CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 75-326

CORRESPONDENCE

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

mailed
7/2/99

June 28, 1999

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20857

NDA ORIG AMENDMENT

Reference: ***MINOR AMENDMENT***
Ticlopidine Hydrochloride Tablets, 250 mg
ANDA 75-326

Dear Ms. Fang:

Pursuant to the letter of Jun 16, 1999 commenting on our Abbreviated New Drug Application submitted on January 30, 1998 for Ticlopidine Hydrochloride Tablets, 250 mg. The following are our responses to the minor deficiencies in the letter.

1. **Drug Substance: The calculations for the drug substance assay do not take into account standard purity. The assay is calculated on the dried basis, but the method does not indicate to dry the drug substance or compensate during calculations.**

Response

The calculations for the drug substance assay do take into account the standard purity. You can see in the calculation definitions section on p.10 of Eon Labs in-house method **T-45 (Attachment 1)** that the Std Wt = Standard weight in mg, adjusted for potency, of ticlopidine hydrochloride.

The assay result was calculated on the dried basis as you can see from the limits on p.11 of method **T- 45.** The chemists know how to calculate potencies on the dried basis using the LOD, however to reinforce this, we have adjusted the assay calculation for better clarification as [illegible] p. 9 of method **T-45 (Attachment 1)**.

CENTER FOR DRUG EVALUATION AND RESEARCH
REC'D
JUN 29 1999
OGD

2. **Drug Product: The calculations for the drug product assay do not take into account standard purity.**

The calculations for the drug product assay do take into account the standard purity. On p. 7 of Eon Labs **Product Monograph T001QC**, you can see in the calculations definitions section that Std Wt = Standard weight in mg, adjusted for potency **(Attachment 2)**.

3. **The assay for the drug substance, drug product and the dissolution all include a specification for standard comparison, however if the comparison specification is not met then a correction factor is used. The methods do not state what this correction factor is to be used for.**

This standard comparison was not included in the assay for the drug substance because it is inappropriate for a test with a narrow limit range. For the finished product, when a standard comparison correction factor is needed, the final result (percent label claim for assay or percent dissolved for dissolution) is multiplied by the Correction Factor. To clarify this for the chemist we have added statements to the standard comparison sections on pages 6 and 10 of Product Monograph T001QC **(Attachment 2).**

Comment

We await response to the deficiencies of DMF from the holder. The deficiencies in the DMF would have to be corrected before the approval of the ANDA.

We acknowledge that the approval of our ANDA will be dependent on the satisfactory response to the DMF deficiences. Also enclosed is a copy of the letter from the to the FDA stating that has successfully answered the DMF deficiency letter **(Attachment 3)**.

We hope that our responses satisfactorily address the deficiencies noted in your letter. If you need further information or clarification, please do not hesitate to call me at (718) 276-8607 ext.404.

Sincerely,
Eon Labs Manufacturing, Inc.

Eva Sultana Khan.
Eva S. Khan, M.S., Pharm.D.
Regulatory Affairs Associate

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

Noted (rvs) 6/30/99

7/23/99 Educational plan is acceptable

/S/

NEW CORRESP

N, C

June 22, 1999

Charles Hoppes
Team Leader
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Document Room, HFD-613
Metro Park North II, Room E 150
7500 Standish Place
Rockville, Maryland 20852

Re: General Correspondence - Educational Program
Ticlopidine Hydrochloride Tablets, 250 mg
ANDA 75-326

Dear Mr. Hoppes:

As per our conversation on June 17, 1999 submitted herein is a post-approval educational plan to address the important issues outlined in the agency's letter dated June 15, 1999.

At this time our educational program is targeted to physicians, nurse practitioners, physician assistants and the dispensing pharmacists. Our educational program will be a three step process which will include the following:

1. We will distribute a 'Dear Doctor' letter to all the physicians who have prescribed ticlopidine in the last two years. We will obtain the targeted list of the prescribing physicians from either IMS or Walsh America (prescription audit firms). Each of the targeted physicians will receive a letter upon launch of the product which will have the educational components described in your notice.

2. Upon the launch of our product we will start to advertise the educational material in the Journal of the American Medical Association (JAMA) periodically. We will supplement our ads in JAMA with advertising to Nurse Practitioners and Physician's Assistants in journals specifically targeted to these audiences.

