

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

Approval Package for:

APPLICATION NUMBER:

83-133

Generic Name: Folic Acid 1mg Tablets

Sponsor: Tablicaps, Inc.

Approval Date: April 24, 1973

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

83-133

CONTENTS

Reviews / Information Included in this ANDA Review.

Approval Letter(s)	X
Tentative Approval Letter(s)	
Final Printed Labeling	X
CSO Labeling Review(s)	X
Medical Officer Review(s)	
Chemistry Review(s)	X
Microbiology Review(s)	
Bioequivalence Review(s)	
Administrative Document(s)	X
Correspondence	X

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

83-133

APPROVAL LETTER

O
NDA 83-133

AF: None

APR 24 1973

Tablicaps, Inc.
Attention: Mr. Richard T. Jackson
P.O. Box 5555
Franklinville, New Jersey 08322

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1.0 mg.

We have completed the review of this abbreviated new drug application and have concluded that the drug is safe and effective for use as recommended in the submitted labeling. Accordingly, the application is approved.

Any significant change in the conditions outlined in this abbreviated new drug application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 130.9 of the new drug regulations.

This Administration should be advised of any change in the marketing status of this drug.

The enclosures summarize the conditions relating to the approval of this application.

The communication dated March 15, 1973, pertaining to the distributor, Columbia Medical Company, will be handled in another communication.

cc:

NWK-DO

Dup BD-69 BD-66 BD-106 BD-242 BD-100 BD-310

JHEilert/JLMeyer/RJWolters/4-16-73

R/D init. JLMeyer/4-16-73

Final typing/rt/4-18-73

Approved

JHEilert
4-19-73
JLMeyer
4/23/73

Sincerely yours,

Marion Seide for
Paul A. Bryan, M.D.

Director

Drug Efficacy Study Implementation

Project Office

Bureau of Drugs

Enclosures:

Records and Reports Requirement

Conditions of Approval of a New Drug Application

RJWolters
4-18-73

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

83-133

FINAL PRINTED LABELING

FOLIC ACID

DESCRIPTION

Each scored tablet contains 1.0 mg. of Folic acid, also known as pteroyl-glutamic acid.

ACTIONS

Folic acid is one of the hematopoietic factors necessary for normal red cell development. The exact mechanism of action is not clearly understood at this time.

INDICATIONS

Folic acid is effective in the treatment of megaloblastic anemias due to a deficiency of folic acid as may be seen in tropical or non-tropical sprue, in anemias of nutritional origin, pregnancy, infancy, or childhood.

WARNINGS

Folic acid alone is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where vitamin B₁₂ is deficient.

PRECAUTIONS

Folic acid especially in doses above 1.0 mg. daily may obscure pernicious anemia, in that hematologic remission may occur while neurological manifestations remain progressive.

ADVERSE REACTIONS

Allergic sensitization has been reported following both oral and parental administration of folic acid.

DOSAGE AND ADMINISTRATION

Oral administration: Folic acid is well absorbed and may be administered orally with satisfactory results except in severe instances of intestinal malabsorption.

Usual therapeutic dosage: In adults: 0.25 mg. to 1.0 mg. daily. In children (regardless of age): 0.25 to 1.0 mg. daily. Resistant cases may require larger doses.

Maintenance dosage: When clinical symptoms have subsided and the blood picture has become normal, a maintenance dose of 0.1 mg. to 0.25 mg. daily should be used, but never less than 0.1 mg. per day. Patients should be kept under close supervision and adjustment of the maintenance dose made if relapse appears imminent.

In the presence of alcoholism, pregnancy, hemolytic anemia, anticonvulsant therapy, or chronic infection, the maintenance dose should be at least doubled.

How supplied:

Compressed tablets bottled in 100's and 1000's.

TC R 9/12/72

**APPEARS THIS WAY
ON ORIGINAL**

Control No.

FOLIC ACID

U.S.P.

1 mg.

A
S
T
X

1000 TABLETS

Mfg. by Tablicaps, Inc.
Franklinville, N.J. 08322

Caution: Federal law prohibits
dispensing without prescription.

See insert for full particulars

Control No.

FOLIC ACID

U.S.P.

1 mg.

A
S
T
X

100 TABLETS

Mfg. by Tablicaps, Inc.
Franklinville, N.J. 08322

Caution: Federal law prohibits
dispensing without prescription.

See insert for full particulars

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

83-133

CSO LABELING REVIEW(S)

REVIEW OF RESUBMISSION

DATE COMPLETED: 11-21-72

ANDA #: 83-133

F.R. DATE: 4-9-71

CO. NAME: Tablicaps, Inc.
Blackwood Road
Franklinville, N.J. 08322

NAME OF DRUG: Trade & Generic: Folic Acid Tablets, 1 mg. U.S.P.
in bottles of 100 and 1,000

DATE OF SUBMISSION: 11-3-72

TYPE OF SUBMISSION: FPL container labels.

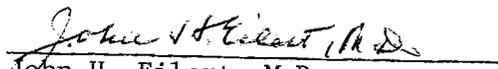
CLINICAL EVALUATION:

1. Review of Studies: Chemist to review.
2. Review of Labeling:
I Immediate container: Approvable.

Package insert: Approved by M.D. review of 10-3-72.

CONCLUSION: 1. Requires chemist review.
2. Labeling approvable.

RECOMMENDATIONS: 1. Approve labeling.
2. Chemist to review.



John H. Eilert, M.D.

cc:
Dup
BD-69
JHEilert/wlb/11-22-72

REVIEW OF ANDA

DATE COMPLETED: 8-11-72

ANDA #: 83-133

F.R. DATE: 4-9-71

CO. NAME: Tablicaps, Inc.
Blackwood Road
Franklinville, N.J. 08322

NAME OF DRUG: Trade & Generic: Folic Acid Tablets 1 mg. U.S.P.
in bottles of 100 and 1,000

DATE OF SUBMISSION: JULY 13, 1972

TYPE OF SUBMISSION: ANDA

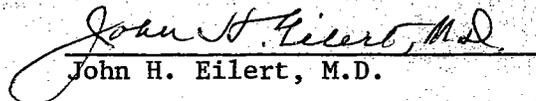
CLINICAL EVALUATION:

1. Review of Studies: Bioavailability study requirement deferred.
Chemist to review.

2. Review of Labeling: Container labels acceptable.
Package insert: Remove ~~_____~~
paragraph from Dosage and Administration. Provide
a How Supplied section.

