

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

Approval Package for:

APPLICATION NUMBER:

80-691

Generic Name: Folic Acid 1mg Tablets

Sponsor: Towne, Paulsen & Co., Inc.

Approval Date: July 31, 1973

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-691

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Reviews / Information Included in this ANDA Review.

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Correspondence	X

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-691

APPROVAL LETTER

NDA 80-691

AF 1-992

Towme, Paulsen & Co., Inc.
Attention: Mr. Harold G. Brock
140 East Duarte Road
Monrovia, CA 91016

JUL 31 1973

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, 0.25 and 1.0 mg.

Reference is also made to your communications dated June 15 and June 21, 1973, amending the application.

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.

Dup
BD-69 BD-66 BD-106 BD-242 BD-100
MSeife/JMeyer/GMiller 7-19-73
R/D not init.
Final typing/wlb/7-23-73
Approved.

JMeyer 7/30/73

Enclosures:

Conditions of Approval of a New Drug Application
Records and Reports Requirements

cc:
SAN-DO

M. Seife 7/30/73

Sincerely yours,

Chell 7/21/73
Paul A. Bryan M.D. 7/30/73
Paul A. Bryan, M.D.
Acting Deputy Director for
Medical Affairs
Office of Scientific Evaluation
Bureau of Drugs

**CENTER FOR DRUG
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RESEARCH**

APPLICATION NUMBER:

80-691

FINAL PRINTED LABELING

31 JUL 1973

APPROVED
FOLIC ACID

DESCRIPTION

Folic Acid Tablets contain not less than 90 percent and not more than 115 percent of the labeled potency of the drug. *DM*

Folic acid is a yellowish orange crystalline powder which is readily soluble in dilute alkali hydroxides and carbonates. It is insoluble in alcohol, chloroform and ether; and very slightly soluble in water.

ACTIONS

Folic acid is a hematopoietic vitamin which is enzymatically reduced in the body to tetrahydrofolic acid, the biologically active coenzyme form. The function of tetrahydrofolic acid is to transfer one-carbon molecular fragments from one compound to another. These molecular fragments serve as building units in the metabolic synthesis of certain purines, pyrimidines and amino acids which are necessary for the normal body processes.

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 B-12 is deficient.

PRECAUTIONS

Folic acid especially in doses above 1.0 mg. daily may obscure pernicious anemia, in that hematologic remission

JUL 1 8

APPROVED

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.

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 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

FOLIC ACID TABLETS U.S.P.

0.25 mg. Folic Acid (yellow, scored):
bottles of 100's and 1000's.
1.0 mg. Folic Acid (yellow, double scored):
bottles of 100's and 1000's.

Issued May 1972



pharmaceutical chemists
140 East Duarte Road - Monrovia, Calif. 91016

III
II
III
TOWNE, PAULSEN & CO., INC.
Monrovia, California 91016
NDC-157-0873-01

List No. 873

FOLIC ACID
Tablets 1 mg.
Towne

CAUTION: Federal law prohibits
dispensing without prescription.

See accompanying insert for indica-
tions, contraindications, warnings,
precautions, adverse reactions, do-
sage and administration.

B-A

APPROVED 100 TABLETS

III
II
III
TOWNE, PAULSEN & CO., INC.
Monrovia, California 91016
NDC-157-0873-10

List No. 873M

FOLIC ACID
Tablets 1 mg.
Towne

CAUTION: Federal law prohibits
dispensing without prescription.

See accompanying insert for indica-
tions, contraindications, warnings,
precautions, adverse reactions, do-
sage and administration.

B-A

APPROVED 1000 TABLETS

**CENTER FOR DRUG
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RESEARCH**

APPLICATION NUMBER:

80-691

CSO LABELING REVIEW(S)

REVIEW OF ANDA

Date Completed: 10/26/71

ANDA #: 80-691

F.R. Statement Date: 4/9/71

Co. Name: Towne Paulsen & Co.
Monrovia, Calif.

NAME OF DRUG: Trade:)
Generic:) Folic Acid Tablets, 0.25 mg. and 1.0 mg.

