

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

Approval Package for:

APPLICATION NUMBER:

80-686

Generic Name: Folic Acid 1mg Tablets

Sponsor: Richlyn Laboratories, Inc.

Approval Date: July 20, 1973

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-686

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:

80-686

APPROVAL LETTER

NDA 80-686
AF 28-724

Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rebollo
Castor & Kensington Avenues
Philadelphia, PA 19124

JUL 20 1973

Gentlemen:

Reference is made to your abbreviated new drug application submitted October 7, 1971, pursuant to Section 305(b) of the Federal Food, Drug, and Cosmetic Act for Folic Acid Tablets, 1.0 mg.

Reference is also made to your communications dated January 17, 1972; March 2, 1972; March 23, 1972; April 14, 1972; May 15, 1972; May 25, 1972 (two); May 26, 1972; August 7, 1972; September 14, 1972; November 10, 1972; December 7, 1972; December 8, 1972; and May 21, 1973, enclosing printed labeling and distributor labeling.

The application provides for you to market 100, 1000 and 5000 tablet containers of the drug under your own label.

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 changes 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 requirement for adequate data to assure the biologic availability is being deferred at the present time. However, our action in approving this application is based upon an understanding that if this requirement is reinstated you will perform the appropriate procedures.

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

Your application provides for distributors (names listed in a separate enclosure). We are enclosing with a copy of this letter to the distributor, the conditions relating to the approval of this application.

Sincerely yours,

Marion Seife for 7/17/73
Paul A. Bryan, M.D.
Acting Deputy Director
for Medical Affairs
Office of Scientific Evaluation
Bureau of Drugs

cc: PHI-D0

Dup

BD-69

BD-66

BD-106

BD-242

BD-100

JHEilert/CSmith/JLMeyer/

R/D init. by MSeife/JMeyer/7-18-73

Final typing/kim/7-18-73

cm. Smith 7-19-73
JMeyer 7/19/73

Enclosures:

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

Approved

Your application provides for you to label containers of the drug in 1 mg. potencies with a label showing your distributor to be:

- 7 Approved Pharmaceutical Corp.
Syracuse, NY 13201
(100's & 1000's)
- 4 Barre Drug Co., Inc.
Baltimore, MD 21215
(100's & 1000's)
- 1 Arcum Pharmaceutical Corp.
Vienna, VA 22180
(100's & 1000's)
- 2 Spencer-Need, Inc.
Valley Stream, NY
(100's)
- 5 United Pharmaceutical, Inc.
Oakland, CA 94601
(100's & 1000's)
- 6 Bicine Laboratories, Inc.
Brooklyn, NY 11203
(1000's)
- 8 Sherry Pharmaceutical Co., Inc.
Bayshore, L.I., NY
(100's & 1000's)
- 9 Rugby Laboratories, Inc.
Inwood, L.I., NY
(1000's)
- 7 Cooper Drug Co.
Troy, MI 98084
(100's & 1000's)

**CENTER FOR DRUG
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APPLICATION NUMBER:

80-686

FINAL PRINTED LABELING

FOLIC ACID TABLETS, U.S.P.
1 mg.

DMB

DESCRIPTION: Each scored, yellow, compressed tablet contains 1 mg. of folic acid. Folic acid is a yellow or yellowish orange, odorless, crystalline powder. It is very slightly soluble in water; insoluble in alcohol, chloroform, and ether. It is readily soluble in solutions of alkalis. Folic acid is stable in neutral or alkaline solution but its stability decreases as the pH is reduced below 6. Considerable destruction of folic acid occurs below pH 4.

ACTIONS: Folic acid is an important growth factor for a large variety of animal, plant, and microbial cells. Its function, in the form of its active metabolite, tetrahydrofolic acid, is to transfer one-carbon molecular fragments such as formyl, hydroxymethyl or methyl from one compound to another. These fragments serve as building units in the synthesis of certain purines, pyrimidines, and amino acids. The methylation of deoxyuridine to thymidine is one of the more important reactions in which folic acid participates, this being a preliminary step in the synthesis of deoxyribonucleic acid (DNA). Deficiency in the synthesis of DNA may interfere with mitosis and be responsible for the gigantic cells (megaloblasts) that are characteristic of megaloblastic anemias. Other important reactions requiring folic acid are the metabolic degradation of histidine to glutamic acid and the conversion of serine to glycine.

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 parenteral administration of folic acid.

DOSAGE AND 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.

CAUTION: Federal law prohibits dispensing without prescription.

HOW SUPPLIED: Each scored, yellow, compressed tablet contains 1 mg. of folic acid.

MARCH, 1972

3585 100 TABLETS C. T. Yellow

FOLIC ACID

TABLETS, U. S. P.

1 mg.

CAUTION: Federal law prohibits dispensing without prescription.
See insert for full particulars

RICHLYN LABORATORIES, INC.
PHILADELPHIA, PA. 19124

Usual* Adult Daily Dosage--
Therapeutic: 0.25 mg. to 1.0 mg.
Maintenance: 0.1 mg. to 0.25 mg.
*Resistant cases may require larger doses (see insert).

Lot No.

3585 1000 TABLETS C. T. Yellow

FOLIC ACID

TABLETS, U. S. P.

1 mg.

CAUTION: Federal law prohibits dispensing without prescription.
See insert for full particulars

RICHLYN LABORATORIES, INC.
PHILADELPHIA, PA. 19124

Usual* Adult Daily Dosage--
Therapeutic: 0.25 mg. to 1.0 mg.
Maintenance: 0.1 mg. to 0.25 mg.
*Resistant cases may require larger doses (see insert).

Lot No.

3585 5000 TABLETS C. T. Yellow

FOLIC ACID

TABLETS, U. S. P.

1 mg.

CAUTION: Federal law prohibits dispensing without prescription.
See insert for full particulars

RICHLYN LABORATORIES, INC.
PHILADELPHIA, PA. 19124

Usual* Adult Daily Dosage--
Therapeutic: 0.25 mg. to 1.0 mg.
Maintenance: 0.1 mg. to 0.25 mg.
*Resistant cases may require larger doses (see insert).

Lot No.

1000 TABLETS C.I. Yellow

FOLIC ACID
TABLETS, U. S. P.

1 mg.

CAUTION: Federal law prohibits
dispensing without prescription.
See insert for full particulars

Manufactured for
COOPER DRUG CO.
TROY, MICHIGAN 48064

Usual* Adult Daily Dosage--
Therapeutic: 0.25 mg. to 1.0 mg.
Maintenance: 0.1 mg. to 0.25 mg.

*Resistant cases may require
larger doses (see insert).

Lot No.

amb

FOLIC ACID

U.S.P.
1 mg.

CAUTION: Federal law prohibits dispensing without prescription.
See insert for full particulars.

1000 TABLETS



Distributed By
APPROVED
PHARMACEUTICAL CORP
SYRACUSE, NEW YORK 13201

Usual* Daily Dosage
Therapeutic: 0.25 mg.
Maintenance: 0.1 mg.
*Resistant cases may require larger doses (see insert).

FOLIC ACID

U.S.P.
1 mg.

CAUTION: Federal law prohibits dispensing without prescription.
See insert for full particulars.

100 TABLETS



Distributed By
APPROVED
PHARMACEUTICAL CORPORATION
Syracuse, New York 13201

Usual* Daily Dosage
Therapeutic: 0.25 mg.
Maintenance: 0.1 mg.
*Resistant cases may require larger doses (see insert).

See insert for full particulars

ams

FOLIC ACID TABLETS
U.S.P.

1 MG. EACH

CAUTION: Federal law prohibits dispensing without prescription.

100 TABLETS

Usual* daily dosage—
Therapeutic: 0.25mg to 1.0mg
Maintenance: 0.1mg to 0.25mg

*Resistant cases may require larger doses (see insert).

BARRE DRUG CO., INC.
Baltimore, Md. 21215 Distributors

See insert for full particulars

ams

FOLIC ACID TABLETS
U.S.P.

1 MG. EACH

CAUTION: Federal law prohibits dispensing without prescription.

100 TABLETS

Usual* daily dosage—
Therapeutic: 0.25mg to 1.0mg
Maintenance: 0.1mg to 0.25mg

*Resistant cases may require larger doses (see insert).

BARRE DRUG CO., INC.
Baltimore, Md. 21215 Distributors

Usual* daily dosage:
Therapeutic: 0.25 mg. to
1.0 mg. Maintenance: 0.1
mg. to 0.25 mg.
*Resistant cases may
require larger doses (see
insert).

100 Tablets
NDC 357-0841-01 C.T. Yellow

**FOLIC ACID
TABLETS, U.S.P.**

1 Milligram

CAUTION: Federal law prohibits
dispensing without prescription.
See insert for full particulars.

Manufactured for
ARCUM
Pharmaceutical Corp.
Vienna, Va. 22180

ems

Usual* daily dosage:
Therapeutic: 0.25 mg. to
1.0 mg. Maintenance: 0.1
mg. to 0.25 mg.
*Resistant cases may
require larger doses (see
insert).

1000 Tablets
NDC 357-0841-10 C. T. Yellow

**FOLIC ACID
TABLETS, U.S.P.**

1 Milligram

CAUTION: Federal law prohibits
dispensing without prescription.
See insert for full particulars.

Manufactured for
ARCUM
Pharmaceutical Corp.
Vienna, Va. 22180

ems



1000 TABLETS

C.T. Yellow

FOLIC ACID

TABLETS, U.S.P.

1 mg.

CAUTION: Federal law prohibits
dispensing without prescription.
See insert for full particulars.

MANUFACTURED FOR
SPENCER-MEAD INC.
VALLEY STREAM, NEW YORK 11582

MS

Usual Adult Daily Dosage...
Therapeutic: 0.25 mg. to 1.0 mg.
Maintenance: 0.1 mg. to 0.25 mg.
Resistant cases may require
larger doses (see insert).
Lot No.

Usual* Adult Daily Dosage—
Therapeutic: 0.25 mg. to 1.0 mg.
Maintenance: 0.1 mg. to 0.25 mg.

UNITED *cms*
FOLIC ACID
TABLETS, U.S.P.
1 mg.

CAUTION: Federal law prohibits dispensing without prescription.
See insert for full particulars.

100 TABLETS

Distributed by
UNITED PHARMACEUTICALS, INC.
Oakland, Calif. 94601

*Resistant cases may require larger doses (see insert).

NDC 416-0139-01

Usual* Adult Daily Dosage—
Therapeutic: 0.25 mg. to 1.0 mg.
Maintenance: 0.1 mg. to 0.25 mg.

UNITED *cms*
FOLIC ACID
TABLETS, U.S.P.
1 mg.

CAUTION: Federal law prohibits dispensing without prescription.
See insert for full particulars.

1000 Tablets

Distributed by
UNITED PHARMACEUTICALS, INC.
Oakland, Calif. 94601

*Resistant cases may require larger doses (see insert).

NDC 416-0139-10

1000 TABLETS

C. T. Yellow

FOLIC ACID

TABLETS, U. S. P.

1 mg.

CAUTION: Federal law prohibits
dispensing without prescription.

See insert for full particulars

Manufactured for

BIOLINE LABORATORIES, INC.
BROOKLYN, N.Y. 11203

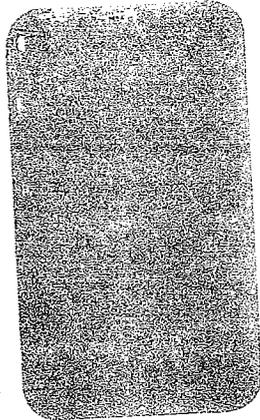
ms
Usual* Adult Daily Dosage--

Therapeutic: 0.25 mg. to 1.0 mg.

Maintenance: 0.1 mg. to 0.25 mg.

*Resistant cases may require
larger doses (see insert).

Lot No.



Sherry

emb

100 TABLETS

C.T. Yellow

FOLIC ACID

TABLETS, U.S.P.

1 mg.

CAUTION: Federal law prohibits dispensing without prescription.

See insert for full particulars.

MANUFACTURED FOR
SHERRY PHARMACEUTICAL CO., INC.
BAYSHORE, L. I., N. Y. 11706

Usual Adult Daily Doseage:
Therapeutic: 0.25 mg. to 10 mg.
Maintenance: 0.1 mg. to 0.25 mg.
Resistant cases may require
larger doses (see insert).
100 Tablets

RUGBY

#38465

1000 TABLETS C.T. Yellow

FOLIC ACID

TABLETS, U. S. P.

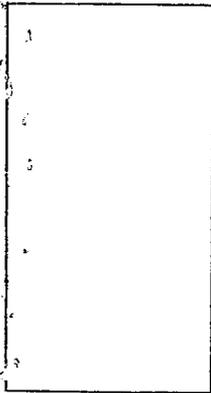
1 mg.

CAUTION: Federal law prohibits
dispensing without prescription.
See insert for full particulars

Usual* Adult Daily Dosage--
Therapeutic: 0.25 mg. to 1.0 mg.
Maintenance: 0.1 mg. to 0.25 mg.

*Resistant cases may require
larger doses (see insert).

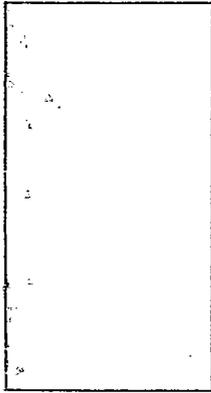
Lot No.



