

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

Approval Package for:

APPLICATION NUMBER:

80-755

Generic Name: Folic Acid 1mg Tablets

Sponsor: Sperti Drug Products, Inc.

Approval Date: March 20, 1973

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

80-755

CONTENTS

Reviews / Information Included in this ANDA Review.

Approval Letter(s)	X
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Correspondence	X

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-755

APPROVAL LETTER

NDA 80-755

AF 24-516 (Sperti)
AF 23-201 (Carroll)
AF 22-968 (Stanlabs)

Sperti Drug Products, Inc.
Attention: Dr. Norbert J. Berberich, Jr.
One Sperti Drive
Fort Mitchell, Kentucky 41017

MAR 20 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 January 30, 1973, enclosing printed labeling and manufacturing information.

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

Stanlabs, Inc.
Portland, Oregon 97214

Carroll Chemical Company
Baltimore, Maryland 21223

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

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

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

The

APPEARS THIS WAY
ON ORIGINAL

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

Sincerely yours,

M. Seife for
Paul A. Bryan, M.D. 3/19/73
Director
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

Enclosures

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

cc:

ATL-DO

Dup

BD-69

BD-66

BD-100

BD-106

BD-242

JHEilert/JLMeyer/RJWolters

R/D init. JLMeyer, MSeife 3/12/73

Final typing bhy 3/15/73

Approved

JHEilert
3-16-73

RJWolters
3-16-73

JLMeyer 3/19/73

M Seife 3/19/73

**CENTER FOR DRUG
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FINAL PRINTED LABELING

FOLIC ACID ORAL

Hematopoietic;

Vitamin B-Complex Component

DESCRIPTION

Folic Acid is a yellow, crystalline powder that occurs naturally and can be prepared synthetically. Its molecular formula is $C_{19}H_{19}N_7O_6$ and it has a molecular weight of 441.4. It makes up an important part of the B complex vitamin group.

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 (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 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

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

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

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

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

CAUTION: Federal law prohibits dispensing without prescription.

HOW SUPPLIED

Folic Acid 1.0 mg. tablets in bottles of 100 and 1000.

Revised March 1972

For dosage and other information, see package insert.

NDC 242-76-50

folic acid
U.S.P.

(Pteroylglutamic Acid)

1 mg.

100 TABLETS

STANLABS, INC.
Portland, Ore. 97214

Caution: Federal law prohibits dispensing without prescription.



NDC 242-654-30

FOLIC ACID
U.S.P.

1 mg.

100 TABLETS

Distributed by

STANLEY DRUG PRODUCTS, INC.
PORTLAND, OREGON 97214

For dosage and other information, see package insert.

CAUTION: Federal law prohibits dispensing without prescription.

For dosage and other information, see package insert.

NDC 242-76-75

folic acid

U.S.P.

(Pteroylglutamic Acid)

1 mg.



Caution: Federal law prohibits dispensing without prescription.



1000 TABLETS

STANLABS, INC.,
PORTLAND, ORE. 97214

For dosage and other information, see package insert.



NDC 242-654-75

FOLIC ACID

U. S. P.

1 mg.

CAUTION: Federal law prohibits dispensing without prescription.

1000 TABLETS

Distributed by

STANLEY DRUG PRODUCTS, INC.
PORTLAND, OREGON 97214

For dosage and other information, see package insert.

For dosage and other information, see package insert.

List 76
FOLIC ACID
(Pteroylglutamic Acid)
U.S.P.
1 mg.

CAUTION: Federal law prohibits
dispensing without prescription.

For dosage and other information,
see package insert.

Control:

TABLETS

Attention—This is bulk merchandise intended for re-
packaging which must be done in accordance with the
regulations of the Food, Drug and Cosmetic Act., The
Stanley Drug Products Inc., assumes no responsibility
under the Act for any subsequent labeling.

STANLEY DRUG PRODUCTS, INC.
Portland, Oregon 97214

List 76
FOLIC ACID
(Pteroylglutamic Acid)
U.S.P.
1 mg.

CAUTION: Federal law prohibits
dispensing without prescription.

For dosage and other information,
see package insert.

Control:

TABLETS

Attention—This is bulk merchandise intended for re-
packaging which must be done in accordance with the
regulations of the Food, Drug and Cosmetic Act., The
Stanley Drug Products Inc., assumes no responsibility
under the Act for any subsequent labeling.

STANLEY DRUG PRODUCTS, INC.
Portland, Oregon 97214

List 76
FOLIC ACID
(Pteroylglutamic Acid)
U.S.P.
1 mg.

CAUTION: Federal law prohibits
dispensing without prescription.

For dosage and other information,
see package insert.

Control:

TABLETS

Attention—This is bulk merchandise intended for re-
packaging which must be done in accordance with the
regulations of the Food, Drug and Cosmetic Act., The
Stanley Drug Products Inc., assumes no responsibility
under the Act for any subsequent labeling.

STANLEY DRUG PRODUCTS, INC.
Portland, Oregon 97214

List 76
FOLIC ACID
(Pteroylglutamic Acid)
U.S.P.
1 mg.

CAUTION: Federal law prohibits
dispensing without prescription.

For dosage and other information,
see package insert.

Control:

TABLETS

Attention—This is bulk merchandise intended for re-
packaging which must be done in accordance with the
regulations of the Food, Drug and Cosmetic Act., The
Stanley Drug Products Inc., assumes no responsibility
under the Act for any subsequent labeling.

