ANDA 75-588

APR 17 2001

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

Dear Sir:

This is in reference to your abbreviated new drug application dated February 19, 1999, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act (Act), for Ibuprofen and Pseudoephedrine Hydrochloride Tablets USP, 200 mg and 30 mg, respectively.

Reference is also made to your amendments dated April 26, 1999; and January 17, January 22, March 2, March 8, and March 12, 2001.

We have completed the review of this abbreviated application and have concluded that, based upon the information you have presented to date, the drug product is safe and effective for use as recommended in the submitted labeling. Therefore, the application is **tentatively approved**. This determination is based upon information available to the Agency at this time (i.e., information in your application and the status of current good manufacturing processes (CGMPs) of the facilities used in the manufacture and testing of the drug product). The determination is subject to change on the basis of new information that may come to our attention.

The listed drug product referenced in your application, Advil Cold and Sinus Tablets of Whitehall Laboratories, inc., is subject to a period of patent protection which expires on October 9, 2004 (U.S. Patent No. 4,552,899). Your application contains a patent certification to this patent under Section 505(j)(2)(A)(vii)(IV) of the Act stating that your manufacture, use or sale of this drug product will not infringe on the patent and/or the patent is invalid. Section 505(j)(5)(B)(iii) of the Act provides that approval shall be made effective immediately unless an action is brought for infringement of the patent which is the subject of the certification before the expiration of

forty-five days from the date the notice provided under paragraph (2)(B)(i) is received. You have notified FDA that Pharmaceutical Formulations, Inc. has complied with the requirements of Section 505(j)(2)(B) of the Act and that no action for patent infringement was brought against Pharmaceutical Formulations, Inc. within the statutory forty-five day period.

However, we are unable to grant full approval to your application at this time because another abbreviated application for Ibuprofen and Pseudoephedrine Hydrochloride Tablets USP, 200 mg/30 mg, containing a Paragraph IV Certification was accepted for filing by this office prior to receipt of your application. Accordingly, your application will be eligible for final approval beginning on the date that is one hundred and eighty days after the date the Agency receives notice of the first commercial marketing of the drug under the previous application, or the date of a court decision described under section 505(j)(5)(B)(iv), whichever is earlier. We refer you to the Agency's guidance document "180-Day Generic Drug Exclusivity Under the Hatch-Waxman Amendments" (June 1998), for additional information.

To reactivate your application prior to final approval, please submit an amendment between 60 to 90 days prior to the date you believe your application will be eligible for final approval. This amendment should identify changes, if any, in the conditions under which the product was tentatively approved, and should include updated information such as final-printed labeling, chemistry, manufacturing, and controls data as appropriate. Please note that this amendment should be submitted even if none of these changes were made. The amendment should be designated clearly in your cover letter as a MINOR AMENDMENT. In addition to this amendment, the Agency may request at any time prior to the final date of approval that you submit an additional amendment containing the information described above.

Failure to submit such an amendment requested by the Agency will prompt a review of the application which may result in rescission of the tentative approval status of your application, or may result in a delay in the issuance of the final approval letter.

Any significant changes in the conditions outlined in this abbreviated application as well as changes in the status of the manufacturing and testing facilities' compliance with current

good manufacturing practices (CGMPs) are subject to Agency review before final approval of the application will be made.

Please note that this drug product may not be marketed without final Agency approval under Section 505 of the Act. The introduction or delivery for introduction into interstate commerce of this drug product before the final approval date is prohibited under Section 501 of the Act and 21 U.S.C. 331(d). Also, until the Agency issues the final approval letter, this drug product will not be deemed approved for marketing under 21 U.S.C. 355 and will not be listed in the "Approved Drug Products with Therapeutic Equivalence Evaluations" list (the "Orange Book"), published by the Agency. Should you believe that there are grounds for issuing the final approval letter prior to the date of final approval, you should amend your application accordingly.

