NDA 19-833

S-011

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 19-833/S-011

JAN 26 1998

Whitehall-Robins Healthcare
Attention: Sharon Heddish
Vice President, Regulatory Affairs Worldwide
5 Giralda Farms
Madison, NJ 07940-0871

Dear Ms. Heddish:

Please refer to your supplemental new drug application dated May 22, 1996, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Advil (ibuprofen oral suspension) Suspension, 100 mg/5 mL. We also refer to our approvable letter of December 15, 1996.

We acknowledge receipt of your submissions dated October 8, 1997 and January 21, 1998.

The supplemental application provides for revised labeling that deletes the overlapping indications between the OTC product and the Rx product.

We have completed the review of this supplemental application including the submitted draft labeling and have concluded that adequate information has been presented to demonstrate that the drug product is safe and effective for use as recommended in the draft labeling submitted on January 22, 1998. Accordingly, the supplemental application is approved effective on the date of this letter.

The final printed labeling (FPL) must be identical to the enclosed marked-up labeling submitted on January 22, 1998. Marketing the product with FPL that is not identical to this draft labeling may render the product misbranded and an unapproved new drug.

Please submit 20 copies of the FPL as soon as it is available, in no case more than 30 days after it is printed. Please individually mount ten of the copies on heavy-weight paper or similar material. For administrative purposes, this submission should be designated "FINAL PRINTED LABELING" for approved supplemental NDA 19-833/S-011. Approval of this submission by FDA is not required before the labeling is used.

Please submit labeling consistent with the NSAID class labeling template of December 20, 1996.

Should additional information relating to safety and effectiveness of the drug become available, revision of that labeling may be required.

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

If you have any questions, please contact Sandra N. Cook, Project Manager, at (301) 827-2090.

Sincerely,

J E H 1-26-98

John E. Hyde, Ph.D., M.D.
Deputy Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Enclosure: Labeling

cc:

NDA 19-833/S-011
HFD-550/Div. Files
HFD-550/CSO/S.Cook
HFD-550/Hyde
HFD-40/DDMAC
HFD-92/DDM-DIAB
HFD-613/OGD
HFD-735/DPE
DISTRICT OFFICE

Drafted by: Cook/January 20, 1998/19833ap.s11
Initialed by:
final:

APPROVAL

FINAL PRINTED LABELING HAS NOT BEEN SUBMITTED TO THE FDA

DRAFT LABELING IS **NO LONGER** BEING SUPPLIED SO AS TO ENSURE ONLY CORRECT AND CURRENT INFORMATION IS DISSEMINATED TO THE PUBLIC.

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

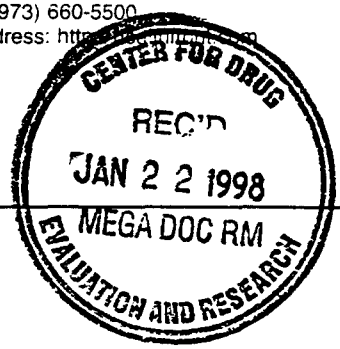
16 pages

WHITEHALL ROBINS

Whitehall-Robins
Five Giralda Farms
Madison, NJ 07940-0871
Telephone (973) 660-5500
Website address: http

AMENDMENT

ORIGINAL



January 21, 1998

NDA 19-833
Advil® (ibuprofen oral suspension) Suspension, 100mg/5mL

AMENDMENT TO SUPPLEMENT 011 - RESPONSE TO FDA REQUEST FOR REVISED LABELING

Michael Weintraub. MD
Acting Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmic Drug Products (HFD-550)
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN.: Document Control Room
9201 Corporate Boulevard
Rockville, MD 20850

Dear Dr. Weintraub:

Reference is made to NDA 19-833 for Advil (ibuprofen oral suspension) Suspension, 100mg/5mL and our supplemental application (S-011) to provide for revised labeling that deleted the overlapping indications between the OTC product and the prescription product.

