CENTER FOR DRUG EVALUATION AND RESEARCH

75-217

APPLICATION NUMBER:

CORRESPONDENCE

PERRIGO®

June 9, 1998
VIA FEDERAL EXPRESS

Office of Generic Drugs, OPS, CDER, FDA
Document Control Room, MPN II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Rashmikant M. Patel, Ph.D.
Director, Div. of Chemistry I

NDA ORIG AMENDMENT
AM

RE: Ibuprofen Oral Suspension USP, 40 mg/mL
ANDA 75-217
Minor Amendment

Dear Dr. Patel:

This letter is in response to the Agency's communication dated June 9, 1998. In that communication, the Agency commented on the Abbreviated New Drug Application for ANDA 75-217, Ibuprofen Oral Suspension USP, 40 mg/mL.

A. Deficiencies

[redacted]

to the approval of this ANDA.

Response:

[redacted]

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

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.

Response:

The L. Perrigo Company acknowledges that 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. The L. Perrigo Company notes that the Agency has requested an evaluation from the Division of Manufacturing and Product Quality. The L. Perrigo Company received the attached letter from the Detroit, Michigan District FDA office on June 12, 1998 recommending approval of ANDA 75-217.

As required by 21 CFR 314.94(d)(5), the L. Perrigo Company certifies that a "field copy," which is a true copy of this Minor Amendment submitted to the FDA headquarters, has been submitted to the Detroit District Field Office.

If you have any questions, please feel free to contact me by telephone at (616) 673-7604, by FAX at 616-673-7655 or by E-mail at glutke@perrigo.com.

Respectfully submitted,

Virginia G. Lutke

Virginia G. Lutke
Regulatory Affairs
enc.
xc: B. Schuster, G. Boerner

RECEIVED
JUN 23 1998
GENERIC DRUGS

117 Water Street
Allegan, Michigan 49010
(616) 673-8451

JUN 9 1998

38. Chemistry Comments to be Provided to the Applicant

ANDA: 75-217 APPLICANT: L. Perrigo Company

DRUG PRODUCT: Ibuprofen Oral Suspension USP, 40 mg/mL

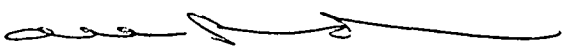
The deficiencies presented below represent MINOR deficiencies.

A. Deficiencies:

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

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.

Sincerely yours,



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

PERRIGO®

NEW C...
NC

April 15, 1998

Office of Generic Drugs
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Rockville, MD 20855-2773
Attention: Rashmikant M. Patel, Ph.D

FACSIMILE AMENDMENT

RE: Ibuprofen Oral Drops, 40 mg/mL
ANDA # 75-217
Facsimile Amendment

Dear Dr. Patel:

This Amendment is being filed in response to the Agency's facsimile communication dated 03/16/98 concerning the L. Perrigo Company's Ibuprofen Oral Drops ANDA 75-217.

Please see the attached responses to the Agency's comments. If you have any questions or need any additional information, please feel free to contact me by telephone at (616) 673-7604, by FAX at 616-673-7655 or by E-mail at glutke@perrigo.com.

In accordance with 21 CFR 314.50 (revisions effective October 8, 1993), I certify that a field copy which is a true copy of this amendment has been provided to the Detroit District Field Office of the Federal Food & Drug Administration.

Respectfully submitted,

Virginia G. Lutke

Virginia G. Lutke
Regulatory Affairs

xc: B. Schuster
G. Boerner

117 Water Street
Allegan, Michigan 49010
(616) 673-8451

PERRIGO®

NEW CORRESP

NC

NAI 2/3/98

January 28, 1998

Douglas Sporn, Director
Office of Generic Drugs
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Rockville, MD 20855-2773

PATENT AMENDMENT

RE: Ibuprofen Oral Drops, 40 mg/mL
ANDA # 75-217

Dear Mr. Sporn:

This Amendment is being filed as a follow-up to the Amendment filed 01/09/98 for the L. Perrigo Company's Ibuprofen Oral Drops ANDA 75-217.

The L. Perrigo Company sent a "Notice of Non-Infringement of a Patent" to the patent and NDA holder as described in the 01/09/98 Amendment. Since that time, 45 days have passed and neither the patent nor NDA holder has taken legal action against the L. Perrigo Company.

In accordance with 21 CFR 314.50 (revisions effective October 8, 1993), I certify that a field copy which is a true copy of this Patent Amendment has been provided to the Detroit District Field Office of the Federal Food & Drug Administration.