At the time you submit any amendments, you should contact Ms. Elaine Hu, R.Ph., Project Manager, at (301) 827-5848, for further instructions.

Sincerely yours,

/S/

Gary Buehler 4/17/01
Acting Director
Office of Generic Drugs
Center for Drug Evaluation and Research

ANDA 75-588

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

MAR 9 1999

Dear Sir:

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

Reference is made to the telephone conversation dated March 4, 1999 and your correspondence dated March 4, 1999.

NAME OF DRUG: Ibuprofen and Pseudoephedrine Hydrochloride Tablets USP, 200 mg/30 mg

DATE OF APPLICATION: February 19, 1999

DATE (RECEIVED) ACCEPTABLE FOR FILING: February 23, 1999

You have filed a Paragraph IV patent certification, in accordance with 21 CFR 314.94(a)(12)(i)(A)(4) and Section 505(j)(2)(A)(vii)(IV) of the Act. Please be aware that you need to comply with the notice requirements, as outlined below. In order to facilitate review of this application, we suggest that you follow the outlined procedures below:

CONTENTS OF THE NOTICE

You must cite section 505(j)(2)(B)(ii) of the Act in the notice and should include, but not be limited to, the information as described in 21 CFR 314.95(c).

SENDING THE NOTICE

In accordance with 21 CFR 314.95(a):

- Send notice by U.S. registered or certified mail with return receipt requested to each of the following:

1) Each owner of the patent or the representative designated by the owner to receive the notice;

2) The holder of the approved application under section 505(b) of the Act for the listed drug claimed by the patent and for which the applicant is seeking approval.

3) An applicant may rely on another form of documentation only if FDA has agreed to such documentation in advance.

DOCUMENTATION OF NOTIFICATION/RECEIPT OF NOTICE

You must submit an amendment to this application with the following:

- In accordance with 21 CFR 314.95(b), provide a statement certifying that the notice has been provided to each person identified under 314.95(a) and that notice met the content requirements under 314.95(c).

- In accordance with 21 CFR 314.95(e), provide documentation of receipt of notice by providing a copy of the return receipt or a letter acknowledging receipt by each person provided the notice.

- A designation on the exterior of the envelope and above the body of the cover letter should clearly state "PATENT AMENDMENT". This amendment should be submitted to your application as soon as documentation of receipt by the patent owner and patent holder is received.

DOCUMENTATION OF LITIGATION/SETTLEMENT OUTCOME

You are requested to submit an amendment to this application that is plainly marked on the cover sheet "PATENT AMENDMENT" with the following:

- If litigation occurs within the 45-day period as provided for in section 505(j)(4)(B)(iii) of the Act, we ask that you provide a copy of the pertinent notification.

- Although 21 CFR 314.95(f) states that the FDA will presume the notice to be complete and sufficient, we ask that if you are not sued within the 45-day period, that you provide a letter immediately after the 45 day period elapses, stating that no legal action was taken by each person provided notice.

- You must submit a copy of a final order or judgement from which no appeal may be taken (which might not be the one from the District Court), or a settlement agreement between the parties, whichever is applicable, or a licensing agreement between you and the patent holder, or any other relevant information. We ask that this information be submitted promptly to the application.

If you have further questions you may contact Peter Rickman, Chief, Regulatory Support Branch, at (301)827-5862.

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:

Bonnie McNeal
Project Manager
(301) 827-5848

Sincerely yours,

/S/

Robert L. West, M.S., R.Ph.
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

cc: ANDA 75-588
DUP/Jacket
Division File
Field Copy
HFD-610/R.West
HFD-92
HFD-615/M.Bennett

Endorsement: HFD-615/PRickman, Chief, RSB /S/ date 3/9/99
HFD-615, GDavis, CSO /S/ 3/5/99 date
HFD-623, VSayeed, Sup. Chem. _____ date

ANDA Acknowledgment Letter!

PFI Pharmaceutical Formulations, Inc.

