

**CENTER FOR DRUG EVALUATION AND RESEARCH**

**APPLICATION NUMBER: 83607**

**ADMINISTRATIVE/CORRESPONDENCE DOCUMENTS**

# MEMORANDUM

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

TO : BD-105  
ATTN: Stanley Stringer

DATE: April 26, 1973

83-607

FROM : BD-340

SUBJECT: Applicant: Richlyn Laboratories, Philadelphia, Penna.

RE:

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:

Lack of master formulas for each formulation and batch size

Inadequate identification of raw materials and released products

Lack of manufacturing records for some intermediates and intermediate granulations

Lack of adequate control in potency adjustment during manufacture of products

Inadequate investigation and determination of reasons for failure of batches to meet specifications, both in-process and finished products.

In addition, the firm has had at least eight subpotent samples reported in programs by BD-320 and one recall in FY73 involving disintegration failure of Potassium Chloride Tablets.

The firm is currently the subject of contempt action filed in U.S. Court, 2/1/73, on the following motions:

Plaintiffs brief in reply to defendants brief in opposition to plaintiffs motion to vacate dismissal and reinstate injunction, and petition to show cause in criminal contempt.

This action involves Civil #36583 and includes approximately nine numbers of adulteration, misbranding and/or GMP (501(a)(2)(B)). PHI-DO informs us no additional inspections are planned until current litigation is resolved.

In view of the above, we find that we can not approve any NDA's until both litigation and GMP deficiencies are resolved.

 /S/ Jonas L. Bassen

NDA 83-607  
AF 28-724

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

FEB 06 1974

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 Hydrochlorothiazide Tablets.

We acknowledge receipt of your communications dated October 30, November 2 and November 9, 1973, amending the application.

Reference is also made to our letters through January 7, 1974.

The application 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 distributor to be:

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:

That previously requested.

Please let us have your response promptly.

/S/ 111  
74  
Marvin Seife, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

111  
111

**RICHLYN  
LABORATORIES  
INC.**

**NDA ORIG AMENDMENT**

*Very E*

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

November 9, 1973

FPL

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

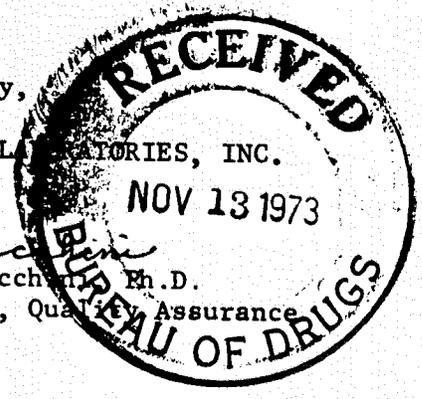
25 mg.

100's

Sincerely,

RICHLYN LABORATORIES, INC.

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



LPC/ mes  
Encl.  
AL-F01  
6-72

RESUBMISSION

NDA ORIG AMENDMENT <sup>ORIG</sup> Cable Address "RICHLYN"

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

November 2, 1973 *orig*

FPL

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

25 mg.

1000's

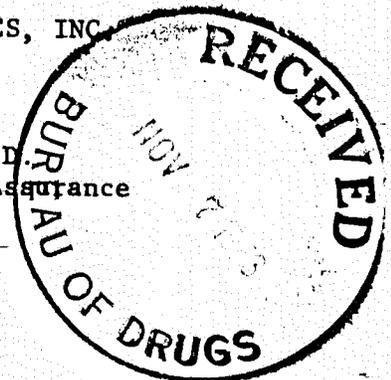
Sincerely,

RICHLYN LABORATORIES, INC.

*L.P. Cecchini*

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

LPC/ mes  
Encl.  
AL-F01  
6-72



NDA 83-607

AF 28-724

JAN 07 1974

Richlyn Laboratories, Inc.  
Attention: Mr. E. M. Rebollo  
Castor & Kensington Avenues  
Philadelphia, PA 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 Hydrochlorothiazide Tablets.

We acknowledge receipt of your communication dated October 25, 1973, amending the application.

Reference is also made to our letters through December 25, 1973.

The application 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 distributor to be:

Interstate Drug Exchange  
Plainview, NY 11803  
(50 mgs. in 100 & 1000)

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:

That previously requested.

Please let us have your response promptly.

Sincerely yours,

/S/

Marvin Seife, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

any 1-4-74

**RICHLYN  
LABORATORIES  
INC.**

RESUBMISSION

OKIE

**NDA ORIG AMENDMENT**

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

**FPL**    October 25, 1973

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: Interstate Drug Exchange  
Plainview, L.I., N.Y. 11803

(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

50 mg.

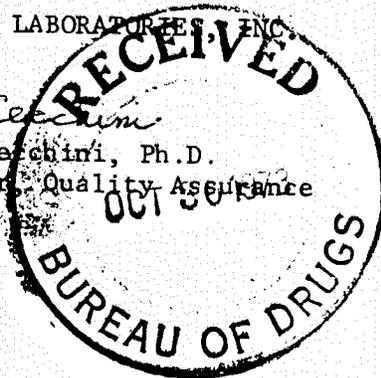
PACKAGING UNIT

100's & 1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*L. P. Cecchi*  
L. P. Cecchi, Ph.D.  
Director, Quality Assurance



LPC/ mes  
Encl.  
AL-F01  
6-72

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS

RESUBMISSION

ANTIBIOTICS      GENERICS

Cable Address "RICHLYN"

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

NDA ORIG AMENDMENT

OCT 11 1973

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607  
Additional Information Requested

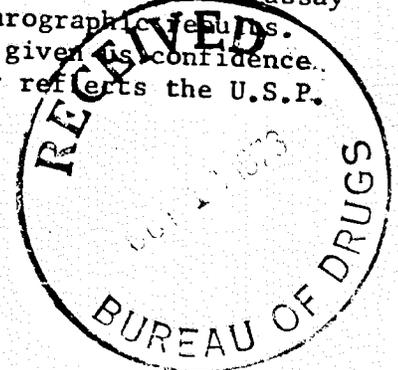
Gentlemen:

This triplicate submission is in response to your 8/24/73 and 9/17/73 requests for additional information.

The bioavailability testing contractor's ) response to DCR's 8/24/73 requests is enclosed. Aside from the superseding data and analyses, it should be noted that, per commitment, subjects abstained from other drugs and alcohol for a period of one week prior to each administration/sampling day.\*

In response to your 9/17/73 requests:

1. Subject supplier and presumed (only company referenced in bulk package labeling and protocol certificate of analysis, illustrative copy enclosed) manufacturer of context active ingredient raw material is, as previously stated,
2. The testing laboratory certification was revised to submitted version per specific request by FDA, Rockville. However, we have re-revised it, per your 9/17/73 guidelines, and herewith enclose the final product executed by the contractors.
3. Our 3/22/73 co-submission, without explanation, of the U.S.P. testing procedures and an "Alternative Assay Procedure" (AAP) for the finished tablets has naturally caused confusion. The explanation is as follows. All testing of the active ingredient and finished product -- except for the latter's content uniformity -- is per U.S.P. Identification and assay are performed by outside laboratories since we do not possess a polarograph. However, we routinely perform the composite assay (tablets) per the AAP and compare the results against the polarographic results. This experience, along with the initial validation study, has given us confidence in the validity of the AAP -- not surprising, since the latter refers the U.S.P. method for subject dissolution.



DRUG Received in DRUG R24

- Thus we now state our commitment to perform (or have performed on our behalf) the U.S.P. testing procedures (including the applicable assay) for the drug with one exception -- the content uniformity testing will employ the validated-comparable AAP.

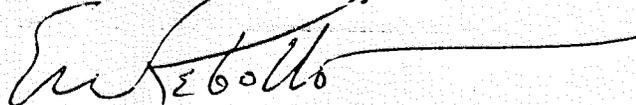
4. Please see paragraph 2 for data adequate to insure bioavailability.

5. Enclosed are the requested samples of active ingredient (A.I. -- 1 gram, our Control #21356, and finished tablets (F.P. -- 1 x 100, 25 mg., Lot #26491, and 1 x 100, 50 mg., Lot #26543.

As stated in our 9/6/73 meeting, this company intends to comply with your request to separate this application, and others, so that you will have an individual application for each dosage form strength. Some delay is needed to allow for our compliance with other FDA regulations (Drug Listing Act, Vitamin/mineral relabeling, periodic reporting, etc.). We request your patience during this period.