DATE OF SUBMISSION: 10/9/71

TYPE OF SUBMISSION: ANDA

CLINICAL EVALUATION:

1. Review of Studies:

Bioavailability: Chemist to assess conformity to USP XVIII

Manufacturing - control data: Chemist to appraise

2. Review of Labeling:

Container label: Remove Warning as this product is Rx.
Change dosage instructions to "See
package insert."

Package insert: Federal dispensing Rx caution to be inserted.
How Supplied: State tablet strength and
quantity as marketed.

CONCLUSIONS: 1. Chemist to appraise.
2. Labeling requires revision.

RECOMMENDATIONS: 1. Chemist to appraise
2. Revise container label and package insert as
detailed above.

cc:

Dup

BD-100

BD-69

JHEilert/bhy 10/26/71

Init. by MAclark


John H. Eilert, M.D.

REVIEW OF RESUBMISSION

DATE COMPLETED: 5-9-73

ANDA #: 80-691

F.R. DATE: 4-9-71

CO. NAME: Towne Paulsen & Co., Inc.
140 E. Duarte Road
Monrovia, Calif. 91016

NAME OF DRUG: Trade & Generic: Folic Acid Tablets 0.25 mg. and 1.0 mg.

DATE OF SUBMISSION: 11-10-72

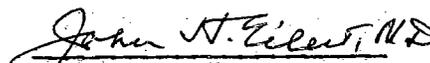
TYPE OF SUBMISSION: Labeling changes, manufacturing data

CLINICAL EVALUATION:

1. Review of Studies: Chemist to evaluate.
2. Review of Labeling: Container labels and insert have been revised as requested.

CONCLUSION: 1. Requires chemist evaluation.
2. Approve labeling.

RECOMMENDATIONS: 1. Review by chemist.
2. Approve labeling.


John H. Eilert, M.D.

cc:
Dup
BD-69
JHEilert/rt/5-24-73

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-691

CHEMISTRY REVIEW(S)

Name and Address of Applicant (City and State) ORIG: 10/2/71

Towne, Paulsen and Company, Inc.
Monrovia, California 91016

NDA Number
80-681
Supplement Date and

Category of Drug
FOLIC ACID

Nonproprietary Name
CIB

Applicant Date(s)
11/2/72

Purpose of Supplement

Other Date(s)

Pharmacological Category
vitamin

How Dispensed
 Rx OTC

AF Number
1-992

Dosage Form(s)
tablet

Potency(ies)
0.25 and 1.0 mg

Related NDA/IND/OTC

Factory Labeling
 Date Due as per '70's review (Jheidert)

Factory Components, Composition, Manufacturing and Controls
 Date Due see below

Factory Biologic Availability
 Date Due as per bio committee
Is data on current formulation? YES NO

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

Dispatch Inspection
in compliance: ~~BD-340~~
per BD-340 5/8/73

Recalls
bio-scan [in compliance BD-340 memo 4/12/73 =]
bio-technics. " ~~BD-340~~
both testors in compliance 5/21/73

Labeling of drug in commercial channels required?
at what level: YES NO

- request: 1. full certifications from testors (as above)
- 2. packaging -light-resistance / light

APPEARS THIS WAY ON ORIGINAL

Revisions
rev w/f
rev w/f

Chell 6/14/73
gmillar

ABBREVIATED NEW DRUG APPLICATION OR SUPPLEMENT		Statement Date	SUPPLEMENT <input type="checkbox"/>
Name & Address of Applicant (City & State) towne, paulsen & Co., Inc montevia, ca. 91016			RDA Number 80-691
Name of Drug folic acid	Nonproprietary Name	Amendment Date(s) 6/15+6/21/73	
Purpose of Supplement		Other Date(s)	
Pharmacological Category vitamin	How Dispensed R _x <input checked="" type="checkbox"/> O.T.C. <input type="checkbox"/>	AF Number 1-992	
Dosage Form(s) tablet	Potency (ies) 0.25 & 1.0 mg.	Related IND/NDA/ME(s)	

Satisfactory Labeling Date Due as per mo(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 in compliance: as per bd-340 memo of 5/8/73
bio-scan = in compliance as per bd-340 memo of 4/12/73

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

Remarks

APPEARS THIS WAY
ON ORIGINAL

Conclusions approved.