STANLEY DRUG PRODUCTS, INC.
Portland, Oregon 97214

CARROLL *h* Cat. No. 1554

FOLIC ACID FOLIC ACID

CAUTION: Federal law prohibits dispensing without prescription.

For dosage see package **APPROVED** U.S.P. **1 mg** **500 TABLETS** **MAR 20 1971**

Distributed by: CARROLL CHEMICAL CO.
Division SPERTI DRUG CORP., Baltimore, MD 21223 U.S.A.

Labeling: Original
MDA No: 80-735 Re'd 5-30-77
Reviewed By: [Signature]
3-573

NDC 242-76-50

folic acid
U.S.P.
(Pteroylglutamic Acid)

1 mg.
100 TABLETS
STANLABS, INC.
Portland, Ore. 97214

For dosage and other information, see package insert.

Caution: Federal law prohibits dispensing without prescription.

NDC 242-76-75

folic acid
U.S.P.
(Pteroylglutamic Acid)

1 mg.

Caution: Federal law prohibits dispensing without prescription.

1000 TABLETS

STANLABS, INC.
PORTLAND, ORE. 97214

For dosage and other information, see package insert.

Labeling: ORIGINAL
MDA No: 80-755 Re'd 9-14-72
Reviewed By: [Signature]
35173

STANLEY

NDC 242-854-75

FOLIC ACID
U. S. P.
1 mg.

CAUTION: Federal law prohibits dispensing without prescription.

1000 TABLETS

Distributed by

STANLEY DRUG PRODUCTS, INC.
PORTLAND, OREGON 97214

For dosage and other information, see package insert.

For dosage and other information, see package insert.

STANLEY

NDC 242-854-50

FOLIC ACID
U. S. P.
1 mg.

CAUTION: Federal law prohibits dispensing without prescription.

100 TABLETS

Distributed by

STANLEY DRUG PRODUCTS, INC.
PORTLAND, OREGON 97214

For dosage and other information, see package insert.

CAUTION: Federal law prohibits dispensing without prescription.

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-755

CSO LABELING REVIEW(S)

REVIEW OF ANDA

DATE COMPLETED: 12-14-71

ANDA#: ~~80-755~~

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

CO. NAME: Sperti Drug Products, Inc.
Ft. Mitchell, Ky. 41017

NAME OF DRUG: Trade: Folic Acid Tablets, 1 mg.

Generic: Pteroylglutamic acid

DATE OF SUBMISSION: 11-24-71

TYPE OF SUBMISSION: ANDA

CLINICAL EVALUATION:

1. Review of Labeling:

(a) Container Label:

Medically acceptable.

(b) Package Insert:

1. In the ACTIONS section, delete the statement _____, as this is an inaccurate description of demonstrated pharmacologic/physiologic actions. In this section information should be added that folic acid metabolites are essential to certain amino acid conversions, purine synthesis and methylation processes required to prevent the disease conditions resulting from such deficiencies. 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 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.

CONCLUSION: Package insert requires revisions as stated above.

RECOMMENDATIONS: Request FPL with revisions.

Raymond Kimbrough, M.D.
Raymond Kimbrough, M.D.

cc:
BD-69
BD-100
RKimbrough/nlp 12/16/71

**APPEARS THIS WAY
ON ORIGINAL**

REVIEW OF RESUBMISSION

DATE COMPLETED: 7/19/72

ANDA # 80-755

F.R. Date: 4/9/71
Sperti Drug Products, Inc.
Seven Sperti Drive
Ft. Mitchell, Kentucky 41017

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

DATE OF SUBMISSION: 5/23/72

TYPE OF SUBMISSION: Resubmission

CLINICAL EVALUATION:

NOTE: This ANDA is submitted by Sperti drugs, Stanlabs, Inc. is the manufacturer and Carroll Chemical Co is a distributor.

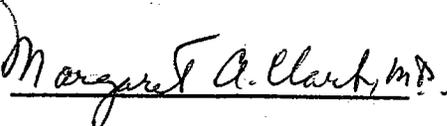
1. Review of Labeling:

- a. Bulk Labels: These are for Stanley Drug Products and are satisfactory.
- b. Package Insert: Satisfactory.
- b. Container Labels: Stanlabs, Inc. labels for containers of 100 & 1,000 are satisfactory.

Carroll Chemical labels for containers of 100: At the time of the next printing the present phrase "Distr. by" should be revised to read "Distributed by".

CONCLUSIONS: The labeling provides for the safe and effective use of this drug. The Carroll labels should be revised at the next printing.

RECOMMENDATIONS: The submission is medically approvable. Advise firm to revise Carroll labels at the next printing.



Margaret A. Clark, M.D.

cc:
Dup.
BD-69
MAClark/mc/7/19/72

REVIEW OF RESUBMISSION

DATE COMPLETED: 2-9-73

ANDA #: 80-755

F.R. DATE: 4-9-71

CO. NAME: Sperti Drug Products, Inc.
Seven Sperti Drive
Ft. Mitchell, Ky. 41017

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

DATE OF SUBMISSION: 1-30-73

TYPE OF SUBMISSION: Manufacturing data, container label.

CLINICAL EVALUATION:

1. Review of Studies: Chemist to review.
2. Review of Labeling: Container labeling for Carroll Chemical Co., for 100 tablets is acceptable.

CONCLUSION: 1. Requires chemist review.
2. Acceptable container label.