- CONCLUSION:
1. Chemist to review.
 2. Acceptable container labels.
 3. Unacceptable insert.

- RECOMMENDATIONS:
1. Review by chemist.
 2. Approve container labels.
 3. Improve insert as detailed above.


John H. Eilert, M.D.

cc:
Dup
BD-69
John H. Eilert, M.D./kim/8-14-72

REVIEW OF RESUBMISSION

DATE COMPLETED: 10-3-72

ANDA #: 83-133

F.R. DATE: 4-9-71

CO. NAME: Tablicaps, Inc.
Blackwood Road
Franklinville, N.J. 08322

NAME OF DRUG: Trade & Generic: Folic Acid Tablets, 1 mg. U.S.P.
in bottles of 100 and 1,000

DATE OF SUBMISSION: 9-15-72

TYPE OF SUBMISSION: Revised FPL (9-12-72) and manufacturing data
in response to FDA 9-8-72 communication.

CLINICAL EVALUATION:

Review of Studies: Chemist to review

Review of Labeling:

PACKAGE INSERT: Approvable

CONCLUSION: 1. Chemist to evaluate submitted data.
2. Insert approvable.

RECOMMENDATION: 1. Review by chemist.
2. Approve insert.


John H. Eilert, M.D.

cc:
Dup
BD-69
John H. Eilert, M.D./kim/10-3-72

REVIEW OF AMENDMENT

DATE COMPLETED: 3-22-73

ANDA #: 83-133

F.R. DATE: 4-9-71

CO. NAME: Tablicaps, Inc.
Blackwood Road
Franklinville, N.J. 08322

NAME OF DRUG: Trade:
& Folic Acid Tablets 1 mg. U.S.P. in bottles of 100
Generic:

DATE OF SUBMISSION: 3-14-73

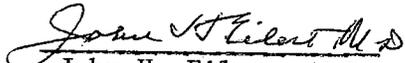
TYPE OF SUBMISSION: _____

CLINICAL EVALUATION:

1. Review of Studies: Chemist to evaluate
2. Review of Labeling: Container labels submitted for bottles of 100 tablets. Insert lists 100 and 1,000 tablet bottles. Discrepancy present, otherwise approvable.

- CONCLUSION:
1. Requires chemist review.
 2. Discrepancy in quantity availability.
 3. Preparation has not been approved.

- RECOMMENDATIONS:
1. Review by chemist.
 2. Request reconciliation of quantity availability between container and insert labeling.


John H. Eilert, M.D.

cc:
Dup
BD-69
JHEilert/rt/3-26-73

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

83-133

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
4-9-71

NDA Number
83-133
Cover letter
7-13-72

Name & Address of Applicant (City & State)
Tablicaps, Inc.
P.O. Box 5555
Franklinville, New Jersey 08322

Original
Amendment
Supplement
Other

Name of Drug
Nonproprietary Name
Folic Acid

Purpose of Supplement

Date(s) of Submission(s)

Pharmacological Category
Vitamin
How Dispensed
R_x O.T.C.

AF Number

Dosage Form(s)
Tablet
Potency (ies)
1.0 mg.

Related NDA & MF

Satisfactory Labeling
 Date Due To be revised (JHEilert)

Satisfactory Components, Composition, Manufacturing and Controls
 Date Due See below

Satisfactory Biologic Availability
 Date Due NA
Is data on current formulation? YES NO

Satisfactory Probably or Possibly Effective Indications
 (if in labeling)
Date Data Due

Establishment Inspection
Satisfactory 10-21-71 per TWX 7-72
Tablicaps Unsatisfactory 4-5 to 12-72

Relabeling of drug in commercial channels required?
so, what level: YES NO

- Remarks
- Request:
1. Revise labeling per MO's review.
 2. Sign form FD 360 to be submitted.
 3. Full list of articles used as components.
 4. Name of other labs if use.
 5. Clarify omission of residue of Ignition test on active ingredient.
 6. Clarify term USP XVII for _____ as this is a NF item.
 7. Revise _____, specs for _____ to conform to the third supplement.
 8. A satisfactory inspection.

Conclusions

rev w/f

RJ Walters
RJWalters 9-6-72

OWNER: SIGNATURE: DATE:

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
4-9-71

NDA Number
83-133

Name & Address of Applicant (City & State)
Tablicaps, Inc.
P.O. Box 5555
Franklinville, New Jersey 08322

Original _____
Amendment 9-18-72

Cover letter 9-15-72
Supplement _____

Name of Drug

Nonproprietary Name
Folic Acid

Other _____

Purpose of Supplement
Printed package insert and manufacturing information.

Date(s) of Submission(s)

Pharmacological Category
Vitamin

How Dispensed
R_x O.T.C.

AF Number _____

Dosage Form(s)
Tablet

Potency (ies)
1.0 mg.

Related NDA & MF

Satisfactory Labeling
 Date Due Satisfactory

Satisfactory Components, Composition, Manufacturing and Controls
 Date Due See below

Satisfactory Biologic Availability
 Date Due NA
Is data on current formulation? YES NO

Satisfactory Probably or Possibly Effective Indications
 (if in labeling)
Date Data Due _____

Establishment Inspection
Satisfactory TWX 7-72
Tablicaps Unsatisfactory 4-7-72

Recalls

If relabeling of drug in commercial channels required? YES NO
If so, what level:

Remarks
**Request: 1. 12 copies of container labels/
2. Include the HOW SUPPLIED section the potency of the drug.
3. Specifications for folic acid comply with the NF XIII.
However Folic acid is a USP item.
4. A satisfactory inspection.**

Conclusions **rev w/f**

RJ Walters 10-26-72
RJWalters

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
4-9-71

NDA Number
83-133

Name and Address of Applicant (City and State)
Tablicaps, Inc.
Blackwood Road
Franklinville, New Jersey 08322

Original _____
Amendment 11-3-72

Name of Drug
Folic Acid

Nonproprietary Name
Folic Acid

Supplement _____

Purpose of Supplement
FPL and manufacturing information.