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo  
Vice President

EWR:mes

Encl.: HRC response re BA study  
Specimen, Supplier's certificate of analysis  
Testing laboratories' certifications (2)  
Samples, A.I. and F.P.

- \*Specifically, the answers to your 8/24/73 letter are:
1. Differences detected, set significance/power levels -- see p.37, HRC supplement.
  2. Abstinence from other drugs and alcohol -- actually 2 weeks pre-, and during, study (in excess of original commitment). -- See HRC "Addendum". Also note that the fasting state actually extended from 10 hours pre-dose to 4 (vs. claimed 2) hours post-dose.
  3. Evidence that analytical method is appropriate -- see HRC "Addendum", p.7a, where reference is made to HRC's subject feasibility study conducted for FDA (Contract No. 70-210).
  4. Revised analysis of variance -- HRC's supplement replaces, in total, the statistical analysis previously submitted. The method of analysis now conforms with DCR's 8/24/73 requirements. The clinical data previously submitted remain, of course, unchanged and should be regarded as part of the original submission.

RICHLYN  
LABORATORIES  
INC.

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

October 22, 1973

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

FPO

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

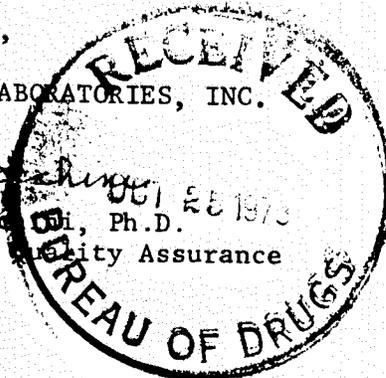
25 mg.  
50 mg.

100's  
1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*L. P. Cecchi*  
L. P. Cecchi, Ph.D.  
Director, Quality Assurance



LPC/ mes  
Encl.  
AL-F01  
6-72

**RICHLYN  
LABORATORIES  
INC.**

ORIG NEW COPIES *July*

Cable Address "RICHLYN"

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

October 8, 1973

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Certain (A)NDA Commitments

Gentlemen:

This triplicate submission is in response to prior correspondence, culminating with my 10/4/73 telephone discussion with Mr. Jack Meyer of your Administration, regarding:

- (A). Employment of "g." (period and plural forms optional) as the abbreviation for "gram" ; and,
- (B). separation of several (A)NDAs (notably #80-767, #83-267, and #83-607) to provide an individual application for each dosage form strength.

(A). This company herewith stipulates commitment to employing "g." (period and plural forms optional) in its labeling of drug products. Since we wish to avoid a bifid system ("g." only for U.S.P. products), we are instituting, immediately effective, the following system:

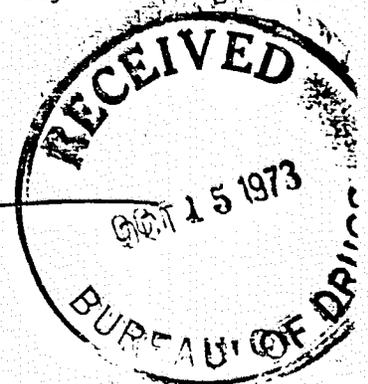
1. all new labeling (and reference thereto, with the exception of Drug Listing Act of 1972 submissions -- where FDA requires the "currently non-accepted 'GM'") will employ "g." notation.
2. all context non-conforming labeling will be ordered revised to "g." notation at true time of next printing (thus allowing reasonable easement from the usual 180-day equivalent for "next printing" in the anticipatedly few instances of slow-moving items).

(B). This company herewith stipulates commitment to separate the aforementioned applications, thus providing an individual application for each dosage form strength. This separation system, scheduled to begin with ANDA #83-607 for Hydrochlorothiazide Tablets, will be initiated as soon as possible. However, some delay is necessary to permit our compliance with other FDA requirements (Drug Listing Act, vitamin/mineral relabeling, periodic reporting, etc.). We request your patience during this period. Furthermore, we request that all such collective ANDAs be considered viable as such until superseded by your approval of the strength-separated applications -- after which the original ANDA will serve as the lead application, applicable to only one dosage form strength.

Sincerely,

RICHLYN LABORATORIES, INC.

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



EWR:mes

RICHLYN  
LABORATORIES  
INC.

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

*Orig*

SEP 24 1973

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607  
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.
- (v): Provision for participation by outside firm.

Appropriate exhibits are attached.\*

Sincerely,

RICHLYN LABORATORIES, INC.

*E. W. Rebollo*

E. W. Rebollo  
Vice President

EWR/1s  
Encl.

\*Alternate supplier, active ingredient (raw material):

RECEIVED  
SEP 27 1973  
IGS

RECEIVED  
SEP 27 1973  
RUIDE

NDA 83-607

AF 28-724

OCT 17 1973

Richlyn Laboratories, Inc.  
Attention: Mr. E. W. Rebell  
Castor & Kensington Avenues  
Philadelphia, PA 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 Hydrochlorothiazide Tablets.

We acknowledge receipt of your communication dated August 24, 1973, amending the application with information pertaining to a distributor.

Reference is also made to our letters through September 17, 1973, commenting upon this application.

The application 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 distributor to be:

Wolins Pharmacal Corp.  
75 Marcus Dr.  
Malville, NY 11746  
(both potencies in 100s & 1000s)

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. Regarding manufacturing, as per our request of September 17, 1973.
2. Regarding bioavailability, as per our comments of August 24, 1973.

Please let us have your response promptly.

/S/ 10/15/73  
MARVIN JALIK, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

S. Meyer 10/12/73  
10/11/73

73  
Garsany 10-11-73

**RICHLYN  
LABORATORIES  
INC.**

**ANDA ORIG AMENDMENT**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

**FPI**

August 24, 1973

Drug Efficacy Study Implementation  
Project Office -- BD-60

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

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: Wolins Pharmacal Corp.  
Melville, New York 11746

(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

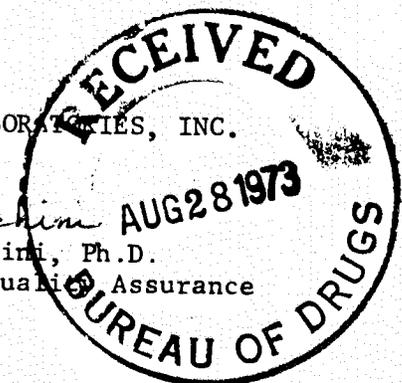
25 mg.

50 mg.

Sincerely,

RICHLYN LABORATORIES, INC.

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



LPC/ mes  
Encl.  
AL-F01  
6-72

**NDA 83-607**

**AF 28-724**

**Richlyn Laboratories, Inc.  
Attention: Mr. H. W. Rebellis  
Coster & Kensington Avenues  
Philadelphia, PA 19124**

**SEP 17 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 Hydrochlorothiazide Tablets.

We also acknowledge receipt of your communications dated June 1 and July 19, 1973, enclosing manufacturing information; and (a) May 14, May 17, May 21, May 29, June 5, June 22 and August 20, 1973 and (b) undated but received on July 16 and July 30, 1973 pertaining to distributors.

Reference is also made to our letter of June 18, 1973.

The application provides for you to market the drug under your own label. It also provides for you to label the drug with a label showing distributors to be:

)  
**The Interstate Drug Exchange, Inc.  
Plainville, NY 11803**  
)

**Spencer-Hoad, Inc.  
Valley Stream, NY 11582**

**Nichlys Laboratories, Inc.**  
**NDA 83-607**

We cannot complete our review of this abbreviated new drug application, however, until the following information - as per our requests of June 18, 1973 - is submitted:

1. The manufacturer of hydrochlorothiazide, including a supplier's protocol.
2. Full certification statements using the terminology of section 130.4(f) of the regulations (21 CFR) from the three testing laboratories.
3. A commitment to perform/have performed on your behalf---the USP procedures for the drug, including the applicable assay.
4. Adequate data to assure bioavailability, in accord with the protocol approved by our Division of Clinical Research.
5. Samples. In this connection, it is noted that you make the commitment to submit the active ingredient and tablets, when available.

Regarding separation of this application, it is requested that you comply with our comments to submit for the 25 mg. potency.

Please let us have your response promptly.