RECOMMENDATIONS: 1. Chemist review.
2. Approve submitted label.


John H. Eilert, M.D.

cc:

Dup

BD-69

JHEilert/wlb/2-12-73

REVIEW OF FPL

DATE COMPLETED: 9-19-72

ANDA #: 80-755

F.R. DATE: 4-9-71

CO. NAME: Sperti Drug Products, Inc.
Seven Sperti Drive
Ft. Mitchell, Ky. 41017

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

DATE OF SUBMISSION: 9-11-72

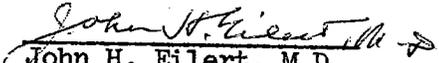
TYPE OF SUBMISSION: Distributor labels

CLINICAL EVALUATION:

Review of Labeling: Container labels for Stanley Drug Products, Inc.
Portland, Oregon 97214
are approvable.

CONCLUSION: Acceptable labeling.

RECOMMENDATIONS: Approve submission


John H. Eilert, M.D.

cc:

Dup

BD-69

John H. Eilert, M.D./kim/9-19-72

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-755

CHEMISTRY REVIEW(S)

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
4/9/71

NDA Number 80-755

Name and Address of Applicant (City and State)
Sperti Drug Products, Inc.
Fort Mitchell, Kentucky 41017

Original 11/3/71
Amendment _____
Supplement _____
Other _____

Name of Drug FOLIC
Nonproprietary Name ACID

DATE(s) of Submission(s)

Purpose of Supplement

Pharmacological Category hematopoietic vitamin
How Dispensed Rx OTC

AF Number sperti=24-516
carroll=23-201

Dosage Form(s)
Potency(ies)

Related IND/NDA/EF Stanley=22-900

Satisfactory Labeling Date Due No be revised (RKimbrough)

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

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

NA

**APPEARS THIS WAY
ON ORIGINAL**

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

Establishment Inspection
Stanley = satisfactory: 9/1/3/71
Carroll = satisfactory: 5/14/71

Recalls

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

Remarks

- Request:
1. Revised labeling, as per M.O.
 2. Full certification
 3. Clarification of procedures for assay (finished tablets); active ingredient; and
 4. Actual mfg & packing methods (in preference to drug MF referral)

Conclusions

rev w/f

gmillar

CHEMIST'S REVIEW FOR
ABBREVIATED NEW DRUG APPLICATION
OR SUPPLEMENT

Federal Register
Statement Date
4-9-71

NDA Number

80-755

Name & Address of Applicant (City & State)

**Sperti Drug Products, Inc.
Seven Sperti Drive
Fort Mitchell, Kentucky 41017**

Original _____

Amendment **5-23-72**

Supplement _____

Name of Drug

Nonproprietary Name

Folic Acid

Other _____

Purpose of Supplement

Revised labeling and manufacturing information

Date(s) of Submission(s)

Sperti 24-516

Carroll 23-301

AF Number **Stanlabs 22-968**

Pharmacological Category

Vitamin

How Dispensed

R_x

O.T.C.

Dosage Form(s)

Tablet

Potency (ies)
1 mg.

Related NDA & MF

Satisfactory

Labeling
Date Due

Satisfactory minor revision in Carroll label (MAClark)

Satisfactory

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

Satisfactory

Biologic Availability
Date Due **NA**

Is data on current
formulation? YES NO

Satisfactory

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

Establishment Inspection

**Stanley Satisfactory 9-13-72
Carroll Satisfactory as a repacker 8-2-72**

Recalls

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

YES NO

Remarks

- Request:**
1. Revise Carroll label per MO's review.
 2. Certification from Carroll per part 133.
 3. Clarify omission of _____ and residue on ignition tests from procedures for active ingredient.
 4. Include procedures for _____
 5. May use test as an alternate. (Assays)
 6. Outline of facilities and controls (no master file referrals).

Conclusions

rev w/f

RJWalters 8-15-72
RJWalters

REVIEWER:

SIGNATURE:

DATE:

CHEMIST'S REVIEW FOR ABBREVIATED NEW DRUG APPLICATION OR SUPPLEMENT		Federal Register Statement Date 4-9-71	NDA Number 80-755
Name & Address of Applicant (City & State) Sperti Drug Products, Inc. Seven Sperti Drive Fort Mitchell, Kentucky 41017		Nonproprietary Name Folic Acid	Original _____ Amendment 9-11-72 Supplement _____ Other _____
Purpose of Supplement Printed labeling for Stanlabs.			Date(s) of Submission(s)
Pharmacological Category Vitamin	How Dispensed R _x <input checked="" type="checkbox"/> O.T.C. <input type="checkbox"/>		AF Number <u>24-516</u> Related NDA & MF
Dosage Form(s) Tablet	Potency (ies) 1 mg.		

Satisfactory Labeling
 Date Due Satisfactory (JHWilert)

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

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 Stanley Satisfactory 9-13-72 Carroll Satisfactory as a packer 8-2-72	Recalls
---	---------

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

Remarks
 Request information required by 130.4(f) be submitted as requested in letter dated 8-16-72.