100 TABLETS C. T. Yellow
FOLIC ACID
 TABLETS, U. S. P.
 1 mg.
 CAUTION: Federal law prohibits
 dispensing without prescription.
 See insert for full particulars

Manufactured for
COOPER DRUG CO.
 TROY, MICHIGAN 98084

ms
 Usual* Adult Daily Dosege --
 Therapeutic: 0.25 mg. to 1.0 mg.
 Maintenance: 0.1 mg. to 0.25 mg.
 *Resistant cases may require
 larger doses (see insert).
 Lot No.



1000 TABLETS C. T. Yellow
FOLIC ACID
 TABLETS, U. S. P.
 1 mg.
 CAUTION: Federal law prohibits
 dispensing without prescription.
 See insert for full particulars

Manufactured for
COOPER DRUG CO.
 TROY, MICHIGAN 98084

ms
 Usual* Adult Daily Dosege --
 Therapeutic: 0.25 mg. to 1.0 mg.
 Maintenance: 0.1 mg. to 0.25 mg.
 *Resistant cases may require
 larger doses (see insert).
 Lot No.

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-686

CSO LABELING REVIEW(S)

REVIEW OF FPL

DATE COMPLETED: 5-22-72

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, Pa. 19124

NAME OF DRUG: Trade & Generic: Folic Acid Tablets 1 mg in bottles
of 100, 1,000 and 5,000.

DATE OF SUBMISSION: 5-15-72

TYPE OF SUBMISSION: FPL (container label)

CLINICAL EVALUATION:

Review of Labeling: Container label approvable.
Insert resubmitted earlier does not list container
quantities in How Supplied.

CONCLUSION: Acceptable container label.

RECOMMENDATION: Approve submission.


John H. Eilert, M.D.

cc:

Dup

BD-69

John H. Eilert, M.D./kim/5-22-72

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-686

CHEMISTRY REVIEW(S)

REVIEW OF ANDA

Date Completed: 10-22-71

ANDA #: 80-686

F.R. Date: 4-9-71

Co. Name: Richlyn Labs., Inc.
Philadelphia, Pa.

Name of Drug: Trade & Generic: Folic Acide Tablets, U.S.P., 1 mg.

Date of Submission: 10-7-71

Type of Submission: ANDA

1. Review of Studies: Bioavailability: Chemist to appraise conformity to U.S.P. XVIII

Chemist to appraise manufacturing-control data.

2. Review of Labeling: Package insert:

Action: Revise, to state that exact mode of therapeutic action has not been determined, followed by statement that the folic acid is enzymatically reduced in the body to tetrahydrofolic acid for activity.

Dosage and Administration: Remove heading

Remove en toto "_____ and sentence following:

How supplied: State strength and number of tablets provided.

Container Label: Satisfactory

- Conclusions: 1. Chemist to review.
2. Labeling requires revision.

- Recommendations: 1. Chemist to review.
2. Package insert requires revision as specified above.


John H. Eilert, M.D.

Dup
BD-69
BD-100
JHEilert/va/10-28-71

Redacted 2

pages of trade

secret and /or

confidential

commercial

information

REVIEW OF ANDA RESUBMISSION

DATE COMPLETED: 12-14-71

ANDA#: 80-686

F.R. STATEMENT DATE: 4-9-71

CO. NAME: Richlyn Labs., Inc.
Philadelphia, Pa.

NAME OF DRUG: Trade: Folic acid tablets, U.S.P. 5 mg.

Generic: Folic acid tablets, U.S.P. 5 mg.

DATE OF SUBMISSION: 11-30-71

TYPE OF SUBMISSION: Response to FDA 11-23-71 letter

CLINICAL EVALUATION:

1. Review of Studies: Chemist to evaluate.
2. Review of Labeling: None submitted.

Description section will require revision. The following paragraph would be acceptable:



Action section will require revision. The following paragraph would be acceptable:

Folic acid is an important growth factor for a large variety of animal, plant, and microbial cells. Its function, in the form of its active metabolite tetrahydrofolic acid, is to transfer one-carbon molecular fragments--formyl, hydroxymethyl, methyl-- from one compound to another. These fragments serve as building units in the synthesis of certain purines, pyrimidines, and amino acids. The methylation of deoxyuridine to thymidine is one of the more important reactions in which folic acid participates, this being a preliminary step in the synthesis of desoxyribonucleic acid (DNA). Deficiency in the synthesis of DNA may interfere with mitosis and be responsible for the gigantic cells (megaloblasts) that are characteristic of megaloblastic anemias. Other important reactions requiring folic acid are the metabolic degradation of histidine to glutamic acid and the conversion of serine to glycine.

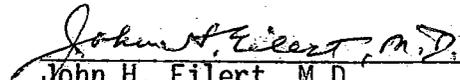
Dosage and Administration and How Supplied section to be revised as per our letter of 11/23/71.

CONCLUSION:

1. Chemist to evaluate.
2. No insert submitted.
3. Revision stated above will be required.

RECOMMENDATION:

1. Chemist to evaluate.
2. Request proposed package insert as requested, in our letter of 11/23/71, and as described above.



John H. Eilert, M.D.

cc:
BD-69
BD-100
JHEilert/nlp 12/17/71

**APPEARS THIS WAY
ON ORIGINAL**

REVIEW OF AMENDMENT

DATE COMPLETED: 1-10-72

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Labs., Inc.
Philadelphia, Pa.

NAME OF DRUG: Trade & Generic: Folic Acid Tablets, U.S.P. 1 mg.

DATE OF SUBMISSION: 12-28-71

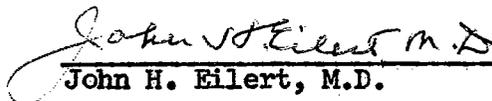
TYPE OF SUBMISSION: Amendments: Statement, credentials, labeling for
ARCUM Pharmaceutical Corp., Vienna, Va.

CLINICAL EVALUATION:

1. Review of Studies: Chemist to review.
2. Review of Labeling: (Refer to my 12-14-71 Review)

CONCLUSION: 1. Chemist to evaluate.
2. Labeling requires revision.

RECOMMENDATIONS: 1. Chemist to review.
2. Revise labeling as recommended 12-14-71 review.


John H. Eilert, M.D.

cc:

Dup

BD-69

JHEilert/wlb/1-11-72

APPEARS THIS WAY
ON ORIGINAL

REVIEW OF AMENDMENTS

DATE COMPLETED: 2/7/72

ANDA #: 80-686

F.R. Date: 4/9/71
Richlyn Laboratories, Inc.
Castor & Kensington Avenues
Philadelphia, Pa. 19124

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

DATES OF SUBMISSIONS: 1/3/72 (Spencer Mead) and 1/17/72 (Approved Pharmaceutical)

TYPES OF SUBMISSIONS: Distributor amendments for: Spencer Mead, Inc.
270 W. Merrick Road
Valley Stream, New York 11582

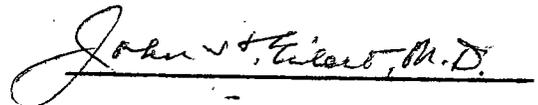
and: Approved Pharmaceutical Corporation
114-144 Gifford Street
Syracuse, New York 13201

CLINICAL EVALUATION:

1. Review of Studies: Chemist to review statements.
2. Review of Labeling:
 - a. Container Labels for both firms are satisfactory.
 - b. Package Insert: None submitted. Instructions for correction of earlier submission were sent manufacturer under date of Jan. 31, 1972 (later date than submissions.)

CONCLUSIONS: 1. Chemist to review.
2. Container labels for above named distributors are satisfactory.

RECOMMENDATIONS: 1. Chemist to review.
2. Await response to FDA 1/31/72 instructions concerning insert.



John H. Eilert, M.D.

cc:
Dup.
BD-69
JHEilert/mc/2/7/72

REVIEW OF ANDA, AMENDMENT

DATE COMPLETED: 3-15-72

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, Pa. 19124

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

DATE OF SUBMISSION: 3-2-72

TYPE OF SUBMISSION: New distributor, Barre Drug Co., Inc., Baltimore,
Maryland 21215 and container labels.

CLINICAL EVALUATION:

1. Review of Studies: Chemist to appraise, and refer to FDA letter
of 2-28-72.

2.. Review of Labeling:

Container labeling approvable except that right panel should be
corrected to read "Usual Adult Daily Dosage" rather than "Usual
daily dosage".

Package insert not submitted.

CONCLUSION: 1. Chemist to review.
2. Container labels approvable except for changes listed
above to be made at the time of the next printing.
3. No package insert. (The distributor has agreed in writing
to use exactly the same labeling approved for Richlyn Labs.)

RECOMMENDATIONS: Defer review completion, awaiting insert, manufacturing
information requested and EIR.

John H. Eilert M.D.
John H. Eilert, M.D.

cc:

Dup

BD-69

JHEilert/wlb/3-21-72

REVIEW OF RESUBMISSION

DATE COMPLETED: 4-14-72

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, Pa. 19124

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

DATE OF SUBMISSION: 3-23-72

TYPE OF SUBMISSION: Partial response to 1-31-72 and 2-28-72 communications

CLINICAL EVALUATION:

1. Review of Studies: None submitted with this communication
2. Review of Labeling:
 1. Container label not submitted. Requires revision as recommended in 3-31-72 letter.
 2. Package insert: How Supplied section does not list quantities proposed nor type of container.

CONCLUSION: Partial response to 1-31-72 and 2-28-72 letters.
FDA 3-31-72 letter had not been received.

RECOMMENDATION: Await complete response to recommendations.



John H. Eilert, M.D.

cc:
Dup
BD-69
JHEilert/rt/4-17-72
R/D init. by MClark

REVIEW OF RESUBMISSION

DATE COMPLETED: 4-25-72

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, Pa. 19124

NAME OF DRUG: Trade & Generic: Folic Acid Tablets, USP 1 mg.
bottles of 100 and 1,000.

DATES OF SUBMISSIONS: 4-10-72 and 4-14-72

TYPE OF SUBMISSION: Labeling and distributor statements

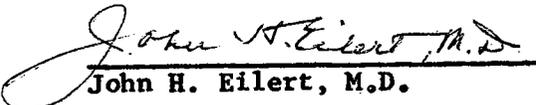
CLINICAL EVALUATION:

1. Review of Studies: Chemist to review
2. Review of Labeling:

4-10-72 Container labeling being corrected: draft is satisfactory.
4-14-72 1. Chemist to review Arcum statements.
Insert and container label approvable.

- CONCLUSION:
1. Chemist to review.
 2. Arcum labeling approvable.
 3. Richlyn container labeling undergoing revision.

- RECOMMENDATION:
1. Await EIR.
 2. Approve labeling for Arcum.


John H. Eilert, M.D.

cc:
Dup
BD-69
JHEilert/wlb/4-27-72

REVIEW OF AMENDMENTS

DATE COMPLETED: 6-7-72

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, Pa. 19124

NAME OF DRUG: Trade & Generic: Folic Acid Tablet 1 mg in bottles of
100 and 1,000 tablets.

DATES OF SUBMISSION: 5-25-72 & 5-26-72

TYPE OF SUBMISSION: New distributors' container labeling.

CLINICAL EVALUATION:

Review of Labeling: Package insert lacks quantity distribution in
'How Supplied' section.
Container labels for 100 and 1,000 tablets bottles for United Pharmaceuticals,
Inc.
Oakland, Calif. 94601

are suitable.

Container labels for Bioline Laboratories, Inc.
Brooklyn, N.Y. 11203
are for 1,000 tablet container only.

CONCLUSION: Acceptable container labeling.

RECOMMENDATIONS: Approve submissions.
Await corrected insert.


John H. Eilert, M.D.

cc:

Dup

BD-69 ?

John H. Eilert, M.D./kim/6-9-72

REVIEW OF AMENDMENT

DATE COMPLETED: 6-16-72

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, PA 19124

NAME OF DRUG: Trade & Generic: Folic Acid 1 mg. in bottles of 100 tablets.

DATE OF SUBMISSION: 5-25-72

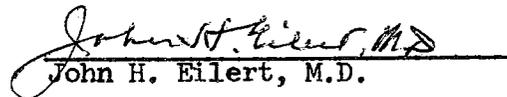
TYPE OF SUBMISSION: Additional distributor, Spencer-Mead Inc.
Valley Stream, N.Y. 11582
container label.

CLINICAL EVALUATION:

Review of Labeling: Container label conforms to those already accepted.

CONCLUSION: Approvable container label.

RECOMMENDATIONS: 1. Chemist to review status.
2. Approve container label.


John H. Eilert, M.D.

cc:

Dup

BD-69

John H. Eilert, M.D./kim/6-19-72

REVIEW OF AMENDMENT

DATE COMPLETED: 9-6-72

ANDA #: 80-686

~~_____~~
F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, Pa. 19124

NAME OF DRUG: Trade & Generic: Folic Acid Tablets, U.S.P. 1 mg.

DATE OF SUBMISSION: 8-7-72

TYPE OF SUBMISSION: Container label for Spencer-Mead, Inc.
Valley Stream, New York 11582
1,000 tablets

CLINICAL EVALUATION:

Review of Labeling: Approvable.

CONCLUSION: 1. Approvable container label.
2. No response to requested inspection.

RECOMMENDATIONS: Approve submission.


John H. Ellert, M.D.

cc:
Dup
BD-69
John H. Ellert, M.D./kim/9-12-72

REVIEW OF AMENDMENTS

DATE COMPLETED: 12-5-72

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, Pa. 19124

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

DATES OF SUBMISSION: 9-14-72, 11-10-72

TYPE OF SUBMISSION: Distributor data, labeling.

CLINICAL EVALUATION:

Review of Studies: For chemist evaluation.