/S/

✓ **Marvin Seife, M.D.**  
**Director**  
**Generic Drug Staff**  
**Office of Scientific Evaluation**  
**Bureau of Drugs**

|  |                                   |                    |
|--|-----------------------------------|--------------------|
| MEMO RECORD  | AVOID ERRORS<br>PUT IT IN WRITING | DATE<br>1/73       |
| FROM: Perry Miller<br>(thru Jack L. Meyer)         |                                   | OFFICE<br>ED-69    |
| TO: Mr. C.G. Broker<br>(thru Stan Stringer ED-105) |                                   | DIVISION<br>ED-349 |

SUBJECT: Collaborative Draft(s)

SUMMARY In connection with NDA 88-007 for [unclear]

The applicant: [unclear]  
[unclear], of [unclear]

RE: 28-724

We acknowledge receipt on  
of  
dated  
for

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

xxx  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

NOTE: an evaluation has originally been made

PLEASE REPLY

SIGNATURE

DOCUMENT NUMBER

# MEMORANDUM

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

TO : BD-105  
ATTN: Stanley Stringer

DATE: June 27, 1973

FROM : BD-340

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

## Re-evaluation

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

**RICHLYN  
LABORATORIES  
INC.**

**NDA ORIG AMENDMENT**

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

August 20, 1973

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

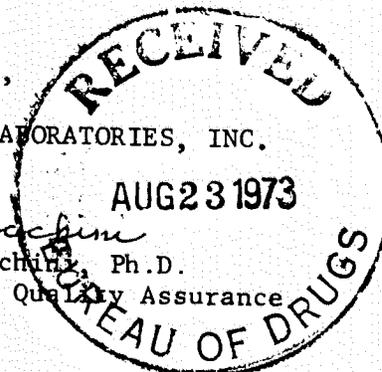
PACKAGING UNIT

1000's

Sincerely,

RICHLYN LABORATORIES, INC.

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



LPC/mes  
-Encl.  
AL-F01  
6-72

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

**RESUBMISSION**

**NDA ORIG AMENDMENT**

Cable Address "RICHLYN"

ORIG

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

JUL 19 1973

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607  
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 6/18/73 request for additional information.

We have relayed your dosage label-statement request for revision to who print their own labels. We will relay their response upon receipt.

Hydrochlorothiazide active ingredient employed in formulation of our tablets utilized in the bioavailability study was supplied (per our 4/22/73, section (1)(ii), commitment) by (

Our control number was #20357;

t number was #5062.

Re your requests for statements (CGMP certification and clarification of procedures, specifications, and tests employed) from the three laboratory contractors referenced, please be advised that these were submitted (3/22/73, section (1)(iii) attachments). As therein indicated, the contractors are required to test per U.S.P. XVIII which does not call for disintegration. However, our laboratory does perform disintegration testing (as indicated in our master laboratory report form) as an optional, additional assurance of product quality. In short, we do more than is required.

We will send, under separate cover, the requested samples of active ingredient and finished tablets (25 mg. and 50 mg. strengths).

Re your request for separate ANDAs for these two strengths, please refer to our 3/22/73 cover letter which confirms that the two tablet strengths share the same formulation. Thus the weight of the 25 mg. strength tablet (1.6 grains) is simply one-half that of the 50 mg. strength tablet (3.2 gr.). This is hardly a basis for separate ANDAs. We respectfully decline.

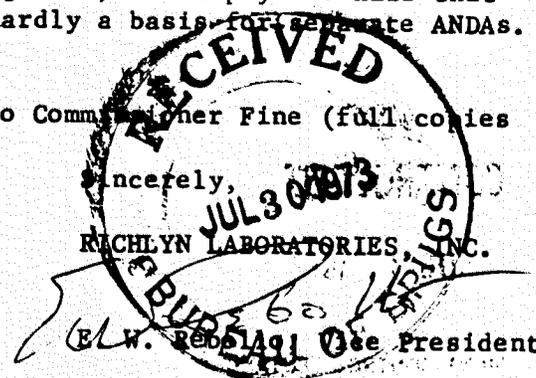
Re our CGMP status, please see our 5/23/73 letter to Commissioner Fine (full copies to Office of Compliance and to your Office).

Sincerely,

RICHLYN LABORATORIES, INC.

EL W. REED, President

EWR:tp



RESUBMISSION

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Drug Efficacy Study Implementation  
Project Office -- BD-60

FPL

ORIG

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

Reference: **HYDROCHLOROTHIAZIDE TABLETS, USP**  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

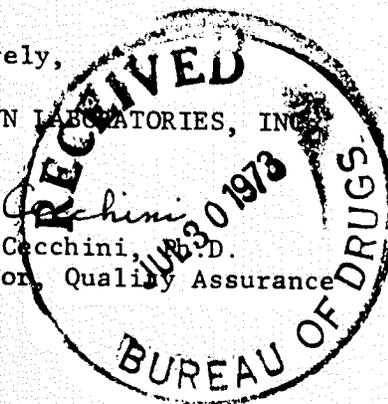
25 mg.

50 mg.

Sincerely,

RICHLYN LABORATORIES, INC.

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



LPC/  
Encl.  
AL-F01  
6-72



1  
RICHLYN  
LABORATORIES  
INC.

ORIG  
NDA ORIG AMENDMENT

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

June 22, 1973

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

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

25 mg.  
50 mg.

PACKAGING UNIT

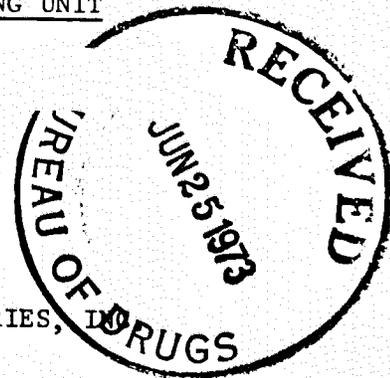
Sincerely,

RICHLYN LABORATORIES, INC.

*L.P. Cecchini*

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

LPC/mes  
Encl.  
AL-F01  
6-72



**RICHLYN  
LABORATORIES  
INC.**

**ANDA ORIG AMENDMENT**

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

**FPL**

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

**Drug Efficacy Study Implementation**  
**Project Office -- BD-60**  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

June 5, 1973

Reference: **Hydrochlorothiazide Tablets, U.S.P.**  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

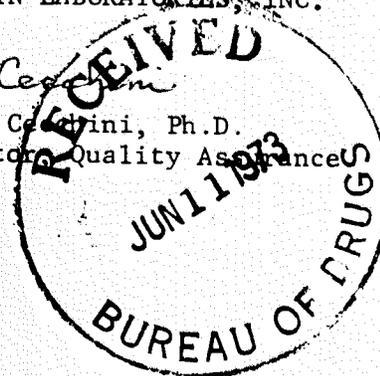
30's

Sincerely,

RICHLYN LABORATORIES, INC.

*L. P. Ceschini*  
L. P. Ceschini, Ph.D.  
Director, Quality Assurance

LPC/  
Encl.  
AL-F01  
6-72



**RICHLYN  
LABORATORIES  
INC.**

**ANDA ORIG AMENDMENT**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

June 1, 1973

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
25 & 50 mg., C.T. Peach Scored  
ANDA #83-607  
Amendment

Gentlemen:

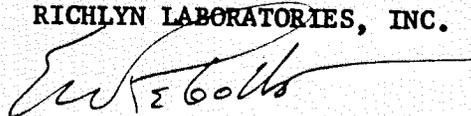
The enclosed triplicate submission provides supplement per 21CFR§130.9  
(a)(4):

- (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,

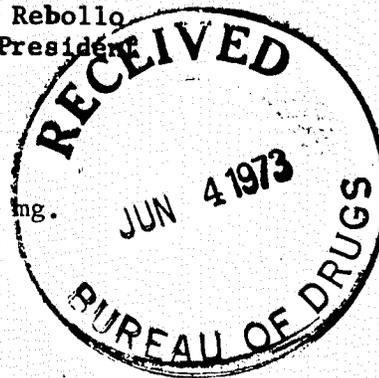
**RICHLYN LABORATORIES, INC.**



E. W. Rebollo  
Vice President

EWR/lrs  
Encl.

\*Corrected Lab Report Form, Finished Product, 25 mg.



ANDA ORIG AMENDMENT

Cable Address "RICHLYN"

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS **FPU** ANTIBIOTICS GENERICS

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

Drug Efficacy Study Implementation  
Project Office -- BD-60

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

May 29, 1973

Reference: HYDROCHLOROTHIAZIDE TABLETS U.S.P.  
25 mg. & 50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

25 mg.

