/or comment.

ii. We note that you have proposed both Child-resistant Closure (CRC) and Non-CRC configurations for both package sizes of 24's and 1000's. Please assure that the closure for your package sizes complies with the "Poison Prevention Packaging" standard. We refer you to the CFR 1700.14 and 1700.15 for your guidance.

b. 24's

Include the storage statement as appears in the carton labeling.

c. 1000's

i. DIRECTIONS

We encourage you to print "Adults:" and "Children:" in bold type.

ii. WARNINGS

We note that the container labels and insert labeling of your reference listed drug do not contain an "Alcohol Warning" statement. However, on September 8, 1993, in conjunction with the Arthritis Drugs Advisory committee, the Agency's Nonprescription Drugs Advisory Committee concluded that an "Alcohol Warning" statement should be required for OTC drug products containing aspirin, ibuprofen, and naproxen sodium. Thus, the Agency is currently developing a proposed regulation to require an "Alcohol Warning" statement for OTC analgesic drug products. The Agency has been encouraging manufactures of OTC drug products containing analgesic active ingredients to voluntarily implement an "Alcohol Warning" statement. Please include the following "Alcohol Warning" statement immediately following the "WARNINGS" section.

ALCOHOL WARNING: If you generally consume 3 or more alcohol-containing drinks per day, you should consult your physician for advice on when and how you should take IBUPROFEN and other pain relievers.

iii. INACTIVE INGREDIENTS

A). Please alphabetize your list of inactive ingredients.

B). We note (b)(4)(TS) [redacted] is listed a[redacted] ingredients. However, it is not found in your Components and Composition statement. Please revise and/or comment.

3. CARTON - 24's

See comments e under CONTAINER.

4. BLISTER PACKAGING CARTON - 24's

See comments e under CONTAINER.

5. BLISTER PACKAGE LABELING

Include the name and place of business of the manufacturer.

6. CONSUMER LABELING LEAFLET

See comments e under CONTAINER.

7. BULK PACKAGE LABELING

Although we do not review bulk package labeling for approval, we have reviewed the labeling for accuracy. Please refer to comments (c)(i) and (c)(ii) under CONTAINER.

Please revise your labels and labeling, as instructed above, and submit in final print, or draft if you prefer.

Please note that we reserve the right to request further changes in your labels and/or labeling based upon changes in the approved labeling of the listed drug or upon further review of the application prior to approval.

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

/S/ [redacted]

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Table of Contents

Section		Pages
I.	**Form 356h**	01 - 02
II.	**Specifications**	
	Raw Material Specifications	03 - 07
	Finished Product Specifications	08 - 09
	Final (b)(4)(T Specifications	10
III.	**Blank Batch Record**	11 - 15
IV.	**Component and Composition Statement**	16
V.	**Table of Excipients**	17
VI.	**National Brand Labeling**	18
VII.	**Labeling**	
	24-count Bottle Label	19 - 23
	24-count Bottle Carton	24 - 36
	1000-count Bottle Label	37 - 49
	24-count Blister Packaging Carton	50 - 62
	Blister Packaging Backing	63 - 69
	Insert	70 - 76
	Bulk Product Label	77 - 89
VIII.	**Labeling Comparison**	
	24-count Bottle Label	90 - 93
	24-count Bottle Carton	94 - 97
	1000-count Bottle Label	98 - 101
	24-count Blister Packaging Carton	102 - 105
	Blister Packaging Backing	106 - 109
	Insert	110 - 113
	Bulk Product Label	114 - 117

PFI Pharmaceutical Formulations, Inc.

AMENDMENT

N/A B

December 24, 1997

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Re: ANDA 74-782 Ibuprofen Capsules 200 mg.

Gentlemen:

Reference is made to a December 23, 1997 telephone conversation between myself and Nancy Chamberlain of the Division of Bioequivalence. Ms. Chamberlain requested that we submit the expiration date of the reference listed drug used in our bioequivalence study submitted September 8, 1997.

(b)(4)(CC) bioequivalence study number 19958 utilized the following reference listed drug:

Motrin IB Gelcaps
Lot 01AXX
Exp. 09/99

This information may be found on page 83 (attached) of our 12/8/97 amendment.

Sincerely,

Brian Barbee

Brian Barbee,
V.P. of Scientific Affairs

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DEC 24 1997
GENERIC DRUGS

BB/mc
Att.

460 Plainfield Avenue, Edison, NJ 08818 Tel: 732-985-7100 Fax: 732-819-3330

PFI Pharmaceutical Formulations, Inc.