Review of Labeling:

Immediate container: 9-14-72: Cooper Drug Co., 1233 Combermere, Troy,
Michigan 48084

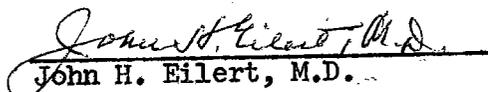
100 and 1,000 tablet containers. Zip # on label
is 98084, on letter is 48084.

11-10-72: Sherry Pharmaceutical Co., Inc. 1550 Fifth
Avenue, Bayshore, N.Y. 11706. 100 and 1,000
tablet containers.

Package insert: To use approvable insert.

CONCLUSION: 1. Requires chemist survey.
2. Cooper label contains California zip number.

RECOMMENDATION: 1. Review by chemist.
2. Reject Cooper label, request correction.


John H. Eilert, M.D.

cc:

Dup

BD-69

John H. Eilert, M.D./kim/12-5-72

REVIEW OF AMENDMENTS

DATE COMPLETED: 1-10-73

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc.
Castor & Kensington Aves.
Philadelphia, Pa. 19124

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

DATES OF SUBMISSION: 12-7-72 12-8-72

TYPE OF SUBMISSION: Distributor notifications.

CLINICAL EVALUATION:

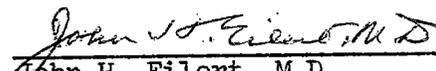
Review of Labeling:

Dec. 7, 1972: Rugby Laboratories, Inc. 420 Doughty Boulevard, Inwood,
L.I., N.Y. 11696, 1,000 tablets. Approvable.

Dec. 8, 1972: Cooper Drug Co., Troy, Mich. 48084, 100 tablets and
1,000 tablets. Approvable.

CONCLUSION: 1. Acceptable container labeling.
2. No commitment from Cooper Drug Co.

RECOMMENDATIONS: 1. Approve labeling.
2. Request required information in re Cooper Drug Co.


John H. Eilert, M.D.

cc:

Dup

BD-69

John H. Eilert, M.D./kim/1-11-73

REVIEW OF AMENDMENT

DATE COMPLETED: 6-27-73

ANDA #: 80-686

F.R. DATE: 4-9-71

CO. NAME: Richlyn Laboratories, Inc
Castor & Kensington Aves
Philadelphia, PA 19124

APPROVAL DATE: None

NAME OF DRUG: Folic Acid Tablets, USP 1 mg. in bottles of 1,000

DATE OF SUBMISSION: 5-21-73

TYPE OF SUBMISSION: New distributor and labeling

CLINICAL EVALUATION:

1. Review of Studies: Chemist to review
2. Review of Labeling: ARCUM Pharmaceutical Corp., Vienna, VA 22180
approvable.

CONCLUSION: Approvable distributor label.

RECOMMENDATIONS: Approve container label.


John H. Eilert, M.D.

cc:

Dup

BD-69

JHEilert/wlb/6-27-73

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
April 9, 1971

NDA Number
80-686

Name and Address of Applicant (City and State)

Richlyn Laboratories
Phila., Pa. 19124

Original 10-7-71
1-17-72; 3-2-72
Amendment 3-23-72;
4-14-72; 5-15-72
Supplement 5-25-72
5-26-72; 8-7-72
9-14-72; 11-10-72
12-7-72; 12-8-72
Other 5-21-73

Name of Drug

Folic Acid

Nonproprietary Name

Purpose of Supplement

Date(s) of Submission(s)

Pharmacological Category

vitamin

How Dispensed

R_x



O.T.C.



Dosage Form(s)

tablet

Potency (ies)

1 mg

AF Number
28-724

Related IND/NDA/MF

Satisfactory



Labeling

Date Due _____

Satisfactory



Components, Composition, Manufacturing and Controls

Date Due _____

Satisfactory



Biologic Availability

Date Due deferred

Is data on current

formulation?

YES

NO

Satisfactory



Probably or Possibly Effective Indications (if in labeling)

Date data Due _____

Establishment Inspection

Recalls

Is relabeling of drug in commercial channels required? YES No

If so, what level?

Remarks

APPEARS THIS WAY
ON ORIGINAL

Conclusions

approve for applicant and distributors:

Approved Pharmaceutical Corp; Barre Drug Co., Inc; Arcum Pharmaceuticals, Inc.;
Spencer-Mead, Inc.; Cooper Drug Co., Sherry Pharmaceutical Co., Inc.;
Bioline Laboratories, Inc.; Rugby Laboratories and United Pharmaceutical, Inc.

Am. Smith

CHEMIST'S REVIEW FOR ABBRVIATED NEW DRUG APPLICATION OR SUPPLEMENT	Federal Register Statement Date	ORIGINAL <input type="checkbox"/> SUPPLEMENT <input type="checkbox"/>
---	------------------------------------	--

Name & Address of Applicant (City & State) Dome Laboratories West Haven, CT 06516	NDA Number 80-972 Supplement Date and Number
---	--

Name of Drug vitamin A	Nonproprietary Name	Amendment Date(s)
---------------------------	---------------------	-------------------

Purpose of Supplement	Other Date(s) Report 6-8-73 AF Number 1-105
-----------------------	---

Pharmacological Category vitamin	How Dispensed R _x <input checked="" type="checkbox"/> O.T.C. <input type="checkbox"/>	Related IND/NDA/AF(s)
-------------------------------------	---	-----------------------

Dosage Form(s)	Potency (ies)	
----------------	---------------	--

Satisfactory <input type="checkbox"/>	Labeling Date Due <u>firm to submit container labels with report per medical officer's review</u>
---------------------------------------	--

Satisfactory <input type="checkbox"/>	Components, Composition, Manufacturing and Controls Date Due _____
---------------------------------------	---

Satisfactory <input type="checkbox"/>	Biologic Availability Date Due _____ Is data on current formulation? YES <input type="checkbox"/> NO <input type="checkbox"/>	APPEARS THIS WAY ON ORIGINAL
---------------------------------------	---	---

Satisfactory <input type="checkbox"/>	Probably or Possibly Effective Indications (if in labeling) Date Data Due _____
---------------------------------------	---

Establishment Inspection	Recalls
--------------------------	---------

If relabeling of drug in commercial channels required? YES NO

If so, what level: _____

Remarks

in the future firm to submit both container labels and package insert.

Conclusions

ack majarski

CHEMIST'S REVIEW FOR REVISED NEW DRUG APPLICATION OR SUPPLEMENT
Federal Register Statement Date 4/9/71
ORIGINAL 10/7/71
SUPPLEMENT

Name & Address of Applicant (City & State)
Richlyn Laboratories, Inc.
Philadelphia, Pennsylvania 19124
NDA Number 80-686
Supplement Date and Number

Name of Drug
Folic Acid
Nonproprietary Name
Amendment Date(s)

Purpose of Supplement
Other Date(s)
AF Number

Pharmacological Category
vitamin
How Dispensed
R_x O.T.C.
Related IND/NDA/ME(s) 28-724

Dosage Form(s)
tablet
Potency (ies)
1.0 mg

Satisfactory Labeling
 Date Due _____ To be revised (JHEilert)

Satisfactory Components, Composition, Manufacturing and Controls
 Date Due _____ see below

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

APPEARS THIS WAY ON ORIGINAL

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

Establishment Inspection
Unsatisfactory: TWX 8/2/71
Recalls

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

Remarks
Request: 1. Revised labeling, as per M.O.'s report
2. Clarification of procedures on _____
_____ asks for clarification
3. Satisfactory inspection

Conclusions
rev w/f
Chill 11/11/71
gmillar

CHEMIST'S REVIEW FOR
RELATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
4/9/71

ORIGINAL 10/7/71
SUPPLEMENT

Name and Address of Applicant (City & State)
Richlyn Laboratories, Inc.
Philadelphia, Pennsylvania 19124

NDA Number
80-686

Name of Drug
Folic Acid

Nonproprietary Name

Amendment Date(s)
11/30/71 +12/28/71

Use of Supplement

Other Date(s)

Pharmacological Category
vitamin

How Dispensed
Rx O.T.C.

AF Number
28-724

Drug Form(s)
tablet

Potency (ies)
1.0 mg

Related IND/NDA/ME(s)

Satisfactory Labeling
 Date Due _____ To be revised (JHEilert)

Satisfactory Components, Composition, Manufacturing and Controls
 Date Due _____ Certification from Arcum (repackager, distributor)

Satisfactory Biologic Availability
 Date Due _____ na

Is data on current formulation? YES NO

APPEARS THIS WAY ON ORIGINAL

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

Establishment Inspection
Unsatisfactory: TTX 8/2/71
ARCUM = satisfactory = 9/28/71

Recalls
YES NO

Is relabeling of drug in commercial channels required?
If so, what level?

Remarks
Request: Revised labeling, as per H.O.'s report
Certification from Arcum
Satisfactory inspection, as requested 11/23/71

Conclusions
rev w/f
guillár 1/13/72

CHIEF'S REVIEW FOR
 ABREVIATED NEW DRUG APPLICATION
 (OR SUPPLEMENT)

Federal Register
 Statement Date
 4/9/71

NDA Number 80-686

Name and Address of Applicant (City and State)
 Richlyn Laboratoires, Inc.
 Philadelphia, Pennsylvania 19124

Original xxx
 Amendment _____
 Supplement _____
 Other _____

Name of Drug
 FOLIC ACID

DATE(s) of Submission(s)
 1/3/72 + 1/17/72

Purpose of Supplement

Pharmacological Category
 vitamin

How Dispensed
 Rx OTC

AF Number 28-724

Dosage Form(s)
 tablet

Potency(ies)
 1.0 mg.

Related IND/NDA/MT

Satisfactory Labeling Date Due Containers (for 2 new distributors) = satisfactory

Satisfactory Components, Composition, Manufacturing and Controls Date Due NA Satisfactory (differential purch)

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

**APPEARS THIS WAY
 ON ORIGINAL**

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

Establishment Inspection
 Unsatisfactory: TWX 8/2/71

Recalls

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

Remarks
 NOTE: firm only submitted container labels (+ statements for 2 new distributors)
 Request: all the information previous requested (1/31/72)

Conclusions
 rev w/f
 Chull
 gmillar 2/15/72

ABREVIATED NEW DRUG APPLICATION

Statement Date

4/9/71

NDA Number 80-686

Name and Address of Applicant (City and State)
 Richlyn Laboratoires, Inc.
 Philadelphia, Pennsylvania 19124

Original xxx
 Amendment _____
 Supplement _____
 Other _____

Name of Drug
 Nonproprietary Name
 FOLIC ACID

DATE(s) of Submission(s)
 1/3/72 + 1/17/72
 3/2/72

Purpose of Supplement

Pharmacological Category
 vitamin

How Dispensed
 Rx OTC

AF Number 28-724

Dosage Form(s)
 tablet

Potency(ies)
 1.0 mg.

Related IND/NDA/ME

Satisfactory Labeling
 Date Due Container revised at next printing(JHEilert)

Satisfactory Components, Composition, Manufacturing and Controls
 Date Due _____ Requested but not submitted

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 _____

**APPEARS THIS WAY
 ON ORIGINAL**

Establishment Inspection
 Not in compliance: TWX 8/2/71

Recalls

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

Remarks
 request: 1. Container revision, at next printing
 2. all other information previously requested

Conclusions
 rev w/f
 Miller 3/21/72
 gmillar

NEW DRUG APPLICATION OR SUPPLEMENT Statement Date 4/2/71
 & Address of Applicant (City & State) Richlyn Laboratories, Inc. Philadelphia, Pennsylvania 19124
 SUPPLEMENT NDA Number 80-686
 Supplement Date and No.

Name of Drug Nonproprietary Name Folic Acid
 Amendment Date(s) 11/30/71 +12/28/71 3/23+4/10+5/15+5/25(2)+5/26

Indication of Supplement
 Other Date(s)

Pharmacological Category New Dispensed
 AF Number 28-724

Therapeutic Category vitamin
 Rx O.T.C.
 Related IND/NDA/NE(s)

Dosage Form(s) tablet Potency (ies) 1.0 mg

Satisfactory Labeling Date Due satisfactory (jheilert)

Satisfactory Components, Composition, Manufacturing and Controls Date Due requested, but not submitted

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
 APPEARS THIS WAY ON ORIGINAL

Establishment Inspection NOT in compliance : TWX 8/2/71
 Recalls

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

Remarks Request: 1. manufacturing information as per previous letters 2. satisfactory inspection report.

Conclusions rev w/f
 gmillar

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
(NDA SUPPLEMENT)

Federal Register
Statement Date
4-9-71

NDA Number

Name and Address of Applicant (City and State)

80-686

Richlyn Laboratories, Inc.
Philadelphia, Pennsylvania 19124

Original
Amendment XXX
Supplement
Other

Name of Drug

Nonproprietary Name

Folic Acid

DATE(s) of Submission(s)

8-7-72

Purpose of Supplement

Pharmacological Category

How Dispensed

vitamin

Rx OTC

AF Number
28-724

Dosage Form(s)

Potency(ies)

tablet

1.0 mg.

Related IND/NDA/EF

Satisfactory

Labeling

Date Due satisfactory per M.O.R.