February 19, 1999

505(j)(2)(A) OK
3/5/99

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

Re: **Ibuprofen Cold & Sinus (Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP)**

Gentlemen:

Pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act, enclosed is our abbreviated new drug application for Ibuprofen Cold & Sinus (Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP). 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, Advil Cold & Sinus, in conditions for use, active ingredients, route of administration, strength and labeling.

We certify, pursuant to 21CFR314.94 (d) (5) that a complete and accurate copy of the Chemistry, Manufacturing, and Controls section of this application has been provided to the FDA New Jersey District Office.

Thank you for your attention to this application.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

RECEIVED
FEB 25 1999
GENERIC DRUGS

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

PFI *Pharmaceutical Formulations, Inc.*

March 4, 1999

NEW CORRESP
NC

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

Re: **ANDA 75-588 Ibuprofen Cold & Sinus**
(Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP)

Dear Mr. Davis:

Reference is made to our conversation on March 4, 1999 concerning ANDA 75-588 for Ibuprofen Cold & Sinus (Ibuprofen/Pseudoephedrine HCl Tablets USP).

As per your request, enclosed please find the following:

1. A revised Patent Certification for ANDA 75-588 to incorporate the patent expiration dates listed in the Orange Book.

2. A bioequivalence waiver request for the round-shaped Ibuprofen/Pseudoephedrine HCl Tablets USP.

If you have any questions or desire any additional information, please contact me.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

RECEIVED
MAR 0 5 1999
GENERIC DRUGS

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

PFI Pharmaceutical Formulations, Inc.

Bioequivalence Telephone Amendment

April 26, 1999

ORIG AMENDMENT

AB

Office of Generic Drugs
CDER, FDA
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attn: Elaine Hu, Project Manager

Re: **ANDA 75-588 Ibuprofen Cold & Sinus**
(Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP)

Dear Ms. Hu:

Reference is made to our conversation on March 16, 1999 concerning ANDA 75-588 for Ibuprofen Cold & Sinus (Ibuprofen/Pseudoephedrine HCl Tablets USP).

Please find enclosed diskettes in ASCII format containing the concentration and pharmacokinetic data for the bioequivalence studies performed under Protocols 299-04(t)and 299-05(

If you have any questions or desire any additional information, please contact me.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

RECEIVED

APR 27 1999

GENERIC DRUGS

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

PFI *Pharmaceutical Formulations, Inc.*

NEW CORRESP

PATENT AMENDMENT

April 19, 1999

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

Re: **ANDA 75-588 Ibuprofen Cold & Sinus**
(Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP)

Dear Sir:

Reference is made to a letter from Robert L. West dated March 9, 1999 listing our notification requirements after filing a Paragraph IV patent certification (21 CFR 314.94(a)(12)(i)(A)(4)).

Please amend our application, in accordance with 21 CFR 314.96(a)(1) as follows:

1. In accordance with 21 CFR 314.95(b), please find on page 3 a certification with regards to the notice provided to each person identified under 314.95(a) and that the notices met the content requirements under 314.95(c). A copy of the cover letters can be found on pages 4 - 6.

2. In accordance with 21 CFR 314.95(e), please find on pages 7 - 10 copies of the return receipts acknowledging the receipt by each person provided the notice.

If you have any questions or desire any additional information, please contact me.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

RECEIVED
APR 21 1999
GENERIC DRUGS

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

PFI *Pharmaceutical Formulations, Inc.*

MINOR LABELING AMENDMENT

May 21, 1999

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

NDA ORIG AMENDMENT
N/AF

Re: **ANDA 75-588 Ibuprofen Cold & Sinus**
(Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP)

Dear Sir:

On March 17, 1999, a final rule standardizing the labeling for OTC drug products was published. In accordance with this rule, please amend our application, in accordance with 21 CFR 314.96(a)(1), as follows:

1. On pages 3 - 24, please find revised labeling for the unit dose cartons and bulk labels in accordance with 21 CFR 201.66 [format and content requirements for over-the-counter (OTC) drug product labeling], replacing pages 23 - 44 of the original submission dated February 19, 1999. We have been unable to locate labeling, revised in accordance with 21 CFR 201.66 for the reference listed drug (Advil Cold & Sinus).

