CENTER FOR DRUG EVALUATION AND RESEARCH

74-937

APPLICATION NUMBER:

CORRESPONDENCE

PERRIGO®

May 4, 1998

VIA FACSIMILE (301-594-0183) AND FEDERAL EXPRESS

Mr. Douglas L. Sporn
Director, Office of Generic Drugs
Center for Drug Evaluation and Research (HFD-600)
Food and Drug Administration
Metro Park North #2
7500 Standish Place
Rockville, Maryland 20855

Re: 180-Day Exclusivity and ANDA 74-937

Dear Mr. Sporn:

For the reasons discussed below, we request that the Food and Drug Administration not grant 180-day generic drug exclusivity to any abbreviated new drug application (ANDA) submitted for children's ibuprofen suspension drug product until the Agency amends the exclusivity regulatory provision, 21 C.F.R. § 314.107, or issues a new regulation, in response to the recent Mova and Granutec appellate decisions, which rejected FDA's "successful defense" requirement. Any regulation promulgated by FDA must conform to the courts' recommendations (particularly those of the Mova court) concerning implementation of the 180-day exclusivity statutory provision discussed below. In addition, Perrigo requests clarification from FDA on two issues relating to its interpretation of the 180-day exclusivity provision as a result of these two court cases.

Perrigo's regulatory counsel, Mr. Alan Minsk, has spoken with Messrs. Donald Hare and Gordon Johnston in your office on these issues. Both FDA officials recommended to Mr. Minsk that Perrigo submit its requests and comments in writing to you.

On September 5, 1997, FDA granted tentative approval to Perrigo for its Children's Ibuprofen Suspension ANDA 74-937, subject to the June 16, 1998, expiration of the 3-year exclusivity period for the brand name drug, Children's Motrin, NDA 20-516. On January 9, 1998, FDA also granted tentative approval to ompetitor product, and we acknowledge that there may be other applicants as well. In its ANDA, Perrigo submitted a "paragraph IV" statement certifying that the patent which claims the brand name drug will not be infringed by the manufacture, use or the sale of the new drug for which the Perrigo ANDA was submitted. We suspect, but are not certain, that o submitted a paragraph IV certification. The NDA owner/patent holder did not sue Perrigo for patent infringement and, to our knowledge, has not sued r any other applicant.

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

Perrigo requested 180-day exclusivity from FDA, as permitted under prescribed conditions in the Federal Food, Drug, and Cosmetic Act (FDC Act), but FDA responded that Perrigo was ineligible because it was not the first applicant to submit a substantially complete ANDA with a paragraph IV certification (FDA letter of October 31, 1997, reference # 97-325).

Before the two recent appellate court decisions in the Mova and Granutec cases, FDA would not have granted 180-day exclusivity to any children's ibuprofen suspension ANDA because there had been no successful defense of a patent infringement suit, as required by 21 C.F.R. § 314.107(c). However, in light of the two decisions, which rejected the "successful defense" requirement, it would appear, now, that the first to file a substantially complete ANDA with a paragraph IV certification may receive exclusivity, even though there was no patent infringement lawsuit, much less one where the ANDA applicant successfully defended the lawsuit.

To date, FDA has not issued any formal statement or policy in response to the courts' rejection of the successful defense requirement. In addition, FDA has not directly communicated with Perrigo on how the Agency will address the children's ibuprofen exclusivity issue. Time is of the essence. The NDA holder's 3-year exclusivity expires on June 16, 1998, and Perrigo, relying on 21 C.F.R. § 314.107 and FDA's policy reiteration in November 1997 that generic drug exclusivity would not be a barrier to market entry for its ANDA product (because there was no patent infringement case brought and, thus, no successful defense), is now faced with the possibility that FDA will delay approval of its ANDA for up to 180 days.

Perrigo requests that FDA notify us as soon as possible whether we may begin marketing our product when the NDA holder's 3-year exclusivity expires, assuming ANDA 74-937 is otherwise approvable.