Satisfactory

Components, Composition, Manufacturing and Controls

Date Due per compendium

Satisfactory

Biologic Availability

Date Due NA

Is data on current
formulation? YES NO

APPEARS THIS WAY
ON ORIGINAL

Satisfactory

Probably or Possibly Effective Indications

(if in labeling)

Date data Due

Establishment Inspection

Recalls

TWX 9-20-72 unsatisfactory

Is relabeling of drug in commercial channels required? YES NO

If so, what level:

Remarks

recent inspection unsatisfactory

(Distributor statement for Spencer - mail dated 12-29-71
submitted 1-3-72)

Conclusions

rev w/f majarski

M. A. Jarski 9/27/72

ABBREVIATED NEW DRUG APPLICATION OR SUPPLEMENT

FEDERAL REGISTER Statement Date

NDA Number 80-686

Name and Address of Applicant (City and State) Richlyn Laboratories Philadelphia, Pennsylvania 19124

Original _____ Amendment XXX _____

Name of Drug Folic Acid Nonproprietary Name

Supplement _____

Purpose of Supplement

Other _____

Pharmacological Category vitamin How Dispensed Rx [X] O.T.C. []

Date(s) of Submission(s) 9-14-72 10-16-72 11-10-72

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

AF Number 28-727 Related IND/NDA/MF

Satisfactory Labeling Date Due Cooper Drug unsatisfactory

Satisfactory Components, Composition, Manufacturing and Controls Date Due clarification of "alternate formulation"

Satisfactory Biologic Availability Date Due deferred Is data on current formulation? YES [] NO []

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

Establishment Inspection 9-20-72 unsatisfactory Recalls

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

Remarks Note: Submissions of 7-28-72 & 10-5-72 are No Reply! APPEARS THIS WAY ON ORIGINAL

Conclusions rev w/f mak jarski M.A. Jarski 12/8/72

CHEMIST'S REVIEW FOR
ADVERTISED NEW DRUG APPLICATION
(NDA) SUPPLEMENT

Federal Register
Statement Date

NDA Number
80-686

Name and Address of Applicant (City and State)
Richlyn Laboratories, Inc.
Phila., Penna

Original
Amendment XXX
Supplement _____
Other _____

Name of Drug
Folic Acid

Nonproprietary Name

DATE(s) of Submission
12-7-72
12-8-72
1-16-73

Purpose of Supplement

Pharmacological Category
vitamin

How Dispensed
 Rx OTC

AF Number
28-724

Dosage Form(s)
tablet

Potency (ies)
1 mg.

Related IND/NEA/NE

Satisfactory Labeling
Date Due satisfactory per medical officer

Satisfactory Components, Composition, Manufacturing and Controls
Date Due additional information

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

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

Establishment Inspection
referred to compliance 3-21-73

Recalls

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

Remarks
Note: Firm provides for an "alternate formulation" - this is essentially a change in batch size and not a new formulation. (see attached)

APPEARS THIS WAY
ON ORIGINAL

Conclusions
rev w/f majarski

majarski 3/28/73

Amulation

Redacted _____

pages of trade

secret and /or

confidential

commercial

information

COMBINED REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date

ORIGINAL

Name & Address of Applicant (City & State)
Richlyn Laboratories, Inc.
Philadelphia, PA. 19124

SUPPLEMENT
NDA Number
80-686

Name of Drug
folic acid

Nonproprietary Name

Supplement Date and Name
Amendment Date(s)
4-11-73

Purpose of Supplement

Other Date(s)

Pharmacological Category
vitamin

How Dispensed
Rx O.T.C.

AF Number
28-724
Related IND/INDA/IF(s)

Dosage Form(s)
tablet

Potency (ies)
1.0 mg.

Satisfactory Labeling
 Date Due ~~satisfactory~~

Satisfactory Components, Composition, Manufacturing and Controls
 Date Due satisfactory

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

APPEARS THIS WAY
ON ORIGINAL

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

Establishment Inspection
not in compliance see memo BD-340 dated 4-26-73

Recalls

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

Remarks
Firm to achieve a satisfactory inspection

Conclusions
ack majarski M.A. Jarski 5/31/73

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-686

**ADMINISTRATIVE
DOCUMENTS**

3-21-73

FROM:

M.A. Jarski

(thru Jack L. Meyer)

OFFICE

BD-69

TO:

Mr. B.T. Loftus, Gen. Dir. Office of Compliance ^{DIVISION} (thru Stan Stringer)

BD-300

SUBJECT:

collaborative draft(s)

SUMMARY

; In connection with NDA 80-686 for Folic Acid Tablets, 1.0 mg.

The applicant Richlyn Laboratories, Inc.

AF 28-724

1-22-73

We acknowledge receipt on 11-72, 12-12-72 and of communications dated 12-7-72, 12-8-72 and 1-16-73 for

ANDA

In accordance with the 2/27/73 directive, Office of Compliance a request is made for:

REQUESTED

1. establishment inspection report on
- a. the applicant
- b. others
2. evaluation of compliance with CGMPR
3. recommendation for approval/disapproval of the application/communication/supplement based on your evaluation of compliance with CGMPR

PLEASE EXPEDITE

NATURE

M.A. Jarski

DOCUMENT NUMBER

80-686

a. Each label, or other labeling, should be clearly identified to show its position on, or the manner in which it accompanies, the market package.

b. If the drug is to be offered over the counter, labeling on or within the retail package should include adequate directions for use by the layman under all the conditions for which the drug is intended for lay use or is to be prescribed, recommended, or suggested in any labeling or advertising sponsored by or on behalf of the applicant and directed to the layman. If the drug is intended or offered for uses under the professional supervision of a practitioner licensed by law to administer it, the application should also contain labeling that includes adequate information for all such uses, including all the purposes for which the over-the-counter drug is to be advertised to, or represented for use by, physicians.

c. If the drug is limited in its labeling to use under the professional supervision of a practitioner licensed by law to administer it, its labeling should bear information for use under which such practitioners can use the drug for the purposes for which it is intended, including all the purposes for which it is to be advertised or represented, in accord with §1.106(b) (21 CFR 1.106(b)). The application should include any labeling for the drug intended to be made available to the layman.

d. If no established name exists for a new-drug substance, the application shall propose a nonproprietary name for use as the established name for the substance.

e. Typewritten or other draft labeling copy may be submitted for preliminary consideration of an application. An application will not ordinarily be approved prior to the submission of the final printed label and labeling of the drug.

f. No application may be approved if the labeling is false or misleading in any particular. (When mailing pieces, any other labeling, or advertising copy are devised for promotion of the new drug, samples shall be submitted at the time of initial dissemination of such labeling and at the time of initial placement of any such advertising for a prescription drug (see §130.13 of the new-drug regulations). Approval of a supplemental new-drug application is required prior to use of any promotional claims not covered by the approved application.)

5. A statement as to whether the drug is (or is not) limited in its labeling and by this application to use under the professional supervision of a practitioner licensed by law to administer it.

6. A full list of the articles used as components of the drug. This list should include all substances used in the synthesis, extraction, or other method of preparation of any new-drug substance, and in the preparation of the finished dosage form, regardless of whether they undergo chemical change or are removed in the process. Each substance should be identified by its established name, if any, or complete chemical name, using structural formulas when necessary for specific identification. If any proprietary preparation is used as a component, the proprietary name should be followed by a complete quantitative statement of composition. Reasonable alternatives for any listed substance may be specified.

7. A full statement of the composition of the drug. The statement shall set forth the name and amount of each ingredient, whether active or not, contained in a stated quantity of the drug in the form in which it is to be distributed (for example, amount per tablet or per milliliter) and a batch formula representative of that to be employed for the manufacture of the finished dosage form. All components should be included in the batch formula regardless of whether they appear in the finished product. Any calculated excess of an ingredient over the label declaration should be designated as such and percent excess shown. Reasonable variations may be specified.

8. A full description of the methods used in, and the facilities and controls used for, the manufacture, processing, and packing of the drug. Included in this description should be full information with respect to any new-drug substance and to the new-drug dosage form, as follows, in sufficient detail to permit evaluation of the adequacy of the described methods of manufacture, processing, and packing and the described facilities and controls to determine and preserve the identity, strength, quality, and purity of the drug:

a. A description of the physical facilities including building and equipment used in manufacturing, processing, packaging, labeling, storage, and control operations.

b. A description of the qualifications, including educational background and experience, of the technical and professional personnel who are responsible for assuring that the drug has the safety, identity, strength, quality, and purity it purports or is represented to possess, and a statement of their responsibilities.

c. The methods used in the synthesis, extraction, isolation, or purification of any new-drug substance. When the specifications and controls applied to such substance are inadequate in themselves to determine its identity, strength, quality, and purity, the methods should be described in sufficient detail, including quantities used, times, temperatures, pH, solvents, etc., to determine these characteristics. Alternative methods or variations in methods within reasonable limits that do not affect such characteristics of the substance may be specified.

d. Precautions to assure proper identity, strength, quality, and purity of the raw materials, whether active or not, including the specifications for acceptance and methods of testing for each lot of raw material.

e. Whether or not each lot of raw materials is given a serial number to identify it, and the use made of such numbers in subsequent plant operations.

f. If the applicant does not himself perform all the manufacturing, processing, packaging, labeling, and control operations for any new-drug substance or the new-drug dosage form, his statement identifying each person who will perform any part of such operations and designating the part; and a signed statement from each such person fully describing, directly or by reference, the methods, facilities, and controls in his part of the operation.

g. Method of preparation of the master formula records and individual batch records and manner in which these records are used.

h. The instructions used in the manufacturing, processing, packaging, and labeling of each dosage form of the new drug, including any special precautions observed in the operations.

i. Adequate information with respect to the characteristics of and the test methods employed for the container, closure, or other component parts of the drug package to assure their suitability for the intended use.

j. Number of individuals checking weight or volume of each individual ingredient entering into each batch of the drug.

k. Whether or not the total weight or volume of each batch is determined at any stage of the manufacturing process subsequent to making up a batch according to the formula card and, if so, at what stage and by whom it is done.

l. Precautions to check the actual package yield produced from a batch of the drug with the theoretical yield. This should include a description of the accounting for such items as discards, breakage, etc., and the criteria used in accepting or rejecting batches of drugs in the event of an unexplained discrepancy.

m. Precautions to assure that each lot of the drug is packaged with the proper label and labeling, including provisions for labeling storage and inventory control.

n. The analytical controls used during the various stages of the manufacturing, processing, packaging, and labeling of the drug, including a detailed description of the collection of samples and the analytical procedures to which they are subjected. The analytical procedures should be capable of determining the active components within a reasonable degree of accuracy and of assuring the identity of such components. If the article is one that is represented to be sterile, the same information with regard to the manufacturing, processing, packaging, and the collection of samples of the drug should be given for sterility controls. Include the standards used for acceptance of each lot of the finished drug.

o. An explanation of the exact significance of the batch control numbers used in the manufacturing, processing, packaging, and labeling of the drug, including the control numbers that appear on the label of the finished article. State whether these numbers enable determination of the complete manufacturing history of the product. Describe any methods used to permit determination of the distribution of any batch if its recall is required.

p. A complete description of, and data derived from, studies of the stability of the drug, including information showing the suitability of the analytical methods used. Describe any additional stability studies underway or contemplated. Stability data should be submitted for any new-drug substance, for the finished dosage form of the drug in the container in which it is to be marketed, including any proposed multiple-dose container, and if it is to be put into solution at the time of dispensing, for the solution prepared as directed. State the expiration date(s) that will be used on the label to preserve the identity, strength, quality, and purity of the drug until it is used. (If no expiration date is proposed, the applicant must justify its absence.)

q. Additional procedures employed which are designed to prevent contamination and otherwise assure proper control of the product.

(An application may be refused unless it includes adequate information showing that the methods used in, and the facilities and controls used for, the manufacturing, processing, and packaging of the drug are adequate to preserve its identity, strength, quality, and purity in conformity with good manufacturing practice and identifies each establishment, showing the location of the plant conducting these operations.)

9. Samples of the drug and articles used as components, as follows: a. The following samples shall be submitted with the application or as soon thereafter as they become available. Each sample shall consist of four identical, separately packaged subdivisions, each containing at least three times the amount required to perform the laboratory test procedures described in the application to determine compliance with its control specifications for identity and assays:

i. A representative sample or samples of the finished dosage form(s) proposed in the application and employed in the clinical investigations and a representative sample or samples of each new-drug substance, as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

ii. A representative sample or samples of finished market packages of each dosage form of the drug prepared for initial marketing and, if any such sample is not from a commercial-scale production batch, such a sample from a representative commercial-scale production batch; and a representative sample or samples of each new-drug substance as defined in §130.1(g), from the batch(es) employed in the production of such dosage form(s).

iii. A sample or samples of any reference standard and blank used in the procedures described in the application for assaying each new-drug substance and other assayed

components of the finished drug: *Provided, however,* That samples of reference standards recognized in the official U.S. Pharmacopoeia or The National Formulary need not be submitted unless requested.

b. Additional samples shall be submitted on request.

c. Each of the samples submitted shall be appropriately packaged and labeled to preserve its characteristics, to identify the material and the quantity in each subdivision of the sample, and to identify each subdivision with the name of the applicant and the new-drug application to which it relates.

d. There shall be included a full list of the samples submitted pursuant to Item 9a; a statement of the additional samples that will be submitted as soon as available; and, with respect to each sample submitted, full information with respect to its identity, the origin of any new-drug substance contained therein (including in the case of new-drug substances, a statement whether it was produced on a laboratory, pilot-plant, or full-production scale) and detailed results of all laboratory tests made to determine the identity, strength, quality, and purity of the batch represented by the sample, including assays. Include for any reference standard a complete description of its preparation and the results of all laboratory tests on it. If the test methods used differed from those described in the application, full details of the methods employed in obtaining the reported results shall be submitted.

e. The requirements of Item 9a may be waived in whole or in part on request of the applicant or otherwise when any such samples are not necessary.

f. If samples of the drug are sent under separate cover, they should be addressed to the attention of the Bureau of Medicine and identified on the outside of the shipping carton with the name of the applicant and the name of the drug as shown on the application.