Chill 7/21/73
gmillar

Name and Address of Applicant (City and State)		Supplement No.
Towne, Paulsen and Company, Inc. Monrovia, California 91016		NDA Number 80-691
Name of Drug	Nonproprietary Name	Supplement Date and
FOLIC ACID		Amendment Date(s)
Purpose of Supplement		Other Date(s)
Pharmacological Category	How Dispensed	AF Number
vitamin	<input checked="" type="checkbox"/> Rx <input type="checkbox"/> OTC	1-992
Dosage Form(s)	Potency (ies)	Related IND/NDA/NF(s)
tablet	0.25 and 1.0 mg	

Satisfactory Labeling <input type="checkbox"/> Date Due _____	To be revised (JHE alert)
Satisfactory Components, Composition, Manufacturing and Controls <input type="checkbox"/> Date Due _____	see below

Factory Biologic Availability Date Due _____	Y
Is data on current formulation? YES <input type="checkbox"/> NO <input type="checkbox"/>	na
Factory Probably or Possibly Effective Indications (if in labeling) Date Data Due _____	APPEARS THIS WAY ON ORIGINAL

Dispatchment Inspection Unsatisfactory LOs-DO 6/14-18/71	Recalls
--	---------

Labeling of drug in commercial channels required? YES NO

at what level:

Request revised labeling; and satisfactory inspection clarification of _____ test on _____

Revisions
rev w/f
Chella 11/30/71
gmillar

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-691

**ADMINISTRATIVE
DOCUMENTS**

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER

80-691

DATE APPROVAL LETTER ISSUED

JUL 31 1973

TO:

Press Relations Staff (PA-40)

FROM:

Bureau of Drugs

Bureau of Veterinary Medicine

APPROVAL OF ORIGINAL ATTENTION ABBREVIATED NDA
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

ORIGINAL NDA

SUPPLEMENT TO NDA

ABBREVIATED ORIGINAL NDA

SUPPLEMENT TO ANDA

CATEGORY

HUMAN

VETERINARY

TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG

folic acid

DOSAGE FORM

tablet

HOW DISPENSED

RX

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, 0.25 & 1.0 mg.

NAME OF APPLICANT (Include City and State)

Towne, Faulsen & Co., Inc.
Monrovia, CA 91016

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

hematopoietic vitamin

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

APPEARS THIS WAY
ON ORIGINAL

NAME

G Miller

FORM PREPARED BY

G Miller

DATE

7/24/73

NAME

JL Meyer

FORM APPROVED BY

JL Meyer

DATE

7/30/73

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

DATE: May 8, 1973

BD-105

ATTN: Stanley Stringer

80-691

BD-340

SUBJECT: Applicant: Towne, Paulsen Co., Inc., Monrovia, Calif.

RE: Approval of NDA's: 80-916 14-464/S006
 83-338 80-799
 80-496 80-800

We have evaluated the operations of the above referenced applicant as they relate to conformity with Current Good Manufacturing Practice Regulations (21 CFR, Part 133). Based on this evaluation, we would have no objection to your approving the above referenced NDA's in so far as they relate to the firm's compliance with GMP in these pending applications.


Jonas L. Bassen

NOTE: If there are other pending ANDA's for above firm not indicated in our memo, they should be included in this approval. Advise us of ANDA numbers to be added.

CC:

NDA orig.

NDA dup.

BD-105

BD-316

BD-340, Log

BD-340, Subject File

BD-340, Laderman

CA-226

LOS-DO (NDA trip.)

RSLADERMAN:lr

MEMORANDUM

DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION

TO : BD-105
ATTN: Stanley Stringer

DATE: May 21, 1973

(80-691)

FROM : BD-340

SUBJECT: Disapproval of ANDA's 80-799 for _____
80-800
Reevaluation
Applicant: Towne-Paulsen, Monrovia, Calif.