Perrigo also seeks clarification from FDA on two issues relating to the Agency's interpretation of the 180-day exclusivity provision, in light of the Mova and Granutec decisions. It is unclear whether FDA will grant 180 days of exclusivity to an ANDA applicant when no patent infringement lawsuit has been brought. Without the lawsuit condition, the NDA holder and the ANDA applicant set to receive exclusivity could collude to prevent any generic competition for at least 180 days, if not longer. For example, the NDA holder might propose that it will not bring an infringement action against the ANDA applicant, so long as the ANDA applicant does not market the product. The NDA holder could also pay the ANDA applicant a hefty fee not to exercise its exclusivity advantage. Neither the FDC Act nor the appellate courts' decisions appear to close this loophole, which could effectively prevent generic competition indefinitely. This result would be unfair and inequitable to other generic manufacturers and would contradict the Congressional intent to encourage the entry of generic drugs on the market and likely lead to increased health care costs.

Thank you for your prompt attention to this matter. Please feel free to call me if you have any questions at 616-673-7595.

Sincerely,

David Jespersen
Director, Technical Affairs
Perrigo Company

PERRIGO®

April 24, 1998

ORIG
N/ANL

Office of Generic Drugs
CDER, FDA
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Rashmikant M. Patel, Ph.D.

RECEIVED
APR 27 1998
GENERIC DRUGS

RE: ANDA 74-937
Ibuprofen Oral Suspension, 100 mg/5 mL
Minor Amendment

Dear Dr. Patel:

This letter is in regard to the Agency's communication dated 02/05/98 concerning the L. Perrigo Company's ANDA 74-937 for Ibuprofen Oral Suspension, 100 mg/5 mL.

In the 02/05/98 communication, the Agency had two comments on the application:

1. The proposal for deletion of color ingredient to create an alternate formula does not fall under 21 CFR 314.70 (d)(4) as suggested in your amendment. This change requires that the proposed change be filed under 505 (j) of the Federal Food, Drug, and Cosmetic Act.

2. The proposed change in container/closure system is not covered under 21 CFR 314.70 as suggested in your amendment. To support this change, you are required to provide three months accelerated stability in the proposed container/closure system.

In response to comment one, the L. Perrigo Company withdraws all references to the formulation which were made in communications to the Agency on 11/07/97 and 02/09/98. This withdrawal is being made without prejudice to future refiling of this information to the ANDA. It is our understanding that OGD Policy and Procedure Guide 20-90 is now being revised and may, in the future, include a provision which will allow the inclusion of more than one formulation in a single ANDA for an oral liquid suspension.

In response to comment two, three-month accelerated test data is included in this minor amendment to support the change in the container/closure system. In addition, the exhibit batch stability samples have been stored under controlled room temperature conditions of 25°-30°C at ambient humidity through 3/1/98. On 3/1/98, the controlled room temperature storage conditions were changed to 25°± 2°C at 60%± 5% RH. These conditions will be maintained for future production batches following approval of this application. A revised stability protocol, noting the change in storage conditions, will be submitted in the first annual report as indicated in the FDA's letters of August 18, 1995 and May 8, 1996 regarding implementation of ICH recommended storage conditions. The revised conditions will not have any effect on this liquid suspension drug product.

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

As stated in our 02/09/98 correspondence, it is our understanding that McNeil was requested by the Agency to revise the Aspirin Sensitive Warning statement on their Children's Motrin® (NDA 20-516) labeling in March of 1997 and submit it as a changes being effected supplemental application. Although McNeil has begun using a revised warning on this product they do not have Agency approval for it. Per conversations with Mr. Chan Parks of the Agency, it is our understanding that the L. Perrigo Company will not be required to revise the Aspirin Sensitive Warning prior to our final approval of this application when exclusivity expires for McNeil's Children's Motrin® on June 16, 1998. After McNeil has received approval on a revised warning and after our final approval of this application, the L. Perrigo Company can submit a changes being effected supplemental application for a revised Aspirin Sensitive Warning which will follow the labeling of the listed drug. We further understand that the currently submitted Perrigo labeling will be acceptable for final approval even if McNeil receives approval for the new warning statement on their Children's Motrin® labeling.