Respectfully submitted,

Virginia G. Lutke

Virginia G. Lutke
Regulatory Affairs

xc: B. Schuster
G. Boerner

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FEB 0 2 1998

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117 Water Street
Allegan, Michigan 49010
(616)673-8451

PERRIGO®

January 9, 1998

NEW CORRESP
NC

Douglas Sporn, Director
Office of Generic Drugs
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Rockville, MD 20855-2773

PATENT AMENDMENT

NAI 2/3/98
Gregory S Davi

RE: Ibuprofen Oral Drops, 40 mg/mL
ANDA # 75-217
Patent Amendment

Dear Mr. Sporn:

The L. Perrigo Company is amending its proposed ANDA # 75-217 Ibuprofen Oral Drops, in accordance with 21 CFR 314.95(a) and (b), and the Agency's letter of November 24, 1997 as follows:

The L. Perrigo Company certifies that the Notice of Certification of Non-infringement of a Patent has been provided to each owner of the patent which is the subject of the certification and to the holder of the approved application under section 505 (b) of the Federal Food, Drug, and Cosmetic Act ("the Act"), for the listed drug that is claimed by the patent and for which the L. Perrigo Company is seeking approval. Further, the Notice met the content requirements under section 505(j)(2)(B)(ii) of the Act and 21 CFR 314.95(c).

Documentation of receipt and evidence of the date of "Notice of Non-Infringement of a Patent" (hereinafter Notice) is attached which was sent to the patent owner, Johnson & Johnson, and holder of the approved New Drug Application, McNeil Consumer Products (hereinafter McNeil), for the listed drug. This Notice was sent to Johnson & Johnson and McNeil via certified mail, return receipt requested.

The Receipt for the Notice addressed to McNeil is postmarked December 5, 1997 by the U. S. Postal Service. A copy of the "DOMESTIC RETURN RECEIPT" PS Form 3811 (hereinafter Receipt) is attached which serves to document receipt by McNeil of the Notice sent to them. The date of delivery stamped in box no. 7 of the form is December 8, 1997.

The Receipt for the Notice addressed to Johnson & Johnson is postmarked December 5, 1997 by the U. S. Postal Service. Unfortunately, PS Form 3811 has not been returned for the Notice sent to Johnson & Johnson. However, please see attached letter from Johnson & Johnson indicating that they did receive the Notice.

If you have any questions or need any additional information, please feel free to contact me by telephone at (616) 673-7604, by fax at (616) 673-7655 or by E-mail at glutke@perrigo.com.

Respectfully submitted,

Virginia G Lutke

Virginia G. Lutke
Regulatory Affairs

xc: B. Schuster

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JAN 12 1998
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Nadine

117 Water Street
Allegan, Michigan 49010
(616)673-8451

BIOEQUIVALENCY COMMENTS

ANDA: 75-217 APPLICANT: L. Perrigo Co.

DRUG PRODUCT: Ibuprofen Oral Drops, 40 mg/mL (or 50 mg/1.25 mL)

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

The dissolution testing will need to be incorporated into your stability and quality control programs as specified in USP 23.

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

Sincerely yours,

Dale Conner

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

PERRIGO®

505(j)(ii)a ok
11/17/97
Gregory S Davis

September 30, 1997

Douglas Sporn, Director
Office of Generic Drugs
CDER, FDA
MPN II, HFD-600
7500 Standish Place
Rockville, MD 20855-2773

RE: Abbreviated New Drug Application
Ibuprofen Oral Drops, 40mg/mL
Over-the-Counter Product

Dear Mr. Sporn:

The L. Perrigo Company is submitting for your review and approval, an ANDA for Ibuprofen Oral Drops, 40mg/mL pursuant to 505(j) of the Federal Food, Drug, Cosmetic Act. The L. Perrigo Company's Ibuprofen Oral Drops are identical in strength, indications, active ingredient, route of administration and dosage form to McNeil Consumer Products Co., Children's Motrin® Drops.

Children's Motrin® Drops (NDA #20-603) is listed in the Seventeenth Edition of *Approved Drug Products with Therapeutic Equivalence Evaluations* as an OTC drug with patent and exclusivity protection. A Paragraph IV Patent Certification is enclosed in Section 3 of this application which states that the unexpired patent will not be infringed by Perrigo's proposed new drug product. Children's Motrin® Drops has market exclusivity until June 16, 1998.

Bioequivalence studies conducted under fasted and fed conditions, sponsored by the L. Perrigo Company, are also included in this ANDA. There are 7 volumes for this ANDA - one CMC volume and 6 volumes for the bioequivalence study.

Attached is an additional copy of this cover letter. Please stamp the date of your receipt on it and return in the enclosed self-addressed, stamped envelope.

Should you require additional information, please contact me directly by telephone at 616-673-7604, by FAX at 616-673-7655, by E-mail at glutke@perrigo.com, or the address on this letterhead.

Thank-you for your prompt handling of this submission.

Respectfully submitted,

Virginia G. Lutke

Virginia G. Lutke
Regulatory Affairs

xc: B. Schuster
G. Boerner

RECEIVED
OCT 0 3 1997
GENERIC DRUGS

117 Water Street
Allegan, Michigan 49010
(616)673-8451

PERRIGO®

November 12, 1997

Office of Generic Drugs,
Food and Drug Administration, CDER
Document Control Room, MPN II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: Ibuprofen Oral Drops, 40 mg/mL
ANDA (# to be assigned)

Dear Sir or Madam:

Reference is made to the telephone request for additional information received on November 10, 1997, from Greg Davis in the Office of Generic Drugs regarding Ibuprofen Oral Drops, 40 mg/mL. The ANDA was submitted dated September 30, 1997, and an ANDA number is to be assigned.