Conclusions
 R. J. Wilert
 10-25-70

Abbreviated New Drug Application
 ON SUPPLEMENT

Statement Date
 4/9/71

NDA Number 80-755

Name and Address of Applicant (City and State)
 Sperti Drug Products, Inc.
 Fort Mitchell, Kentucky 41017

Original 11/3
 Amendment _____
 Supplement _____
 Other _____

Name of Drug
 FOLIC
 Nonproprietary Name
 ACID

DATE(s) of Submission
 9/29/72

Purpose of Supplement

Pharmacological Category
 hematopoietic vitamin
 How Dispensed
 RX OTC

AF Number sperti=24-515
 carroll=23-201
 stanias=22-52

Dosage Form(s)
 Potency(ies)

Satisfactory Labeling Date Due _____ NA

Satisfactory Components, Composition, Manufacturing and Controls Date Due _____ NA

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

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

Establishment Inspection
 NA

Recalls
**APPEARS THIS WAY
 ON ORIGINAL**

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

Remarks

NOTE: firm makes commitments, as per previous requests;
 But questions need for submission of mfg info.
 Send firm regs outlined in red.

Conclusions

rev w/f

Chill
 gmillar 12/14/72

TYPE FOR DRUG APPLICATION		FEDERAL REGISTER Statement Date 4-9-71	80-755
NAME & ADDRESS OF APPLICANT (City & State) Sperti Drug Products, Inc. Fort Mitchell, Kentucky 41017		Original _____ Amendment <u>1-30-73</u> Supplement _____ Other _____	
Name of Drug	Nonproprietary Name Folic Acid		
Purpose of Supplement RE FPL for Carroll and manufacturing information		Date(s) of Submission(s)	
Pharmacological Category Vitamin	How Dispensed R _x <input checked="" type="checkbox"/> O.T.C. <input type="checkbox"/>		AF Number Sperti 24-516 Carroll 23-201, Stanlabs Related NDA & MF 22-968
Dosage Form(s) Tablet	Potency (ies) 1 mg.		
Satisfactory Labeling <input type="checkbox"/>	Date Due <u>Satisfactory (JHEilert)</u>		
Satisfactory Components, Composition, Manufacturing and Controls <input type="checkbox"/>	Date Due <u>Active ingredient and drug dosage form complies to USP specs.</u>		
Satisfactory Biologic Availability <input type="checkbox"/>	Date Due <u>NA</u> Is data on current formulation? YES <input type="checkbox"/> NO <input type="checkbox"/>		
Satisfactory Probably or Possibly Effective Indications <input type="checkbox"/>	(if in labeling) Date Data Due _____		
Establishment Inspection Stanley Satisfactory 9-13-72 Carroll Satisfactory as repacker 8-2-72		Recalls	
If relabeling of drug in commercial channels required? If so, what level:		YES <input type="checkbox"/> NO <input type="checkbox"/>	
Remarks <p style="text-align: center;">APPEARS THIS WAY ON ORIGINAL.</p>			
Conclusions Approved		<i>RJ Walters 3-16-73</i> RJWalters	

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-755

**ADMINISTRATIVE
DOCUMENTS**

ORIG

<p align="center">NOTICE OF APPROVAL NEW DRUG APPLICATION OR SUPPLEMENT</p>		NDA NUMBER 80-755
		DATE APPROVAL LETTER ISSUED MAR-20 1973
TO: Press Relations Staff (CE-300)	FROM: <input checked="" type="checkbox"/> Bureau of Drugs <input type="checkbox"/> Bureau of Veterinary Medicine	
<p align="center">APPROVAL OF ORIGINAL ABBREVIATED NDA</p> <p align="center">Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.</p>		
TYPE OF APPLICATION <input type="checkbox"/> ORIGINAL NDA <input checked="" type="checkbox"/> ABBREVIATED <input type="checkbox"/> SUPPLEMENT TO NDA		CATEGORY <input checked="" type="checkbox"/> HUMAN <input type="checkbox"/> VETERINARY
TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG <p align="center">Folic Acid</p>		
DOSAGE FORM <p align="center">Tablet</p>		HOW DISPENSED <input checked="" type="checkbox"/> RX <input type="checkbox"/> OTC
ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.) <p align="center">Folic Acid 1 mg.</p>		
<p align="right">APPEARS THIS WAY ON ORIGINAL</p>		
NAME OF APPLICANT (Include City and State) <p align="center">Spertia Drug Products, Inc. Fort Mitchell, Kentucky 41017</p>		
PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY <p align="center">Vitamin</p>		
COMPLETE FOR VETERINARY ONLY		
ANIMAL SPECIES FOR WHICH APPROVED		
COMPLETE FOR SUPPLEMENT ONLY		
CHANGE APPROVED TO PROVIDE FOR		
FORM PREPARED BY		
NAME R.J. Wolters	DATE	
FORM APPROVED BY		
NAME J.L. Meyer	DATE	

[DESI 5897; 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.
 Pfeston Franklin Pharmacal Co.
 Richlyn Labs.
 Robinson Laboratory, Inc.
 Spencer-Mead, Inc.
 Stanlabs, Inc.
 Supreme Pharmaceutical Co., Inc.
 Thompson, Wm. T., Co.
 Towne, Paulson and Co., Inc.
 Vitamin Research Corp.
 Vita-Pore Products Co.

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

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

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

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

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

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

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

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

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

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

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

FOLIC ACID

DESCRIPTION

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

ACTIONS

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

INDICATIONS

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

WARNINGS

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

PRECAUTIONS

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

ADVERSE REACTIONS

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

DOSAGE AND ADMINISTRATION

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

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

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

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

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

D. Previously approved applications.

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

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

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

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

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

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

b. 180 days for updating information.