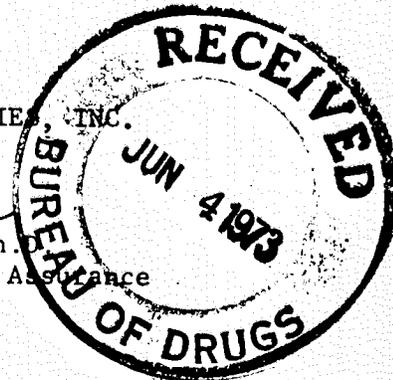
50 mg.

Sincerely,

RICHLYN LABORATORIES, INC.

*L. P. Cecchini*

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



LPC/tp  
Encl.  
AL-F01  
6-72

RICHLYN  
LABORATORIES  
INC.

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

*Orig*

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

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

May 21, 1973

Reference: Hydrochlorothiazide Tablets  
U.S.P. 25 Mg. & 50 Mg.  
C.T. Peach Scored ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: The Interstate Drug Exchange, Inc.  
Engineers Hill, Plainview, L.I., NY 11803

(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

25 Mg.

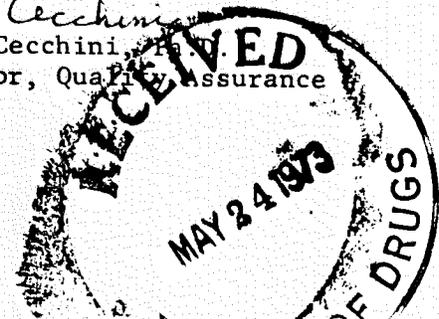
50 Mg.

Sincerely,

RICHLYN LABORATORIES, INC.

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

LPC/mes  
Encl.  
AL-F01  
6-72



RICHLYN  
LABORATORIES  
INC.

RESUBMISSION

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

May 17, 1973

FPL

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg & 50 mg C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

25 mg.

100's & 1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*L. P. Cecchini*

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

LPC/mes  
Encl.  
AL-F01  
6-72



**RICHLYN  
LABORATORIES  
INC.**

**NDA ORIG AMENDMENT**

*Original*  
Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

**FPLJ** May 14, 1973

Reference: Hydrochlorothiazide Tablets, U.S.P.  
25 mg & 50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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.

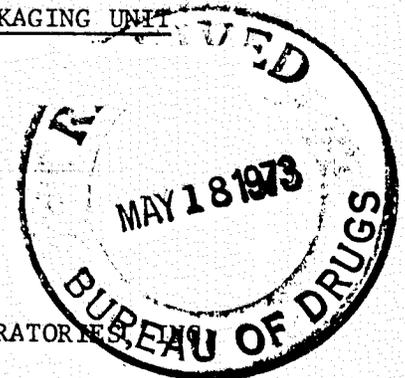
Label(s) & insert.

Labeling submission is  original  revised.

DOSE STRENGTH

50 mg.

PACKAGING UNIT



Sincerely,

RICHLYN LABORATORIES, INC.

*L. P. Cecchini*

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

LPC/ mes  
Encl.  
AL-F01  
6-72

NDA 83-607  
AF 28-724

AUG 24 1973

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

Gentlemen:

Reference is made to your bioavailability study for Hydrochlorothiazide Tablets U.S.P., 25 mg. and 50 mg.

This study has been reviewed by our Division of Clinical Research and they have the following comments:

The following information is required before an adequate review of the data submitted can be made:

1. The difference that can be detected between test and reference products at a significance level of 0.05 and a power of the test of 0.80.
2. The period of time that the subjects abstained from other drugs and alcohol.
3. The sensitivity, specificity, and linearity of the laboratory method employed must be determined by the laboratory at the level of drug expected in the clinical specimens. All standard curves, recovery data, etc. must be submitted.
4. The analysis of variance employed did not contain reference to all the variables desired. It should include subject, period or time effects, drug, and sequence effects. A similar analysis will be required for cumulative urine excretion.

RECOMMENDATION:

The applicant should submit the data requested above.

Sincerely yours,

*S/*  
M. Selfe, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

*11 - 1*  
*3/23*

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

*Orig*

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

May 14, 1973

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg., C.T. Peach Scored  
ANDA #83-607  
Bioavailability Study  
Additional Information Requested

Gentlemen:

This triplicate submission provides subject data and analysis. Pertinent analysis of 50 mg. strength tablet samples from subject clinical testing supply provided the following data.

| <u>Test Product</u>                            | <u>Reference Product</u>                 |
|--|--|
| Mfr.: Richlyn Laboratories, Inc.<br>Lot #25785 | Mfr.: Merck, Sharp & Dohme<br>Lot #P1666 |
| Av. Weight/Tablet: 0.206 g.                    | Av. Weight/Tablet: 0.223 g.              |
| Composite Assay: 99.4%                         | Composite Assay: 100.6%                  |
| Content Uniformity:                            | Content Uniformity:                      |
| 101.6%      103.2%                             | 100.3%      105.8%                       |
| 103.5%      101.6%                             | 103.2%      107.4%                       |
| 100.0%      100.3%                             | 98.4%      96.2%                         |
| 96.5%      101.6%                              | 104.8%      103.8%                       |
| 98.4%      100.6%                              | 103.8%      103.2%                       |

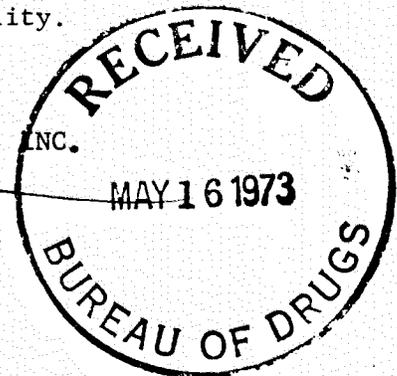
Note: Assay data reported as % of label claim, active ingredient; data represent average value, duplicate determinations.

We respectfully submit this evidence of isobioavailability.

Sincerely,  
RICHLYN LABORATORIES, INC.

*E. W. Rebollo*

E. W. Rebollo  
Vice President



Encl.: (3 sets), reference evidence  
EWR:mes

NDA 83-607  
~~AP 28-724~~

**Richlyn Laboratories, Inc.**  
**Attention: Mr. Edward Rebolle**  
**Castor & Kensington Avenues**  
**Philadelphia, Pennsylvania 19124**

APR 25 1973

Gentlemen:

Reference is made to your protocol for bioavailability studies for Hydrochlorothiazide Tablets, 25 and 50 mg.

This protocol has been reviewed by our Division of Clinical Research and they have the following comments:

1. The study will employ 12 normal male volunteers 21-55 years of age, weighing 135-200 pounds. The applicant should be informed that the number of subjects employed should be sufficient to determine a reasonable difference between test and reference drugs at a significance level of 0.05 and a power of the test of 0.80. This difference should be reported. Also, the subject weights should be within 10% of those contained in the Metropolitan Life Insurance Company's Statistical Bulletin '40'. Nov.-Dec., 1959.
2. The protocol indicates that the subjects will abstain from other drugs for at least one week prior to the study. They should, however, abstain from other drugs for two weeks and from alcohol for 48 hours prior to dose administration.
3. Laboratory studies will include WBC, hematocrit, hemoglobin, urinalysis (including microscopic) calcium, phosphorus, glucose, BUN, LDH, uric acid, cholesterol, total bilirubin, serum alkaline phosphatase, and glucose-6-phosphate dehydrogenase. An SGOT should be included.
4. Urine collection will occur at 0, 2, 4, 6, 8, 12, 16 and 24 hours. It should be better fractionated, however. Collection at 0, 1, 2, 3, 4, 6, 8, 12, and 24 hours is recommended.

5. Eight ounces of water should be ingested at each urine collection to insure an adequate urinary flow.

6. The urine collected will be measured for volume and 100 mg will be retained for lab analysis. This is satisfactory if the drug content can be quantitated by the analytical methodology employed. In addition, however, pH should be determined.

7. The crossover interval was not given but should have been. It should not occur until after 10 half-lives of the drug. For hydrochlorothiazide we recommend an interval of one week.

8. Hydrochlorothiazide levels in urine will be determined by the method of Sheppard, et al. The applicant should be informed that the sensitivity, specificity, and linearity of the method must be determined by the laboratory at the level of the drug expected in the clinical specimen. All standard curves, recovery data, etc. should be submitted with the final report.

9. The test and reference product should be assayed for potency and content uniformity.

**RECOMMENDATION:**

The protocol is acceptable provided that the above 9 points are satisfactorily incorporated into the protocol.