Reference is also made to FDA's letter of December 15, 1996 informing us of the approvable status of S-011. Following receipt of the approvable letter, FDA's letter of December 20. 1996 was received requesting that holders of approved new drug applications for NSAID products update the labeling of these products in accordance with class labeling. Accordingly, the labeling submitted to respond to FDA's approvable letter of December 15, 1996 complied with the class labeling format (submitted on October 8. 1997 as an amendment to S-011).

NAI (approval letter sent 1-25-98)
J Hyde 2-1-98

Whitehall-Robins Healthcare
Amendment To Supplement 011 - Response To FDA Request For Revised Labeling

NDA 19-833
Advil® (ibuprofen oral suspension) Suspension, 100mg/5mL

On January 20, 1998, Ms. Sandra Cook of your Division called to indicate that labeling should be submitted that is identical to the version included with the December 15, 1996 approvable letter in order to obtain immediate approval. As requested, attached are four copies of the labeling as was provided with the approvable letter with the following exception:

> The section **Precautions** - *Pre-existing Asthma* (page 9) was not included in FDA's version, although the section was referred to under the section, **Anaphylactoid Reactions** (page 6). Therefore, the attached labeling was prepared with the section **Precautions** - *Pre-existing Asthma* included.

Should you have any comments regarding this submission, please contact the undersigned at (973) 660-5753 or Joanne Robinett at (973) 660-6167. We look forward to obtaining approval of S-011 as soon as possible since this is impacting approval of NDA 20-812 for the Children's Advil Drops.

Sincerely,

WHITEHALL-ROBINS HEALTHCARE

Joanne Robinett for

Sharon Heddish
Vice President
Regulatory Affairs Worldwide

NAI

PAW. 12-31-96

AMERICAN HOME PRODUCTS CORPORATION

FIVE GIRALDA FARMS, MADISON, NEW JERSEY 07940. (201) 660-5000, FAX: (201) 660-7160 (5988), TELEX: 125751

December 18, 1996

SUPPL MED

NDA No. 19-833/S-011

Wiley A. Chambers, M.D., Acting Director
Division of Anti-Inflammatory, Analgesic,
and Ophthalmic Drug Products (HFD-550)
Center for Drug Evaluation and Research
Document Control Room
Food and Drug Administration
5600 Fishers Lane
Rockville, MD 20857-1706

Dear Dr. Chambers:

Reference is made to American Home Products Corporation's approved New Drug Application No. 19-833 for Advil® (ibuprofen oral suspension) Suspension, and to the December 15, 1996 "approvable" letter from the Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products (DAAODP) in regard to supplemental application 011. As noted in the approvable letter, supplemental application 011, submitted May 22, 1996,

The purpose of this letter is to advise you that as per the provisions of 21 CFR 314.110 (a) (1), we intend to exercise our option to amend Advil Suspension supplemental application 011.

Sincerely,

WYETH-AYERST LABORATORIES

James J. O'Shaughnessy
Associate Director
U.S. Regulatory Affairs

1148.adv

DEC 2 - 1996
HFD

Sharon C. Heddish
Senior Director, Regulatory Affairs

Whitehall-Robins
Five Giralda Farms
Madison, NJ 07940-0871
Telephone (973) 660-5753
Fax #: (973) 660-7187
E-mail address: heddiss@ahp.com

WHITEHALL ROBINS

NDA SUPPL AMENDMENT
ORIGINAL

October 8, 1997

NDA 19-833
Children's Advil Suspension®
(Ibuprofen 100mg/5mL)

AMENDMENT TO SUPPLEMENT 011 - RESPONSE TO APPROVABLE LETTER
EXPEDITED REVIEW REQUESTED

Michael Weintraub, M.D., Acting Director
Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products **(HFD-550)**
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN.: Document Control Room N115
9201 Corporate Blvd.
Rockville, MD 20850

Dear Dr. Weintraub:

Reference is made to NDA 19-833 for Advil (ibuprofen oral suspension) Suspension, 100mg/5mL, sponsored by American Home Products Corporation ("AHPC")

Reference is also made to FDA's letter of December 15, 1996 informing us of the approvable status for S-011. The letter stated that approval would be granted upon receipt of Final Printed Labeling that was identical in content to the labeling included with the approvable letter. Following receipt of the approvable letter, FDA's letter of December 20, 1996, was received requesting that holders of all approved new drug applications for NSAID products update the labeling of these products to comply with the template for NSAID class labeling.