2. Please delete pages 51 - 55 (carton insert labeling) of the original submission dated February 19, 1999. All information required on the insert is listed on the revised unit dose cartons and we therefore believe the insert to be repetitive and unnecessary. The insert included in the reference listed drug (Advil Cold & Sinus) packaging was originally included as the product was bottled and the bottle label did not contain all of the required warnings.

If you have any questions or desire any additional information, please contact me.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
MAY 25 1999
OGD

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

PFI Pharmaceutical Formulations, Inc.

LABELING AMENDMENT

March 17, 2000

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

RE: **Labeling Amendment**
ANDA 75-588 Ibuprofen/Pseudoephedrine HCl Tablets USP 200 mg/30 mg

Gentlemen:

Pursuant to 21 CFR 314.96(a)(1), please amend our above abbreviated new drug application for Ibuprofen/Pseudoephedrine HCl Tablets USP 200 mg/30 mg. Since our major amendment of December 2, 1999 in which revised labeling was submitted, the reference listed drug labeling has been revised.

Proposed Labeling for the unit dose cartons is in accordance with the most recently approved labeling for the reference listed drug. The reference listed drug (Advil® Cold & Sinus) utilizes a new format.

Carton insert labeling has been removed from this amendment due to the fact that the reference listed drug does not use an insert. All information required on the insert is listed on the proposed unit dose cartons. Blister Pack Backing artwork has been included in this amendment.

In support of this Labeling Amendment, we are submitting the following information:

1) Reference Listed Drug Labeling

2) PFI's Proposed Labeling

3) Side by Side Annotated Comparison of Reference Listed Drug Labeling with PFI's Proposed Labeling

If you have any questions or desire any additional information, please feel free to contact me.

CENTER FOR DRUG EVALUATION AND RESEARCH
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MAR 20 2000
OGD

Sincerely,

Brian W. Barbee

Brian W. Barbee
V.P. Scientific Affairs

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

1 Copy

PFI *Pharmaceutical Formulations, Inc.*

NDA DRG AMENDMENT

MAJOR AMENDMENT

December 2, 1999

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

RE: **ANDA 75-588 Ibuprofen/Pseudoephedrine HCl Tablets USP 200 mg/30 mg**

Gentlemen:

Reference is made to Joseph Buccine's facsimile of October 12, 1999 containing letters from Rashmikant M. Patel, Ph.D., Dale P. Conner, Pharm.D., and Robert L. West, M.S., R.Ph., listing chemistry, bioequivalence and labeling comments to the above abbreviated new drug application dated February 19, 1999.

Pursuant to 21CFR314.101(b)(3), please amend our application to correct these deficiencies.

The deficiencies are summarized on the following pages and are followed by our response. We trust that we have satisfactorily answered all deficiencies.

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 Office.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
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OGD

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

PFI Pharmaceutical Formulations, Inc.

PATENT AMENDMENT

May 28, 1999

NEW CORRESP
NC

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

Re: **ANDA 75-588 Ibuprofen Cold & Sinus**
(Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP)

Dear Sir:

Reference is made to a letter from Robert L. West dated March 9, 1999 listing our notification requirements after filing a Paragraph IV patent certification (21 CFR 314.94(a)(12)(i)(A)(4)).

Please amend our application, in accordance with 21 CFR 314.96(a)(1) as follows:

In accordance with 21 CFR 314.95(f), please find on page 3 a certification that the 45-day period during which the persons identified under 314.95(a) could file litigation against Pharmaceutical Formulations, Inc. has expired and that no legal action was taken by such individuals during the 45-day period.