Other _____

Pharmacological Category
Vitamin

How Dispensed
R_x O.T.C.

Date(s) of Submission(s)

Dosage Form(s)
Tablet

Potency (ies)
1 mg.

AF Number
None

Related IND/NDA/MF

Satisfactory Labeling
Date Due **Satisfactory (JHEilert)**

Satisfactory Components, Composition, Manufacturing and Controls
Date Due **Satisfactory**

Satisfactory Biologic Availability
Date Due **NA**
Is data on current formulation? YES NO

Satisfactory Probably or Possibly Effective Indications (if in labeling)
Date data Due _____

Establishment Inspection
Satisfactory TWX 7-11-72
Tablicaps Unsatisfactory 4-72
Requested inspection 12-11-72

Recalls

Is relabeling of drug in commercial channels required? YES No
If so, what level?

Remarks
Request a satisfactory inspection.

Conclusions
rev w/f

RJWalters 12-13-72
RJWalters

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
4-9-71

ORIGINAL

SUPPLEMENT

Name & Address of Applicant (City & State)

Tablicaps, Inc.
P.O. Box 5553
Franklinville, New Jersey 08322

NDA Number
83-133

Supplement Date and Number

Name of Drug

Nonproprietary Name

Amendment Date(s)

Folic Acid

Purpose of Supplement

Other Date(s)

Pharmacological Category

Vitamin

How Dispensed

R_x

Q.T.C.

AF Number

Related IND/NDA/ME(s)

Dosage Form(s)

Tablet

Potency (ies)

1.0 mg.

Satisfactory

Labeling

Date Due Satisfactory (JHEilert)

Satisfactory

Components, Composition, Manufacturing and Controls

Date Due Active ingredient and drug dosage form complies to USP specs.

Satisfactory

Biologic Availability

Date Due NA

Is data on current
formulation? YES NO

Satisfactory

Probably or Possibly Effective Indications

(if in labeling)

Date Data Due

Establishment Inspection

Satisfactory 7-72

Recalls

Tablicaps Satisfactory BD 340 memo 4-12-73

If relabeling of drug in commercial channels required? YES NO

If so, what level:

Remarks

APPEARS THIS WAY
ON ORIGINAL

Conclusions

Approval

RJWalters
RJWalters 4-18-73

REVIEWER:

SIGNATURE:

DATE:

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

83-133

**ADMINISTRATIVE
DOCUMENTS**

ORIG.

NOTICE OF APPROVAL NEW DRUG APPLICATION OR SUPPLEMENT		NDA NUMBER 83-133
		DATE APPROVAL LETTER ISSUED APR 24 1973
TO: Press Relations Staff (CE-300)	FROM: <input checked="" type="checkbox"/> Bureau of Medicine <input type="checkbox"/> Bureau of Veterinary Medicine	
ATTENTION		
Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.		
TYPE OF APPLICATION <input type="checkbox"/> ORIGINAL NDA <input checked="" type="checkbox"/> ABBREVIATED ORIGINAL NDA <input type="checkbox"/> SUPPLEMENT TO NDA		CATEGORY <input checked="" type="checkbox"/> HUMAN <input type="checkbox"/> VETERINARY
TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG Folic Acid		
DOSAGE FORM Tablet	HOW DISPENSED <input checked="" type="checkbox"/> RX <input type="checkbox"/> OTC	
ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.) Folic Acid 0.1 mg.		
NAME OF APPLICANT (Include City and State) Tablicaps, Inc. Franklinville, New Jersey 08322		
PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY Vitamin		
COMPLETE FOR VETERINARY ONLY		
ANIMAL SPECIES FOR WHICH APPROVED		
COMPLETE FOR SUPPLEMENT ONLY		
CHANGE APPROVED TO PROVIDE FOR		
APPEARS THIS WAY ON ORIGINAL		
FORM PREPARED BY		
NAME R.J. Wolters	DATE	
FORM APPROVED BY		
NAME J.L. Meyer	DATE	

APPROVAL OF ORIGINAL ABBREVIATED NDA

12/18/72

STANLEY A. STRINGER

443-4320

XX

FOOD AND DRUG ADMINISTRATION
NEWARK DISTRICT NWC-050APPLICANT:
TABLICAPS, INC.
FRANKLINVILLE, N.J.
APR NONERE: ANDA 83-133 FOLIC ACID TABLETS
NANDA

THE DESI PROJECT OFFICE IS PRESENTLY CONSIDERING APPROVAL OF THE SUBJECT ABBREVIATED NEW DRUG APPLICATIONS. THESE PRODUCTS ARE TO BE MANUFACTURED AND PACKAGED BY TABLICAPS, INC.

AS YOU ARE AWARE IN THE ANDA THE FIRM CERTIFIES THAT MANUFACTURING, PACKAGING AND TESTING ARE DONE IN CONFORMITY WITH GMP (SEE 130.4(F) OF THE NEW DRUG REGULATIONS REFERENCE ANDAS, PUBLISHED IN THE FEDERAL REGISTER ON APRIL 24, 1970).

WE NOTE YOUR 4/7-12/72 INSPECTION REPORT INDICATES REINSPECTION WAS SCHEDULED FOR OCTOBER 1972. WE REQUEST AN EVALUATION OF THE FIRM'S PRESENT COMPLIANCE STATUS UNDER GMP AND ITS ABILITY TO COMPLY WITH ANDA AND COMPENDIUM COMMITMENTS. IF AN INSPECTION IS INDICATED, PLEASE INSPECT AND REPORT RESULTS.