BIOEQUIVALENCE AMENDMENT

January 23, 1998

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

ORIG AMENDMENT
N/ME

RE: **ANDA 74-782 Ibuprofen Capsules 200 mg**

Gentlemen:

Reference is made to Nancy Chamberlin's facsimile of January 13, 1998 containing a letter from Dale P. Conner listing a bioequivalence deficiency in the above abbreviated new drug application.

Pursuant to 21CFR314.101(b)(3), please amend our application to correct this deficiency. The deficiency is summarized below and is followed by our response.

1. You are advised to conduct dissolution testing under the following conditions:
   Apparatus: USP 23 Apparatus II (paddle) at 50 RPM
   Medium: 900 mL of phosphate buffer pH 7.2 at 37°C
   Sampling Time: 15, 30, 45, and 60 minutes
   Specifications: NLT[redacted] in 45 minutes

   Please find on pages 3 - 4 the new dissolution profiles, utilizing the new apparatus and sampling times, for Ibuprofen Capsules 200 mg manufactured by Private Formulations, Inc. and for Motrin Gelcaps manufactured by Upjohn. Please find on pages 5 - 6 updated Finished Product Specifications for Ibuprofen Capsules 200 mg. Please find on pages 7 - 12 an updated Analytical Method for Ibuprofen Capsules.

We trust that we have satisfactorily answered the deficiency mentioned in your letter.

We certify, pursuant to 21CFR314.96 (b), that a complete and accurate copy this response has been provided to the FDA New Jersey District Office.

Sincerely,

Philip D. Johnson

Philip D. Johnson
Regulatory Affairs Associate

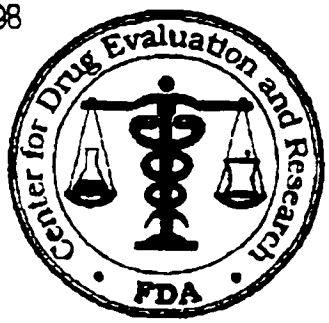
RECEIVED
JAN 26 1998
GENERIC DRUGS

460 Plainfield Avenue, Edison, NJ 08818 Tel: 732-985-7100 Fax: 732-819-3530

BIOEQUIVALENCY AMENDMENT

JAN 13 1998

ANDA 74-782



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

TO: APPLICANT: Private Formulations, Inc. PHONE: 732-985-7100

ATTN: Brian Barbee FAX: 732-819-3310

FROM: Nancy Chamberlin PROJECT MANAGER (301) 827-5847

Dear Sir:

This facsimile is in reference to the bioequivalency data submitted on 9-8-97, 12-15-97, and 12-24-97, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Ibuprofen 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 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 direct any questions concerning this communication to the project manager identified above.

SPECIAL INSTRUCTIONS:

THIS DOCUMENT IS INTENDED ONLY FOR THE USE OF THE PARTY TO WHOM IT IS ADDRESSED AND MAY CONTAIN INFORMATION THAT IS PRIVILEGED, CONFIDENTIAL, OR PROTECTED FROM DISCLOSURE UNDER APPLICABLE LAW. If received by someone other than the addressee or a person authorized to deliver this document to the addressee, you are hereby notified that any disclosure, dissemination, copying, or other action to the content of this communication is not authorized. If you have received this document in error, please immediately notify us by telephone and return it to us by mail at the above address.

X:\new\ogdadmin\glossary\biofax.frm

JAN 13 1998

BIOEQUIVALENCY DEFICIENCIES TO BE PROVIDED TO THE APPLICANT

ANDA: 74-782 APPLICANT: Private Formulations, Inc.

DRUG: Ibuprofen Capsules, 200 mg

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

You are advised to conduct dissolution testing under the following conditions:

Apparatus: USP 23 apparatus II (paddle) at 50 RPM
Medium: 900 mL of phosphate buffer pH 7.2 at 37°C
Sampling Time: 15, 30, 45 and 60 minutes.
Specifications: NLT (b)(4)(C[redacted]n 45 minutes.

Sincerely yours,

/S/ [redacted]

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

PFI Pharmaceutical Formulations, Inc.

TELEPHONE AMENDMENT

May 18, 1998 ORIG AMENDMENT

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

Attn: Jim Wilson, Project Manager
Fax: (301) 594-0180

Re: **ANDA 74-782 Ibuprofen Capsules 200 mg**

Gentlemen:

Reference is made to a telephone conversation on May 14, 1998 between Jim Wilson of the FDA and Brian Barbee and Charles LaRosa of Pharmaceutical Formulations, Inc. citing deficiencies in the above abbreviated new drug application.