If you have any questions or desire any additional information, please contact me.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

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REC'D
JUN 0 1 1999
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460 Plainfield Avenue, Edison, NJ 08818 Tel: 732-985-7100 Fax: 732-819-3330

Paragraph IV Patent Certification
Documentation of Litigation/Settlement Outcome

On February 23, 1999, Pharmaceutical Formulations, Inc. filed ANDA 75-588 containing a Paragraph IV patent certification (21 CFR 314.94(a)(12)(i)(A)(4)) for Ibuprofen and Pseudoephedrine Hydrochloride Tablets USP, 200 mg/30 mg.

On March 26, 1999 and April 7, 1999, Pharmaceutical Formulations, Inc. sent, by certified mail with return receipt, a notice citing 505(j)(2)(B)(ii) of the FD&C Act and including the information described in 21 CFR 314.95(c) to each of the following:

1. Each owner of the patent or the representative designated by the owner to receive the notice.

2. The holder of the approved application under section 505(b) of the Act for the listed drug claimed by the patent and for which Pharmaceutical Formulations, Inc. is seeking approval.

The last of these notices was received by the recipient on April 12, 1999, and the above information was submitted on April 19, 1999 as a patent amendment to ANDA 75-588.

Pharmaceutical Formulations, Inc. hereby certifies, in accordance with 21 CFR 314.95(f), that the 45-day period for the last of the notices expired on May 27, 1999, and no legal action was brought by any of the individuals listed above during the 45-day period.

Brian W. Barbee
Brian W. Barbee
V. P. Scientific Affairs

5/28/99
Date

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

PFI *Pharmaceutical Formulations, Inc.*

MINOR AMENDMENT

October 3, 2000

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

NDA ORIG AMENDMENT
N/Am

Re: **ANDA 75-588 Ibuprofen Cold & Sinus Relief Formula**
(Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP)

Gentlemen:

Reference is made to Elaine Hu's facsimile of August 28, 2000 containing comments from Rashmikant M. Patel, Ph.D., and Wm. Peter Rickman, listing chemistry and labeling deficiencies in the above abbreviated new drug application.

Pursuant to 21CFR314.120(a)(1), please amend our application to correct these deficiencies.

The deficiencies are listed on the following pages and are followed by our response. We trust that we have satisfactorily answered all deficiencies.

We certify, pursuant to 21CFR 314.96 (b), that a complete and accurate copy of this response has been provided to the FDA New Jersey District Office.

Sincerely,

Brian W. Barbee

Brian W. Barbee
Vice President, Scientific Affairs

460 Plainfield Avenue, Edison, NJ 08818 Tel: 732-985-7[illegible] Fax: 732-819-3330

10/4/00

PFI Pharmaceutical Formulations, Inc.

TELEPHONE AMENDMENT

March 12, 2001

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

ORIG AMENDMENT
N/AM

Re: **ANDA 75-588 Ibuprofen and Pseudoephedrine HCl Tablets USP 200 mg / 30 mg**

Gentlemen:

Reference is made to a telephone conversation of March 9, 2001 between myself and Elaine Hu, Dr. Schwartz, and Dr. Khan of the Office of Generic Drugs concerning our Finished Product Specifications for Ibuprofen and Pseudoephedrine HCl Tablets USP. Questions were raised concerning the inclusion of certain impurities in our finished product specifications found on pages 4-7 of our telephone amendment of March 2, 2001.

As was discussed, the product specifications listed both potential process impurities and degradation impurities. The finished product analytical method specifically analyzes for only the degradation impurities. If an unknown peak is found, we use standards of the known process impurities to effect a positive identification.

As agreed upon, the product specifications and stability protocols have been updated to only list impurities of the Ibuprofen and Pseudoephedrine HCl that are known to be degradation impurities. These degradation impurities are specifically analyzed for and quantitated by our analytical method. The process impurities are tested and controlled in the) Since these process impurities do not increase with time, there is no need to test for them in the finished product. This is in conformance with the December 1998 CDER draft guidance "ANDAs: Impurities in Drug Products" Section II.