PAGE 2

APPEARS THIS WAY
ON ORIGINAL

IN YOUR REPLY PLEASE INDICATE WHETHER OR NOT THE ANDA CAN BE APPROVED BASED UPON THE FIRM'S COMPLIANCE WITH GMP. A RECOMMENDATION TO WITHHOLD APPROVAL SHOULD BE BASED UPON CRITICAL OR SIGNIFICANT DEVIATIONS FROM GMP WHICH SHOULD BE LISTED.

WE WOULD APPRECIATE A REPLY BY TWA FOLLOWED BY EIR OR MEMO.

DATA CONTROL CODE: BD-105-054

ESTIMATED TIME: 32 HOURS IF EI NEEDED

REPLY REQUESTED BY: FEBRUARY 4, 1973, IF EI NEEDED

CHARGE TO: BD-100

CONTACT OFFICER: ROBERT J. WOLTERS
PHONE: 301-443-4040

ENDORSE REPORT TO: BD-105

CLEARANCE OFFICER: STANLEY A. STRINGER
OFFICE OF SCIENTIFIC EVALUATION
PHONE: 301-443-4320

CC:
NWK-D50
NYK-F1

BD-100
BD-105
BD-106
BD-69

CA-224
RO-100
BD-69 RJWOLTERS
BD-105 SASTRINGER:JK:12/18/72

FOLIC ACID PREPARATIONS, ORAL AND PARENTERAL FOR THERAPEUTIC USE

Uses for Human Use; Drug Efficacy Study Implementation

The Food and Drug Administration has evaluated reports received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following folic acid preparations:

1. a. Folvite Elixir; 5 mg. folic acid per 5 cc.;
- b. Folvite Tablets; 5 mg. and 20 mg. folic acid per tablet; and
- c. Folvite Parenteral Solution; sodium folate equivalent to 15 mg. folic acid per cc.; marketed by Lederle Laboratories, Pearl River, New York 10965 (NDA 5-897).

2. Folic Acid Tablets; 5 mg. per tablet; marketed by Eli Lilly and Co., Box 618, Indianapolis, Indiana 46206 (NDA 6-135).

3. Folic Acid Injection; 15 mg. folic acid, as the sodium salt, per cc.; marketed by S. F. Durst and Co., Inc., 5317 North Third Street, Philadelphia, Pennsylvania 19120 (NDA 6-333).

In addition to the above products, folic acid preparations for therapeutic use are marketed by other firms. A partial list of other suppliers of folic acid preparations limited to prescription dispensing, as indicated in readily available reference sources, is as follows:

- ABA Pharmaceutical Co., Division of Bergher Distributing Co.
- American Pharmaceutical Co.
- American Drug Products.
- American Quinine Co.
- Approved Pharmaceutical Corp.
- Arcum Pharmaceutical Corp.
- Associated Labs., Inc.
- Barre Drug Co., Inc., The.
- Barry-Martin Pharmaceuticals, Inc.
- Bell Pharmaceutical Co.
- Carroll Chemical Co., The.
- Columbia Medical Co.
- Consolidated Midland Corp., CMC Research Division.
- Corvit Pharmaceuticals.
- Daniels, Robert and Co., Inc.
- DuMont Pharmaceutical Co., Inc.
- Evron Pharmaceutical Co., Inc.
- Faraday Laboratories, Inc.
- Gold Leaf Pharmacal Co., Inc.
- Gotham Pharmaceutical Co., Inc.
- Halsey Drug Co., Inc.
- Harvey Labs., Inc.
- Jan Labs.
- Kirkman Labs., Inc.
- Launett Co., Inc.
- Let Drug Co.
- Lustgarten Laboratories, Inc.
- Millin, McCambridge Co., Inc.
- Penhurst Pharmacal Co.
- Pharmex, Inc.
- Preston Franklin Pharmacal Co.
- Richlyn Labs.
- Robinson Laboratory, Inc.
- Spencer-Mead, Inc.
- Stanlabs, Inc.
- Supreme Pharmaceutical Co., Inc.
- Thompson, Wm. T., Co.
- Towne, Paulson and Co., Inc.
- Vitamin Research Corp.
- Vita-Pore Products Co.

The drugs are regarded as new drugs (21 U.S.C. 321(p)). Supplemental new-drug applications are required to revise the labeling in and to update previously approved applications providing for such drugs. A new-drug application is required from any person marketing such drugs without approval.

The Food and Drug Administration is prepared to approve new-drug applications and supplements to previously approved new-drug applications under conditions described in this announcement.

A. Effectiveness classification. The Food and Drug Administration has considered the Academy reports, as well as other available evidence, and concludes that:

1. Folic acid is effective for the treatment of megaloblastic anemias of tropical and nontropical sprue, nutritional origin, pregnancy, infancy, and childhood.

2. There is a lack of substantial evidence that folic acid is effective for the following labeled indications: "macrocytic anemias associated with pellagra and similar deficiency states" and such vague, unspecific conditions as "macrocytic anemia of gastrointestinal origin" and "megaloblastic anemias other than pernicious anemia."

The Food and Drug Administration also concludes that there is no evidence that doses of folic acid greater than 1 mg. daily have greater efficacy than do those of 1 mg. Further, the usual therapeutic dose, oral or parenteral, should be 0.25 mg. to 1.0 mg. daily, and the maintenance dose should ordinarily be 0.1 to 0.25 mg. daily. Administration of higher doses greatly increases the possibility of masking vitamin B-12 deficiencies and the insidious development of or precipitation of neurological manifestations and/or lesions.

Preparations supplying no more than 0.1 mg. folic acid daily continue to be regarded as dietary supplements (21 CFR 3.42) and may be prescribed when a maintenance dose of 0.1 mg. a day is indicated.

B. Form of drug. Folic acid preparations are in (1) tablet form suitable for oral administration and contain no less than 0.15 mg. and no more than 1.0 mg. folic acid per tablet or (2) solution form suitable for parenteral administration in the dosages recommended in the labeling guidelines below.

C. Labeling conditions. 1. The label bears the statement "CAUTION: Federal law prohibits dispensing without prescription."