This amendment serves to identify all changes in the conditions under which the product was tentatively approved, as required in the September 5, 1997 tentative approval letter. We trust this response will allow adequate review time prior to the final approval on June 16, 1998 when exclusivity expires for the listed drug. Note, the district FDA began the preapproval inspection for this application at the L. Perrigo Company on April 16, 1998.

Should you require additional information, please feel free to contact me directly by telephone at 616-673-7604, by fax at 616-673-7655 or the address on this letterhead.

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

PERRIGO®

NOTED
3/26/98

March 4, 1998

Office of Generic Drugs
CDER, FDA
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Rashmikant M. Patel, Ph.D.

RE: ANDA 74-937
Ibuprofen Oral Suspension, 100 mg/5 mL

NDA ORIG AMENDMENT

Dear Dr. Patel:

This letter is in regard to the Agency's communication dated 02/05/98 concerning the L. Perrigo Company's ANDA 74-937 for Ibuprofen Oral Suspension, 100 mg/5 mL. Reference is also made to the telephone conversation on 02/27/98 with Jim Wilson and Dr. Sied of the Agency with Virginia Lutke of the L. Perrigo Company.

In the 02/05/98 communication, the Agency had two comments on the application:

1. The proposal for deletion of color ingredient to create an alternate formula does not fall under 21 CFR 314.70 (d)(4) as suggested in your amendment. This change requires that the proposed change be filed under 505 (j) of the Federal Food, Drug, and Cosmetic Act.

2. The proposed change in container/closure system is not covered under 21 CFR 314.70 as suggested in your amendment. To support this change, you are required to provide three months accelerated stability in the proposed container/closure system.

In response to comment one, the L. Perrigo Company will withdraw all references to the formulation as recommended by Jim Wilson when stability data on the new proposed container/closure system is submitted to the Agency.

In response to comment two, three-month accelerated test data will be available in April 1998, at which time a minor amendment will be submitted to the Agency as requested in the 02/05/98 communication. We trust this will allow adequate review time prior to the final approval on June 16, 1998 when exclusivity expires for the listed drug.

Should you require additional information, please feel free to contact me directly by telephone at 616-673-7604, by fax at 616-673-7655 or the address on this letterhead.

Respectfully submitted,

Virginia G. Lutke

Virginia G. Lutke
Regulatory Affairs

xc: B. Schuster
G. Boerner

RECEIVED
MAR 5 1998
GENERIC DRUGS

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

PERRIGO®

February 9, 1998

Office of Generic Drugs
CDER, FDA
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Mr. Chan Parks

FPL

NDA ORIG AMENDMENT

N/AF

RE: ANDA 74-937
Ibuprofen Oral Suspension, 100 mg/5 mL
Telephone Amendment

Dear Mr. Parks:

Per your request during a telephone conversation on Tuesday, February 3, 1998, the L. Perrigo Company is submitting this telephone amendment for revised carton labeling for ANDA 74-937 Ibuprofen Oral Suspension, 100 mg/5 mL.

This carton is being submitted as Final Printed Labeling. The changes between this carton and the previously submitted carton are:

1. Deletion of FD&C Red #40 from the inactive ingredient list on the side panel.

As the inactive ingredient list does not appear on the label, a revised label is not being submitted per your instructions. The deletion of FD&C Red #40 gives an orange colored product as was noted in the minor amendment submitted to the Agency dated November 7, 1997 for this application. Please see enclosed Final Printed Labeling for a 4 ounce carton (orange colored product) and side-by-side comparison to previously submitted carton labeling.

In addition, from our recent telephone conversations concerning the National Brand Products for children's ibuprofen oral suspensions, it is my understanding that:

McNeil was requested by the Agency to revise the Aspirin Sensitive Warning statement on their Children's Motrin® (NDA 20-516) labeling in March of 1997 and submit it as a changes being effected supplemental application. Although McNeil has begun using a revised warning on this product they do not have Agency approval for it. Whitehall-Robins Healthcare has received approval for a revised Aspirin Sensitive Warning on their Children's Advil® product (NDA 20-589).