Mr. Davis requested a reconciliation to clarify the packaging operation for the bioequivalence batch number 7P404V which was packaged into two configurations - a 0.5 ounce bottle (packaging lot number 7PA74V) and a 1.0 ounce bottle (packaging lot number 7PA73V). The requested information is enclosed.

If you have any questions or require additional information, please feel free to contact me by telephone at 616-673-9745, by fax at 616-673-7655 or e-mail at bschuste@perrigo.com.

Sincerely,

Brian R. Schuster
Manager, Regulatory Affairs

117 Water Street
Allegan, Michigan 49010
(616)673-8451

BIOEQUIVALENCY COMMENTS

ANDA: 75-217 APPLICANT: L. Perrigo Co.

DRUG PRODUCT: Ibuprofen Oral Drops, 40 mg/mL (or 50 mg/1.25 mL)

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

The dissolution testing will need to be incorporated into your stability and quality control programs as specified in USP 23.

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

Sincerely yours,

Dale Conner

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

Figure 1: Mean Ibuprofen Serum Levels
#116-21-11143
N = 26

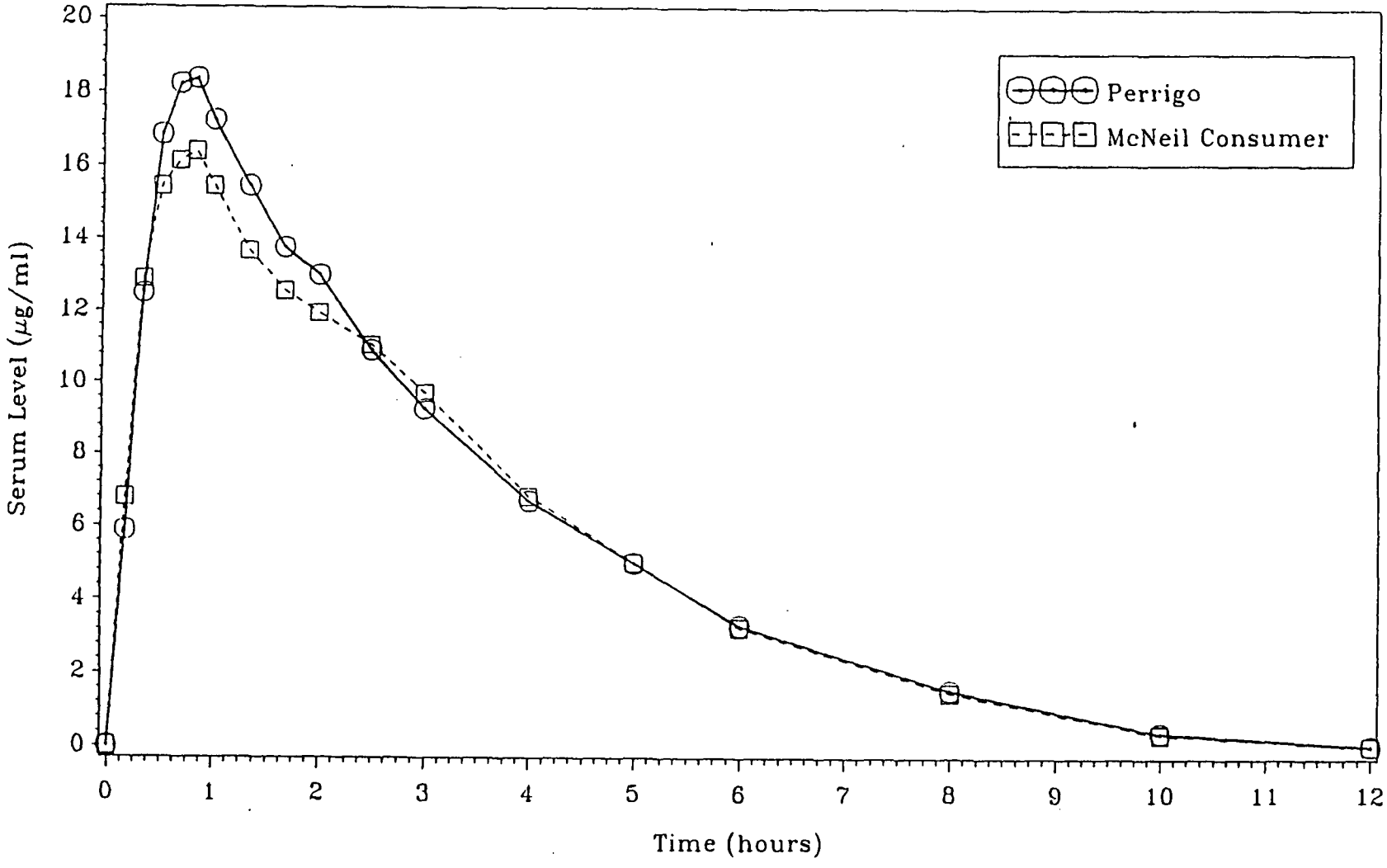

Figure 1: Mean Ibuprofen Serum Levels
#116-22-1144
N = 17