2. The drug is labeled to comply with all requirements of the Act and regulations promulgated thereunder, and those parts of its labeling indicated below are substantially as follows: (Optional additional information, applicable to the drug, may be proposed under other appropriate paragraph headings and should follow the information set forth below.)

(To be supplied by the manufacturer. This is to be confined to an appropriate description of the physical and chemical properties of the drug, and the formulation.)

ACTIONS

(To be supplied by the manufacturer. This is to be confined to an appropriate statement of the demonstrated pharmacologic/physiologic actions of the active ingredients of the drug in humans. When the mode of action has not been determined, this should be clearly indicated.)

INDICATIONS

Folic acid is effective in the treatment of megaloblastic anemias due to a deficiency of folic acid as may be seen in tropical or nontropical sprue, in anemias of nutritional origin, pregnancy, infancy, or childhood.

WARNINGS

Folic acid alone is improper therapy in the treatment of pernicious anemia and other megaloblastic anemias where vitamin B₁₂ is deficient.

PRECAUTIONS

Folic acid especially in doses above 1.0 mg. daily may obscure pernicious anemia, in that hematologic remission may occur while neurological manifestations remain progressive.

ADVERSE REACTIONS

Allergic sensitization has been reported following both oral and parenteral administration of folic acid.

DOSAGE AND ADMINISTRATION

Oral administration: Folic acid is well absorbed and may be administered orally with satisfactory results except in severe instances of intestinal malabsorption.

Parental administration: Intramuscular, intravenous, and subcutaneous routes may be used if the disease is exceptionally severe, or if gastrointestinal absorption may be, or is known to be, impaired.

Usual therapeutic dosage: In adults: 0.25 mg. to 1.0 mg. daily. In children (regardless of age): 0.25 to 1.0 mg. daily. Resistant cases may require larger doses.

Maintenance dosage: When clinical symptoms have subsided and the blood picture has become normal, a maintenance dose of 0.1 mg. to 0.25 mg. daily should be used, but never less than 0.1 mg. per day. Patients should be kept under close supervision and adjustment of the maintenance dose made if relapse appears imminent.

In the presence of alcoholism, pregnancy, hemolytic anemia, anticonvulsant therapy, or chronic infection, the maintenance dose should be at least doubled.

D. Previously approved applications.

1. Each holder of a "deemed approved" new-drug application (i.e., an application which became effective on the basis of safety prior to October 10, 1962) for such drug is requested to seek approval of the claims of effectiveness and bring the application into conformance by submitting supplements containing:

a. Revised labeling as needed to conform to the labeling conditions described herein for the drug, and complete current container labeling, unless recently submitted.

b. Updating information as needed to provide for an oral dosage form containing no less than 0.15 mg. and no more than 1.0 mg. folic acid per tablet or a

0.15

parenteral dosage form containing an amount appropriate for administration as described herein, and to make the application current in regard to items 6 (components), 7 (composition), and 8 (methods, facilities, and controls) of the new-drug application form FD-356H to the extent described for abbreviated new-drug applications, § 130.4(f), published in the FEDERAL REGISTER April 24, 1970 (35 F.R. 6574). (One supplement may contain all the information described in this paragraph.)

2. Such supplements should be submitted within the following time periods after the date of publication of this notice in the FEDERAL REGISTER:

a. 60 days for revised labeling; or, for those products which must be reformulated, 180 days for revised labeling fully in accord with this announcement, provided claims for which substantial evidence of effectiveness is lacking are deleted within 60 days. The supplements should be submitted under the provisions of § 130.9 (d) and (e) of the new-drug regulations (21 CFR 130.9) which permit certain changes to be put into effect at the earliest possible time.

b. 180 days for updating information.

3. Marketing of the drug may continue until the supplemental applications submitted in accord with the preceding subparagraphs 1 and 2 are acted upon, provided that the labeling of the preparation shipped within the jurisdiction of the Act is in accord with the labeling conditions described in this announcement within the time periods described in subparagraph 2a.

E. *New applications.* 1. Any person who distributes or intends to distribute such drug which is intended for the conditions of use for which it has been shown to be effective, as described under A1 above, should submit an abbreviated new-drug application meeting the conditions specified in § 130.4(f) (1) and (2), published in the FEDERAL REGISTER April 24, 1970 (35 F.R. 6574). Such applications should include proposed labeling which is in accord with the labeling conditions described herein.

2. Distribution of any such preparation currently on the market without an approved new-drug application may be continued provided that:

a. Within 60 days from the date of publication of this announcement in the FEDERAL REGISTER, the labeling of such preparation shipped within the jurisdiction of the Act is in accord with the labeling conditions described herein, except that if the preparation must be reformulated, 180 days will be allowed for the dosage recommendations to be in accord with this announcement.

b. The manufacturer, packer, or distributor of such drug submits, within 180 days from the date of this publication, a new-drug application to the Food and Drug Administration.

c. The applicant submits within a reasonable time additional information that may be required for the approval of the application as specified in a written communication from the Food and Drug Administration.

d. The application has not been ruled incomplete or unapprovable.

F. *Opportunity for a hearing.* 1. The Commissioner of Food and Drugs proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act withdrawing approval of all new-drug applications and all amendments and supplements thereto providing for the indications for which substantial evidence of effectiveness is lacking as described in paragraph A2 of this announcement. An order withdrawing approval of the applications will not issue if such applications are supplemented, in accord with this notice, to delete such indications. Promulgation of the proposed order would cause any such drug for human use offered for the indications for which substantial evidence of effectiveness is lacking, to be a new drug for which an approved new-drug application is not in effect. Any such drug then on the market would be subject to regulatory proceedings.