On page 16 of this amendment is found the potential process impurities of Ibuprofen produced by Of the two ibuprofen impurities listed in our revised specifications, was found in our forced degradation study to also be a degradation impurity. The other was identified as a potential degradation impurity by another ibuprofen supplier not part of this application.

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

On pages 17 to 22 is found the potential process impurities and degradation impurities of Pseudoephedrine HCl produced by Of the three impurities listed in our revised specifications, our forced degradation study found the We did not find any

The finished product degradation study found on pages 23 to 33 did not find any of the other known process impurities of Ibuprofen or Pseudoephedrine HCl to also be potential degradation impurities with the exception of the

Pursuant to 21CFR314.120(a)(1), and as agreed in the aforementioned conversation, please amend our application to include the following:

- Finished Product Specifications for Ibuprofen/Pseudoephedrine HCl Tablets
- Stability Protocols for Ibuprofen/Pseudoephedrine HCl Tablets
- Ibuprofen Impurity Profile
- Pseudoephedrine Hydrochloride Impurity Profiles
  - Stress Testing and Degradation Products
  - Potential Impurities: Process Contaminations
- Ibuprofen/Pseudoephedrine HCl Tablets Degradation Study
- Analytical Method for the Analysis of in Ibuprofen/Pseudoephedrine HCl Tablets

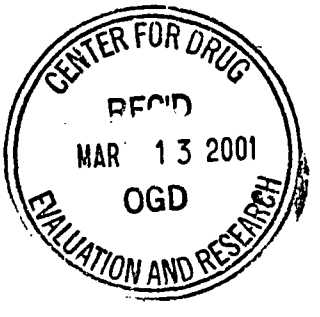
We certify, pursuant to 21CFR 314.96 (b), that a complete and accurate copy of this response has been provided to the FDA New Jersey District Office.

Please feel free to call me at (732)-819-3326 if you have any questions concerning this amendment.

Sincerely,

Brian W. Barbee

Brian W. Barbee
Vice President, Scientific Affairs



PFI *Pharmaceutical Formulations, Inc.*

TELEPHONE AMENDMENT

March 8, 2001

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

ORIG AMENDMENT
N/AM

Re: **ANDA 75-588 Ibuprofen and Pseudoephedrine HCl Tablets USP 200 mg / 30 mg**

Gentlemen:

Reference is made to a telephone conversation of March 6, 2001 between myself and Elaine Hu of the Office of Generic Drugs concerning our Analytical Method for Ibuprofen and Pseudoephedrine HCl Tablets USP. Questions were raised concerning the detection of the impurities listed in our finished product specifications found on pages 4-7 of our telephone amendment of March 2, 2001.

Our current finished product specifications list all known impurities of the Ibuprofen and Pseudoephedrine HCl active pharmaceutical ingredients( ) used in our product. This includes both process impurities and potential degradation impurities. The specifications originally submitted in this application listed only the potential degradation impurities since these are the substances specifically analyzed for by our analytical method. The process impurities are tested and controlled in the . Since these process impurities do not increase with time, there is no need to test for them in the finished product. This is in conformance with the December 1998 CDER draft guidance "ANDAs: Impurities in Drug Products" Section II.

In a minor deficiency letter dated August 28, 2000, deficiency #7, we were requested to "please provide the names of any other identified Ibuprofen impurities and Pseudoephedrine HCl impurities for the finished product specification.' We complied with this request in our minor amendment of October 3, 2000.

Though our finished product method does not specifically test for the process impurities of the , it is capable of detecting and identifying these compounds (exception

CENTER FOR DRUG EVALUATION AND RESEARCH
MAR 09 2001
OGD

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

3-9-01

Therefore, any unidentified peaks found during finished product testing can be compared with a process impurity reference standard to confirm its identity.