In a previous memo of 4/12/73 _____ was approved as _____
_____ for the subject ANDA's. We have reevaluated the operations of
_____ based on additional information received by this
office. On the basis of this reevaluation, we are unable to approve this
_____ for the subject ANDA's as the firm is not operating in
conformity with CGMP Regulations (21 CFR, Part 133) to assure that products
meet the requirements of the Federal Food, Drug, and Cosmetic Act as to
safety, and have the identity and strength, and meet the quality and purity
characteristics which they purport to possess.

Inspection of _____ of 3/14 to 3/16/73 revealed significant
GMP deviations in the _____ of drug ingredients:

In view of these deviations, we are disapproving the use of _____
_____ until corrective action has been effected.

Jonas L. Bassen
Jonas L. Bassen

NOTE: We understand Towne-Paulsen has amended these ANDA's to remove _____

cc:

ANDA File

NDA orig.

NDA dup.

BD-105

BD-316

BD-340, Log

BD-340, Subject File

BD-340, Laderman

CA-226

LOS-DO

RSLADERMAN:lr

APPEARS THIS WAY
ON ORIGINAL

[DESI 597; Docket No. FDC-D-265; NDA 5-897, etc.]

FOLIC ACID PREPARATIONS, ORAL AND PARENTERAL FOR THERAPEUTIC USE

Drugs 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 6-338).

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:

A 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 Pharmacal Co.
 Carroll Chemical Co., The.
 Columbia Medical Co.
 Consolidated Midland Corp., CMC Research Division.
 Corvit Pharmaceuticals.
 Daniels, Robert and Co., Inc.
 DuMont Pharmacal Co.
 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.
 Lannett Co., Inc.
 Lit Drug Co.
 Lustgarten Laboratories, Inc.
 Mifflin, McCambridge Co., Inc.
 Penhurst Pharmacal Co.
 Pharmex, Inc.
 Pfeston 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-Fore Products Co.

West-Ward, Inc.
 Williams Chemical Co.
 Winsale Drug 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.)

FOLIC ACID

DESCRIPTION

(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 (packaging, 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 obtained 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 5897, directed to the attention of the following appropriate office, and addressed (unless otherwise specified) to the Food and Drug Administration, 5600 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; 8:46 am]

[DESI 10423]

LEVALLOPHAN 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 levallophan tartrate; Roche Laboratories, Division of Hoffman-LaRoche, Inc., 340 Kingsland Street, Nutley, New Jersey 07110 (NDA 10-423).

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-691

CORRESPONDENCE



ABBREVIATED
NEW DRUG APPLICATION
pharmaceutical chemists

140 E. Duarte Road, Monrovia, California • Elliott 9-9331
Cable Address "Towne"

80-691

October 9, 1971

Department of Health, Education & Welfare
Bureau of Drugs
Food & Drug Administration
Rockville, Maryland 20852

Gentlemen:

In accordance with regulations provided for in section 505 (b) of the Federal Food, Drug and Cosmetic Act, as amended, we hereby submit this original abbreviated new drug application. Attached hereto, submitted in triplicate and in the form described in part 130.4 (f) of the new drug regulations, is the full information and data required by the published notice in the Federal Register, Vol. 36, No. 69, Friday, April 9, 1971.

Sincerely,

TOWNE, PAULSEN & CO., INC.

A handwritten signature in cursive script, appearing to read "Harold G. Brock".

Harold G. Brock
Technical Director

HGB:mb



pharmaceutical chemists

140 E. Duarte Road, Monrovia, California - Elliott 9-9331
Cable Address "Towne"

October 9, 1971

Department of Health, Education & Welfare
Bureau of Drugs
Food and Drug Administration
Washington, D.C. 20204

Original Abbreviated New Drug Application

Title 21, Code of Federal Regulations § 130.4 (f)

Name of Applicant: Towne, Paulsen & Co., Inc.
Address: 140 East Duarte Road
Monrovia, California 91016

Date: October 9, 1971

Name of Drug: FOLIC ACID TABLETS U.S.P.



OCT 22 1971

NDA 80-691

AF 1-992

Towne, Paulsen & Co., Inc.
Attention: Mr. Harold G. Brock
140 East Duarte Road
Monrovia, California 91016

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, 0.25 mg. and 1.0 mg.