Pursuant to 21CFR314.96(a)(1), please amend our application to correct these deficiencies. The deficiencies are summarized below and are followed by our response.

A) Chemistry Deficiencies

(b)(4)(TS)

[redacted]

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MAY 19 1998

460 Plainfield Avenue, Edison, NJ 08818 Tel: 732-985-7100 Fax: 732-819-3330

GENERIC DRUGS

(b)(4)(TS)

[redacted]

We trust that we have satisfactorily answered all deficiencies mentioned in the telephone conversation of May 14, 1998.

We certify, pursuant to 21CFR314.96, that a complete and accurate copy this response has been provided to the FDA New Jersey District Office.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

1-732-
817-
3322

DEPARTMENT OF HEALTH AND HUMAN SERVICES
FOOD AND DRUG ADMINISTRATION

APPLICATION TO MARKET A NEW DRUG, BIOLOGIC, OR AN ANTIBIOTIC DRUG FOR HUMAN USE

(Title 21, Code of Federal Regulations, 314 & 601)

Form Approved: OMB No. 0910-0338
Expiration Date: April 30, 2000
See OMB Statement on last page.

FOR FDA USE ONLY

APPLICATION NUMBER

APPLICANT INFORMATION

NAME OF APPLICANT: Pharmaceutical Formulations, Inc.

DATE OF SUBMISSION: May 18, 1998

TELEPHONE NO. *(Include Area Code)*: (732) 985-7100

FACSIMILE (FAX) Number *(Include Area Code)*: (732) 819-3310

APPLICANT ADDRESS *(Number, Street, City, State, Country, ZIP Code or Mail Code, and U.S. License number if previously issued)*:
460 Plainfield Avenue
Edison, New Jersey 08818

AUTHORIZED U.S. AGENT NAME & ADDRESS *(Number, Street, City, State, ZIP Code, telephone & FAX number)* IF APPLICABLE

PRODUCT DESCRIPTION

NEW DRUG OR ANTIBIOTIC APPLICATION NUMBER, OR BIOLOGICS LICENSE APPLICATION NUMBER (If previously issued) 74-782

ESTABLISHED NAME *(e.g., Proper name, USP/USAN name)*: Ibuprofen Capsules

PROPRIETARY NAME *(trade name)* IF ANY:

CHEMICAL/BIOCHEMICAL/BLOOD PRODUCT NAME *(If any)*: (±)-2-(p-Isobutylphenyl)propionic acid

CODE NAME *(If any)*:

DOSAGE FORM: Capsule (Solid-Filled)

STRENGTHS: 200 mg

ROUTE OF ADMINISTRATION: Oral

(PROPOSED) INDICATION(S) FOR USE:
Temporary relief of minor aches and pains associated with the common cold, headache, toothache, muscular aches, backache, for the minor pain of arthritis for the pain of menstrual cramps and for reduction of fever.

APPLICATION INFORMATION

APPLICATION TYPE (check one)
☐ NEW DRUG APPLICATION (21 CFR 314.50)
☒ ABBREVIATED APPLICATION (ANDA, AADA, 21 CFR 314.94)
☐ BIOLOGICS LICENSE APPLICATION (21 CFR part 601)

IF AN NDA, IDENTIFY THE APPROPRIATE TYPE ☐ 505 (b) (1) ☐ 505 (b) (2) ☐ 507

IF AN ANDA, OR AADA, IDENTIFY THE REFERENCE LISTED DRUG PRODUCT THAT IS THE BASIS FOR THE SUBMISSION
Name of Drug: Midol Ibuprofen Capsules
Holder of Approved Application: Sterling Drug

TYPE OF SUBMISSION (check one)
☐ ORIGINAL APPLICATION ☒ AMENDMENT TO A PENDING APPLICATION ☐ RESUBMISSION
☐ PRESUBMISSION ☐ ANNUAL REPORT ☐ ESTABLISHMENT DESCRIPTION SUPPLEMENT ☐ SUPAC SUPPLEMENT
☐ EFFICACY SUPPLEMENT ☐ LABELING SUPPLEMENT ☐ CHEMISTRY MANUFACTURING AND CONTROLS SUPPLEMENT ☐ OTHER