10. Full reports of preclinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate preclinical tests by all methods reasonably applicable to a determination of the safety and effectiveness of the drug under the conditions of use suggested in the proposed labeling.

b. Detailed reports of the preclinical investigations, including all studies made on laboratory animals, the methods used, and the results obtained, should be clearly set forth. Such information should include identification of the person who conducted each investigation, a statement of where the investigations were conducted, and where the underlying data are available for inspection. The animal studies may not be considered adequate unless they give proper attention to the conditions of use recommended in the proposed labeling for the drug such as, for example, whether the drug is for short- or long-term administration or whether it is to be used in infants, children, pregnant women, or women of child-bearing potential.

c. Detailed reports of any pertinent microbiological and *in vitro* studies.

d. Summarize and provide a list of literature references (if available) to all other preclinical information known to the applicant, whether published or unpublished, that is pertinent to an evaluation of the safety or effectiveness of the drug.

11. List of investigators. a. A complete list of all investigators supplied with the drug including the name and post office address of each investigator and, following each name, the volume and page references to the investigator's report(s) in this application and in any documents incorporated by reference, or the explanation of the omission of any reports.

b. The unexplained omission of any reports of investigations made with the new drug by the applicant, or

submitted to him by an investigator, or the unexplained omission of any pertinent reports of investigations or clinical experience received or otherwise obtained by the applicant from published literature or other sources, whether or not it would bias an evaluation of the safety of the drug or its effectiveness in use, may constitute grounds for the refusal or withdrawal of the approval of an application.

12. Full reports of clinical investigations that have been made to show whether or not the drug is safe for use and effective in use. a. An application may be refused unless it contains full reports of adequate tests by all methods reasonably applicable to show whether or not the drug is safe and effective for use as suggested in the labeling.

b. An application may be refused unless it includes substantial evidence consisting of adequate and well-controlled investigations, including clinical investigations, by experts qualified by scientific training and experience to evaluate the effectiveness of the drug involved, on the basis of which it could fairly and responsibly be concluded by such experts that the drug will have the effect it purports or is represented to have under the conditions of use prescribed, recommended, or suggested in the proposed labeling.

c. Reports of all clinical tests sponsored by the applicant or received or otherwise obtained by the applicant should be attached. These reports should include adequate information concerning each subject treated with the drug or employed as a control, including age, sex, conditions treated, dosage, frequency of administration of the drug, results of all relevant clinical observations and laboratory examinations made, full information concerning any other treatment given previously or concurrently, and a full statement of adverse effects and useful results observed, together with an opinion as to whether such effects or results are attributable to the drug under investigation and a statement of where the underlying data are available for inspection. Ordinarily, the reports of clinical studies will not be regarded as adequate unless they include reports from more than one independent, competent investigator who maintains adequate case histories of an adequate number of subjects, designed to record observations and permit evaluation of any and all discernible effects attributable to the drug in each individual treated and comparable records on any individuals employed as controls. An application for a combination drug may be refused unless there is substantial evidence that each ingredient designated as active makes a contribution to the total effect claimed for the drug combination. Except when the disease for which the drug is being tested occurs with such infre-

quency in the United States as to make testing impractical, some of the investigations should be performed by competent investigators within the United States.

d. Attach as a separate section a completed Form FD-1639, Drug Experience Report (obtainable, with instructions, on request from the Food and Drug Administration, Department of Health, Education, and Welfare, Washington, D.C. 20204), for each adverse experience or, if feasible, for each subject or patient experiencing one or more adverse effects, described in Item 12c, whether or not full information is available. Form FD-1639 should be prepared by the applicant if the adverse experience was not reported in such form by the investigator. The Drug Experience Report should be cross-referenced to any narrative description included in Item 12c.

e. All information pertinent to an evaluation of the safety and effectiveness of the drug received or otherwise obtained by the applicant from any source, including information derived from other investigations or commercial marketing (for example, outside the United States), or reports in the scientific literature, involving the drug that is the subject of the application and related drugs. An adequate summary may be acceptable in lieu of a reprint of a published report which only supports other data submitted. Reprints are not required of reports in designated journals, listed in §130.38 of the new-drug regulations, about related drugs; a bibliography will suffice. Include any evaluation of the safety or effectiveness of the drug that has been made by the applicant's medical department, expert committee, or consultants.

f. If the drug is a combination of previously investigated or marketed drugs, an adequate summary of pre-existing information from preclinical and clinical investigation and experience with its components, including all reports received or otherwise obtained by the applicant suggesting side effects, contraindications, and ineffectiveness in use of such components. Such summary should include an adequate bibliography of publications about the components and may incorporate by reference information concerning such components previously submitted by the applicant to the Food and Drug Administration.

g. The complete composition and/or method of manufacture of the new drug used in each submitted report of investigation should be shown to the extent necessary to establish its identity, strength, quality, and purity if it differs from the description in Item 6, 7, or 8 of the application.

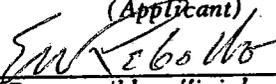
13. If this is a supplemental application, full information on each proposed change concerning any statement made in the approved application.

Observe the provisions of §130.9 of the new-drug regulations concerning supplemental applications.

Richlyn Laboratories, Inc.

(Applicant)

Per


(Responsible official or agent)

Vice President

(Indicate authority)

(Warning: A willfully false statement is a criminal offense. U.S.C. Title 18, sec. 1001.)

NOTE: This application must be signed by the applicant or by an authorized attorney, agent, or official. If the applicant or such authorized representative does not reside or have a place of business within the United States, the application must also furnish the name and post office address of and must be countersigned by an authorized attorney, agent, or official residing or maintaining a place of business within the United States.

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER
80-686 *Orig*
DATE APPROVAL LETTER ISSUED
7-20-73

Press Relations Staff (PA-40)

FROM:

- Bureau of Drugs
 Bureau of Veterinary Medicine

ATTENTION

APPROVAL OF ORIGINAL 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 1.6 mg

APPEARS THIS WAY
ON ORIGINAL

NAME OF APPLICANT (Include City and State)

Richlyn Laboratories, Inc.
Philadelphia, Pa.

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

vitamin

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

NAME

C. M. Smith

FORM PREPARED BY

C.M. Smith

DATE

NAME

J. L. Meyer

FORM APPROVED BY

DATE

[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:

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 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.
 Pfegston 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: "megaloblastic anemias associated with pellagra and similar deficiency states" and such vague, unspecific conditions as "megaloblastic 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 (dosage, 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:

80-686

CORRESPONDENCE

RICHLYN
LABORATORIES
INC.

ABBREVIATED
NEW DRUG APPLICATION Case Address "RICHLYN"

PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES • PHILADELPHIA, PENNSYLVANIA 19124 • 215 CU 9-2220

OCT 7 1971

80-486

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food and Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Gentlemen:

Enclosed in triplicate is an Original Abbreviated New Drug
Application re:

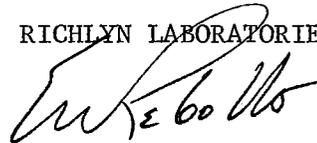
Folic Acid Tablets, U.S.P. - 1 mg. - C.T. Yellow.

Labeling is in accord with 36 F.R. 6843 (DESI 5897), April 9, 1971.

Your cooperation is appreciated.

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo
Vice-President

EWR/lrs
Encl.



MEMBER

OCT 21 1971

NDA 80-686

AF 280724

Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rehollo
Castor and Kensington Avenues
Philadelphia, Pennsylvania 19124

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 APPLICATION: October 7, 1971

DATE of RECEIPT: October 13, 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. 10/21/71

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

cc:

PHI-DO

Dup

BD-69

BD-300

BD-67

BD-22

JLMeyer/wlb/10-15-71

Ack.

JLMeyer 10/21/71

Gene Carroll, M.D. 10/21/71

JRW... 10/21/71

Salmon

NDA 80-686

AF 28-724

NOV 23 1971

Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rebollo
Castor and Kensington Avenues
Philadelphia, Pennsylvania 19124

Gentlemen:

Reference is made to your abbreviated new drug application dated October 7, 1971, 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 package insert:

1. In the DESCRIPTION section, add an appropriate description of the physical and chemical properties of the drug.
2. Revise the ACTIONS section to state that the exact mode of therapeutic action has not been determined. Follow this by a statement that the folic acid is enzymatically reduced in the body to tetrahydrofolic acid for activity.
3. In the DOSAGE and ADMINISTRATION section, remove the heading, ' _____ ' and the entire section devoted to ' _____ '.
4. In the HOW SUPPLIED section, state the strength and number of tablets per container size.

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

A clarification of the analytical procedures used to assure that the components and the final dosage form will comply with the specifications and tests described in an official compendium (naming the 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 drug and its components are adequate to assure their identity, strength, quality and purity, since it is noted that:

APPEARS THIS WAY
ON ORIGINAL

1. The generic name is not given for the component, _____
2. The procedures for the _____ are not listed.
3. The procedures for _____ are not listed.
4. The identification test for _____ is included in the _____ monograph.

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 Philadelphia District Office. We suggest you contact them and arrange for an inspection.

Please let us have your response promptly.

Sincerely yours,

Paul A. Bryan, M.D. 11/23/71

Paul A. Bryan, M.D.

Director

Drug Efficacy Study Implementation
Project Office

Bureau of Drugs

cc:
PHI-DO
Dup
BD-67
BD-69
BD-22
BD-100
BD-242

*JHEilert
11-17-71*

Miller 11/17/71
JHEilert/JIMeyer/GMiller 11-11-71

Final typed/rt 11/15/71

Rev w/f

JIMeyer 11/19/71

GM. Carroll M.D. 11/22/71

**RICHLYN
LABORATORIES
INC.**

Orig. *Rev w/F* *E*
Cable Address "RICHLYN"
PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES • PHILADELPHIA, PENNSYLVANIA 19124 • 215 CU 9-2220

November 30, 1971

**RESUBMISSION
NDA ORIG AMENDMENT**

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P. - 1 mg.
C.T. Yellow
ANDA #80-686
Additional Information Requested.

Gentlemen:

Herewith in triplicate is our response to your 11/23/71 letter.

Package Insert.

1. DESCRIPTION. We attempted to provide "appropriate" description by limiting same to physical description of the finished dosage unit--the only characteristic normally accessible to evaluation by the prescribing physician or the dispensing pharmacist (the originally intended readers of such inserts).
2. ACTIONS. Present phrasing appears more appropriate since we don't know the exact mode of action for the prophylactic or therapeutic activity. Your proposed reference to Tetrahydrofolic acid (THFA) is duly noted. We don't grasp the clinical significance of this biochemical fragment out of the full 6-page context afforded it in Goodman and Gilman; but we will include it if you insist.
3. DOSAGE AND ADMINISTRATION. The full wording (including the "Parenteral Administration" section) set forth in 36F.R.6843 (4/9/71) was employed in the belief that it provides a useful, possibly vital, clinical reminder to the physician. We included this information for his benefit, not ours (we do not market a parenteral form).
4. HOW SUPPLIED. It is our style to state the dosage unit strength under "DESCRIPTION". It is also generally desirable for us to avoid insert-statement of container contents since, in generic manufacturing, such packaging varies widely and unpredictably. Package content is always covered by package label.

MEMBER

**RICHLYN
LABORATORIES
INC.**

Cable Address "RICHLYN"

PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

Folic Acid Tablets, U.S.P.-1 mg.
C.T. Yellow
ANDA #80-686
Additional Information Requested cont'd.
11/30/71
Page 2

Test.

1. _____ " is a proprietary specialty (no established common or usual name) supplied and represented to us by _____

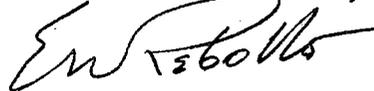
[
As stated in our 10/7/71 submission, our acceptance specifications, as described, conform with those of said supplier (in the absence of compendial or official reference).

2. _____ Specifications and references are enclosed.
3. _____ Specifications and references are enclosed.
4. _____ Identification for _____ is included because the _____, specifications for _____

We acknowledge your comments regarding inspectional status. We await your response re aforementioned labeling observations before proceeding to any revision.

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo
Vice President

EWR/lrs
Encl.



MEMBER

E

**RICHLYN
LABORATORIES
INC.**

Cable Address "RICHLYN"

PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES • PHILADELPHIA, PENNSYLVANIA 19124 • 215 CU 3-2220

December 28, 1971

NDA ORIG AMENDMENT

FRL

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
Original ANDA #80-686
Supplemental Application
Additional Packer (Repackaging) & Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(4)(v)--

Designated Repackager and Distributor:
Arcum Pharmaceutical Corp.
P.O. Box 38
Vienna, Virginia 22180

Applicant's Statement : previously herewith submitted
Applicant's Credentials: previously herewith submitted
Applicant's Labeling* : previously herewith submitted
*(4 copies, each of 3 sets; total: 12)

Sincerely,

RICHLYN LABORATORIES, INC.

L.P. Cecchini

L. P. Cecchini, Ph.D.
Director, Quality Assurance

LPC/1s
Att.



MEMBER

**RICHLYN
LABORATORIES
INC.**

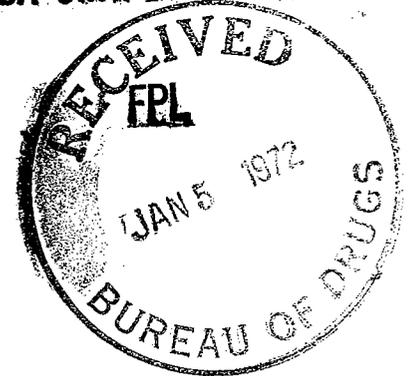
E
Cable Address "RICHLYN"

PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES • PHILADELPHIA, PENNSYLVANIA 19124 • 215 CU 9-2220

January 3, 1972

NDA ORIG AMENDMENT



Orig

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs .
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
Original ANDA #80-686
Supplemental Application
Additional Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(6) --

- (i) Designated Distributor: Spencer Mead, Inc.
270 W. Merrick Road
Valley Stream, New York 11582
- (ii) Applicant will conform.
- (iii) Distributor's Statement: previously submitted
 herewith submitted
- (iv) Labeling (4 copies, each of 3 sets; total: 12) herewith submitted.