/S/ 25/73  
Marvin Seife, M.D.  
Director  
Division of Actions Implementation  
Drug Efficacy Study Implementation  
Project Office  
Bureau of Drugs

**NDA 83-607**

**AF 28-724**

**JUN 18 1973**

**Richlyn Laboratories, Inc.  
Attention: Mr. E. W. Rebellis  
Caster & Kensington Avenues  
Philadelphia, PA 19124**

**Gentlemen:**

**Reference is made to your abbreviated new drug application dated March 22, 1973, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets.**

**We also acknowledge receipt of your communications dated April 11, and April 16, 1973, amending the application with information pertaining to a distributor and environmental impact.**

**The application 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 distributor to be:**

**y**

**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. Revised labels for your distributor on which the indications and specific dosages are replaced with the statement: "Usual Dose: See Package Insert."**
- 2. Information pertaining to the manufacturer of the hydrochlorothiazide, as per your bioavailability study.**
- 3. Certification statements from:**

**nc.**

that the methods used in, and the facilities and controls used for, testing the drug are in conformity with current good manufacturing practice in accord with Part 133 (21CFR) of the regulations.

4. A clarification of the procedures to be performed by these testing firms.  
A clarification of the specifications and tests used to assure the identity, strength, quality and purity of the drug dosage form, since it is noted that you also include disintegration testing.
5. Samples of (a) the active ingredient and (b) 50 mg. tablets. In this regard, it is also requested that information pertaining to and samples of 25 mg. tablets be submitted as a separate abbreviated new drug application—incorporating the information requested above.

That part of your submission pertaining to bioavailability was commented upon in a letter of April 25, 1973.

The Bureau of Drugs, Office of Compliance, has reviewed your establishment inspection report(s) and have the following comments:

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 September 12, 1972, revealed numerous significant CGP deviations including:

Lack of master formulas for each formulation and batch size

Inadequate identification of raw materials and released products

Lack of manufacturing records for some

Lack of adequate control in potency adjustment during manufacture of products

Inadequate investigation and determination of reasons for failure of batches to meet specifications, both in-process and finished products.

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,  
*[Handwritten signature]*  
/S/

HARVEY SALVE, M.D.  
Director  
Division of Actions Implementation  
Drug Efficacy Study Implementation  
Project Office  
Bureau of Drugs  
K 11113

- 93

3



Page (s) \_\_\_\_\_ / \_\_\_\_\_

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

*Labeling agreement*

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

ORIG

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

April 11, 1973

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg., C.T. Peach Scored  
ANDA #83-607  
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 4/5/73 request (received 4/11/73) for additional information.

Please find enclosed reference environmental impact analysis report.

Also enclosed are the return-receipt certified (#46406) slips that accompanied your request, but which were inadvertently ignored by the delivering postman. The latter oversight was undoubtedly due to the U.S. Post Office's concern with prompt delivery.

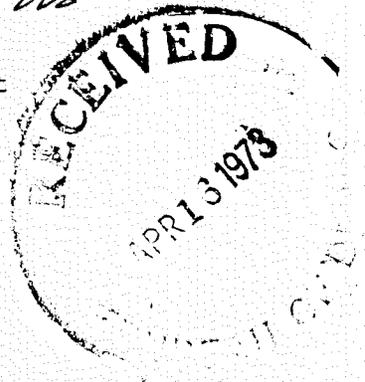
We trust that our EIAR will prove adequate to your careful consideration, thus permitting expeditious review of subject application.

Sincerely,

RICHLYN LABORATORIES, INC.

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

EWR/lrs  
Encl.: EIAR.



NDA 83-607

AF 28-724

APR 5 1973

**CERTIFIED MAIL  
RETURN RECEIPT REQUESTED**

Richlyn Laboratories, Inc.  
Attention: Mr. Edward Rebelle  
Castor & Kensington Avenues  
Philadelphia, Pennsylvania 19124

Gentlemen:

This is in regard to your recent submission of your abbreviated new drug application received on March 27, 1973.

The Food and Drug Administration published in the Federal Register of March 15, 1973 (38 F.R. 7001) regulations establishing procedures for preparation of Environmental Impact Statements (Part 6 - Environmental Impact Considerations). Section 6.1(a) of these regulations requires that the applicant include an environmental impact analysis report as part of any new-drug application. Failure to submit an environmental impact analysis report is grounds for refusing to file or to approve an application (21 CFR 130.5(a)(8) or 130.12(a)(7)).

The effective date for the Environmental Impact Considerations regulation (21 CFR Part 6) is March 15, 1973. Since your new-drug application was submitted after that date, you are required to include an environmental impact analysis report as part of your application. In view of the limited time to review the application and the requirements for environmental consideration, please submit by April 30, 1973, an environmental impact analysis report for the subject new-drug application (or abbreviated new-drug application.)

The format for the environmental impact analysis report is described in Section 5.1(g).

The FDA encourages that the required analysis report be submitted as promptly as possible since approval of a new-drug application cannot be made until the environmental effects are carefully considered. A copy of the Regulation is enclosed for your ready reference.

Sincerely yours,

*IS/*  
Janis Sells, M.D.  
Director  
Division of Actions Implementation  
Drug Efficacy Study Implementation  
Project Office  
Bureau of Drugs

*5/73*

NDA 83-607

AF 28-724

APR 5 1973

Richlyn Laboratories, Inc.  
Attention: Mr. Edward Rebollo  
Castor & 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: Hydrochlorothiazide Tablets, 25 mg. and 50 mg.

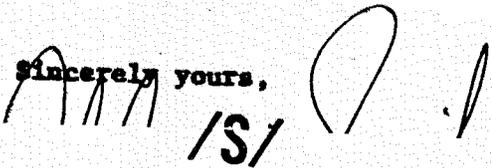
DATE of APPLICATION: March 22, 1973

DATE of RECEIPT: March 27, 1973

We will communicate 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,

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

RICHLYN  
LABORATORIES  
INC.

ABBREVIATED  
NEW DRUG APPLICATION Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

MAR 22 1973

83-607

Drug Efficacy Study Implementation  
Project Office -- BD-60  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
25 mg. & 50 mg., C.T. Peach Scored  
Original ANDA

Gentlemen:

Herewith in triplicate is reference submission.

Labeling is in accord with 37 F.R.14896 (DESI 11145), 7/26/72.

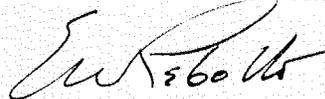
Please note (Section 3) our proposed bioavailability study to be performed

We plan to use the 50 mg. strength tablet (scored) in this study. The results will cover the 25 mg. tablet as well, since the master formulations are identical -- i.e., the weight of a 25 mg. strength tablet is precisely one-half that of a 50 mg. strength tablet.

Your cooperation in expediting review of our protocol will be greatly appreciated, since the study will not proceed without your approval.

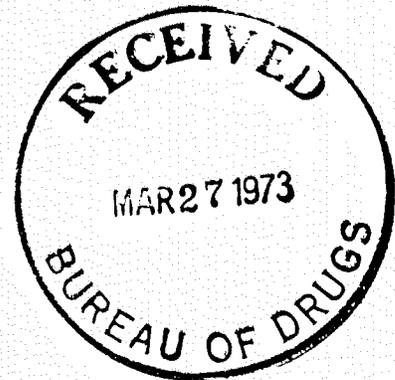
Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo  
Vice President

EWR/lrs  
Encl.





MAY -6 1977

NDA 83-607

Richlyn Laboratories, Inc.  
Attention: Mr. E.W. Rebollo  
Castor & Kensington Avenues  
Philadelphia, PA 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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communication dated February 11, 1977, containing data to assure the bioavailability of your drug dosage form.

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. The per tablet composition of lot #30234 used in the study and information as to whether it differs from previously submitted formulations.
2. An updating of the manufacturing and control sections of this application in light of the time between initial submission and submission of the bioavailability data.
3. Copies of labeling - it is requested that information pertaining to distributors NOT be submitted until the application is approved.

That part of your submission pertaining to bioavailability - as per the above referenced submission - has been reviewed by our Division of Biopharmaceutics. Their comment is that your preparation "is bioequivalent" to the reference drug.

Please let us have your response promptly.

Sincerely yours,

*[Handwritten signature]*  
MARVIN SEIRE, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs  
*[Handwritten initials]* 1/6/77

5/1/77

FROM: Marvin Seife, M.D.

OFFICE

TO: Division of Biopharmaceutics

DIVISION

HF-D-530

SUBJECT:

SUMMARY

Attention: Dr. Harold Murdock

NDA

83-607

Hydrochlorothiazide Tabs 50mg  
Richlyn Labs

Please review the bioavailability study on the above drug.