3. The patient package insert (PPI) previously submitted in our March ammendment, also has the components of the educational material included in your notice and will act as an educational tool for the dispensing pharmacists.

Upon approval of our educational program plan we will be prepared to implement the program upon the distribution and marketing of ticlopidine.

We hope that our responses satisfactorily addresses the important issues outlined in your notice. If you need further information or clarification, please do not hesitate to call me at (718) 276-8607 ext. 330.

Sincerely,
Eon Labs Manufacturing, Inc.

Sadie Ciganek
VP, Regulatory Affairs

ANDA 75-326

JUN 15 1999

Eon Labs Manufacturing, Inc.
Attention: Sadie M. Ciganek
227-15 North Conduit Avenue
Laurelton, New York 11413

Dear Madam:

This is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Ticlopidine Hydrochloride Tablets, 250 mg (Ticlopidine).

In light of several new applicants seeking to market Ticlopidine, inquiries from those applicants, and the November 27, 1998, citizen petition from Hoffmann-LaRoche, Inc., as well as other correspondence, the Agency has reevaluated the measures that it believes may enhance the safe use of Ticlopidine.

Our letter of September 21, 1998, informed you that Hoffman-LaRoche, Inc., manufacturer of the reference listed drug, TICLID® tablets, has in place a number of steps intended to encourage the safe use of their product. These steps include offering free blood monitoring to patients and providing educational materials to health-care professionals to make them aware of potentially life-threatening hematological adverse reactions associated with the drug and to help ensure appropriate monitoring of patients on Ticlopidine.

The Agency has reevaluated the utility of Hoffman-LaRoche's post-marketing program in light of information gathered from their seven years of experience marketing TICLID®. We have concluded that the provision of white cell count monitoring, offered free of charge, does not significantly enhance the safe use of the product. Accordingly, although monitoring remains an important part of the safe use of Ticlopidine, we will not expect applicants to offer this free service in the future. We continue to believe strongly, however, that a post-approval educational program directed towards prescribing physicians and other health-care professionals may enhance the safe use of Ticlopidine.

The Agency believes that an effective educational program for Ticlopidine should include the following characteristics:

1. Target audience for an adequate educational campaign.

    a. Physicians, including those within a health-care system such as an HMO or PPO, who prescribe Ticlopidine.

    b. Other health-care professionals, such as nurse practitioners, physician assistants, and dispensing pharmacists, who are in a position in a given health-care system to educate patients and/or monitor compliance.

2. Substantive elements of an adequate educational campaign.

    a. A clear statement that Ticlopidine is approved for use only in patients who are intolerant or allergic to aspirin therapy or who have failed aspirin therapy.

    b. Discussion of the known risks of Ticlopidine therapy and how to mitigate them. An adequate discussion would include not only information about the frequency and potential severity of adverse events, but also informaiton about the role that clinical observation and blood monitoring can play in preventing/minimizing their clinical severity. The discussion should include information about the following known adverse events:

        (i) Neutropenia/agranulocytosis;

        (ii) Thrombotic thrombocytopenic purpura (TTP); and

        (iii) Aplastic anemia.

    c. Information delineating the schedule for blood and clinical monitoring during the first three months of treatment, and describing the steps to be taken should the results of such monitoring be abnormal.

    d. A statement reinforcing the need for all health-care professionals to report observed serious and fatal adverse events with Ticlopidine administration to MedWatch.

Within 10 days of receiving this notice, we ask that you submit your post-approval plan to address the important issues outlined above. You should be prepared to implement your educational program upon distribution and marketing of Ticlopidine under an approved application. You should also provide, in each annual report, a brief summary of your implementation efforts, as well as any other relevant data, associated with the educational program described above.

We await your prompt response. If you have further questions or need clarification on any of the elements listed above, please contact Mr. Charlie Hoppes, Team Leader - Division II; Labeling Review Branch at (301) 827-5846.

Sincerely yours,

/S/ 6/15/99

Douglas L. Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

April 27, 1999

labeling reviewer drafted 6/10/99 AVerjee

Robert L. West
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20857

Reference: **LABELING AMENDMENT**
Ticlopidine HydrochlorideTablets, 250 mg
ANDA 75-326

Dear Mr. West:

In regards to the labeling deficiency letter dated March 11, 1999 for Ticlopidine Hydrochloride Tablets, 250 mg, ANDA 75-326, we have made all the necessary corrections indicated in your letter as well as the changes related to the previous labeling correspondence forwarded by the fax received on August 1998, we are submitting the final printed labels (FPLs) as ***Attachment 1.*** A side-by-side comparison of the changes comparing the new insert to the previously submitted insert as well as a table of annotations is provided for your reference as ***Attachment 2***.