Per the telephone conversation on Thursday, February 5, 1998 between yourself, Brian Schuster (Perrigo) and myself, it is our understanding that the L. Perrigo Company will not be required by the Agency to revise the Aspirin Sensitive Warning prior to our final approval of this application when exclusivity expires for McNeil's Children's Motrin® on June 16, 1998. After McNeil has received approval on a revised warning and after our

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FEB 10 1998
GENERIC DRUGS

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[illegible]
[illegible]

final approval of this application, the L. Perrigo Company can submit a changes being effected supplemental application for a revised Aspirin Sensitive Warning which will follow the labeling of the listed drug. We further understand that the currently submitted Perrigo labeling will be acceptable for final approval even if McNeil receives approval for the new warning statement on their Children's Motrin® labeling.

Should you require additional information, please feel free to contact me directly by telephone at 616-673-7604, by fax at 616-673-7655 or the address on this letterhead.

Respectfully submitted,

Virginia G Lutke

Virginia G. Lutke
Regulatory Affairs

xc: B. Schuster

PERRIGO®

November 7, 1997

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

NDA ORIG AMENDMENT

RE: Ibuprofen Oral Suspension 100 mg/5 mL
ANDA 74-937
Minor Amendment

Dear Sir or Madam:

On September 5, 1997, the L. Perrigo Company received a tentative approval letter for ANDA 74-937, Ibuprofen Oral Suspension 100 mg/5 mL. That letter contained a request that Perrigo submit, at least 60 days prior to the expiration of the applicable exclusivity protection (June 16, 1998), an amendment to the application to identify any changes in the conditions under which the product was tentatively approved. This minor amendment is being submitted to fulfill that requirement. If changes beyond those described in this amendment are implemented prior to June 16, 1998, an additional minor amendment will be filed to describe those changes.

In order to provide complete information, this amendment includes reference to changes which may be reported in an Annual Report under 21 CFR 314.70. The following changes in this application are proposed:

1) Changes in Container

a. Minor revision to bottle specifications and change in bottle manufacturer
b. Change in resin type

a) Minor revision to bottle specifications and change in bottle manufacturer- In order to ensure

The label claim of 120 mL remains unchanged with the revised bottle. The headspace in both the original and revised bottles is approximately the same volume, as described in item 2 below.

Allegan, Michigan 49010

A specification and drawing for the revised bottle, part number 410276, and a DMF Referral letter from Drug Plastics & Glass Company, are enclosed in Attachment 1.

b. Change in resin type- The

2) Revised fill weight - The fill weight for the revised bottle has been adjusted from a target of grams to a target of ms in order to meet the USP Deliverable Volume specifications as well as to provide a headspace volume which is comparable to the bottles which were packaged for the original submission batch. A master packaging card is included in Attachment 2 which includes this adjustment.

3) Revised ibuprofen assay procedure - The procedure for the Assay of Ibuprofen (drug substance) has been updated to USP supplement 7 which includes a specification for
A copy of procedure 1257 - Assay of Ibuprofen by s included in Attachment 3.

4) Revised ibuprofen specification - The specification for ibuprofen drug substance (code 8768) has been revised for the assay to reflect calculation of potency on the anhydrous basis, consistent with USP requirements. A copy of the revised specification is enclosed in Attachment 4.

5) Revised glycerin specification - The specification for glycerin has been updated to revise the wording for the identification test per the USP. The raw material specification for Glycerin is included in Attachment 5.

6) Revised dissolution test procedure - The procedure for the Dissolution Testing of Ibuprofen Oral Suspension has been updated to include the following:

-Added the ibuprofen concentrations to the dissolution sample section.
-Changed the injection volume to
-Added USP tangent plate count to system suitability tests.

Procedure 1431- Dissolution Testing of Ibuprofen Oral Suspension is included in Attachment 6.