Date of application: October 9, 1971

Date of receipt: October 15, 1971

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,

Paul A. Bryan, M.D. 10/22/71

Paul A. Bryan, M.D.
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
LOS-DO

Dup
BD-67 BD-69
BD-22
BD-100 BD-242
JLMeyer/va/10-21-71

Ack. *JLMeyer 10/21/71*

o.m. Farrell 10/24/71
J.R. Williams 10/22/71

DEC 8 1971

Salmon

NDA 80-691
AF 1-992

Towne, Paulsen and Company, Inc.
Attention: Mr. Harold G. Brock
140 East Duarte Road
Monrovia, California 91016

Gentlemen:

Reference is made to your abbreviated new drug application dated October 9, 1971, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 0.25 and 1.0 mg.

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

1. Container label: Remove both the Warning section and the specific dosage amounts, since the reference to the package insert is sufficient.
2. Package insert:

In the HOW SUPPLIED section, state the tablet strength.

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

A clarification of the procedures used to assure that the components will comply with the specifications and tests described in an official compendium, since it is noted that the _____ test is not performed on the _____

APPEARS THIS WAY
ON ORIGINAL

Page 2 - Toome, Paulsen and Company, Inc.
NDA 80-691

Before we can take final action, it will be necessary for you to have a satisfactory inspection of your manufacturing methods facilities and controls to assure the strength, identity, purity, and quality of the drug. A copy of this letter has been sent to our Los Angeles District Office. We suggest you contact them and arrange for an inspection.

Please let us have your response promptly.

Sincerely yours,

Paul A. Bryan
Paul A. Bryan, M.D.
Director
Drug Efficiency Study Implementation
Project Office
Bureau of Drugs
12/7/71

cc:

LOS-DO

Dup

BD-67

BD-69 *© Jim Carroll (M.D.), 12/7/71*

BD-22

BD-100

BD-242

JHEllert/JIMeyer/CMillar 11-24-71

Initialed by Dr. Clark rt/11-29-71

Rev w/f

Sumner 12/7/71

SALMOY



Rev. w/f orig

RESUBMISSION
NDA ORIG AMENDMENT

E

pharmaceutical chemists

140 E. Duarte Road, Monrovia, California 91016 • (213) 359-9331
Cable Address "Towne"

FPL

November 10, 1972

D.E.S.I. Project Office
Bureau of Drugs (BD-60)
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Reference: NDA 80-691/~~XXXX~~
Folic Acid Tablets U.S.P.

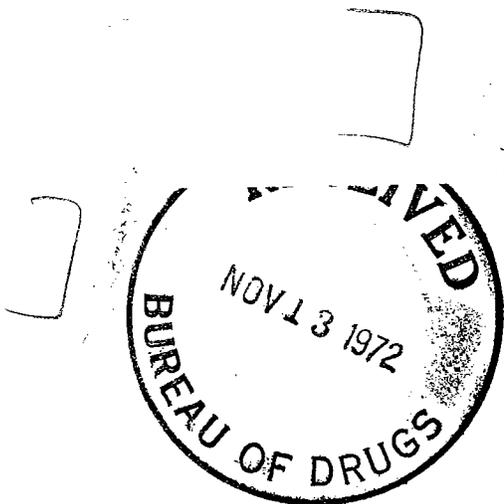
Gentlemen:

In response to your review of our abbreviated new drug application we are submitting the necessary additional information and corrections as follows:

1. Container labels have been changed to delete the usual dosage statement. Reference is made to the package insert. Additionally, our National Drug Code number has been added to the label along with a "bleed line" code on the label margin to help prevent label mix-ups.
2. The package insert (Issued May 1972) has been corrected to add the available tablet strengths to the HOW SUPPLIED section.
3. A clarification of the procedures used to assure that the components of the drug comply with the specifications and tests described in the official compendium is as follows:

A. The _____ test for the absence of _____ and _____ in the raw material _____ has been added as a Towne, Paulsen & Co., Inc. specification for this inert raw material ingredient. This test will be performed for Towne, Paulsen & Co., Inc. by a qualified _____ from the following list:

[
[
[



NDA 80-691

AF 1-992

JUN 14 1973

Towne, Paulsen and Company, Inc.
Attention: Mr. Harold G. Brock
140 East Duarte Road
Monrovia, California 91016

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, 0.25 and 1.0 mg.