We are also submitting final printed labeling for the Patient Information Leaflet (patient package insert) which we intend to distribute with the packaged product as pads of 12 sheets in each tray of 30's and 60's, and as pads of 100 sheets in each tray of 500's. Each sheet will be torn off from the pad by the pharmacist and given to the patient upon dispensing.

We hope our responses satisfactorily address the labeling deficiencies and that the approval of our application can move forward pending resolution of all chemistry issues. If you need further information please feel free to contact me at (718) 276-8607 ext. 404.

Sincerely,
Eon Labs Manufacturing, Inc.

Eva Sultana Khan.
Eva S. Khan, M.S., Pharm.D.
Regulatory Affairs Associate

RECEIVED
APR 26 1999
GENERIC DRUGS

DEPARTMENT OF HEALTH & HUMAN SERVICES

PUBLIC HEALTH SERVICE
PHILADELPHIA DISTRICT
FOOD AND DRUG ADMINISTRATION
SCIENCE BRANCH

MEMORANDUM

DATE: March 12,1999

FROM: Director, Science Branch
Philadelphia District, HFR-CE160

SUBJECT: ANDA 75-326: Ticlopidine HCl Tablets, 250mg, and Bulk Drug Substance
Eon Labs, Laurektin, NY 114413
RE: 43218

TO: Radhika Rajagopalan, Review Chemist
CDER/OGD, HFD-645

The Philadelphia District Laboratory performed the analysis of Ticlopidine HCl Tablets, and Bulk Drug Substance, using the firm's method and samples provided. Attached are the summary of results, worksheets, and comments for the subject ANDA.

Based on the analytical results, the ANDA method appears to be suitable for regulatory control of this product. No other problems were encountered with the analytical methods.

W. Charles Becoat

W. Charles Becoat

cc:

YH:WCB

ATTACHMENTS

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

March 17, 1999

Frank Holcombe, Ph.D.
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20857

Subject: ***Ticlopidine Hydrochloride Tablets, 250 mg***
ANDA 75-326

Reference: ***MAJOR (I) Deficiency Letter dated June 30, 1998***
Major Amendment submitted July 1998
MAJOR (II) Deficiency Letter dated Feb 12, 1999

Letter from Ms. Sadie Ciganek to Mr. Doug Sporn dated March 4, 1999

Dear Dr. Holcombe:

In accordance with my telephone conversation of March 10, 1999, with Ms. Rita Hassall, we are providing herein documentation which supports our request for a re-evaluation of a second major deficiency letter received February 12, 1999 for Ticlopidine Hydrochloride Tablets, 250 mg. Copies of relevant pages from previous filings are being submitted to assist in your review along with a brief explanation commenting on each deficiency in the Feb.12, 1999 letter.

Also provided for your review is a copy of our July 1998 major amendment responses (text only) as **ATTACHMENT 1**. This amendment represents the responses to the first major deficiency letter of June 30, 1998. As stated in our earlier communication to Mr. Sporn, we are requesting a re-classification of the major status for the reasons discussed below:

1. Comment

We notice your response regarding the master batch record to support the proposed commercial batch size of . tablets. Please provide a master batch record for the maximum production batch size to be manufactured or confirm that .ablets is the maximum production size to be manufactured.

Response

The Master Batch Record for the proposed commercial batch size of tablets was previously filed in the original ANDA application, Volume 2, pages 0282-0305. The Master Batch Record (MBR) was preceded by a summary statement, page No 0281, which listed the intended commercial batch size as tablets. A copy of the summary page is provided as **ATTACHMENT 2.**

The proposed commercial batch size of tablets was also provided in our August 1998 major amendment as part of the response to comment # 4.

2. **Comment**

We notice your statements regarding question #7 on in-process testing. Please provide us a copy of the test results obtained on 7/17/97.

Response

test results obtained on 7/17/97 were filed in the original application in Volume 2, page 0376. A copy is provided as **ATTACHMENT 3.**

3. **Comment**

Please clarify what Normal Plant Environmental Conditions are. Please explain if temperature and humidity are controlled.