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

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

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

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

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

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

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

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

2. In accordance with the provisions of section 505 of the Act (21 U.S.C. 355) and the regulations promulgated thereunder (21 CFR Part 130), the Commissioner will give the holders of any such applications, and any interested person who would be adversely affected by such an order, an opportunity for a hearing to show why such indications should not be deleted from labeling. A request for a hearing must be filed within 30 days after the date of publication of this notice in the FEDERAL REGISTER. A request for a hearing may not rest upon mere allegations or denials, but must set forth specific facts showing that a genuine and substantial issue of fact requires a hearing, together with a well-organized and full-factual analysis of the clinical and other investigational data. The objector is prepared to prove in a hearing. Any data submitted in response to this notice must be previously unsubmitted and include data from adequate and well-controlled clinical investigations (identified for ready review) as described in § 130.12(a) (5) of the regulations published in the FEDERAL REGISTER of May 8, 1970 (35 F.R. 7250). Carefully conducted and documented clinical studies 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]

LEVALLORPHAN TARTRATE INJECTION

Drugs for Human Use; Drug Efficacy Study Implementation

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

Lorfan Injection, containing levallorphan tartrate; Roche Laboratories, Division of Hoffman-La Roche, Inc., 340 Kingsland Street, Nutley, New Jersey 07110 (NDA 10-423).

REPORTS

TRANSMITTAL OF PERIODIC REPORTS FOR DRUGS FOR HUMAN USE <small>(21 CFR 130.13, 136.35, and 146.14)</small>		DATE SUBMITTED 7-11-73	Form Approved Budget Bureau No. 57-R0035												
INSTRUCTIONS Submit a separate form (parts 1 through 4-carbons intact) for each NDA or Antibiotic Application for which the periodic report contains required reporting information. Attach two copies of report to the form. Where the same item of information applies to more than one NDA or Antibiotic Application for preparations containing a common active ingredient, that information may be submitted as part of the report for only one such application provided all application numbers to which that part of the report applies are listed in Item 7 and provided a separate form, with duplicate copies of all other required information, is submitted for each number. Forward form and attachments to Department of Health, Education, and Welfare, Food and Drug Administration (MD-14), 200 C Street, S.W., Washington, D.C. 20204.		1. NDA NUMBER <table border="1" style="width:100%; text-align: center;"> <tr> <td>1</td><td>2</td><td>3</td><td>4</td><td>5</td><td>6</td> </tr> <tr> <td>N</td><td>8</td><td>0</td><td>7</td><td>5</td><td>5</td> </tr> </table>		1	2	3	4	5	6	N	8	0	7	5	5
1	2	3	4	5	6										
N	8	0	7	5	5										
4. APPLICANT <p style="text-align: center;">STANLEY DRUG PRODUCTS, INC.</p>		2. REPORT NO. (FDA Complete) R- <table border="1" style="width:100%; text-align: center;"> <tr> <td style="width: 20px;">8</td><td style="width: 20px;">9</td> </tr> <tr> <td style="font-size: 2em;">φ</td><td style="font-size: 2em;">1</td> </tr> </table>		8	9	φ	1								
8	9														
φ	1														
5. DRUG NAME <p style="text-align: center;">Folic Acid 1 mg.</p>		3. CFR SECTION NUMBER (Antibiotic only) 6. TYPE OF REPORT (Check one (10)) <input checked="" type="checkbox"/> QUARTERLY <input type="checkbox"/> SEMIANNUAL <input type="checkbox"/> ANNUAL <input type="checkbox"/> OTHER													
7. OTHER NDA/ANTIBIOTIC APPLICATION NUMBERS (List all numbers if any part of report applies to more than one number.) <p style="text-align: center;">None</p>		8. PERIOD COVERED BY REPORT <table border="1" style="width:100%; text-align: center;"> <tr> <td colspan="2">FROM (11-14)</td> <td colspan="2">TO (15-18)</td> </tr> <tr> <td>YEAR</td><td>MONTH</td><td>YEAR</td><td>MONTH</td> </tr> <tr> <td>1973</td><td>4</td><td>1973</td><td>6</td> </tr> </table>		FROM (11-14)		TO (15-18)		YEAR	MONTH	YEAR	MONTH	1973	4	1973	6
FROM (11-14)		TO (15-18)													
YEAR	MONTH	YEAR	MONTH												
1973	4	1973	6												
9. REPORT INFORMATION REQUIRED (See §§ 130.13 (a) or 146.14 (a) for description) (Enter an "X" in Column A if you have nothing to report. Enter identification of type of information attached in Column C.) (ALWAYS INCLUDE INFORMATION REQUIRED UNDER "f" AND "g".)															
NONE	TYPE OF INFORMATION	IDENTIFICATION (Volume No.(s)/Tab(s)/Page(s) of Report)													
A (19)	B														
X	a. CLINICAL DATA	<i>Review submitted No Reply Mr R. W. Wells 8-21-73</i>													
X	b. ADVERSE REACTION(S)														
X	c. ANIMAL DATA														
X	d. CHEMICAL OR PHYSICAL DRUG PROPERTIES														
X	e. MANUFACTURING OR CONTROL CHANGES (§§ 130.9 (a) (5))														
X	f. CURRENT PACKAGE LABELING (Whether or not previously submitted)			See Attached											
X	g. QUANTITY DISTRIBUTED	See Attached													
TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT <p style="text-align: center;">Ted Tamaki Vice President, Quality Control</p>		FDA USE ONLY													
SIGNATURE 		10. DATE OF RECEIPT <table border="1" style="width:100%; text-align: center;"> <tr> <td>24</td><td>25</td><td>26</td><td>27</td><td>28</td><td>29</td> </tr> <tr> <td>7</td><td>3</td><td></td><td>1</td><td>6</td><td>7</td> </tr> </table>		24	25	26	27	28	29	7	3		1	6	7
		24	25	26	27	28	29								
7	3		1	6	7										
APPLICANTS RETURN ADDRESS (Type within the window envelope tic marks) <p style="text-align: center;">Stanley Drug Products, Inc. P.O. Box 3108 Portland, Oregon 97208</p>		11. REPORT FILED IN NDA NO. <table border="1" style="width:100%; text-align: center;"> <tr> <td>30</td><td>31</td><td>32</td><td>33</td><td>34</td><td>35</td> </tr> <tr> <td>N</td><td>8</td><td>0</td><td>7</td><td>5</td><td>5</td> </tr> </table>		30	31	32	33	34	35	N	8	0	7	5	5
30	31	32	33	34	35										
N	8	0	7	5	5										
		12. DIV CODE (1) TYPE CARD (28) 14. FDA ACKNOWLEDGMENT 													