1

/S/

Marvin Seife, M.D.

*[Handwritten signature]*

SIGNATURE

DOCUMENT NUMBER

RICHLYN  
LABORATORIES  
INC.

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

February 11, 1977

Bureau of Drugs, HFD #530  
Attn.: Document Control Room #16-72  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

ORIG NEW CORRES

Ref.: Hydrochlorothiazide Tablets, 50 mg.  
ANDA #83-607  
Additional Information Requested

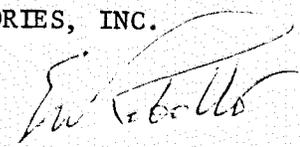
Gentlemen:

This triplicate submission, per your request, provides the bioavailability study report on our referenced product. Pertinent in-vitro testing data are given on the third page of the report, following "Table of Contents", tabbed as "Drug Analysis".

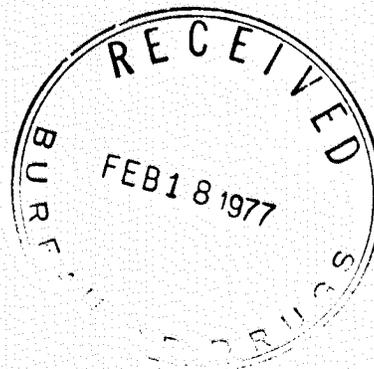
Sincerely,

RICHLYN LABORATORIES, INC.

E. W. Rebollo  
Vice President



Encl.: cited.



JAN 11 1977

NDA 83-607

Richlyn Laboratories, Inc.  
Attention: Mr. E.W. Rebollo  
Castor & Kensington Avenues  
Philadelphia, PA 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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communications dated July 25 August 5 & 6, 1976 pertaining to distributors.

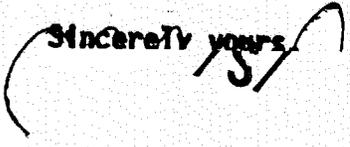
Reference is also made to you communication of June 23, 1976 containing a bioavailability protocol.

Before we are able to reach a final conclusion, however, it is requested that you submit adequate data to assure the bioavailability of your drug dosage form in accord with this protocol.

It is again requested that further amendments to provide for additional distributors not be submitted as per Agency Policy for this drug dosage form.

The material submitted (for distributors) is being retained in our files.

Sincerely yours,

  
Martin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

*Handwritten initials and date:* A  
11/10/77

17  
11/10/77

NDA 83-607

JAN 04 1977

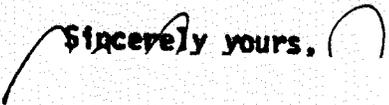
**Richlyn Laboratories, Inc.**  
**Attention: Mr. E.W. Rebelle**  
**Castor & Kensington Avenues**  
**Philadelphia, PA 19124**

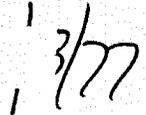
**Gentlemen:**

**Reference is made to the protocol you submitted for bioavailability studies for Hydrochlorothiazide Tablets, 50 mg.**

**The protocol has been reviewed by our Division of Biopharmaceutics and they have the following comments:**

**The protocol, as submitted, is acceptable.**

Sincerely yours, 

  
  
/ **Marvin Seife, M.D.**  
**Director**  
**Division of Generic Drug Monographs**  
**Office of Drug Monographs**  
**Bureau of Drugs**

9/23/76

FROM:

Marvin Seife, M.D.

OFFICE

TO:

Division of Biopharmaceutics

DIVISION

HPD 530

SUBJECT:

SUMMARY

Attention: Dr. Harold Murdock

NDA

83-607  
Hydrochlorothiazide Tabs 50mg  
Reblyn

Please review the bioavailability protocol on the above drug.

MS

Marvin Seife, M.D.

SIGNATURE

DOCUMENT NUMBER

**RICHLYN  
LABORATORIES  
INC.**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA

215 CU 9-2220

June 23, 1976

Bureau of Drugs -- HFD-530  
Attn.: Document Control Room #16-72  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

**ORIG NEW CORRES**

Ref.: Hydrochlorothiazide Tablets, 50 mg.  
ANDA #83-607  
Bioavailability Study Protocol

Gentlemen:

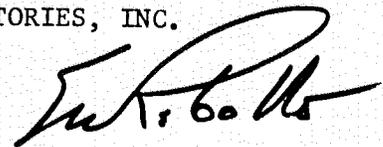
This triplicate submission provides our proposed bioavailability study protocol.

Confirming my recent discussion with Dr. Seife, we request promptest possible review and comments on this proposal since study initiation awaits your response.

Sincerely,

RICHLYN LABORATORIES, INC.

E. W. Rebollo  
Vice President



Encl.: cited



Page (s) 1

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

*Labeling agreement.*

**RICHLYN  
LABORATORIES  
INC.**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

August 5, 1975

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

**NDA ORIG AMENDMENT  
FPL**

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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.

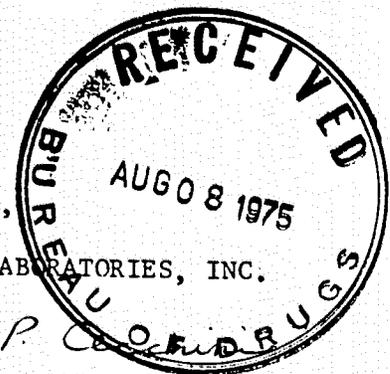
DOSE STRENGTH  
50 mg.

PACKAGING UNIT  
1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*  
Louis P. Cecchini, Ph.D.  
Director, Quality Assurance



Encl.  
AL-F01  
6-72

**RICHLYN  
LABORATORIES  
INC.**

*Craig*

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

July 25, 1975

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

**NDA ORIG AMENDMENT**

**FPL**

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: ;  
;

(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.

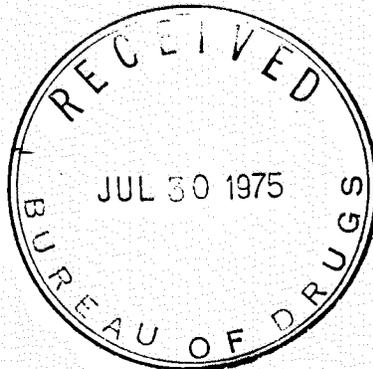
Labeling submission is  original  revised.

DOSE STRENGTH

50 mg.

PACKAGING UNIT

1000's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.  
AL-F01  
6-72

NDA 83-607

DEC 09 1975

Richlyn Laboratories, Inc.  
Attention: Mr. E. W. Rebollo  
Castor & Kensington Avenues  
Philadelphia, PA 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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communications dated June 27 (two) and July 3, 1975, pertaining to distributors.

The application provides for you to market the drug under your own label. It also provides for you to label the drug with a label showing distributors to be:

R. A. McNeil Co.  
Chattanooga, TN 37416  
(100s, trade name - M-Zide)

your Mutual labels  
(100s + 1000s)

Before we are able to reach a final conclusion, however, it is requested that you submit adequate data to assure the bioavailability of your drug dosage form—as per previous requests to complete filing in this area in response to our comments of April 15, 1974.

It is again suggested that further amendments to provide for additional distributors not be submitted until the bioavailability status of your application is clarified.

The material submitted is being retained in our files with review deferred.

Sincerely yours,

Marvin Seife, M.D.  
Director

Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

9/75

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

July 3, 1975

FPL

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: Richlyn Laboratories, Inc.  
Philadelphia, PA 19124

(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.

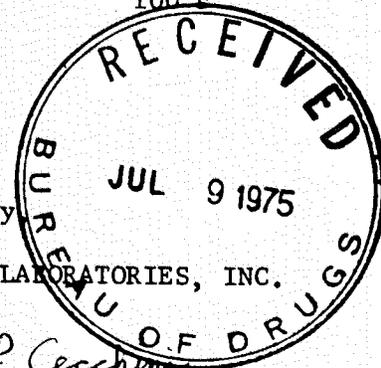
Labeling submission is  original  revised.

DOSE STRENGTH

50 mg.

PACKAGING UNIT

100's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.  
AL-F01  
6-72

**RICHLYN  
LABORATORIES  
INC.**

**NDA ORIG AMENDMENT**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

June 27, 1975

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

FPL

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: Richlyn Laboratories, Inc.  
Philadelphia, PA 19124

(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.