An explanation of Normal Plant Environmental Conditions (NPEC) was previously provided in the original application in Vol 3, Page 0471, **ATTACHMENT 4.** NPEC is the ambient temperature and relative humidity in the warehouse and applies to short term holding of drug product.

4. **Comment**

We notice your response regarding system suitability testing. Explain how the analyst will identify and quantitate the impurities based on retention times if the mobile phase composition and flow rate will be changed during analyses as they prefer. We strongly recommend the removal of the note sections in your assay method, and further establish resolution between impurity B which elutes at 6.4 minutes and ticlopidine (elution time roughly 9.4 minutes).

This comment is a matter of tightening specifications on existing records. It does not require additional analytical work or generation of new data. We believe this to be a small issue that should not require a significant amount of time to review the changes since no analytical data or methods are involved.

6. **Comment**

We notice your response regarding the weight variation methods as per USP 23, Supplement 7 (page 3984). This is acceptable officially for products manufactured after November 15, 1997 and for future commercial batches. However, the biobatch was manufactured and released during the middle of the year (release date 7/21/97). Hence please provide us uniformity data based on chemical analysis.

Response

THIS IS AN INCORRECT STATEMENT!! The Bio/ANDA batch that was released on 7/8/1997 was tested for uniformity of dosage using **ASSAY** (chemical analysis) method and not weight variation. This can be confirmed by reference to the Finished Product Specification and Release Form which states "Uniformity of Dosage <905> (content uniformity)" ; analytical methods ARMR 081, and USP Page 3219-3220 . A copy of the relevant documents from the specification sheet, ARMR, and USP <905> are provided in **ATTACHMENT 7**.

To further understand our position on this comment, please refer to our response to comment No.13 (b) in the August 1998 major amendment. The reviewer seems to be confused with the content uniformity issue. The first deficiency letter states in both comment 13 (b) and 14 that weight variation is not accepted. The language is fairly strong in that regard.

We responded by saying that compendial changes were published in the USP 23 which allowed for weight variation for this product. We provided the relevant page from the USP as a reference. As seen by the above comment, the reviewer **now** acknowledges the USP 23 criteria for uniformity of dose by weight variation, but states that our Bio/ANDA batch was released before that method became official in the USP 23. As stated above, this is not correct.

7. **Comment**

We recommend reporting the stability evaluation data based on individual known impurities, individual unknown impurities and total impurities. Please provide us the data submitted on pages 85-88 (of the amendment) using the above classification between different types of impurities

Response

This comment is a new issue and was not included in the first deficiency letter. It requires Eon Labs to report the stability data in a different manner or format from that submitted in the ANDA. It does not effect or alter the analytical method or the raw data recorded in the analysts notebooks. Nor does it affect the chromatograms on file. It only requires new calculations of the existing data to be reported as individual known, individual unknown, and total. We were reporting the impurities as any impurity, known or unknown, and total. Once again, this change should not require a lengthy review.

We agree to report the stability data based on individual known impurities, individual unknown impurities, and total impurities. Enclosed herewith are the amended CRT Stability Reports reflecting the new reporting format in **ATTACHMENT 8**.

Based on the above, we believe that we have already addressed six of the seven deficiencies in the Feb 1999 letter and the one remaining issue is minor in scope. Please re-evaluate the information submitted herein and give consideration to our request.

I hope we can satisfactorily resolve this matter quickly so we can proceed with addressing any remaining deficiencies to obtain a timely approval of our ANDA application. If you require additional information, I can be reached directly at (718) 276-8607 x330.

I thank you for your consideration in this matter and look forward to hearing from you in the near future.

Sincerely,
Eon Labs Manufacturing, Inc.

Patricia Kaufold for
Sadie M. Ciganek
Vice President Regulatory Affairs

cc:
A. Amann, Ph.D.
Florence Fang, Ph.D.
Bernhard Hampl, Ph.D.

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

March 4, 1999

Mr. Douglas Sporn
Director
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20857

NC

Subject: ***Ticlopidine Hydrochloride Tablets, 250 mg***
ANDA 75-326

Reference: ***MAJOR (I)Deficiency Letter dated June 30, 1998***
MAJOR (II) Deficiency Letter dated Feb 12, 1999

Dear Mr. Sporn:

Eon Labs submitted an Abbreviated New Drug Application in January 1998 for Ticlopidine Hydrochloride Tablets, 250 mg, ANDA 75-326. Subsequent to the filing, we received two MAJOR DEFICIENCY letters from the FDA, dated June 1998, and February 1999 respectively, commenting on the chemistry and manufacturing controls filed in the application. A copy of each letter is provided for your review and discussed in greater detail herein.