Pursuant to 21CFR314.120(a)(1), and as agreed in the aforementioned conversation, please amend our application to include the following:

- Analytical Method for Ibuprofen/Pseudoephedrine HCl Tablets or Caplets USP Product Codes 22450F and 22453F
- Analytical Method Validation for Ibuprofen/Pseudoephedrine Tablets or Caplets Product Codes 22450F and 22453F – Additional Specificity Studies
- Measurement of Impurities in Finished Product of Ibuprofen/Pseudoephedrine HCl Tablets or Caplets Product Codes 22450F and 22453F
- Addendum to the Analytical Method Validation Report for the Assay and Chromatographic Purity of Ibuprofen Raw Material Code # J09010
- Analytical Method Validation for the Assay and Chromatographic Purity of Ibuprofen Raw Material Code # J09010 – Additional Specificity Studies

We certify, pursuant to 21CFR 314.96 (b), that a complete and accurate copy of this response has been provided to the FDA New Jersey District Office.

Please feel free to call me at (732)-819-3326 if you have any questions concerning this application.

Sincerely,

Brian W. Barbee

Brian W. Barbee
Vice President, Scientific Affairs

PFI *Pharmaceutical Formulations, Inc.*

TELEPHONE AMENDMENT

March 2, 2001

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

NDA ORIG AMENDMENT
N/Am

Re: **ANDA 75-588 Ibuprofen and Pseudoephedrine HCl Tablets USP 200 mg / 30 mg**

Gentlemen:

Reference is made to a telephone conversation of March 2, 2001 between myself and Elaine Hu and Dr. Paul Schwartz of the Office of Generic Drugs concerning the limit of ( ) in our finished product specifications and stability protocols. The specifications and protocols were submitted on January 17, 2001 in our Minor Amendment to ANDA 75-588 for Ibuprofen and Pseudoephedrine HCl Tablets USP, 200 mg / 30 mg.

Pursuant to 21CFR314.120(a)(1), and as agreed in the aforementioned conversation, please amend our application to revise the limit of ( ) from ( )%. The revised finished product specifications can be found on pages 4-7, and the stability protocols can be found on pages 8-17 of this amendment.

We certify, pursuant to 21CFR 314.96 (b), that a complete and accurate copy of this response has been provided to the FDA New Jersey District Office.

Please feel free to call me if you have any questions concerning this application at (732)-819-3326.

Sincerely,

Brian W. Barbee

Brian W. Barbee
Vice President, Scientific Affairs

CENTER FOR DRUG EVALUATION AND RESEARCH
MAR 05 2001
OGD

460 Plainfield Avenue, Edison, NJ 08818 Tel: 732-985-7100 Fax: 732-819-3326

PFI *Pharmaceutical Formulations, Inc.*

MINOR AMENDMENT

January 17, 2001

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

ORIG AMENDMENT
N/AM

Re: **ANDA 75-588 Ibuprofen and Pseudoephedrine HCl Tablets USP 200mg / 30mg**

Gentlemen:

Reference is made to Elaine Hu's facsimile of December 27, 2000 containing comments from Rashmikant M. Patel, Ph.D., and Wm. Peter Rickman, listing chemistry and labeling deficiencies in the above abbreviated new drug application.

Pursuant to 21CFR314.120(a)(1), please amend our application to correct these deficiencies.

The deficiencies are listed on the following pages and are followed by our response. We trust that we have satisfactorily answered all deficiencies.

We certify, pursuant to 21CFR 314.96 (b), that a complete and accurate copy of this response has been provided to the FDA New Jersey District Office.

Sincerely,

Brian W. Barbee

Brian W. Barbee
Vice President, Scientific Affairs

CENTER FOR DRUG
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JAN 18 2001
OGD
EVALUATION AND RESEARCH

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

NW 1-23-01

PFI Pharmaceutical Formulations, Inc.

NC to Am
ORIG AMENDMENT

January 22, 2001

Elaine Hu
Project Manager
Office of Generic Drugs
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
(P) – 301-827-5754, (F) – 301-594-0180

Re: **ANDA 75-588 Ibuprofen and Pseudoephedrine HCl Tablets USP 200mg / 30mg**

Dear Elaine:

Reference is made to our Minor Amendment dated January 17, 2001 containing our responses to deficiencies in the above abbreviated new drug application.