REASON FOR SUBMISSION: Chemistry Telephone Deficiency of May 14, 1998

PROPOSED MARKETING STATUS (check one) ☐ PRESCRIPTION PRODUCT (Rx) ☒ OVER THE COUNTER PRODUCT (OTC)

NUMBER OF VOLUMES SUBMITTED 1

THIS APPLICATION IS ☒ PAPER ☐ PAPER AND ELECTRONIC ☐ ELECTRONIC

ESTABLISHMENT INFORMATION

Provide locations of all manufacturing, packaging and control sites for drug substance and drug product (continuation sheets may be used if necessary). Include name, address, contact, telephone number, registration number (CFN), DMF number, and manufacturing steps and/or type of testing (e.g. Final dosage form, Stability testing) conducted at the site. Please indicate whether the site is ready for inspection or, if not, when it will be ready.

All manufacturing, packaging, and testing is performed at the above address.
Reg #:2242470/NWK [redacted] (b)(4)(CC) Contact: Brian W. Barbee
Phone: (732) 819-3326
This site is ready for inspection.

Cross References (list related License Applications, INDs, NDAs, PMAs, 510(k)s, IDEs, BMFs, and DMFs referenced in the current application)

DMF [redacted] (b)(4)(CC)
DMF

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MAY 19 1998
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FORM FDA 356h (4/97)

EF

PHARMACEUTICAL FORMULATIONS, INC.
460 Plainfield Avenue
Edison, New Jersey 08818

J09010

QUALITY CONTROL DEPARTMENT
ANALYTICAL PROCEDURE

Raw Material Specification Ibuprofen USP 23, Pages 785-786, 3897-3898	Page 1 of 2
PREPARED BY: Philip Johnson	DATE: 5/15/98
APPROVED BY: Brian Barber	DATE: 5/15/98

TEST	SPECIFICATION
1. Description	White to off-white crystalline powder, having a slight, characteristic odor.
2. Identification A) The infrared Absorption <197M>. Do not dry specimens.	Exhibits maxima only at the same wavelengths as that of a similar preparation of USP Ibuprofen RS.
B) Ultraviolet Absorption <197U> Solution: 250 µg per mL Medium: 0.1N Sodium Hydroxide	Respective absorptivities, calculated on the anhydrous basis, at 264nm and 273nm do not differ by more than 3.0 %.
C) The chromatogram of the *Assay preparation* obtained as directed in the *Assay*.	Exhibits a major peak for Ibuprofen the retention time of which, relative to that of the internal standard, corresponds to that exhibited in the chromatogram of the *Standard preparation* obtained as directed in the *Assay*.
3. Water, Method I <921>	NMT 1.0 %
4. Residue on Ignition <281>	NMT 0.5 %
5. Heavy Metals, Method II <231>	0.002 %
6. Chromatographic Purity USP Pg. 786	NMT 0.3 % of any individual impurity is found, and the sum of all the individual impurities found does not exceed 1.0 %.
* 7. Organic Volatile Impurities Method V <467>	None of the specific toxic impurities are used in the process. The material if tested will comply with USP.

PHARMACEUTICAL FORMULATIONS, INC.
460 Plainfield Avenue
Edison, New Jersey 08818

J09010

QUALITY CONTROL DEPARTMENT
ANALYTICAL PROCEDURE

Raw Material Specification Ibuprofen USP 23, Pages 785-786, 3897-3898	Page 2 of 2
PREPARED BY: Philip Johnson	DATE: 5/15/98
APPROVED BY: Brian Barbee	DATE: 5/15/98

TEST	SPECIFICATION
8. Assay, USP Pg. 3897-3898	NLT 97.0 % and NMT 103.0 % calculated on the anhydrous basis.
9. Limit of 4-isobutylacetophenone	NMT 0.1 %
*10. Median Particle Size	(b)(4)(CC) [redacted]
11. Retest Date	(b)(4)(CC) [redacted]
12. Approved Supplier	(b)(4)(CC) [redacted]
13. Supplier's Certificate of Analysis	Required

* The tests and specifications meet USP 23 requirements and they are based on the Supplier's Certificate of Analysis.

PFI Pharmaceutical Formulations, Inc.

Ibuprofen Capsules 200 mg
Bulk Product Commitment

For ANDA 74-782 for Ibuprofen Capsules 200 mg, Pharmaceutical Formulations, Inc. commits to the following regarding the bulk sale for repackaging of the product:

1. All customers purchasing bulk Ibuprofen Capsules 200 mg will be informed of the approved market container/closure systems and that they must utilize these systems when repackaging the product.