7) Removal of color ingredient - In order to also offer an orange colored product, the FD&C Red #40 will be removed from the formula to create an alternate formula. The L. Perrigo Company will offer both a red colored product (which was submitted in the original application) and an orange colored product (alternate formula, product code 897). Once production of this alternate formula has begun, stability data will be generated and submitted in the first annual report for this product in accordance with 21 CFR 314.70 (d)(4). The In-Process, Finished Product and Stability specifications for the

alternate formula will be identical to the original formula, except for a change in the description of the product from a red to an orange color.

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.

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.

Respectfully submitted,

Virginia G. Lutke

Virginia G. Lutke
Regulatory Affairs

xc: B. Schuster
G. Boerner

PERRIGO

June 23, 1997

NEW CORRESP
NC

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

Telephone Amendment

RE: Ibuprofen Oral Suspension 100 mg/5mL
ANDA 74-937

Dear Sir or Madam:

This Telephone Amendment is in response to the request for additional information received on June 11, 1997, from James Wilson and Dr. Sied in the Office of Generic Drugs regarding Ibuprofen Oral Suspension, 100 mg/5mL, ANDA 74-937. Please note that an amendment to provide final printed labeling has been submitted dated June 23, 1997.

We hereby amend ANDA 74-937 to address the following comments.

Comment 1: In regard to the flavor, the product labeling states "Berry Flavored Liquid", however, the flavor is described elsewhere in the ANDA as " . Identify the correct flavor and revise appropriate documents to reference consistently.

The product is correctly described in the labeling as berry flavored. The flavor manufacturer's certificate of analysis (enclosed on page 151 of the original ANDA) uses the term " flavor" (artificial punch) to describe exactly the same flavoring. Although the description of the taste was not identical, please note that the usage and tracking of this material at Perrigo is entirely controlled by the Raw Material (or Item) number "4655" and the Material description "
These numbers are found in the original ANDA on page 151 (manufacturer's certificate of analysis), page 152 (Perrigo Raw Material Specifications), and page 226 (drug product manufacturing order).

To ensure consistency in referencing this flavor, we have contacted the manufacturer, to request a revision of the flavor description. A representative certificate of analysis is enclosed in Attachment 1 which indicates "Artificial Berry Flavor" as the taste description. All future shipments of this ingredient will include this description to ensure consistency with the drug product labeling.

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JUN 25 1997
GENERIC DRUGS

Comment 2: Provide the composition of the flavoring ingredient.

We have contacted the manufacturer, to request a composition list for the Artificial Berry Flavor. The formulation of the flavor is proprietary, however, the listing that

Madeline

could be provided is enclosed in Attachment 2. As described in item 3, below, the manufacturer has provided a statement and certification regarding the safety of all ingredients.

Comment 3: Provide a CFR reference for the components of the flavoring ingredient.

has provided a comprehensive certification regarding the FDCA and FEMA/GRAS status of all flavor ingredients. This certification is enclosed in Attachment 3.

In accordance with 21 CFR 314.94, I certify that a field copy which is a true copy of this amendment has been mailed to the Detroit District FDA Office.

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

Brian Schuster
Manager, Regulatory Affairs

PERRIGO

NDA ORIG AMENDMENT

N / FA

June 23, 1997
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: Jerry Phillips
Director, Div. of Labeling and Program Support

FACSIMILE AMENDMENT

RE: Ibuprofen Oral Suspension USP, 100 mg/5 mL
ANDA 74-937
Facsimile Amendment

Dear Mr. Phillips:

This letter is in response to the Agency's facsimile dated June 18, 1997. In this communication, the Agency commented on the labeling for the L. Perrigo Company's ANDA 74-937 Ibuprofen Oral Suspension, USP, 100 mg/5 mL submitted 02/14/97.

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.