Sincerely,

RICHLYN LABORATORIES, INC.

L. P. Cecchini

L. P. Cecchini, Ph.D
Director, Quality Assurance

LPC/ 1s

Att. (3 sets of 1000; 3 sets of 100 - Spencer Mead Inc.)

MEMBER

Orig

E

Cable Address "RICHLYN"

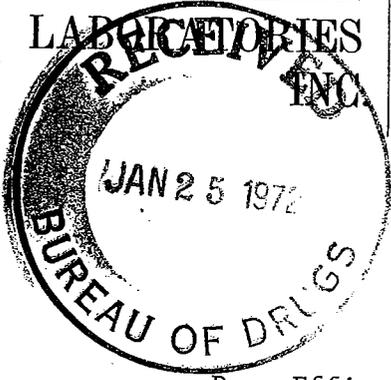
RICHLYN
LABORATORIES
INC.

PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

January 18, 1972

NDA ORIG AMENDMENT



Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
Original ANDA #80-686
Supplemental Application

Gentlemen:

The enclosed triplicate submission provides supplement per
21CFR§130.9 (a)(4)(iii).

Subject: Revision in manufacturing and control procedures--

Manufacturing:
--Alternate Master Formula Sheet (specimen attached).

Sincerely,

RICHLYN LABORATORIES, INC.

E. W. Rebollo
Vice President

EWR/lrs
Encl.

MEMBER

orig. mailed

NDA 80-686

AF 28-724

JAN 31 1972

Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rebollo
Castor and Kensington Avenues
Philadelphia, Pennsylvania 19124

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 communications dated November 30, 1971, and December 28, 1971, amending the application.

Your application, as amended, provides for you to market the drug under your own label. It also provides for you to label the drug with a label showing the repackager and distributor to be:

Arcum Pharmaceutical Corporation
Vienna, Virginia 22180

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

1. Replace the DESCRIPTION section with the following statement:

Folic acid is yellow or yellowish orange, odorless, crystalline powder. It is very slightly soluble in water; insoluble in alcohol, chloroform, and ether. It is readily soluble in solutions of alkalis. Folic acid is stable in neutral or alkaline solution but its stability decreases as the pH is reduced below 6. Considerable destruction of folic acid occurs below pH 4.

2. Revise the ACTIONS section. The following paragraph would be acceptable.

Folic acid is an important growth factor for a large variety of animal, plant, and microbial cells. Its function, in the form of its active metabolite tetrahydrofolic acid, is to transfer one-carbon molecular fragments such as formyl, hydroxymethyl or methyl from one compound to another. These fragments serve as building units

in the synthesis of certain purines, pyrimidines, and amino acids. The methylation of deoxyuridine to thymidine is one of the more important reactions in which folic acid participates, this being a preliminary step in the synthesis of deoxyribonucleic acid (DNA). Deficiency in the synthesis of DNA may interfere with mitosis and be responsible for the gigantic cells (megaloblasts) that are characteristic of megaloblastic anemias. Other important reactions requiring folic acid are the metabolic degradation of histidine to glutamic acid and the conversion of serine to glycine.

3. In the DOSAGE and ADMINISTRATION section, remove the heading, _____ " and the entire section devoted to _____ as was requested in our letter of November 23, 1971.
4. In the HOW SUPPLIED section, state the strength of your dosage form, as was also requested on November 23, 1971.

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

1. Certification from Arcum Pharmaceutical Corporation that the methods used in, and the facilities and controls used for, the packing and holding of the drug are in conformity with current good manufacturing practice in accord with Part 133 (21 CFR) of the regulations.
2. A satisfactory inspection report, as was also requested on November 23, 1971.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife 1/31/72

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

cc:
PHI-DO
Dup
BD-69
BD-67
BD-22
BD-242

JHEilert/JLMeyer/GMi Mar 1/13/72
Init. by MAClark/JLMeyer 1/14/72
sam/1/28/72

Chiller 1/28/72
S. Meyer 1/28/72

rev w/f

NDA 80-686

AF 28-724

Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rebollo
Castor and Kensington Avenues
Philadelphia, Pennsylvania 19124

FEB 28 1972

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 also acknowledge receipt of your communications dated January 3, 1972, January 17, 1972 and January 18, 1972, amending the application.

Reference is also made to our letter of January 31, 1972, reviewing your application.

Your application, as amended, provides for you to market the drug under your own label. It also provides for you to label the drug with labels showing the distributors to be:

Spencer-Mead Inc.
Valley Stream, New York 11582

Approved Pharmaceutical Corporation
Syracuse, New York 13201

Before we can complete the review of this abbreviated new drug application, however, it will be necessary for you: to revise the labeling; to submit the manufacturing information; and to provide for the satisfactory inspection requested on January 31, 1972.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife 2/28/72

Marvin Seife, M.D.

Director

Division of Actions Implementation
Drug Efficacy Study Implementation

Project Office

Bureau of Drugs

CC:

PHI-DO

Dup

BD-69 BD-67

BD-242 BD-22

JHEilert/JLMeyer/GMillar: 2/15/72

R/D init. MAClark, JLMeyer 2/17/72

Final typing bhy 2/23/72 Rev. W/F

*JHEilert
2-24-72*

JMeyer 2/23/72

Chull

**RICHLYN
LABORATORIES
INC.**

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

PHARMACEUTICALS ANTIBIOTICS GENERICS

FPL

CASTOR & KENSINGTON AVENUES • PHILADELPHIA, PENNSYLVANIA 19124 • 215 CU 3-2220

March 2, 1972

ORIG

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Supplemental Application
Additional Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(6) --

(i) Designated Distributor: Barre Drug Co., Inc.
Baltimore, Maryland 21215

(ii) Applicant will conform.

(iii) Distributor's Statement: previously submitted
 herewith submitted

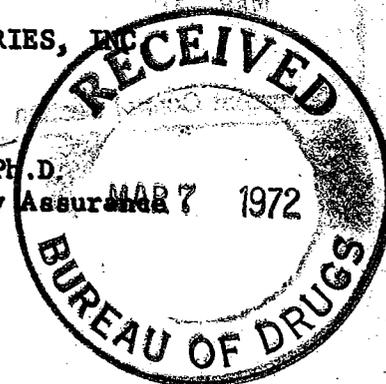
(iv) Labeling (4 copies, each of 3 sets; total: 12) herewith submitted.

Sincerely,

RICHLYN LABORATORIES, INC

L. P. Cecchini

L. P. Cecchini, Ph.D.
Director, Quality Assurance



LPC/lis

Att. (3 sets of 100's); (3 sets of 1000's)

MEMBER

**RICHLYN
LABORATORIES
INC.**

D/W/T = E
ORIG

Cable Address "RICHLYN"

PHARMACEUTICALS ANTIBIOTICS GENERICS

FPL

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

MAR 23 1972

**RESUBMISSION
NDA ORIG AMENDMENT**

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 1/31/72 and 2/28/72 requests for additional information.

Enclosed are specimens of package insert revised per your 1/31/72 guidelines.

Arcum Pharmaceutical Corporation's CGMP statement and insert revision have been requested and will be submitted as soon as available.

We acknowledge your request for a satisfactory inspection report. We anticipate the latter in the very near future.

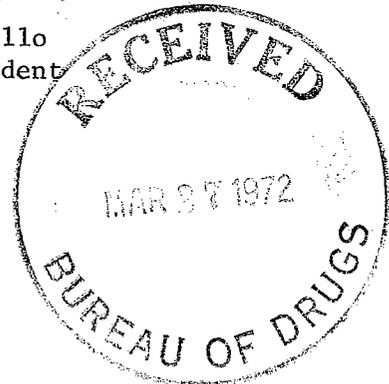
Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo
Vice President

EWR/lrs
Encl.



MEMBER

Salva

March 28, 1972

Theodore E. Byers
Director, Office of Compliance BD-300

BD-105

ANDAs (GMP Certification Violations)

1. As you are aware the DESI Project Office withholds approval of ANDAs because district inspections have shown that the firms are not in compliance with GMP as they have certified in each application.
2. DESI has had a tremendous amount of voluntary correction with some violative firms by denying approval of ANDAs because of critical or significant GMP violations.
3. However there are several firms which have not corrected violative conditions and continue to manufacture ANDA products without approval. Since these ANDAs are not approvable because of significant GMP problems, it would appear that we should consider taking legal action to have each ANDA product withdrawn from the market.
4. I am listing three examples of firms and products below. There are others.

I. _____

ANDAs - []

II. Bel-Mar Labs, Inwood, New York

- ANDAs - _____
- 80-710 Lidocaine HCL Inj.
 - 80-711 Procaine HCL Inj. 1%
 - 80-712 Thiamine HCL Inj. 200mg
 - 80-718 Thiamine HCL Inj. 100mg
 - 80-741 Testosterone Propionate Inj. 25mg
 - 80-742 Testosterone Propionate Inj. 50mg
 - 80-743 Testosterone Propionate Inj. 100mg
 - 80-758 Procaine HCL 1% w/Epinephrine
 - 80-759 Procaine HCL 2% w/Epinephrine
 - 80-760 Lidocaine HCL Inj. 2%

Page Two - ANDAs (GMP Certification Violations)

80-761 Pyridoxine HCL Inj. 100mg
80-756 Procaine HCL Inj. 2%
80-757 Lidocaine HCL Inj w/Epinephrine
80-820 Lidocaine HCL 1% w/Epinephrine
80-821 Chlorpheniramine Maleate Inj.
80-822 Diphenhydramine HCL Inj.

III Richlyn Laboratories Inc., Philadelphia, Penna.

80-079 Triple Sulfa Tabs
80-081 Sulfadiazine Tabs

80-109 Sulfisoxazole Tabs
80-151 Thyroglobulin Tabs
80-153 Isoniazid Tabs
80-686 Folic Acid Tabs
80-785 Triplennamine HCL Tabs
80-767 Methyltestosterone Tabs
80-780 Prednisolone Tabs 5mg orange
80-781 Hydrocortisone Tabs 20mg
80-782 Prednisone Tabs 5mg white
80-807 Diphenhydramine HCL Tabs
80-808 Pyrilamine Maleate Tabs
80-809 Chlorpheniramine Maleate Tabs
80-874 Pyserazine Citrate Tabs
80-880 Chloroquine Phos. Tabs
80-881 Dimenhydrinate Tabs

Bruce E. Byer - BD-105
Office of Scientific Evaluation

cc:

BD-100

BD-105

BD-310

BD-69 c/o Jack Meyer.

BD-310 c/o Ted Byers

BD-105 c/o BEByer/mw/4/4/72

NDA 80-686

AF 28-724

Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rebollo
Castor and Kensington Avenues
Philadelphia, Pennsylvania 19124

MAR 31 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.

We also acknowledge receipt of your communication dated March 2, 1972, amending the application.

Reference is also made to our letter of January 31, 1972, reviewing your application.

Your application, as amended, also provides for you to label the drug with the label showing the distributor to be:

Barre Drug Company, Inc.
Baltimore, Maryland 21215

We have reviewed this abbreviated new drug application and have the following comments regarding the proposed container label:

The "Usual Daily Dose" statement should be revised as follows:
"Usual Adult Daily Dosage."

This revision, however, may be made at the time of the next printing.

Before we can complete the review of this application, however, it will be necessary for you: to revise the labeling; to submit the

APPEARS THIS WAY
ON ORIGINAL

manufacturing information; and to provide for the satisfactory inspection requested on January 31, 1972.

Please let us have your response promptly.

Sincerely yours,

Margaret Clark M.D. for

Marvin Seife, M.D.

3/30/72

Director

Division of Actions Implementation

Drug Efficacy Study Implementation

Project Office

Bureau of Drugs

cc:

PHI-DO

Dup

BD-69

BD-67

BD-22

BD-242

JHEilert/JLMeyer/GMiHar: 3/21/72

R/D init. MAClark, JLMeyer 3/24/72

Final typing bhy 3/30/72

Rev. W/F

JLMeyer 3/30/72

Miller 3/30/72

*M. Seife
3/30/72*

APPEARS THIS WAY
ON ORIGINAL

RICHLYN
LABORATORIES
INC.

PHARMACEUTICALS

ANTIBIOTICS

GENERIC^S

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

April 10, 1972

Rev. of RESUBMISSION
NDA ORIG AMENDMENT *E*

Cable Address "RICHLYN"

ORIG.

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 3/31/72 request for additional information.

In response to your 1/31/72 and 2/28/72 communications, please see our 3/23/72 submission covering package insert revision and manufacturing information (Arcum Pharmaceutical Corporation's CGMP statement and insert revision; our anticipation of satisfactory inspection report in the near future).

Regarding your 3/31/72 comments on container label, enclosed is our printing revision order this date. Resultant label specimens will be submitted upon our receipt of same.

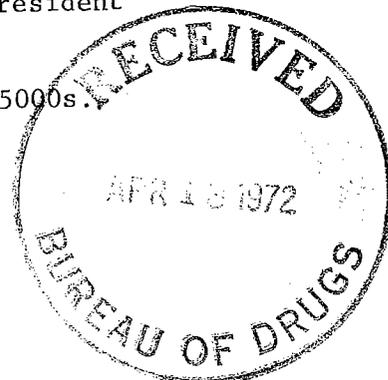
Sincerely,

RICHLYN LABORATORIES, INC.