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**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

80-755

CORRESPONDENCE

D.C.M.C. 12-9-71

Cable Address "SPERTI"



SPERTI DRUG PRODUCTS, INC.
SEVEN SPERTI DRIVE, FT. MITCHELL, KENTUCKY 41017
606-331-0800

ABBREVIATED
NEW DRUG APPLICATION

80-755

November 24, 1971

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

Re: Desi 5897

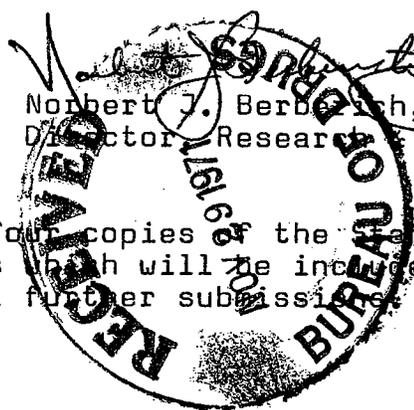
Gentlemen:

Enclosed are four copies of the Original Abbreviated New Drug Application for Folic Acid Tablets 1 mg submitted by Sperti Drug Products, Inc. The submission is incomplete only with respect to labels and inserts for Carroll Chemical Co. and bulk labels for Stanley Drug Products, Inc., these are in the process of printing and will be submitted shortly.

Sincerely yours,

Norbert J. Berberich, Jr.
Norbert J. Berberich, Jr. Ph.D.
Director, Research & Development

Enclosed also find four copies of the Standard Operation Procedures which will be included by reference for all further submissions.



DMF #
Assigned

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

NDA 80-755
AF 24-516

DEC 3 1971

Sperti Drug Products Inc.
Attention: Dr. Norbert J. Berberich, Jr.
Seven Sperti Drive
Fort Mitchell, Kentucky 41017

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 Tablet, 1 mg.

DATE of APPLICATION: November 3, 1971

DATE of RECEIPT: November 29, 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. 12/2/71

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

cc:

ATL-DO

Dup

BD-69

BD-67

BD-100

BD-22

JIMeyer/wlb/12-1-71

Ack.

JTM 12/1/71

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.

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

1. Certification statements from both Stanlabs, Inc. and Carroll Chemical Company that the methods used in, and the facilities and controls used for, the manufacturing, processing, 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 clarification of the procedures used to assure that the drug dosage form and components will comply with the specifications and tests described in an official compendium, since it is noted that:
 - a) No procedures are given for the active ingredient.
 - b) The procedures listed for the final dosage form differ from those of the U.S.P.
 - c) And the procedures for the ——— used in the formulation of the tablets are omitted.
3. An outline of the methods actually used in, and the facilities, and controls used for, the processing, packing and holding of the drug, in preference to master file referrals (from both Stanlabs and Carroll Chemical).

APPEARS THIS WAY
ON ORIGINAL



Please let us have your response promptly.

Sincerely yours,

Marvin Seife 1/28/72

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

cc:

ATL-DO

SEA-DO

BLT-DO

Dup

BD-69

BD-67

BD-22

BD-242

RKimbrough/JLMeyer/GMi Mar 1/12/72

Init. by MAClark/JLMeyer/ 1/12/72

sam/1/27/72

rev w/f

RKimbrough 1/27/72
JLMeyer 1/27/72
Chubb 1/27/72

APPEARS THIS WAY
ON ORIGINAL



SPERTI DRUG PRODUCTS, INC.
SEVEN SPERTI DRIVE, FT. MITCHELL, KENTUCKY 41017
606-331-0800

3-3-72 *E*
Cable Address "SPERTI"

RESUBMISSION
NDA ORIG AMENDMENT

EPL
ORIG

May 23, 1972

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

REF: NDA 80-755

Gentlemen:

Reference is made to your letter of January 31, 1972. Please find enclosed the following information.