2. In accordance with the provisions of section 505 of the Act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Part 130), the Commissioner will give the holders of any such applications, and any interested person who would be adversely affected by such an order, an opportunity for a hearing to show why such indications should not be deleted from labeling. A request for a hearing must be filed within 30 days after the date of publication of this notice in the FEDERAL REGISTER. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing, together with a well-organized and full-factual analysis of the clinical and other investigational data the objector is prepared to prove in a hearing. Any data submitted in response to this notice must be previously unsubmitted and include data from adequate and well-controlled clinical investigations (identified for ready review) as described in § 130.12(a) (5) of the regulations published in the FEDERAL REGISTER of May 8, 1970 (35 F.R. 7250). Carefully conducted and documented clinical studies conducted under uncontrolled or partially controlled situations are not acceptable as a sole basis for approval of claims of effectiveness, but such studies may be considered on their merits for corroborative support of efficacy and evidence of safety. If a hearing is requested and justified by the response to this notice, the issues will be defined, a hearing examiner will be named, and he shall issue a written notice of the time and place at which the hearing will commence.

G. *Unapproved use or form of drug.* 1. If the article is labeled or advertised for use in any condition other than those provided for in this announcement, it may be regarded as an unapproved new drug subject to regulatory proceedings until such recommended use is approved in a new-drug application, or is otherwise in accord with this announcement.

2. If the article is proposed for marketing in another form or for use other than

the use provided for in this announcement, appropriate additional information as described in § 130.4 or § 130.9 of the regulations (21 CFR 130.4, 130.9) may be required, including results of animal and clinical tests intended to show whether the drug is safe and effective.

Representatives of the Administration are willing to meet with any interested person who desires to have a conference concerning proposed changes in the labeling set forth herein. Requests for such meetings should be made to the Office of Scientific Evaluation at the address given below, within 30 days after the publication of this notice in the FEDERAL REGISTER.

A copy of the NAS-NRC report has been furnished to each firm referred to above. Any other interested person may obtain a copy by request to the appropriate office named below.

Communications forwarded in response to this announcement should be identified with the reference number DESI 5397, directed to the attention of the following appropriate office, and addressed (unless otherwise specified) to the Food and Drug Administration, 5650 Fishers Lane, Rockville, Maryland 20852:

Supplements (Identify with NDA number):
Office of Scientific Evaluation (BD-100),
Bureau of Drugs.

Original abbreviated new-drug applications (Identify as such): Drug Efficacy Study Implementation Project Office (BD-5), Bureau of Drugs.

Request for Hearing (Identify with Docket number): Hearing Clerk, Office of General Counsel (GC-1), Room 6-62, Parklawn. All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (BD-5), Bureau of Drugs.

Requests for NAS-NRC report: Press Relations Office (CE-200), 200 C Street SW., Washington, D.C. 20204.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-53, as amended; 21 U.S.C. 352, 355) and under authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: March 19, 1971.

SAM D. FINE,
Associate Commissioner
for Compliance.

[FR Doc. 71-4952 Filed 4-8-71; 2:46 am]

[DESI 10423]

LEVALLORPHAN TARTRATE INJECTION

Drugs for Human Use; Drug Efficacy
Study Implementation

The Food and Drug Administration has evaluated a report received from the National Academy of Sciences-National Research Council, Drug Efficacy Study Group, on the following drug for intravenous use:

Lorfan Injection, containing levallorphan tartrate; Roche Laboratories, Division of Hoffman-LaRoche, Inc., 310 Kingsland Street, Nutley, New Jersey 07110 (NDA 10-423).

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

83-133

CORRESPONDENCE



83-133
ABBREVIATED
NEW DRUG APPLICATION

For Quality Generic Pharmaceuticals

July 13, 1972

Letter Ref: 7-72-T2-T5-10

Food and Drug Administration
Bureau of Drugs
5600 Fishers Lane
Rockville, Maryland 20852

Gentlemen:

We are hereby submitting, in triplicate, our Abbreviated New Drug Application for Folic Acid 1.0 Mg. Compressed Tablets for your review and consideration.

This submission, as well as similar documents submitted by Tablicaps, attempts to conform to the requirements of the Drug Efficacy Study Implementation Programs. It should be noted that Tablicaps questions the legality and intent of these requirements, however Tablicaps has no recourse at this time, except object to, but comply with these requirements.

We thank you for giving this matter your attention and look forward to hearing from you in the very near future since we are preparing a marketing program for this product.

Very truly yours,

TABLICAPS, INC.

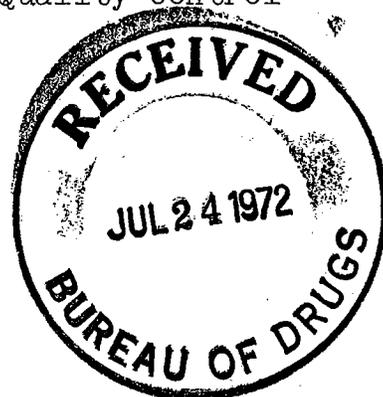
Robert L. Pillarella
President

Richard T. Jackson
Director of Quality Control

RLP/RTJ:kc

Enclosures

RECEIVED / COPY
PHOTOSTATS OF
COVER LETTER MADE
FOR DUP _____ TRIP _____



JUL 28 1972

NDA 83-133

AF None

Tablicaps, Inc.
Attention: Mr. Robert L. Pillarella
P.O. Box 5555
Blackwood Road
Franklinville, New Jersey 08322

Gentlemen:

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

NAME of DRUG: Folic Acid Tablets, 1 mg.

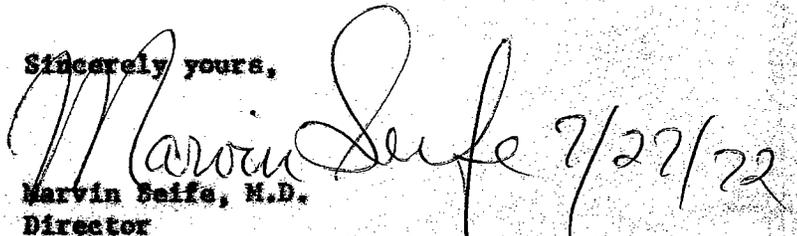
DATE of COVER LETTER: July 13, 1972

DATE of RECEIPT: July 24, 1972

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 NDA number shown above.