Upon providing responses to the comments listed in the December 27, 2000 facsimile, we seem to have inadvertently included the Ibuprofen Raw Material Specification from another ANDA. Please update our amendment to this application using the Ibuprofen Raw Material Specification included in this packet, to replace pages 5-6 of the Minor Amendment dated January 17, 2001. We apologize for the inconvenience.

Thank you for your assistance with this matter.

Sincerely,

Scott D. Tomsky
Regulatory Affairs Supervisor

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

PFI *Pharmaceutical Formulations, Inc.*

TELEPHONE AMENDMENT

March 8, 2002

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

NEW CORRESP
NC to FAX

Re: ANDA 75-588 Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP, 200mg/30mg

Gentlemen:

Reference is made to a telephone conversation between myself and Sara Ho, Gil King, and James Fan concerning our minor amendment of January 25, 2002 to the above application.

A question was raised concerning the Ibuprofen specification on page 6 of the amendment being different from that tentatively approved in our application.

Attached is the revised Ibuprofen specification for ANDA 75-588. The specification included in the amendment is for another of our approved ANDA'S. Please accept our apologies for the inconvenience which this has caused.

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

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

RECEIVED
MAR 1 1 2002
OGD / CDER

460 Plainfield Avenue, P.O. Box 1904, Edison, NJ 08818-1904 Tel: 732-985-7100 Fax: 732-819-3330

PFI *Pharmaceutical Formulations, Inc.*

MINOR AMENDMENT

January 25, 2002

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

N/Am

ORIG AMENDMENT

Re: ANDA 75-588 Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP, 200mg/30mg

Dear Sir:

Reference is made to our April 17, 2001 Tentative Approval letter for the above abbreviated new drug application. This letter stated that 60 to 90 days prior to the expiration of exclusivity, we should submit a minor amendment to reactivate our application.

We understand that the exclusivity for ANDA 74-567 held by Ohm Labs will expire in April 2002. Therefore, we are submitting this amendment to update our application.

On November 15, 2001 we submitted an amendment to revise our labeling to 'Drug Facts' format in accordance with 21CFR314.96(a)(1). In this amendment we are submitting revised raw material specifications changing the reference from USP24/NF19 to USP25/NF20. There are no actual changes to the tests or specs.

There have been no other revisions to this application since the date of tentative approval.

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

CENTER FOR DRUG EVALUATION AND RESEARCH
JAN 28 2002

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

1/28/02

460 Plainfield Avenue, P.O. Box 1904, Edison, NJ 08818-1904 Tel: 732-985-7100 Fax: 732-819-3330

PFI *Pharmaceutical Formulations, Inc.*

MINOR LABELING AMENDMENT

November 15, 2001

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

AF

Re: ANDA 75-588 Ibuprofen/Pseudoephedrine Hydrochloride Tablets USP, 200mg/30mg

Dear Sir:

On March 17, 1999 a final rule standardizing the labeling for OTC drug products was published. On May 23, 2001 the FDA Division of Over-the-Counter Drug Products approved drug facts format labeling for NDA 19-771/S-20 Advil Cold and Sinus, the reference listed drug for our application.

In accordance with 21 CFR314.96(a)(1) please amend our tentatively approved application to include our product labeling in Drug Facts format. Included in this amendment are 12 pieces each of our proposed final printed labeling for the tablets and caplets cartons. Also included is a side-by-side comparison of our proposed Drug Facts labeling with our currently "approved" labeling.

If you have any questions or desire any additional information, please contact me.

Sincerely,

Brian W. Barbee

Brian W. Barbee
V. P. Scientific Affairs

460 Plainfield Avenue, P.O. Box 1904, Edison, NJ 08818-1904 Tel: 732-985-7100 Fax: 732-819-3330