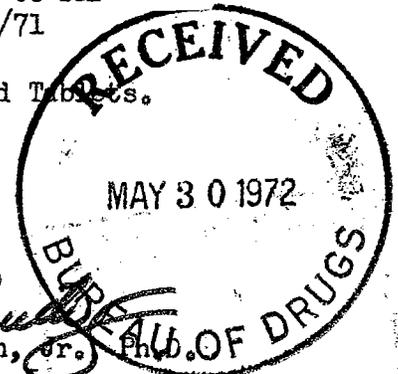
1. Revised package inserts as requested.
2. Container labels for Carroll Chemical Co. showing them as a distributor.
3. Container labels for Stanlabs Inc., showing them as the manufacturer.
4. Bulk container labels for shipment of bulk tablets from Stanlab plant to Carroll Chemical plant.
5. Certification statements from Stanlabs and Carroll Chemical Co.
6. Assay procedures for Folic acid raw material and final dosage form.
7. Requirements for the — used in the manufacture of the tablets.
8. For manufacturing methods, facilities, and controls used for the processing packaging and holding of the drug refer to DMF submitted to the Office of Technical Affairs 12/13/71

These documents should complete our file for Folic Acid Tablets.

RECEIVED 1 COPY
PHOTOSTATS MADE
FOR DUP _____ TRIP _____

Sincerely yours,

Norbert J. Herberich, Jr.
Norbert J. Herberich, Jr.
Sperti Drug Products Inc.



NDA 80-755

AF 24-516 (Sperti)
AF 23-201 (Carroll)
AF 22-968 (Stanlabs)

AUG 16 1972

Sperti Drug Products, Inc.
Attention: Dr. Norbert J. Berberich, Jr.
Seven Sperti Drive
Fort Mitchell, Kentucky 41017

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 May 23, 1972, enclosing printed labeling and manufacturing information.

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

Stanlabs, Inc.
Portland, Oregon 97214

Carroll Chemical Company
Baltimore, Maryland 21223

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

Carroll Chemical Company container label: At the time of the next printing, revise the phrase "Distr. by" to read "Distributed by".

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

1. Certification statement from Carroll Chemical Company, that the methods used in, and the facilities and controls used for the processing, 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. Procedures used to assure that the drug dosage form and components will comply with the specifications and tests described in an official compendium.
 - a) Clarify the omission of the _____ and residue on ignition tests performed on the active ingredient.
 - b) Include the testing procedures for _____ used in the formulation of the tablets, as requested in our letter of January 31, 1972.
 - c) It is noted that the assays for folic acid both as an active ingredient and a finished dosage form does not comply with the USP XVIII procedures. It is recommended that the proposed procedure be used only as an alternate procedure.
3. An outline of the facilities and controls, in preference to master file referrals, as requested in our letter of January 31, 1972.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife 8/14/72
Marvin Seife, M.D.
Director
Division of Actions Implementation
Drug Efficacy Study Implementation
Project Office
Bureau of Drugs

cc:
ATL-DO

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

MAClark/JLMeyer/RJWalters/8-7-72
R/D init. by MC JMeyer/8-11-72
Final typing/kim/8-15-72
Rev wf/

JMeyer 8/15/72
RJWalters 8-15-72



ORIG NEW CORRES.

E

FPL

STANLEY DRUG PRODUCTS, INC.

DIVISION OF SPERTI DRUG PRODUCTS, INC.

ORIG

MANUFACTURERS AND DISTRIBUTORS OF FINE PHARMACEUTICAL PRODUCTS

CABLE ADDRESS: "STANDRUG"
TELEPHONE: AREA 503 - 234-0432

P. O. BOX 3108
PORTLAND, OREGON 97208

September 11, 1972

Bureau of Drugs
Dept. of Health, Education and Welfare
Food and Drug Administration
Rockville, Maryland 20852

Re: N.D.A. #80-755
Folic Acid Tablets

Gentlemen,

Enclosed are our "Stanley" container label samples for Folic Acid tablets.
Please add these as supplement to our N.D.A. submitted through Sperti
Drug Products, Inc.

Thank you for your cooperation.

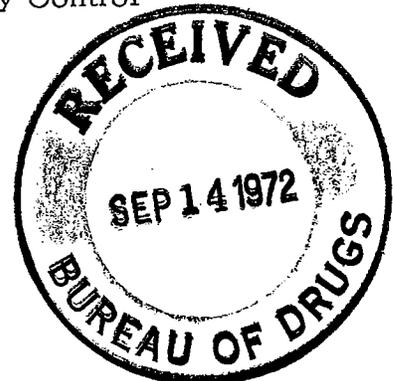
Sincerely yours

STANLEY DRUG PRODUCTS, INC.

Ted Tamaki
Vice President, Quality Control

TT:da
Encls.
cc:Jack Berberich

RECEIVED 1 COPY
PHOTOSTATS MADE
FOR DUP _____ TRIP _____





SPERTI DRUG PRODUCTS, INC.
SEVEN SPERTI DRIVE, FT. MITCHELL, KENTUCKY 41017
606-331-0800

Kevin W. F.
RESUBMISSION *E*
Cable Address "SPERTI"
NDA ORIG AMENDMENT

ORIG

September 29, 1972

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

Ref: NDA 80-755 Folic Acid Tablets 1.Omg.