2. All customers purchasing bulk Ibuprofen Capsules 200 mg will be informed that the expiration date of the product in its bulk container is 3 months and the expiration date of the product in the market container/closure system is 2 years.

Brian W. Barbee
V. P. Scientific Affairs

5/18/98
Date

460 Plainfield Avenue, Edison, NJ 08818 Tel: 732-985-7100 Fax: 732-819-3330

NDC 10916-954-00

CODE #: (b)(4)(CC)

IBUPROFEN CAPSULES, 200 MG

PAIN RELIEVER / FEVER REDUCER

WARNING: ASPIRIN SENSITIVE PATIENTS. DO NOT TAKE THIS PRODUCT IF YOU HAVE HAD A SEVERE ALLERGIC REACTION TO ASPIRIN, E.G. ASTHMA, SWELLING, SHOCK OR HIVES, BECAUSE EVEN THOUGH THIS PRODUCT CONTAINS NO ASPIRIN OR SALICYLATES, CROSS-REACTIONS MAY OCCUR IN PATIENTS ALLERGIC TO ASPIRIN.

ALCOHOL WARNING: If you generally consume 3 or more alcohol-containing drinks per day, you should consult your physician for advice on when and how you should take IBUPROFEN and other pain relievers.

INDICATIONS: For the temporary relief of minor aches and pains associated with the common cold, headache, toothache, muscular aches, backache, for the minor pain of arthritis, for the pain of menstrual cramps and for the reduction of fever.

DIRECTIONS: **Adults:** Take 1 gel caplet every 4 to 6 hours while symptoms persist. If pain or fever does not respond to 1 gel caplet, 2 gel caplets may be used but do not exceed 6 gel caplets in 24 hours, unless directed by a doctor. The smallest effective dose should be used. Take with food or milk if occasional and mild heartburn, upset stomach, or stomach pain occurs with use. Consult a doctor if these symptoms are more than mild or if they persist. **Children:** Do not give this product to children under 12 except under the advice and supervision of a doctor.

WARNINGS: Do not take for pain for more than 10 days or for fever for more than 3 days unless directed by a doctor. If pain or fever persists or gets worse, if new symptoms occur, or if the painful area is red or swollen, consult a doctor. These could be signs of serious illness. If you are under a doctor's care for any serious conditions, consult a doctor before taking this product. As with aspirin and acetaminophen, if you have any condition which requires you to take prescription drugs or if you have had any problems or serious side effects from taking any non-prescription pain reliever do not take Ibuprofen gel caplets without first discussing it with your doctor. If you experience any symptoms which are unusual or seem unrelated to the condition for which you took Ibuprofen, consult a doctor before taking any more of it. Although Ibuprofen is indicated for the same conditions as aspirin and acetaminophen, it should not be taken with them except under a doctor's direction. Do not combine this product with any other Ibuprofen containing product. As with any drug, if you are pregnant or nursing a baby, seek the advice of a health professional before using this product. **IT IS ESPECIALLY IMPORTANT NOT TO USE IBUPROFEN DURING THE LAST 3 MONTHS OF PREGNANCY UNLESS SPECIFICALLY DIRECTED TO DO SO BY A DOCTOR BECAUSE IT MAY CAUSE PROBLEMS IN THE UNBORN CHILD OR COMPLICATIONS DURING DELIVERY.**

Keep this and all drugs out of the reach of children. In case of accidental overdose, seek professional assistance or contact a poison control center immediately.

ACTIVE INGREDIENT: Each gel caplet contains Ibuprofen USP 200 mg.
STORE AT ROOM TEMPERATURE. AVOID EXCESSIVE HEAT 40°C (104°F).

Date of Manufacture: Bulk Carton Exp. Date:
Product Exp. Date:

WARNING—KEEP OUT OF THE REACH OF CHILDREN

Revised March 1997

IMPORTANT

PJ 3/11/97
MT 3/17/97

This bulk unit is not for consumer sale. It is to be suitably repacked and relabeled for distribution in retail packages as soon as received. We cannot assume any responsibility for bulk goods that are left in bulk containers or subsequently packaged in any container unsuitable to the product.

No responsibility is assumed, under the provisions of the Food, Drug and Cosmetic Act of 1938, for any subsequent label statements under which this product may be labeled. We guarantee that the contents of this container conform to specifications and were in good condition when shipped. If, upon opening, the contents are found unsatisfactory in any particular, we must be notified immediately in writing as our responsibility ceases upon removal of goods from the original container or 10 days after receipt of this shipment by our