Respectfully submitted,

Virginia G. Lutke

Virginia G. Lutke
Regulatory Affairs

xc: B. Schuster
D. Jespersen

RECEIVED
JUN 25 1997
GENERIC DRUGS

PERRIGO®

N/FA

March 7, 1997

Office of Generic Drugs, OPS, CDER, FDA
Document Control Room, MPN II
7500 Standish Place, Room 150
Rockville, MD 20855-2773
Attention: Mr. Douglas Sporn, Director

Telephone Amendment

RE: Ibuprofen Oral Suspension 100 mg/5mL
ANDA 74-937

Dear Mr. Sporn:

This Telephone Amendment is in response to the request received on March 7, 1997, from James Wilson in the Office of Generic Drugs regarding the L. Perrigo Company's Ibuprofen Oral Suspension 100 mg/5mL application.

We hereby amend ANDA 74-937 to provide a revision to the Finished Product Specifications to include the test for Deliverable Volume performed according to USP <698>. This test is added in conformance to the USP 23 monograph as updated in supplement 3. A copy of the revised specification is enclosed.

In accordance with 21 CFR 314.50, I certify that a field copy which is a true copy of this amendment has been mailed to the Detroit District FDA Office.

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 Schuster
Manager, Regulatory Affairs

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MAR 10 1997
GENERIC DRUGS

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

PERRIGO®

February 14, 1997

NEW CORRESP

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

MINOR AMENDMENT
FACSIMILE AMENDMENT
FAX: 301-827-4337

Re: ANDA 74-937
Ibuprofen Oral Suspension 100mg/5mL

Dear Mr. Wilson:

Please find attached Perrigo's response to the Facsimile Deficiency Letter dated January 15, 1997 with respect to Perrigo's ANDA 74-937 for Ibuprofen Oral Suspension 100mg/5mL.

If you should have any further questions regarding this response or this application, please contact Brian Schuster, Perrigo Regulatory Affairs Manager at telephone 616-673-7745 or facsimile 616-673-7655.

Perrigo appreciates the opportunity to receive and respond to deficiency letters via facsimile.

Respectfully submitted,

Jacqueline M. Eaton

Jacqueline M. Eaton
Regulatory Affairs

RECEIVED
FEB 18 1997
GENERIC DRUGS

117 [illegible] Street
[illegible], Michigan 49010
616-[illegible]-3451

ANDA 74-937

L. Perrigo Company
Attention: Jacqueline M. Eaton
117 Water Street
Allegan MI 49010

FEB - 4 1997

Dear Madam:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505 (j) of the Federal Food, Drug and Cosmetic Act for Ibuprofen Oral Suspension, 10 mg/5 mL.

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

2. The following dissolution testing will need to be incorporated into your stability and quality control programs:

   The testing should be conducted on 12 individual dosage units each of the test and reference product employing 900 ml of phosphate buffer, pH 7.2, at 37°C using USP 23 apparatus II (paddle) at 50 rpm. The test product should meet the following specification:

Please note that the bioequivalency comments expressed in this letter are preliminary. The above bioequivalency comments may be revised after review of the entire application, upon consideration of the chemistry, manufacturing and controls, microbiology, labeling or other scientific or regulatory issues. A revised determination may require additional information and/or studies, or may conclude that the proposed formulation is not approvable.

Sincerely yours,

Rabindra Patnaik, Ph.D.
Acting Director, Division of Bioequivalence
Office of Generic Drugs
Center for Drug Evaluation and Research

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November 13, 1996
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: Keith K. Chan, Ph.D.
Director, Div. of Bioequivalence

MINOR AMENDMENT

RE: Ibuprofen Oral Suspension
ANDA #74-937
Minor Amendment

Dear Dr. Chan:

This letter is in response to the Agency's telephone communication with the L. Perrigo Company on November 12, 1996. In that telephone conversation, the Agency requested information concerning the 6 "drop out" subjects in the bioequivalence study #10838B for the L. Perrigo Company's Ibuprofen Oral Suspension product, ANDA #74-937.

Please see the attached letter from Pharmakinetics Laboratories, Inc. detailing why 6 of 24 subjects did not complete study #10838B. The treatment sequences these 6 subjects were assigned to is also included in the letter from Pharmakinetics.

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 GGREEN@PERRIGO.COM.