E. W. Rebollo
E. W. Rebollo
Vice President

EWR/lrs

Encl.: Printing Revision Order: 100s, 1000s, 5000s.



**RICHLYN
LABORATORIES
INC.**

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

ORIG. **FPL**

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

April 14, 1972

**Drug Efficacy Study Implementation
Project Office -- BD-3
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852**

Reference: **Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-600**

Supplemental Application
Additional Packer (Repackaging)
& Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR8130.9
(a)(4)(v)--

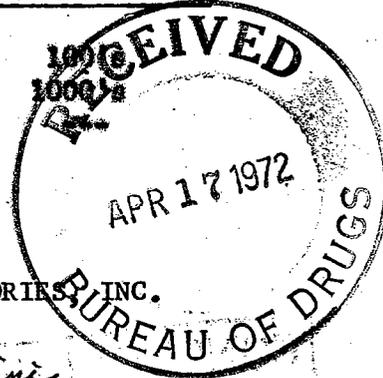
Designated Repackager and Distributor: **Arcum Pharmaceutical Corp.
Vienna, Va. 22180**

Applicant's Statement : previously herewith submitted
Applicant's Credentials : previously herewith submitted
Applicant's Labeling* : original revised
*(4 copies, each of 3 sets; total: 12)

DOSE STRENGTH

1 mg.
1 mg.
Insert

PACKAGING UNIT



Sincerely,

RICHLYN LABORATORIES, INC.

L. P. Cecchini

L. P. Cecchini, Ph.D.
Director, Quality Assurance

LPC/lis
Att.

RICHLYN
LABORATORIES
INC.

PHARMACEUTICALS ANTIBIOTICS GENERICS

FPL

CASTOR & KENSINGTON AVENUES • PHILADELPHIA, PENNSYLVANIA 19124 • 215 CU 3-2220

MAY 15 1972

ORIG

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Supplement

Gentlemen:

The enclosed triplicate submission provides supplement per 21CFR§130.9
(a)(4):

- (i): Revision in labeling.
- (ii): Addition of claim.
- (iii): Revision in manufacturing or control procedures.
- (iv): Change in manufacturing facilities.

Appropriate exhibits are attached.*

Sincerely,

RICHLYN LABORATORIES, INC.

EWR
E. W. Rebollo
Vice President



EWR/1s
Encl.

*Container Label, 100s, 1000s, 5000s -- revised per your

5/11/72 comments

RICHLYN
LABORATORIES
INC.

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

ORIG. FPL

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

May 25, 1972

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Supplemental Application
Additional Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(6) --

(i) Designated Distributor: United Pharmaceuticals, Inc.
Oakland, California 94601

(ii) Applicant will conform.

(iii) Distributor's Statement: previously submitted
 herewith submitted

(iv) Labeling (4 copies, each of 3 sets; total: 12) herewith
submitted.

Labeling submission is X original revised

DOSAGE STRENGTH

1 mg.

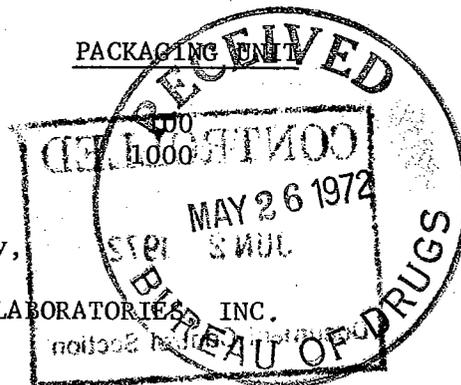
PACKAGING UNIT

Sincerely,

RICHLYN LABORATORIES, INC.

L. P. Cecchini

L. P. Cecchini, Ph.D.
Director, Quality Assurance



NDA 80-686

AF 28-724

Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rebello
Castor and Kensington Avenues
Philadelphia, Pennsylvania 19124

JUL 05 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.

We also acknowledge receipt of your communications dated March 23, 1972, April 10, 1972, April 14, 1972, May 15, 1972, May 25, 1972 (two) and May 26, 1972, amending the application.

Reference is also made to our letter of January 31, 1972 and March 31, 1972, reviewing your application.

Your application, as amended, also provides for you to label the drug with the label showing the distributors to be:

Bioline Laboratories
Brooklyn, New York 11203

United Pharmaceuticals, Inc.
Oakland, California 94601

Before we can complete the review of this application, however, it will be necessary for you to provide for a satisfactory inspection, as previously requested.

Please let us have your response regarding the above request promptly.

Sincerely yours,

Marvin Seife 7/5/72

Marvin Seife, M.D.

Director

Division of Actions Implementation
Drug Efficacy Study Implementation

Project Office

Bureau of Drugs

cc:

PHI-DO

Dup

BD-69 BD-67 BD-242 BD-106

R/D init. by MClark/JMeyer 6-28-72

JHEllert/JIMeyer/GMillar 6-27-72

Final typing/wlb/6-30-72

Rev w/f

RICHLYN
LABORATORIES
INC.

PHARMACEUTICALS

ANTIBIOTICS

GENERICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

Rev. W/F RESUBMISSION *E*
ANDA ORIG AMENDMENT
Cable Address "RICHLYN"

JUL 18 1972

DUP
W reply
made
12-5-72

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Additional Information Requested

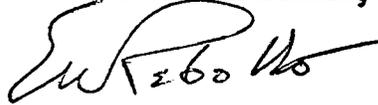
Gentlemen:

This triplicate submission is in response to your 7/5/72 request for additional information.

Regarding your request for a satisfactory establishment inspection report, please be advised that we have requested said inspection by Philadelphia District Office and that we anticipate appropriate resolution of this matter.

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo
Vice President

EWR/Is



RICHLYN
LABORATORIES
INC.

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

FPL

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

August 7, 1972

ORIG

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Reference: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686

Supplemental Application
Additional Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(6) --

(i) Designated Distributor: Spencer-Mead Inc.
Valley Stream, New York 11582

(ii) Applicant will conform.

(iii) Distributor's Statement: previously submitted.
 herewith submitted.

(iv) Labeling (12 copies) herewith submitted thus:

Label(s) only -- approved neutral (Richlyn) insert will be used.

Label(s) & insert.

Labeling submission is original revised.

DOSE STRENGTH

1 mg.

PACKAGING UNIT

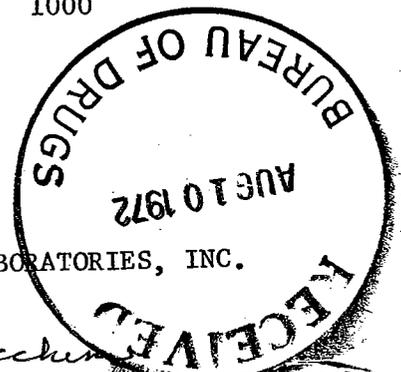
1000

Sincerely,

RICHLYN LABORATORIES, INC.

L. P. Cecchini

L. P. Cecchini, Ph.D.
Director, Quality Assurance



LPC/ls
Encl.
AL-F01
6-72

NDA 80-686

AF 28-727

SEP 28 1972

Richlyn Laboratories
Attention: Mr. L. P. Cecchini
Castor & Kensington Avenues
Philadelphia, Pennsylvania 19124

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 acknowledge receipt of your communication dated August 7, 1972, amending the application.

Your application, as amended, also provides for you to label the drug in 1000 tablet containers with a label showing the distributor to be:

Spencer-Mead, Inc.
Valley Stream, New York 11582

Before we can complete the review of this application, however, it will be necessary for you to have a satisfactory inspection report, as previously requested.

Please let us have your response regarding the above request promptly.

Sincerely yours,

Margaret Clark, MD, for
Marvin Saife, M.D. *9/28/72*
Director
Division of Actions Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:

PHI-DO

Dup

BD-69

BD-66

BD-106 BD-242

JHEilert/JLMeyer/MAJarski

R/D init. MAClark, JLMeyer

Final typing bhy 9/27/72

Rev. W/F

JMeyer 9/28/72

M.A. Jarski 9/27/72

*JHEilert
9-28-72*

Rev. w/f RESUBMISSION
NDA ORIG AMENDMENT *E*

Cable Address "RICHLYN"

RICHLYN
LABORATORIES
INC.

PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

October 5, 1972

Orig

No Reply
M.A. Janssen 12-5-

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 9/28/72 request for additional information.

Regarding your request for a satisfactory establishment inspection report, please be advised that we have requested said inspection by Philadelphia District Office and that we anticipate appropriate resolution of this matter.

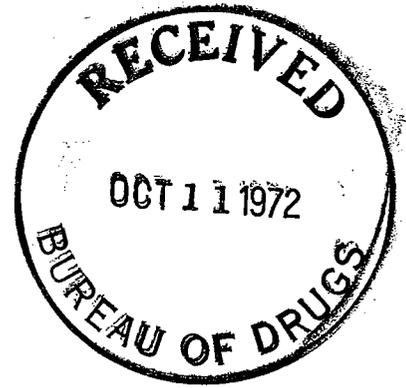
Sincerely,

RICHLYN LABORATORIES, INC.

EWR 1260/16

E. W. Rebollo
Vice President

- EWR/1s



**RICHLYN
LABORATORIES
INC.**

PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

October 16, 1972

ORIG.

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686

Gentlemen:

The enclosed triplicate submission provides supplement per 21CFR§130.9 (a)(4):

- (i): Revision in labeling.
 - (ii): Addition of claim.
 - (iii): Revision in manufacturing or control procedures.
 - (iv): Change in manufacturing facilities.
 - (v): Provision for participation by outside firm.
- Appropriate exhibits are attached.*

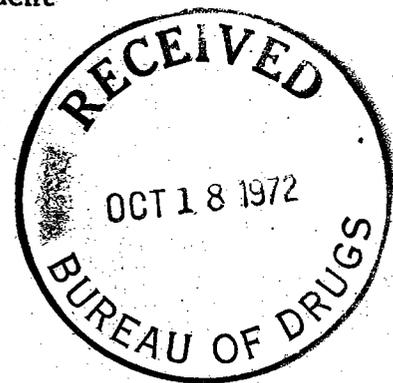
Sincerely,

RICHLYN LABORATORIES, INC.

E. W. Rebollo
Vice President

EWR/lrs
Encl.

*Alternate Formulation.
(essentially, increased batch size).



E

RICHLYN
LABORATORIES
INC.

Cable Address "RICHLYN"

PHARMACEUTICALS ANTIBIOTICS GENERICS

FPU

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

November 10, 1972

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Reference: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686

Supplemental Application
Additional Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(6) --

- (i) Designated Distributor: Sherry Pharmaceutical Co., Inc.
Bayshore, L.I., New York 11706
 - (ii) Applicant will conform.
 - (iii) Distributor's Statement: previously submitted.
 herewith submitted.
 - (iv) Labeling (12 copies) herewith submitted thus:
 - Label(s) only -- approved neutral (Richlyn) insert will be used.
 - Label(s) & insert.
- Labeling submission is original revised.

DOSE STRENGTH

1 mg!

PACKAGING UNIT

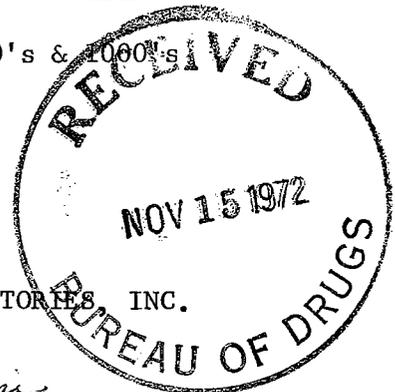
100's & 1000's

Sincerely,

RICHLYN LABORATORIES, INC.

L.P. Cecchini

L. P. Cecchini, Ph.D.
Director, Quality Assurance



LPC/lrs
Encl.
AL-F01
6-72

E

Cable Address "RICHLYN"

PHARMACEUTICALS ANTIBIOTICS GENERICS

FPL

RICHLYN
LABORATORIES
INC.

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

December 7, 1972

ORIG.

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Reference: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686

Supplemental Application
Additional Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(6) --

(i) Designated Distributor: Rugby Laboratories, Inc.
Inwood, L.I., N.Y. 11696

(ii) Applicant will conform.

(iii) Distributor's Statement: previously submitted.
 herewith submitted.

(iv) Labeling (12 copies) herewith submitted thus:

Label(s) only -- approved neutral (Richlyn) insert will be used.

Label(s) & insert.

Labeling submission is original revised.

DOSE STRENGTH

PACKAGING UNIT

1 mg.

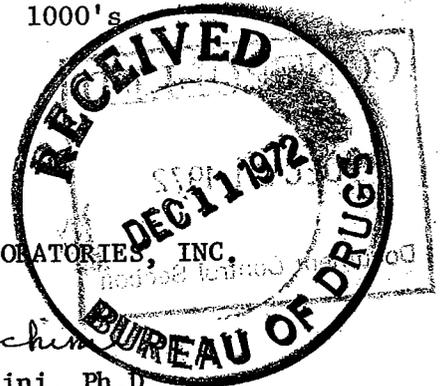
1000's

Sincerely,

RICHLYN LABORATORIES, INC.

L. P. Cecchini

L. P. Cecchini, Ph.D.
Director, Quality Assurance



LPC/1s
Encl.
AL-F01
6-72

E

Cable Address "RICHLYN"

RICHLYN
LABORATORIES
INC.