Accordingly, draft labeling is being submitted herewith in response to FDA's request for submission of labeling for the product and to comply with FDA's request to update labeling to comply with the class labeling. While we have complied with this request in order to expedite Agency review and to obtain the approval of this supplement, it is done with reservation. We feel the warnings presented in the class labeling template cover a very broad spectrum of NSAIDs, not all of which have the same safety profile as that of ibuprofen, especially when used per OTC dosing recommendations.

Attached to this letter is a Table of Contents to assist the reviewers in locating the labeling information provided in this amendment. Included in Attachment 1 is the draft package insert (diskette included) for Advil Suspension prepared to parallel the NSAID class labeling template with appropriate Advil Suspension-specific information referenced. Attachment II contains a mock-up copy of the labeling included with the S-011 approvable letter with revisions delineated to comply with the class labeling template. The reference listing for the Advil-specific information is located in Attachment III. For the ease of review, the December 15, 1996 approvable letter has been included in Attachment IV.

We herewith formally request that FDA expedite the review of this amendment. We look forward to a prompt review and approval of S-011. If you have any questions regarding this information, please contact the undersigned at (973) 660-5753 or Joanne Robinett at (973) 660-6167.

Sincerely,

WHITEHALL-ROBINS HEALTHCARE

Sharon Heddish

Sharon C. Heddish
Sr. Director, Regulatory Affairs

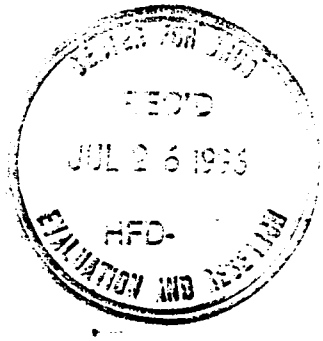
ORIGINAL

WHITEHALL ROBINS

Whitehall-Robins
Five Giralda Farms
Madison, NJ 07940-0871
Telephone (201) 660-5500

S-003,006,00 1-10+all
SUPPL NEW CORRESP

July 25, 1996



NDA 19-833
Advil® (ibuprofen oral suspension) Suspension, 100mg/5mL

GENERAL CORRESPONDENCE

Wiley A. Chambers, MD, Acting Director
Division of Anti-Inflammatory, Analgesic, and Ophthalmic Drug Products (HFD-550)
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN.: Document Control Room
9201 Corporate Blvd.
Rockville, MD 20850

Dear Dr. Chambers:

Reference is made to NDA 19-833 for Advil (ibuprofen oral suspension) Suspension, 100mg/5mL, sponsored by American Home Products Corporation ("AHPC")

and May 22, 1996 (S-011).

The above referenced supplemental applications were submitted through Whitehall-Robins Healthcare, the OTC Division of American Home Products, in order to better coordinate all elements necessary for approval of the Children's Advil Suspension (Rx to OTC) NDA 20-589. With the July 27, 1996 NDA approval of the Children's Advil Suspension (OTC) product, the responsibilities associated with the above referenced pending supplemental applications will now be transferred to Wyeth-Ayerst Laboratories.

Dr. Vern DeVries, Wyeth-Ayerst Laboratories' Assistant Vice President, U.S. Regulatory Affairs, will be the responsible official for NDA 19-833 and will replace Mr. David Olivier, Senior Vice President (AHPC) as the responsible official for the NDA 19-833

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☑ N.A.I. ☐ MEMO
CSO INITIALS: DR 7/29/96 DATE

Mr. James O'Shaughnessy (610-902-3761), Wyeth-Ayerst Laboratories' Associate Director, U.S. Regulatory Affairs, will remain as the primary contact for NDA 19-833 and will replace Ms. Elle Barbo and Ms. Sharon Heddish as the primary contact for the NDA 19-833

If you have any questions related to this letter, please call me at (201) 660-5753.