Sincerely yours,



Marvin Seife, M.D.
Director
Division of Actions Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:

NWK-DO

Dup

BD-69

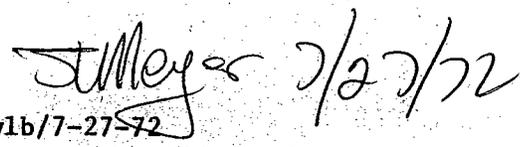
BD-66

BD-406

BD-310

JIMeyer/wlb/7-27-72

Ack.



SEP 8 1972

Tablicaps, Inc.
Attention: Mr. Richard T. Jackson
P.O. Box 5555
Blackwood Road
Franklinville, New Jersey 08322

Gentlemen:

Reference is made to your abbreviated new drug application, cover letter dated July 13, 1972, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1.0 mg.

We have completed the review of this abbreviated new drug application and have the following comments regarding the proposed labeling:

Package insert:

- 1) Delete the _____ paragraph from the DOSAGE and ADMINISTRATION section.
2. Include a HOW SUPPLIED section.

Other information required by section 130.4(f) of the regulations:

1. The signature of the applicant or responsible official or agent on a completed form FD 356H. Four copies are enclosed for your convenience. ✓
2. A full list of articles used as components of the drug. ✓
3. If you elect to employ a laboratory other than _____, the regulation requires the name of the laboratory and a certification statement from the laboratory be submitted as part of your abbreviated new drug application.

APPEARS THIS WAY
ON ORIGINAL

4. Procedures that assure that the components will comply with the specifications and tests described in an official compendium if such article is recognized therein, or, if not listed or if the article differs from the compendium drug, that the specifications and tests applied to the components are adequate to assure their identity, strength, quality, and purity. The following deficiencies are noted:
- a) Clarify the omission of the Residue on Ignition test performed on the component Folic Acid.
 - b) Clarify the term "U.S.P. XVIII" at the top of page 20 "Raw Material Specifications" for the component _____
 - c) Revise the _____ test specification to conform to the N.F. XIII, third supplement, for the component _____

Information in a report of inspection of your facilities, by inspectors of this Administration (covering the methods facilities, and controls used), indicates that there is disagreement between actual current good manufacturing practice and the commitment made in your application. Therefore, before we can take final action on this abbreviated new drug application, we should have a satisfactory inspection report.

A copy of this letter has been sent to our Newark District Office. We recommend that you contact the District and arrange for an inspection after the deficiencies have been corrected.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife 9/7/72
Marvin Seife, M.D.
Director
Division of Actions Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
NW^K-DO
Dup
BD-69
BD-66
BD-106
BD-242

JHEilert/JMeyer/RJWolters/8-31-72

R/D init. by MClark/JMeyer/9-5-72

Final typing/kim/9-6-72

Rev w/p

JMeyer
9/7/72

R.J. Wolters
9-6-72

Rev. w/f

E

P.O. Box 5555
BLACKWOOD ROAD.
FRANKLINVILLE, N.J. 08322



ORIG

**RESUBMISSION
NDA ORIG AMENDMENT**

For Quality Generic Pharmaceuticals

FPL

Letter Ref: 9-72-T5-5

September 15, 1972

Department of Health, Education and Welfare
Public Health Service
Food and Drug Administration
Rockville, Maryland 20852

Gentlemen:

We are hereby submitting in triplicate the following additional information for our Abbreviated New Drug Application No. 83-133 as you requested in your letter of September 8, 1972.

The following comments are submitted as a paragraph by paragraph reply to the above mentioned letter:

1. Package insert:
 - a) Enclosed please find revised copies of our insert for Folic Acid with parental dosage deleted and How Supplied section added.
2. Enclosed please find three signed copies of form FD 365H.
3. Please find on page 24 of our submitted ANDA 83-133 a complete list of articles used as components of the drug.
4.
 - a) A revised Raw Material Specification (see attached) for Folic Acid is being submitted which includes a Residue on Ignition test.
 - b) The term " _____ " for _____ on page 20 was submitted in error. A revised Raw Material Specification for _____ is being submitted (see attached).
 - c) A revised Raw Material Specification _____ is being submitted which includes the 3rd revision for _____

We have contacted the Newark District Office and have requested

Page one of two

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PHOTOSTATS MADE
FOR DUP _____ TRIP _____



Page two of two
September 15, 1972

another inspection of our facilities with special attention to those deficiencies noted in the earlier report.

Very truly yours,

TABLICAPS, INC.

A handwritten signature in cursive script, appearing to read "Richard T. Jackson".

Richard T. Jackson
Director of Quality Control

RTJ:jch

Enclosures

**APPEARS THIS WAY
ON ORIGINAL**

NDA 83-133

AF _____

Tablicaps, Inc.
Attention: Mr. Richard T. Jackson
P.O. Box 5555
Blackwood Road
Franklinville, New Jersey 08322

OCT 30 1972

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1.0 mg.

Reference is also made to your communication dated September 18, 1972, enclosing printed labeling and manufacturing information.

We have completed the review of this abbreviated new drug application and have the following comments regarding the proposed labeling:

1. Submit twelve copies of the container labels for the 100 and 1,000 tablet containers. The labels should be identical in content to the labels submitted on July 13, 1972.
2. At the time of the next printing, it is recommended that the potency of the drug be included in the HOW SUPPLIED section of the package insert.

Regarding the manufacturing information, it is noted that the Raw Material Specifications for Folic Acid comply with the NF XIII. However, Folic Acid is listed in the U.S.P. XVIII. Please clarify.

Also, before we can take final action on this abbreviated new drug application, we should have a satisfactory establishment inspection report, as requested in our letter of September 8, 1972.

Please let us have your response promptly.

cc:
NWK-DO
Dup
BD-69
BD-66
BD-106
BD-242

JHEilert/JLMeyer/RJWalters 10-25-72
R/D init. MClark
Final typing/rt/10-26-72
rev w/f

Sincerely yours,

Marvin Seifs, M.D.

Director

Division of Actions Implementation
Drug Efficacy Study Implementation

Project Office

Bureau of Drugs

Marvin Seifs 10/30/72

JLMeyer 10/30/72 RJ Walters

10-26-72

Rev. w/t

RESUBMISSION
NDA ORIG. AMENDMENT
BLACKWOOD ROAD
FRANKLINVILLE, N.J. 08322

E



FPL
ORIG.