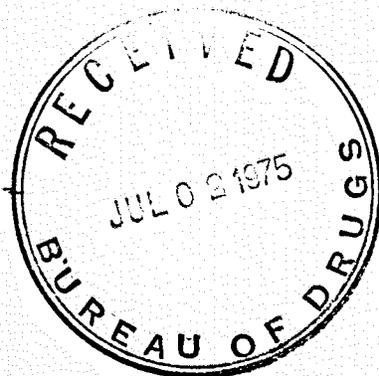
Labeling submission is  original  revised.

DOSE STRENGTH

50 mg.

PACKAGING UNIT

1000's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

Louis P. Cecchini, Ph.D.

Director, Quality Assurance

Encl.  
AL-F01  
6-72

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

June 27, 1975

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

FPL

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: R.A. McNeil Company  
Chattanooga, TN 37416

(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.

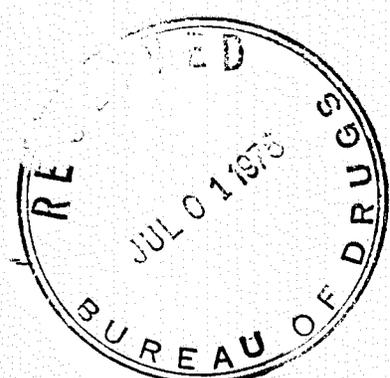
Labeling submission is  original  revised.

DOSE STRENGTH

50 mg.

PACKAGING UNIT

100's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*  
Louis P. Cecchini, Ph.D.  
Director, Quality Assurance

Encl.  
AL-F01  
6-72

NDA 83-607

AF 28-724

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

MAY 23 1975

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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communications dated (1) February 13, 1975 pertaining to a distributor and (2) March 21, 1975 updating your manufacturing records.

The application 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 distributor to be:

Before we are able to reach a final conclusion, however, it is requested that you submit adequate data to assure the bioavailability of your drug dosage form---as per previous requests to complete filing in this area in response to our comments of April 15, 1974.

It is again suggested that further amendments to provide for additional distributors not be submitted until the bioavailability status of your application is clarified.

The material submitted (for this distributor) is being retained in our files with its review deferred.

/S/

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

# NDA ORIG AMENDMENT

Cable Address "RICHLYN" *CRAG*

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

March 21, 1975

Division of Generic Drug Monographs -- HFD-107  
Office of Drug Monographs  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Gentlemen:

The enclosed triplicate submission provides supplement per 21CFR8314.8  
(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*  
E. W. Rebollo  
Vice President

EWR/  
Encl.

\* Superseding replacement, Master Formula 50 mg.: (700M, 1050M)

**RECEIVED**

MAR 23 1975

GENERIC DRUGS

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

FPL  
ORIG

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

February 13, 1975

Division of Generic Drug Monographs -- HFD-107  
Office of Drug Monographs  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg., C.T. Peach, Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

PACKAGING UNIT

100's & 1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Centina*  
Louis P. Centina, Ph.D.  
Director, Quality Assurance  
**RECEIVED**  
FEB 19 1975  
BUREAU OF DRUGS

Encl.  
AL-F01  
6-72

NDA 83-607  
AF 28-724

APR 08 1975

Richlyn Laboratories, Inc.  
Attention: Mr. E. W. Rebollo  
Castor & Kensington Avenues  
Philadelphia, PA 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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communications dated November 21 and December 31, 1974, and January 7 and 31, 1975, pertaining to distributors.

The application provides for you to market the drug under your own label. It also provides for you to label the drug with a label showing distributors to be:

Spencer-Mead, Inc.  
Valley Stream, NY 11582

Interstate Drug Exchange, Inc.  
Plainview, NY 11803

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:

That requested in our letter of July 18, 1974, pertaining to the bioavailability of your formulation.

Richlyn Laboratories, Inc.  
NDA 83-607 Page - 2

It is again suggested that further amendments to provide for additional distributors not be submitted until the bioavailability status of your application is clarified.

The material submitted (for these distributors) is being retained in our files with its review deferred.

/S/

7/8/75

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

Barney 4-7-75

RICHLYN  
LABORATORIES  
INC.

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

January 31, 1975

Division of Generic Drug Monographs -- HFD-107  
Office of Drug Monographs  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

FPL

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg., C.T. Peach, Scored  
ANDA #83-607

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, N Y 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

50 mg.

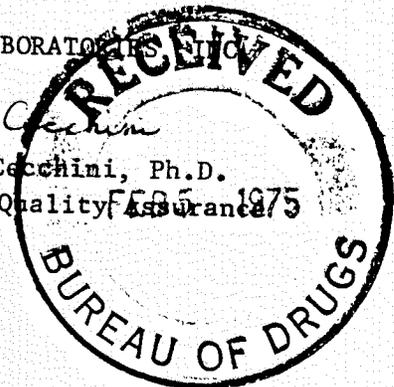
PACKAGING UNIT

1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*  
Louis P. Cecchini, Ph.D.  
Director, Quality Assurance



Encl.  
AL-F01  
6-72

**RICHLYN  
LABORATORIES  
INC.**

**RESUBMISSION  
NDA ORIG AMENDMENT**

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

January 7, 1975

Division of Generic Drug Monographs -- HFD-107  
Office of Drug Monographs  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

FPL

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: Interstate Drug Exchange, Inc.  
Plainview, L.I., N.Y. 11803

(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

50 mg.

PACKAGING UNIT

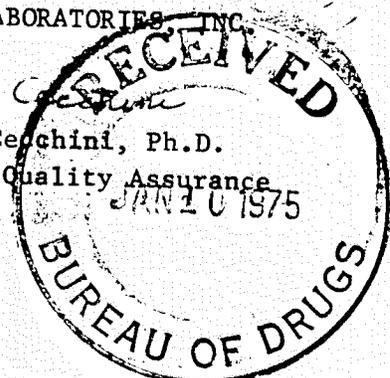
100's & 1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*  
Louis P. Cecchini, Ph.D.

Director, Quality Assurance



Encl.  
AL-F01  
6-72

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

December 31, 1974

Division of Generic Drug Monographs -- HFD-107 **FPL**  
Office of Drug Monographs  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

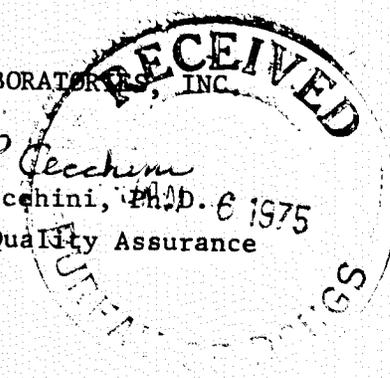
PACKAGING UNIT

1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*  
Louis P. Cecchini, PH.D. 6 1975  
Director, Quality Assurance



Encl.  
AL-F01  
6-72

NDA ORIG AMENDMENT

Cable Address "RICHLYN"

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

FPL

November 21, 1974

Generic Drug Staff -- HFD-107  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg. C.T. Peach Scored  
ANDA #83-607

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, N Y 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

50 mg.

PACKAGING UNIT

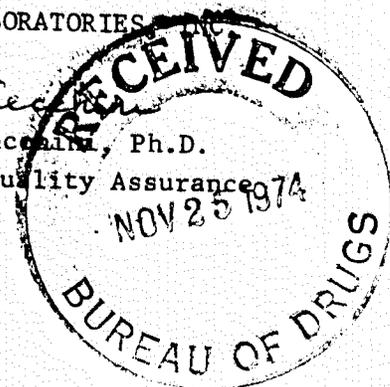
100's

Sincerely,

RICHLYN LABORATORIES

*Louis P. Cecchini*  
Louis P. Cecchini, Ph.D.

Director, Quality Assurance



Encl.  
AL-F01  
6-72

NDA 83-607

AF 28-724

DEC 24 1974

Richlys Laboratories, Inc.  
Attention: Mr. E. W. Rebollo  
Castor & Kensington Avenues  
Philadelphia, PA 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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communication dated November 5, 1974 pertaining to a distributor.

The application 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 distributor to be:

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:

That requested in our letter of July 18, 1974, pertaining to the bioavailability of your formulation.

It is again suggested that further amendments to provide for additional distributors not be submitted until the bioavailability status of your application is clarified.

The material submitted (for this distributor) is being retained in our files with its review deferred.

Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

je 12/24/74

74

RESUBMISSION

*orig* *E*

**RICHLYN  
LABORATORIES  
INC.**

**NDA ORIG AMENDMENT**

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

**FPL**

November 5, 1974

Generic Drug Staff -- HFD-107  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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  
50 mg.