Sincerely,

AMERICAN HOME PRODUCTS CORPORATION

Sharon Heddish

Sharon Heddish
Director, Regulatory Affairs
Whitehall-Robins Healthcare

JUL 27 1996

Division Director's Review of NDA 19-833
Supplement 11

NDA #19-833

Submit date:	5/22/96
Received date:	5/23/96
Review completed:	7/27/96

Drug name: Advil Suspension
Generic name: ibuprofen suspension

Sponsor:
Whitehall-Robins
5 Giralda Farms
Madison, NJ 07940-0871
(201) 660-5493

Pharmacologic Category: Nonsteroidal Anti-inflammatory

Proposed Indication(s): Relief of the signs and symptoms of juvenile arthritis, rheumatoid arthritis, osteoarthritis and primary dysmenorrhea; reduction of fever and mild to moderate pain in adults and pediatric patients ages 6 months to 2 years of age.

Dosage Form(s) and Route(s) of Administration: Oral suspension, 100 mg/5 mL

Submitted:

Supplement 11: Revised labeling deleting the overlapping indications between the OTC product and the Rx product.

Reviewer's Comments:

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

17 pages

Conclusions/Recommendations:

It is recommended that:

1. Supplement 11 of NDA 19-833 be approved with the labeling outlined in this review.

2.

3.

Wiley A. Chambers, M.D.

cc: Orig NDA 19-833
HFD-550
HFD-340
HFD-550/CSO/Raigrodski
HFD-550/CHEM/Yaciw
HFD-550/PHARM/Chen
HFD-550/MO/Hyde
HFD-880/Bashaw
HFD-550/ActgDivDir/Chambers

LABELING REVIEW OF NDA 19-833/S-011

JAN 26 1998

Submission Date: May 22, 1996
October 8, 1997

Action: Approvable letter issued December 15, 1996

Review Date: January 21, 1998

Applicant: Whitehall-Robins Healthcare

Applicant's Representative: Sharon C. Heddish
Sr. Director, Regulatory Affairs

Drug: Children's Advil (ibuprofen suspension) Suspension, 100 mg/5 mL

Pharmacologic Category: Pain reliever/Fever reducer

Submitted: The supplemental application provides for revised labeling that deletes the overlapping indications between the OTC product and the Rx product.

Reviewer's Comment: The requested revisions were incorporated in S-011, submitted on January 22, 1998. Whitehall-Robins added a paragraph under "Precautions", *Pre-existing Asthma*. Convey minor editorial changes to the sponsor.

Recommendation: The labeling is acceptable with minor editorial changes and an approval letter should be issued to the company with marked up labeling.

Sandra N. Cook

1-26-98

John E. Hyde, Ph.D., M.D.

Division Director's Review of NDA 19-833
Supplement 11

DEC - 6 1996

NDA #19-833

Submit date:	5/22/96
Received date:	5/23/96
Review completed:	7/27/96
Revised date:	11/11/96

Drug name: Advil Suspension
Generic name: ibuprofen suspension

Sponsor: Whitehall-Robins
5 Giralda Farms
Madison, NJ 07940-0871
(201) 660-5493

Pharmacologic Category: Nonsteroidal Anti-inflammatory

Proposed Indication(s): Relief of the signs and symptoms of juvenile arthritis, rheumatoid arthritis, osteoarthritis and primary dysmenorrhea; reduction of fever and mild to moderate pain in adults and pediatric patients ages 6 months to 2 years of age.

Dosage Form(s) and Route(s) of Administration: Oral suspension, 100 mg/5 mL

Submitted:

Supplement 11: Revised labeling deleting the overlapping indications between the OTC product and the Rx product.