For Quality Generic Pharmaceuticals

Letter Ref: 11-72-T5-7

November 3, 1972

Marvin Seife, M.D.
Director
Division of Actions Implementation
Drug Efficacy Study Implementation Project Office
Bureau of Drugs
Food and Drug Administration
Rockville, Maryland 20852

Gentlemen:

Reference is made to your letter of October 30, 1972, concerning our NDA #83-133 for Folic Acid 1 MG. compressed tablets. The following comments are in response to those points discussed in your letter:

1. Enclosed are twelve copies of the container labels for the 100 and 1000 tablet container. These are identical in content to the labels submitted on July 13, 1972.
2. At the time of our next printing, the potency of the drug will be included in the "How Supplied" section of the package insert.
3. Enclosed are revised Raw Material Specifications for Folic Acid properly listed as U.S.P. XVIII. The previously submitted specifications were improperly headed NF XIII.
4. We have contacted the Newark District Office and are currently awaiting reinspection of our facilities.

Your prompt attention to this matter will be appreciated.

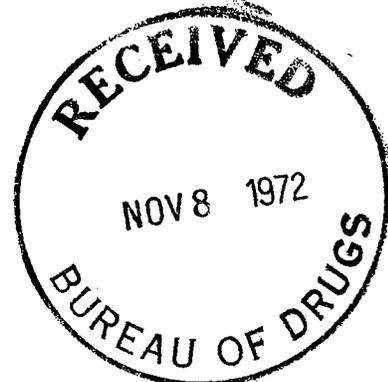
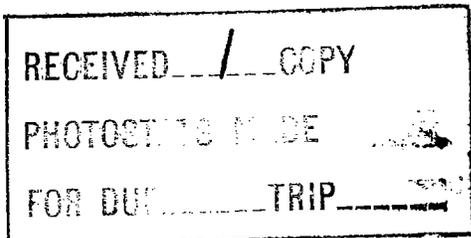
Sincerely yours,

TABLICAPS, INC.

Richard T. Jackson
Director of Quality Control

RTJ/cd

Enclosures



NDA 83-133

AF

DEC 18 1972

Tablicaps, Inc.
Attention: Mr. Richard T. Jackson
P.O. Box 5555
Blackwood Road
Franklinville, New Jersey 08322

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1.0 mg.

Reference is also made to your communication dated November 3, 1972, enclosing printed labeling and manufacturing information.

We have completed the review of this abbreviated new drug application. However, before we are able to reach a final conclusion, it will be necessary for you to have a satisfactory establishment inspection report, as requested in our correspondence since September 8, 1972.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife 12/18/72
Marvin Seife, M.D.

Director
Division of Actions Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
NWK-DO

Dup
BD-69
BD-66
BD-106
BD-242

JHEilert
12-13-72
JHEilert/JLMeyer/RJWolters 12-11-72
R/D init. by MClark/JMeyer
Final typing/wlb/12-13-72

Rev *w/f*

RJ Wolters
12-13-72

Original E

P.O. Box 5555
BLACKWOOD ROAD
FRANKLINVILLE, N.J. 08322



NDA ORIG AMENDMENT

For Quality Generic Pharmaceuticals

EPL

March 15, 1973

Letter Ref: 3-73-T5-16

Department of Health, Education, and Welfare
Public Health Service
Food and Drug Administration
Rockville, Maryland 20852

Gentlemen:

We are submitting, in triplicate, the attached information on behalf of _____ of _____. The purpose of this submission is to supplement our Abbreviated New Drug Application, 83-133, for FOLIC ACID, 1 MG. so that _____ may distribute our product under their label. The product will be manufactured, packaged, and labeled with the copy submitted in this supplement here at TABLICAPS, INC. and shipped to _____ for distribution.

Your prompt review of this information will be greatly appreciated.

Sincerely yours,

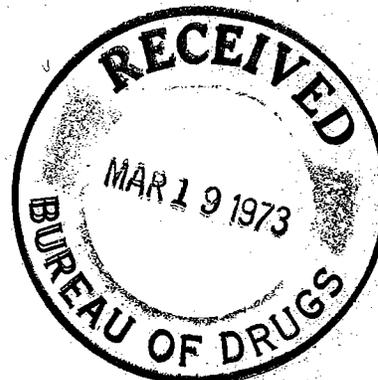
TABLICAPS, INC.

Richard T. Jackson
Director of Quality Control

RTJ/mes

Enclosures

RECEIVED / COPY
PHOTOSTATS MADE
FOR DUP TRIP



NDA 83-133

AF: None

APR 24 1973

Tablicaps, Inc.
Attention: Mr. Richard T. Jackson
P.O. Box 5555
Franklinville, New Jersey 08322

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1.0 mg.

Reference is also made to your communication dated March 15, 1973, enclosing labeling for a _____

The communication provides for you to label the drug with a label showing the _____ to be:



We have completed the review of this communication. However, before we are able to reach a final conclusion, the following additional information is necessary:

1. The application must include a signed statement from the proposed distributor to show that he is regularly and lawfully engaged in the distribution or dispensing of prescription drugs; the category of his operation (repackager, relabeler, wholesaler, retail pharmacy, etc.) and that he agrees to distribute the drug only under the labeling provided for in the application and that no changes will be made in the labeling unless such changes are provided for in a supplement to this application.
2. It is noted that the package insert includes a reference to 100 and 1,000 tablet containers. However, only labels for the 100 tablet containers were submitted. Please clarify.

Please let us have your response promptly.

cc:
NWK-DO
Dup
BD-69 BD-66 BD-106 BD-242
JHEilert/JLMeyer/RJWolters/4-2-73
R/D init. JMeyer/4-16-73
Final typing/rt/4-18-73
rev w/f

Sincerely yours,

Marvin Seife, M.D.
Director
Division of Actions Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

Marvin Seife 4/24/73

*JHEilert
4-19-73
RJWolters
JMeyer 4/23/73
4-18-73*