The first MAJOR DEFICIENCY letter, dated June 1998, had twenty (20) points relating to the chemistry and manufacturing controls of the application. Eon Labs answered the deficiency letter as a MAJOR AMENDMENT dated July 1998, addressing each issue with what we believed were comprehensive and adequate responses. A second MAJOR DEFICIENCY letter was issued to Eon Labs in February 1999 listing seven (7) additional points. Review of the second letter revealed that six of the seven points had already been answered in our August 1998 amendment or had previously been filed in the original ANDA application.

Eon Labs contacted the CSO requesting a conference call to discuss the deficiency letter in an attempt to understand the basis for the major classification. The CSO arranged a conference call with the reviewing chemist and the team leader. In preparation for the conference call, Eon Labs sent a copy of the deficiency letter to the CSO with annotations in the margin indicating the Page No and reference to where the data could be found (attached) At the conclusion of the conference call, Eon Labs was convinced that the deficiencies were trivial in nature and did not warrant a major status. We requested a reduction to the classification of the letter, but the CSO was not able to take such an independent action under her authority.

The matter was subsequently discussed with Dr. Florence Fang, the Director of Division of Chemistry I. Dr. Fang indicated that she personally had not reviewed the jackets of the ANDA and suggested that if Eon Labs wanted to pursue the matter beyond this point, a formal meeting would have to be requested with the agency.

Eon Labs strongly believes that the second MAJOR DEFICIENCY letter has no significant issues and that the letter unfairly penalizes our firm from a timely approval. As stated above, we believe that this second major deficiency letter is unjustified.

We are requesting a formal meeting with the agency to discuss both deficiency letters and to present data which supports our case. Since time is of the essence, we are requesting a meeting at the earliest time possible so that this matter can be resolved quickly and Eon Labs can proceed with answering the final letter agreed upon from the outcome of the meeting. Please consider our request and advise our firm with the details of the meeting. I can be reached directly at (718) 276-8607 x330.

I thank you for your consideration in this matter and look forward to hearing from you in the near future.

Sincerely,
Eon Labs Manufacturing, Inc.

Sadie M. Ciganek
Vice President Regulatory Affairs

cc:
A. Amann, Ph.D.
Florence Fang, Ph.D.
Bernhard Hampl, Ph.D.

ANDA 75-326

Amt 1263

Eon Labs Manufacturing, Inc.
Attention: Sadie M. Ciganek
227-15 North Conduit Avenue
Laurelton, New York 11413

SEP 21 1999

Dear Madam:

This is in reference to your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act, for Ticlopidine Hydrochloride Tablets, 250 mg.

The reference listed drug (Ticlid®; Hoffman La Roche Inc.) provides educational programs for physicians and patients. In addition, a CBC monitoring program is offered free of charge. The reason for this monitoring is that ticlopidine can cause life-threatening hematological adverse reactions, including neutropenia/agranulocytosis and thrombotic thrombocytopenic purpura (TTP). To detect early signs of these conditions and allow intervention when necessary, it is important that patients receiving ticlopidine be hematologically and clinically monitored every 2 weeks for evidence of neutropenia or TTP during the first 3 months of treatment. The Agency also believes that educational programs that alert physicians to the occurrence of neutropenia/agranulocytosis and TTP can enhance the safe use of ticlopidine and strongly encourages you to consider a similar educational program.

In addition, you were recently notified by the Division of Labeling and Program Support of new and important changes in the package insert labeling for ticlopidine. In addition to these requested labeling changes, we ask that you outline any plans you have in addressing these important issues discussed above.

We await your prompt response. If you have further questions concerning this issue, please contact Mr. Charlie Hoppes, Team Leader - Division II; Labeling Review Branch at (301)827-5846.

Sincerely yours,

/S/ 1/21/98

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

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

FPL

MAJOR AMENDMENT

AC

July 30, 1998

Frank O. Holocombe, Jr., Ph.D.
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II
7500 Standish Place
Rockville, MD 20857

Reference: ***MAJOR AMENDMENT***
Ticlopidine Hydrochloride Tablets, 250 mg
ANDA 75-326

Dear Dr. Holocombe:

Pursuant to your letter of June 30, 1998 commenting on our Abbreviated New Drug Application submitted on January 30, 1998 for Ticlopidine Hydrochloride Tablets, 250 mg. The following are our responses to the major deficiencies noted in the letter.