Reviewer's Comments:

THIS SECTION WAS DETERMINED **NOT** TO BE RELEASABLE

19 pages

Conclusions/Recommendations:

It is recommended that:

1. Supplement 11 of NDA 19-833 be approved with the labeling outlined in this review.

2.

3.

Wiley A. Chambers, M.D.

cc: Orig NDA 19-833
HFD-550
HFD-340
HFD-550/CSO/Raigrodski
HFD-550/CHEM/Yaciw
HFD-550/PHARM/Chen
HFD-550/MO/Hyde
HFD-880/Bashaw
HFD-550/ActgDivDir/Chambers

ORIGINAL

NDA NO. [illegible] REF. NO. [illegible]
NDA SUPPL NO. [illegible]

AMERICAN HOME PRODUCTS CORPORATION

FIVE GIRALDA FARMS, MADISON, NEW JERSEY 07940 (201) 660-5000

May 22, 1996

RECD
MAY 23 1996
HFD-

NDA 19-833
Advil® (ibuprofen) Suspension, 100mg/5mL

SUPPLEMENT: Proposed Labeling Change

Wiley A. Chambers, MD, Acting Director
Division of Analgesic, Anti-Inflammatory, and Ophthalmic Drug Products (HFD-550)
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN.: Document Control Room
9201 Corporate Blvd.
Rockville, MD 20850

REVIEWS COMPLETED
CSO ACTION:
☐ LETTER ☐ FAX ☐ MEMO
CSO INITIALS DATE

Dear Dr. Chambers:

Reference is made to NDA 19-833, Advil® (ibuprofen) Suspension, 100mg/5mL, sponsored by American Home Products Corporation (AHPC) and to the final printed labeling (FPL) submitted on May 15, 1996 by the Whitehall-Robins Healthcare division. The FPL was submitted in response to the April 18, 1996 approvable letter from the Division for the addition of an analgesic indication for the product.

Further reference is made to NDA 20-589 for Children's Advil® OTC (ibuprofen oral suspension), 100mg/5mL, and to the April 25, 1996 approvable letter which requested a supplement to NDA 19-833 to delete any overlap in indications of use between the prescription and OTC product labeling (see Attachment 1, item 4 in letter).

Therefore, at this time, enclosed in Attachment 2 is the proposed package insert (4 copies) for the prescription NDA 19-833, Advil® Suspension. For your convenience, a copy of the FPL as submitted to this NDA on May 15, 1996 is also enclosed in Attachment 3 and is highlighted to indicate the changes made to the proposed package insert.

As discussed with you on May 21, 1996, the language in the proposed package insert has been modified to reflect use of the prescription product for reduction of fever and relief of pain in the pediatric patients aged 6 months up to 2 years old. Therefore, the labeling between the prescription and OTC products are no longer overlapping for indications of use in the pediatric population.

We thank you for your clarification regarding this labeling supplement and look forward to your expeditious review. If you have any questions, please call Ms. Elle Barbo at (201) 660-5751 or Mr. Rich Cuprys at (201) 660-5913.

Sincerely,

AMERICAN HOME PRODUCTS CORPORATION

Eleanor F. Barbo
Director, Regulatory Affairs
Whitehall-Robins Healthcare

Enclosure

EFB:mb

ORIGINAL

AMERICAN HOME PRODUCTS CORPORATION

FIVE GIRALDA FARMS, MADISON, NEW JERSEY 07940 (201) 660-5000

June 3, 1996

SUPPL NEW CORRESP

NDA 19-833
Advil® (ibuprofen) Suspension, 100mg/5mL

AMENDMENT TO SUPPLEMENT NO. 011

Wiley A. Chambers, MD, Acting Director
Division of Analgesic, Anti-Inflammatory, and
Ophthalmic Drug Products (HFD-550)
Center for Drug Evaluation and Research
Food and Drug Administration
ATTN.: Document Control Room
9201 Corporate Blvd.
Rockville, MD 20850

Dear Dr. Chambers:

Reference is made to NDA 19-833 for Advil® (ibuprofen) Suspension, 100mg/5mL, sponsored by American Home Products Corporation (AHPC) and to Supplemental Application No. 011 dated May 22, 1996. Further reference is made to NDA 20-589 for Children's Advil® OTC (ibuprofen oral suspension), 100mg/5mL, sponsored by Whitehall-Robins Healthcare, a division of AHPC.