Respectfully submitted,

Virginia K. Green

Virginia K. Green
Regulatory Affairs

xc: J. Eaton
D. Jespersen

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NOV 15 1996
GENERIC DRUGS

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

1 Copy only

PERRIGO®

October 30, 1996

Amendment
ANDA 74-937

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

Re: Ibuprofen Oral Suspension, ANDA #74-937

Dear Mr. Sporn:

As a follow-up to the Amendment filed September 30, 1996, the L. Perrigo Company is filing another amendment to it's proposed ANDA 74-937 Ibuprofen Oral Suspenion, in accordance with 21 CFR 314.95(e).

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 as described in the Amendment dated September 30, 1996. This Notice was sent to Johnson & Johnson and McNeil via certified mail, return receipt requested. A copy of each "DOMESTIC RETURN RECEIPT" PS Form 3811 (hereinafter Receipt) is attached which serves to document receipt by Johnson & Johnson and McNeil of the Notice sent to them.

The Receipt for the Notice addressed to Johnson & Johnson is postmarked October 21, 1996 by the U.S. Postal Service. The date of delivery in box no.7 of the form is blank.

The Receipt for the Notice addressed to McNeil is postmarked October 19, 1996 by the U.S. Postal Service which is the same as the date of delivery stamped in box no. 7 of the form.

Please contact me at telephone 616-673-7670 if you have any questions.

Respectfully submitted,

Jacqueline M. Eaton
Regulatory Affairs Manager

xc: D. Jespersen

Modules 1-31-97

117 Water Street
Allegan, Michigan 49010
616/673-8451

PERRIGO®

October 15, 1996

AMENDMENT
ANDA 74-937

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

RECEIVED
OCT 17 1996
GENERIC DRUGS

NEW CORRESP
NC
Noted
J Bucci
10/31/96

Re: Ibuprofen Oral Suspension
ANDA #74-937

Dear Mr. Sporn:

The L. Perrigo Company is amending its proposed ANDA 74-937 Ibuprofen Oral Suspension, in accordance with 21 CFR 314.95 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 L. Perrigo 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).

The Notice described above was sent to each owner of the patent and to the holder of approved new drug application number 20516-001, on the same day this Amendment is being sent to FDA.

Further, documentation of receipt of notice as described in 21 CFR 314.95(e), will be sent to FDA and L. Perrigo's ANDA amended again, when the receipt is obtained by L. Perrigo.

Respectfully submitted

Jacqueline M. Eaton

Jacqueline M. Eaton
Regulatory Affairs Manager

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

PERRIGO

505(5)(2)(a) info acceptable for filing Anne Marie White 8/19/96 OK 8/19/96

RECEIVED

AUG 2 1996

GENERIC DRUGS

July 26, 1996

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

RE: Abbreviated New Drug Application
Children's Ibuprofen Oral Suspension, 100mg/5mL
Over-the-Counter

Dear Mr. Sporn:

The L. Perrigo Company is submitting for your review and approval, an ANDA for over-the-counter Children's Ibuprofen Oral Suspension, 100mg/5mL pursuant to 505(j) of the Federal Food, Drug, Cosmetic Act. Children's Ibuprofen Oral Suspension is identical in strength, indication, active ingredient, route of administration and dosage form to the listed drug, McNeil Consumer Products Co. Children's Motrin.

Children's Motrin Ibuprofen Oral Suspension (NDA # 20-516) is listed in the Sixteenth Edition of Approved Drug Products with Therapeutic Equivalence Evaluations as an OTC drug with patent protection until December 20, 2011, and market exclusivity until June 16, 1998. The official monograph for Ibuprofen Oral Suspension was published in the Third Supplement to USP23 at pages 2941 and 2942 in the Supplement.

Bioequivalence studies conducted under fed and fasting conditions, sponsored by Perrigo, are also included in this ANDA.

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

Should you require additional information, please contact me directly by telephone at 616-673-7670, by FAX at 616-673-7655, e-mail at JEATON@PERRIGO.COM or the address on this letterhead.

Respectfully submitted,

Jacqueline M. Eaton

Jacqueline M. Eaton
Regulatory Affairs Manager

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