Reference is also made to your communication dated November 10, 1972 amending the application.

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

1. Certification statements from _____ and _____, that the methods used in, and the facilities and the controls used for, testing are in conformity with current good manufacturing practice in accord with Part 133 (21CFR) of the regulations.
2. An outline of the methods used in, and facilities and controls used for, packing and holding of the drug since compendial special specifications call for special handling.

Please let us have your response promptly.

cc:
LOS-DO
BD-69
BD-66
BD-106
BD-242
JHE:ert/JLMeyer/GMillar/6/1/73
R/D init by: JLMeyer 6/1/73
Final Typing/skg/6/11/73

Sincerely yours,

Marvin Seife 6/14/73

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

REV. W./F. *JLMeyer 6/13/73*

*just filed
6-14-73*

Original
NDA ORIG AMENDMENT

E



pharmaceutical chemists
140 E. Duarte Road, Monrovia, California 91016 • (213) 359-9331
Cable Address "Towne"

June 15, 1973

Dr. Marvin Seife, Director
D.E.S.I. Project Office (BD-60)
Bureau of Drugs, F.D.A.
5600 Fishers Lane
Rockville, Maryland 20852

Reference: NDA 80-691
Folic Acid Tablets U.S.P.

Gentlemen:

We have been informed by your office that one of the _____
_____ referred to in our application has not been approved by
an F.D.A. inspection. Therefore, without prejudice, we would like to
withdraw this _____ from our application until such time
as a favorable inspection report of the establishment is received by
your office.

Please remove the name of _____
_____ from this application.

Towne, Paulsen & Co., Inc. will continue to use _____
_____ to perform the
required _____ on the components of the drug.

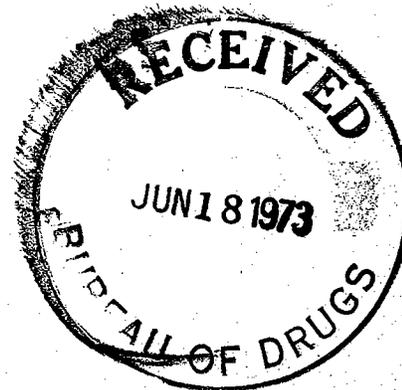
Sincerely,

TOWNE, PAULSEN & CO., INC.

Harold G. Brock

Harold G. Brock
Technical Director

HGB:fh



NDA ORIG AMENDMENT

ERIC



pharmaceutical chemists

140 E. Duarte Road, Monrovia, California 91016 • (213) 359-9331
Cable Address "Towne"

June 21, 1973

Dr. Marvin Seife, Director
D.E.S.I. Project Office (BD-60)
Bureau of Drugs, F.D.A.
5600 Fishers Lane
Rockville, Maryland 20852

Reference: NDA 80-691
Folic Acid Tablets, 0.25 mg. and 1.0 mg.

Gentlemen:

In response to your review of an abbreviated NDA we are submitting the additional information as follows:

- (1) We have withdrawn _____ as a _____ in our letter of June 15, 1973. TOWNE, PAULSEN & CO., INC. will continue to use _____ to perform the required _____ on the components of the drug. A certification statement from _____ is attached.
- (2) An outline of the methods used in special handling of the drug are as follows: In accord with compendial specifications, the raw material drug is stored in well-closed, light resistant containers.

The tablets are made by a _____ method to keep the handling of the drug to a minimum. The _____ tablets are _____

Folic Acid Tablets U.S.P. are filled into well closed _____ according to the U.S.P. specifications. These containers are _____ amber glass bottles or high density polyethylene _____ which are tightly closed with a screw cap closure.

Thank you for your consideration of our application.

Sincerely,

TOWNE, PAULSEN & CO., INC.

Harold G. Brock

Harold G. Brock
Technical Director
HGB:fh