The April 25, 1996 approvable letter for NDA 20-589 requested a supplement to NDA 19-833 to delete any overlap in indications of use between the prescription and OTC product labeling. Accordingly, Supplement No. 011 to NDA 19-833 was submitted with proposed labeling (package insert) in compliance with this request.

On May 30, 1996, a request was made by Ms. Susan Raigrodski to provide the proposed labeling on diskette. Consequently, enclosed are two (2) diskettes containing the proposed package insert in Word 6.0 as Archival and Review copies.

REVIEWS COMPLETED
CSO ACTION
LETTER ✓ MAIL MEMO
CSO INITIALS R DATE 6/10/96

CENTER FOR DRUG
REC'D
JUN 05 1996
HFD
EVALUATION

We look forward to your expeditious review of this supplement. If you have any questions, please call Ms. Elle Barbo at (201) 660-5751.

Sincerely,

AMERICAN HOME PRODUCTS CORPORATION

Eleanor F. Barbo
Director, Regulatory Affairs
Whitehall-Robins Healthcare

Enclosure

NDA 19-833/S-011

DEC 15 1996

American Home Products Corporation
Whitehall-Robins Healthcare
Attention: Rich Cuprys
Assistant Vice President
5 Giralda Farms
Madison, New Jersey 07940-0871

Dear Mr. Cuprys:

Please refer to your May 22, 1996, supplemental new drug application submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Advil® (ibuprofen oral suspension) Suspension, 100 mg/5mL. Your supplemental new drug application submission of May 22, 1996,

We also refer to our approvable letter of April 18, 1996.

We acknowledge receipt of your amendments and correspondence dated April 26, May 7, 15(2), and 22, June 3, July 16, 18, and 25, September 24, October 21 and 29, and November 14, 1996.

The supplemental application provides for revised labeling that deletes the overlapping indications between the OTC product and the Rx product.

We have completed the review of this supplemental application as amended, and it is approvable. Before the application may be approved, however, it will be necessary for you to submit final printed labeling (FPL) for the drug. The labeling should be identical in content to the enclosed draft labeling.

Please submit 20 copies of the printed labels and other labeling, ten of which are individuallly mounted on heavy-weight paper or similar material.

If additional information relating to the safety and effectiveness of the drug becomes available, revision of that labeling may be required.

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

Please submit one copy to this Division and two copies of both the promotional material and the package insert directly to:

Division of Drug Marketing, Advertising and Communications, HFD-40
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20857

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of the other options under 21 CFR 314.110. In the absence of such action, FDA may take action to withdraw the application.

The proposed changes may not be permitted until you have been notified in writing that this supplemental application is approved.

Should you have any questions, please contact Sandra Cook at (301) 827-2090.

Sincerely,

WAC 12/5/96
Wiley A. Chambers, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic, and
Ophthalmic Drug Products, HFD-550
Office of Drug Evaluation V
Center for Drug Evaluation and Research

Attachment: Draft labeling

cc:

HFD-2/Lumpkin
HFD-550/Div. File
DISTRICT OFFICE
HFD-550/MO/Hyde
HFD-550/Biopharm/Bashaw
HFD-550/Chem/Yaciw
HFD-550/Chem TL/Patel
HFD-550/Pharm/Chen
HFD-550/CSO/Cook
HFD-550/SCSO/LoBianco
HFD-725/Stat/Leung
HFD-735/D Barash

drafted: SCook/12-12-96/19833s11.ae
final: Chambers/12-15-96

APPROVABLE