PHARMACEUTICALS ANTIBIOTICS GENERICS

FPL

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

December 8, 1972

ORIG

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Reference: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686

Supplemental Application
Additional Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(6) --

- (i) Designated Distributor: Cooper Drug Co.
Troy, Michigan 48084
- (ii) Applicant will conform.
- (iii) Distributor's Statement: previously submitted.
 herewith submitted.
- (iv) Labeling (12 copies) herewith submitted thus:
 Label(s) only -- approved neutral (Richlyn) insert will be used.
 Label(s) & insert.
Labeling submission is original revised.

DOSE STRENGTH

PACKAGING UNIT

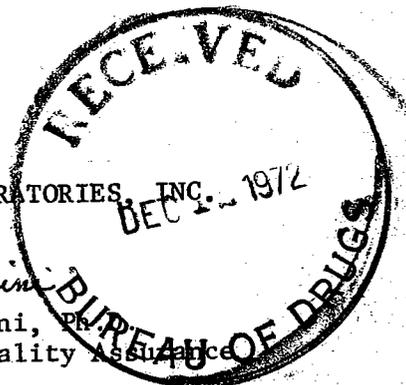
1 mg.

100's & 1000's

Sincerely,

RICHLYN LABORATORIES, INC. 1972

L. P. Cecchini
L. P. Cecchini, PE
Director, Quality Assurance



LPC/lis
Encl.
AL-F01
6-72

NDA 80-686
AF 28-727

DEC 12 1972

Richlyn Laboratories
Attention: Mr. E. W. Rebollo
Castor & Kensington Avenues
Philadelphia, Pennsylvania 19124

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 made to your communications dated September 14, 1972, October 16, 1972, and November 10, 1972, amending the application.

The application as amended provides for the following:

- a) You to label the drug in 100 and 1000 tablet containers with labels showing your additional distributors to be:

Cooper Drug Co.
Troy, Michigan 48064

Sherry Pharmaceutical Co., Inc.
Bayshore, New York 11706

- b) A revision in formulation.

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

1. A revised container label for Cooper Drug Company containing the correct zip code (48064).

APPEARS THIS WAY
ON ORIGINAL

2. A clarification of the use of "Alternate formulation" in your manufacturing procedures. Further, it is recommended that only one mensural system be applied when listing amounts of components in formulation statements.
3. A satisfactory inspection, as previously requested.

Please let us have your response promptly. Submit twelve copies of the revised container label.

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

Sincerely yours,

Marvin Seife 12/11/72

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

12-8-72

M. O. Jarski
JHEilert/JLMeyer/MAJarski 12/8/72
R/D init. by JMeyer/12-6-72
Final typing/kim/12-7-72

Rev w/f *JMeyer* 12/11/72

**RICHLYN
LABORATORIES
INC.**

PHARMACEUTICALS

REV. W/F
RESUBMISSION
NDA ORIG AMENDMENT
ANTIBIOTICS GENERICS

Cable Address "RICH"

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

JAN 16 1973

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 12/12/72 request for additional information.

1. Revised container label specimens (12 copies) for Cooper Drug Co. (correct ZIP code) were submitted to you on 12/8/72 (certified mail receipt returned to us on 12/18/72).
2. "Alternate formulation"--denotes variation from prior submission considered sufficient to warrant separate notation, but insufficient to warrant categorization as a separate pharmaceutical formulation.
Examples: change in batch size, or
In this case, the basic variation was an increase in batch size.
A second variation was a

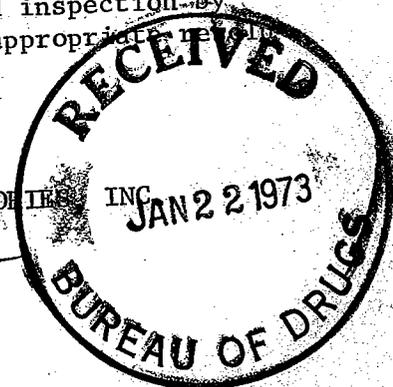
In response to your request for use of one mensural system in formulation statements, please be advised that, re Folic Acid component, 100 mg. = 0.0154 gr. (grains). Thus the latter equivalent may be substituted in either formulation statement, yielding a consistent (apothecary) mensural system usage.

3. Regarding your request for a satisfactory establishment inspection report, please be advised that we have requested said inspection by Philadelphia District Office and that we anticipate appropriate resolution of this matter.

Sincerely,

RICHLYN LABORATORIES, INC.

E. W. Rebollo
E. W. Rebollo
Vice President



NDA 80-686

AF 28-724

Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rebollo
Castor and Kensington Avenues
Philadelphia, Pennsylvania 19124

MAR 29 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, 1.0 mg.

Reference is also made to your communications dated December 7, 1972, December 8, 1972 and January 16, 1973, enclosing distributor labeling and manufacturing information.

The application provides for you to label the drug with labels showing your distributors to be:

Rugby Laboratories, Inc.
Inwood, New York 11696

Cooper Drug Co.
Troy, Michigan 48084

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. A quantitative statement of composition of the proprietary items used in your formulation or authorization to refer to a Drug Master File in connection with this application.
2. The additional information requested in our letter of December 12, 1972.

Also, it is suggested that if you elect to provide for "Alternate Formulations" rather than manufacturing revisions pertaining to

APPEARS THIS WAY
ON ORIGINAL

batch size, these should be appropriately filed as separate abbreviated new drug applications.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife 3/29/73

Marvin Seife, M.D.
Director

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

cc:
PHIL-DO

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

MA Jarski 3/28/73

3-98-73 JHEilert/JLMeyer/MAJarski
R/D init. JLMeyer, MSeife 3/26/73
Final typing bhy 3/27/73
Rev. w/f

JLMeyer 3/28/73

Rev. d/f

**RESUBMISSION
NDA ORIG AMENDMENT**

E
Orig

Cable Address "RICHLYN"

**RICHLYN
LABORATORIES
INC.**

PHARMACEUTICALS ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES PHILADELPHIA, PENNSYLVANIA 19124 215 CU 9-2220

ARR 11 1973

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 3/29/73 request for additional information.

Enclosed is a copy of manufacturer-supplier's authorization to refer to their Drug Master File covering Sterotex in connection with this application.

Regarding your request for a satisfactory establishment inspection report, please be advised that we have requested said inspection by Philadelphia District Office and that we anticipate appropriate resolution of this matter.

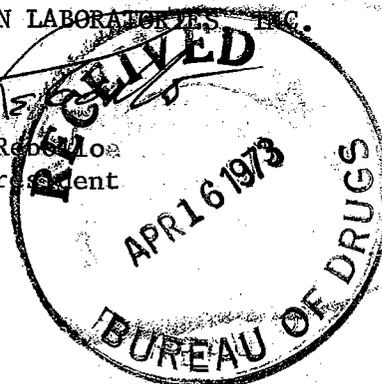
We respectfully submit that the 10/16/72 "Alternate Formulation" submission involved (per iso-date cover letter and 1/16/73 clarification) no more than an increased batch size and a

--hardly a basis for a separate ANDA.

Sincerely,

RICHLYN LABORATORIES, INC.

E. W. Rebo
E. W. Rebo
Vice President



EWR/lr
Encl.

RICHLYN
LABORATORIES
INC.

NDA ORIG AMENDMENT

Cable Address "RICHLYN" B

PHARMACEUTICALS ANTIBIOTICS GENERICS

Original

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

EPLI

May 21, 1973

Reference: Folic Acid Tablets, U.S.P.
1 Mg., C.T. Yellow
ANDA #80-686

Supplemental Application
Additional Distributor

Gentlemen:

The attached triplicate submission provides supplement per 21CFR§130.9
(a)(6) --

(i) Designated Distributor: Arcum Pharmaceutical Corp.
Vienna, VA 22180

(ii) Applicant will conform.

(iii) Distributor's Statement: previously submitted.
 herewith submitted.

(iv) Labeling (12 copies) herewith submitted thus:

Label(s) only -- approved neutral (Richlyn) insert will be used.
 Label(s) & insert.

Labeling submission is original revised.

DOSE STRENGTH

PACKAGING UNIT

1 Mg.

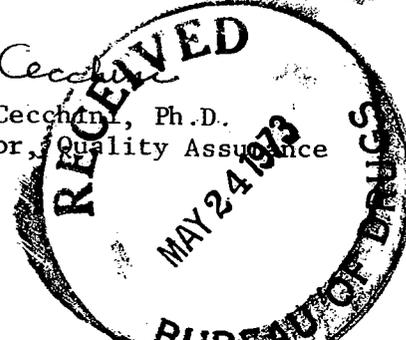
1000's

Sincerely,

RICHLYN LABORATORIES, INC.

L. P. Cecchini
L. P. Cecchini, Ph.D.
Director, Quality Assurance

LPC/ mes
Encl.
AL-F01
6-72



NDA 80-686

AF 28-724

**Richlyn Laboratories, Inc.
Attention: Mr. E. W. Rebollo
Castor & Kensington Avenues
Philadelphia, Pennsylvania 19124**

JUN 5 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, 1.0 mg.

Reference is also made to your communication dated April 11, 1973, pertaining to an increased batch size.

We have reviewed this abbreviated new drug application and have the following comments:

The Bureau of Drugs, Office of Compliance, has evaluated your establishment inspection report(s) and remarks as follows:

We have evaluated the operations of the above referenced firm in so far as they apply to conformity with Current Good Manufacturing Practice Regulations (21 CFR, Part 133). On the basis of this evaluation, we can not approve any NDA's or ANDA's as the firm is not operating in conformity with 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 the firm initiated 9-12-72 revealed numerous significant GMP deviations including:

[]

**APPEARS THIS WAY
ON ORIGINAL**

Richlyn Laboratories, Inc.
NDA 80-686

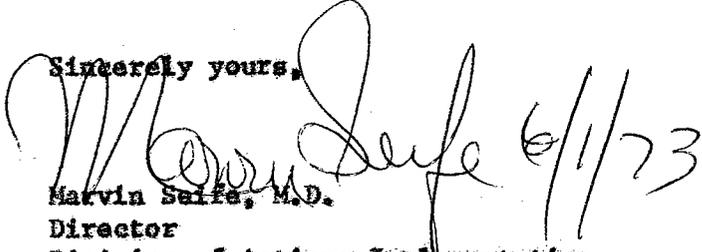
-2-

[]

Such information indicates that there is a disagreement between actual GMP and the commitment in your application. Therefore, before we can take further action on this abbreviated new drug application, we should have a satisfactory inspection report.

The material submitted is being retained as part of your application for this article.

Sincerely yours,

 6/1/73
Marvin Seife, M.D.
Director
Division of Actions Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
PHI-DO
Dup
BD-69
BD-66
BD-106
BD-242
BD-340

JLMeyer/MAJarski
R/D init. MSeife/JMeyer/5-18-73
Final typing/rt/5-30-73
Ack.

JMeyer 5/31/73
M.A. Jarski 5/31/73

APPEARS THIS WAY
ON ORIGINAL

ORIG NEW CORRES

6

RICHLYN
LABORATORIES
INC.

Cable Address "RICHLYN"

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

Original

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

JUN 7 1973

*No Reply
JMMyer
7/11/73*

Drug Efficacy Study Implementation
Project Office -- BD-5
Bureau of Drugs
Food & Drug Administration
5600 Fishers Lane
Rockville, Maryland 20852

Ref.: Folic Acid Tablets, U.S.P.
1 mg., C.T. Yellow
ANDA #80-686
Additional Information Requested

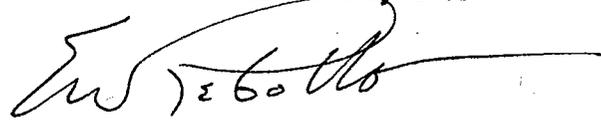
Gentlemen:

This triplicate submission is in response to your 6/5/73 request for additional information.

Re our CGMP status, please see our 5/23/73 letter to Commissioner Fine.

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo
Vice President

EWR:tp



MEMORANDUM

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

BD-105
ATTN: Stanley Stringer

DATE: June 27, 1973

DM : BD-340

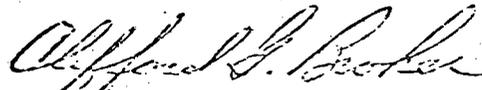
SUBJECT: Applicant; Richlyn Laboratories, Phila., Pa.

RE: Approval of pending NDAs & ANDAs:

9-627	_____	80-686 Jariski	80-767 Jariski
14-322	80-874 Wolters	80-780 Jariski	80-151 Jariski
	_____	80-782 Jariski	80-808 Jariski
	80-153 Millar	80-881 Jariski	83-115 Jariski
	80-159 Jariski	_____	83-347 McKinlay
	_____	80-081 Millar	83-607 Millar
	83-317 Jariski	_____	83-681 Wolters
	80-109 Jariski	80-952 Jariski	83-720 Jariski
	80-951 Jariski	80-782 Jariski	_____
	80-079 Jariski	80-781 Jariski	

Re-evaluation

We have previously disapproved this applicant as not conforming to CGMP Regulations. We have re-evaluated the firm's operations based on a later inspection conducted 5/8 - 18/73. On the basis of this evaluation we would have no objection to your approving the above referenced NDAs/ANDAs insofar as they relate to compliance with Current Good Manufacturing Practice Regulations.



Clifford G. Broker

RSL:jmv

80-079 Mr. Jariski	_____	80-781 Jariski
80-081 Ms. Millar	80-159 Jariski	80-782 Jariski
_____	_____	
80-109 Ms. Jariski	80-686 Jariski	
80-151 Ms. Jariski	80-785 Jariski	
80-153 Ms. Millar	80-767 Jariski	