Dear Doctor Seife;

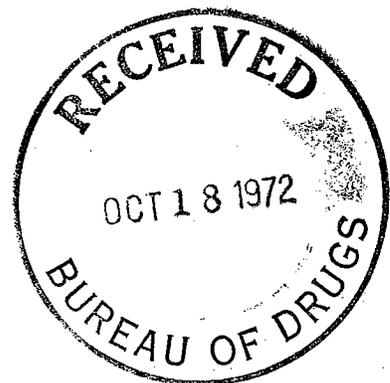
Reference is made to your communication of August 16, 1972. With respect to the marketing of this product as well as with all other tableted products, the following will prevail unless specifically stated. Sperti Drug Products Inc. is the parent corporation, we do not perform any manufacturing at the Kentucky facility. Stanley Drug Products of Portland Oregon does all tablet manufacturing as well as distributing, therefore they will so indicate on their labels according to regulations regarding labeling. On the other hand Carroll Chemical Co. of Baltimore Maryland will be supplied tablets in bulk through Stanley for repackaging and their label will designate them as a distributor.

Regarding the abbreviation "Distr. by" on the Carroll labels we will prepare all future labels to read "Distributed by" as you have recommended.

Regarding the certification statement for Carroll Chemical Co., we have notified them to forward this to us, as soon as it is received you will inturn receive it.

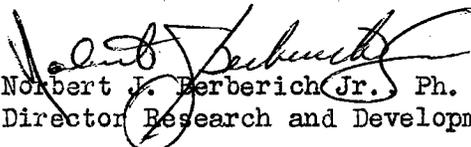
With respect to analytical procedures for the components and the finished dosage form as performed by Stanley we will submit revised analytical procedures which are in compliance will present compendia.

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Regarding your last point wherein you preferentially require individual submission of the outline of facilities and controls rather than reference to a DMF. I submit the following, it was at the suggestion of one of your own people during a meeting in April, 1969 involving discussions of our IND. that it was your preference to have us file a DMF rather than duplicating the submission of material which are of a general nature relating to methods and facilities. We recognize the difference in personal preferences, however we would appreciate a clarification of this matter since we have two obviously different suggestions from the same bureau.

Sincerely,


Norbert J. Berberich Jr., Ph. D.
Director Research and Development

NDA 80-755

AF 24-516
AF 23-201
AF 22-968

Sparti Drug Products, Inc.
Attention: Dr. Norbert J. Berberich, Jr.
Seven Sperti Drive
Fort Mitchell, Kentucky 41017

NOV 2 1972

Gentlemen:

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

Reference is made to the communication dated September 11, 1972, submitted on your behalf by Stanley Drug Products enclosing printed labels.

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:

Submit the information required by Section 130.4(f) of the regulations as requested in our letter dated August 16, 1972.

Please let us have your response promptly.

Sincerely yours,

Marvin Seifa 11/2/72

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

cc:

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JMeyer 10/24/72

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R/D init. MAClark, JLMeyer 10/24/72
Final typing bhy 10/24/72
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RJ Wolters 10-25-72

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~~NDA 80-755~~
AF 24-516 (Sperti)
AF 23-201 (Carroll)
AF 22-968 (Stanlabs)

Sperti Drug Products, Inc.
Attention: Dr. Norbert J. Berberich, Jr.
One Sperti Drive
Fort Mitchell, Kentucky 41017

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.

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

Stanlabs, Inc.
Portland, Oregon 97214

Carroll Chemical Company
Baltimore, Maryland 21223

We acknowledge receipt of your communication dated September 29, 1972.

Reference is also made to our communications of January 31, 1972, and August 16, 1972.

Your communication makes commitments to (1) revise the labels for Carroll Chemical Company (2) provide the requisite certification from Carroll Chemical (3) perform all appropriate compendial procedures for the components and finished dosage form, as per our previous comments and (4) clarified the relationship between the above firms.

Your communication also requested guidance regarding the need for the inclusion of a brief outline of the actual methods used in, and facilities and controls used for, the manufacture, processing and packing of the drug. That part of the regulations requesting inclusion of such materials as part of an abbreviated new drug application is outlined in red in the accompanying material.

APPEARS THIS WAY
ON ORIGINAL

Spartan Drug Products, Inc.
NDA 80-755

-2-

Please submit the above information (a) as per your commitments and
(b) as per our previous requests promptly.

Sincerely yours,

Marvin Seife 12/26/72

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

Enclosure:
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Miller 12/19/72
JMeyer 12/20/72

Rev. W/F

E

Cable Address "SPERTI"



RESUBMISSION

NDA ORIG AMENDMENT

FPL

Orig

SPERTI DRUG PRODUCTS, INC.
SEVEN SPERTI DRIVE, FT. MITCHELL, KENTUCKY 41017
606-331-0800

January 30, 1973

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

Re: NDA 80-755

Dear Dr. Seife:

Enclosed is the following information:

1. Revised labels Carroll Chemical Co.
2. Certification Statement of Carroll Chemical Co.
3. Various analytical procedures as requested in your letter of 8-16-72.

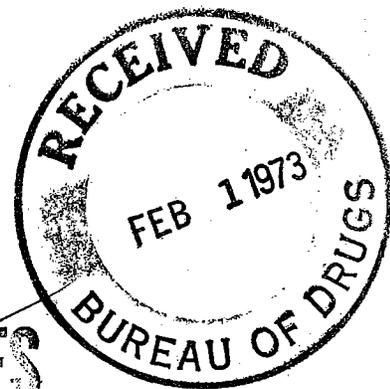
Sincerely,

Norbert J. Berberich, Jr.

NORBERT J. BERBERICH, Jr.
Ph.D.
Director, Research and
Development

NJB/sj

Encl.



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