1. **Comment**

Page(s) 1

Contain Trade Secret, Commercial/Confidential Information and are not releasable.

7/30/98

22. Labeling Deficiencies

Response:

Final printed labels and labeling have been revised to include your observations and are being

submitted ***(ATTACHMENT 15)***. To facilitate review of this submission, included is a side by side comparison of the current insert and the last submission with all the differences annotated and explained ***(ATTACHMENT 16).*** Also included is the Patient Package Insert (PPI) and our plans for supplying the PPI with our product ***(ATTACHMENT 17).***

We hope that our responses satisfactorily address the deficiencies noted in your letter. If you need further information or clarification, please do not hesitate to call me at (718) 276-8607 ext.404.

Sincerely,
Eon Labs Manufacturing, Inc.

Eva Sultana Khan .
Eva Sultana Khan, M.S.
Regulatory Affairs Associate

Eon Labs
The Pharmacy Drug Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laurelton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

April 30, 1998

ORIG AMENDMENT

Jerry Phillips
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research
Food and Drug Administration
Metro park North II
7500 Standish Place, Room 150
Rockville, MD 20855

Re: General Correspondence - Patent Amendment
Ticlopidine Hydrochloride Tablets, 250 mg
ANDA 75-326

Dear Mr. Phillips:

As a follow up to our letter dated March 20, 1998, we are submitting a copy of the return receipt from SYNTEX (U.S.A.) INC., 3401 Hillview Avenue, P.O. Box 10850 Palo Alto, CA 94303. This indicates that they have been notified as per 21CFR 314.95 (a) and (c) of the filing of our Ticlopidine Hydrochloride Tablets, 250 mg, ANDA 75-326 application.

Sincerely,
Eon Labs Manufacturing, Inc.

Sadie M. Ciganek
Vice President, Regulatory Affairs

RECEIVED
MAY 0 5 1998
GENERIC DRUGS

ANDA 75-326

Eon Labs Manufacturing, Inc.
Attention: Sadie M. Ciganek
227-15 North Conduit Avenue
Laurelton, New York 11413

FEB 26 1998

Dear Madam:

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 also made to the telephone conversation dated February 19, 1998 and your correspondence dated February 20, 1998.

NAME OF DRUG: Ticlopidine Hydrochloride Tablets, 250 mg

DATE OF APPLICATION: January 30, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: February 2, 1998

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:

Kassandra Sherrod
Project Manager
(301) 827-5849

Sincerely yours,

/S/

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

cc:

5/98

Eon Labs
A Health Care Company

Eon Labs Manufacturing, Inc.
227-15 N. Conduit Avenue
Laureiton, NY 11413
Telephone 718 276-8600
Fax 718 949-3120

January 30, 1998

Douglas L. Sporn
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Document Control Room
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855-2773

RE: Original ANDA
Ticlopidine Hydrochloride Tablets, 250 mg

Dear Mr. Sporn:

Pursuant to section 505(j) of the Federal Food, Drug and Cosmetic Act, enclosed is an original Abbreviated New Drug Application for Ticlopidine Hydrochloride Tablets, 250 mg. This application consists of the following volumes:

Volume 1 Debarment, patent and exclusivity certifications, Section 505(j)(2)(A) information, labeling, dissolution profiles, certificates of analysis, and components and composition.

Volume 2 Raw material control data, manufacturing and packaging data including executed batch records.

Volume 3 Container/closure, finished product control, methods validation, stability data, control numbers, samples, and environmental impact statement.

Volume 4 through 15 Biostudy summary and test results

A full table of content precedes each appropriately paginated volume.

In addition to the archival and review copies, we are submitting a certified true copy of the chemistry, manufacturing and controls data to the District Field Office, Brooklyn, New York. Subsequent amendments or supplements containing chemistry, manufacturing and controls data will also be submitted to the District Field Office.

If there are any comments or questions about this application, please contact me at (718) 276-8600, extension 330.

Sincerely,
Eon Labs Manufacturing, Inc.

Sadie M. Ciganek
Vice President Regulatory Affairs
Eon Labs Manufacturing, Inc.