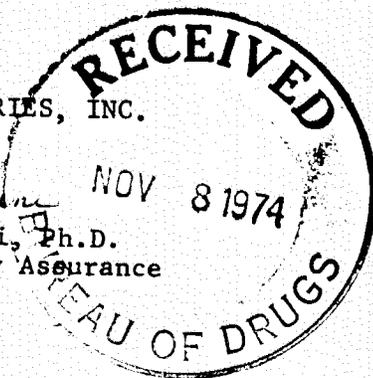
PACKAGING UNIT  
1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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



Encl.  
AL-F01  
6-72

NBA 83-607

AF 28-724

SEP 27 1974

Richlyn Laboratories, Inc.  
Attention: Mr. E. W. Rebolfo  
Castor & Kensington Avenues  
Philadelphia, PA 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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communications dated August 7 and 22, 1974, pertaining to distributors.

Reference is also made to our letter of August 9, 1974.

The application 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 distributors to be:

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:

As per our comments of August 9, 1974.

Please let us have your response promptly.

Sincerely yours,

Marvin Seife, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

1. 1. 1  
j. Masany 9-26-74

NDA ORIG AMENDMENT

←

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS

ANTIBIOTICS

FPL

GENERIC

Cable Address "RICHLYN"

ORIG

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

Generic Drug Staff -- HFD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

August 22, 1974

Reference: HYDROCHLOROTHIAZIDE TABLETS  
50 mg.  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

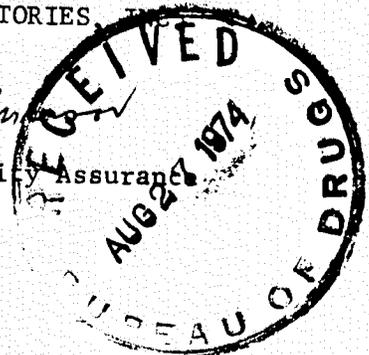
100s

1000s

Sincerely,

RICHLYN LABORATORIES

*W. J. Palmerson*  
Director, Quality Assurance



Encl.  
AL-F01  
6-72

Hydrochlorothiazide  
50 mg Tablets  
ANDA 83-607

Richlyn Laboratories  
Philadelphia, Pennsylvania  
AF #28-724  
Submission Dated:  
October 30, 1974

REPLY TO LETTER FROM THE APPLICANT CONCERNING THE  
BIOAVAILABILITY STUDY

1. In my review of the bioavailability study, dated 4/5/74, I had pointed two deficiencies in the study:

a. individual values of the drug level in the urine were quite erratic, and in 4 out of 13 subjects the area under the curve indicated bioavailability from 24 to 60 percent in reference to Merck's hydrodiuril.

b. The differences detectable at a significance level of 0.05 and a power of the test 0.80 at various sampling times range from 40% to 100%. The detectable differences at the same significance level and the power of the test for AUC's, peak heights and cumulative excretion amount to 50 percent. These differences are much higher than the customarily acceptable value of 20 percent detectable differences.

On the basis of these two arguments the study was deemed unacceptable for approval. The additional information supplied in this submission viz, disintegration times and dissolution rates (99 to 100 percent of the drug in solution in 30 minutes), does meet the compendial specifications and is acceptable. However, this additional information in no way changes the conclusions reached in the previous review (by S. Dighe, dated 4/5/75).

2. In the case of 4 subjects who showed low bioavailability for the Richlyn product, the applicant has submitted, in this letter, urinary output data to demonstrate the effectiveness of the drug. The study was conducted to demonstrate the bioequivalence of the test product with the reference product by determining the unchanged drug in the urine. One cannot use two different yardsticks in evaluating the bioavailability performance of the drug in order to explain away the deficiencies. It is neither consistent nor scientific.

RECOMMENDATION:

The company should be informed that the additional information in no way changes the conclusions reached about the study in the previous review. The company should conduct a new bioequivalency study by determining the unchanged drug in urine or the electrolytes (sodium, potassium and chloride) in the urine.

Shrikant V. Dighe, Ph.D.  
Biopharmaceutics Review Branch

MEMO RECORD

AVOID ERRORS  
PUT IT IN WRITING

DATE

1/7/75

FROM:

Marvin Seife, M.D.

OFFICE

TO:

Division of Biopharmaceutics

DIVISION

of General Drug  
Monographs

SUBJECT:

SUMMARY

Attention: Dr. Harold Murdock

NDA 83-607

Hydrochlorothiazide Tablets, U.S.P. 50mg.  
Richlyn Laboratories, Inc.

Please review <sup>additional</sup> ~~the~~ bioavailability study <sup>data</sup> on the above drug, as requested.

/S/

Marvin Seife, M.D.

SIGNATURE

DOCUMENT NUMBER

RICHLYN  
LABORATORIES  
INC.

RESUBMISSION

Cable Address "RICHLYN"

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

NDA ORIG AMENDMENT

OCT 30 1974

Generic Drug Staff -- HFD-107  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
50 mg., C.T. Peach Scored  
ANDA #83-607  
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 7/18/74 and 8/9/74 requests for additional information regarding our reference and related (25 mg. strength, ANDA #84-029) products' bioavailability.

5/21/74 HRC-FDA meeting re subject bioavailability study. has kindly provided his summary of the has registered no objections to, the contents of this letter which provides: aware of, and

- our understanding of that meeting's results;
- our interpretations of the study's data and methodology;
- new analytic approach proposals;
- additional information; and,
- our request that DCR and your staff review same with a view toward approval of said study.

HRC-FDA Meeting

DCR now concedes that the maximum analytic sensitivity may be as low as 2.5 mcg./ml. (vs. their 4/15/74 judgement of 10 mcg./ml.). Original concerns re "power of the test", "detectable differences", and erraticism of individual values appear to have diminished considerably. DCR states that a relative mean bioavailability of 80% (their "cumulative" calculation: 81.3%) is acceptable in context. However, they maintain that, per their analysis, apparent relative hypobioavailability of our product in 4 of 13 subjects (their calculations' range: 24% - 60%) renders the study unacceptable. They suggest that said disparities may reflect inadequate content uniformity, disintegration, or dissolution characteristics of our product. They admit this suspicion is unsupported by data, but claim they never received pertinent in-vitro information despite their request for same. They kindly invite our response re data, analysis, or conclusions.

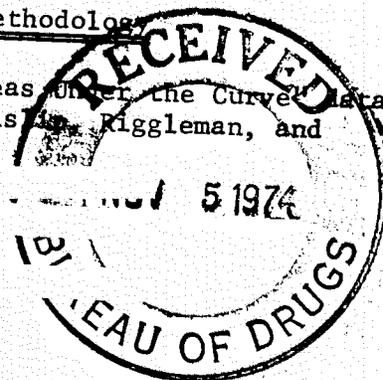
Our Interpretations of the Data and Methodology

Relative Mean Bioavailability. Our calculations, based on "Areas Under the Curve" data, are given in Exhibit A. The 4 obvious outliers are Boyce, Chris, Riggelman, and Shotkosky. However, our calculations are:

Non-Cumulative: RCH/MSD = 87.5%; Outlier Range =

Cumulative: RCH/MSD = 86.1%; Outlier Range =

in contrast with FDA's (presumably cumulative) figures of:  
RCH/MSD = 81.3%; Outlier Range =



**RICHLYN  
LABORATORIES  
INC.**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

Generic Drug Staff -- HFD-107 (continued)

Accepting a 4-outlier range of \_\_\_\_\_, we submit that the study group mean of 86.1% for all 13 subjects indicates:

- quite acceptable relative bioavailability (overall analysis);
- strong compensating trend in the 9 non-outlier subjects (6 subjects' \_\_\_\_\_ values ranged from \_\_\_\_\_)
- basis for suspicion that some of the outlier data may be invalid or non-representative; and,
- need for alternative analysis.

Maximum Sensitivity. Even with the new figure (2.5 mcg./ml.), 39 of the 208 (16 x 13 subjects) non-0-Hour HCT concentration data (1/5 of the data and resultant calculations) still fall below this limit and are thus of questionable reliability. The reference data loci are given in Exhibit B. Note this affects almost twice as many RCH data as MSD data, and is particularly pertinent to most of \_\_\_\_\_'s RCH data and all RCH's 1-Hour data. We share DCR's uncertainty in this matter. Retrospect of the analytical methodology reveals the assumption that high concentrations (12.5-50.0 mcg./ml.) would be found in the 1,2,3,4, and 6-hour samples and that low concentrations (0.0-10.0 mcg./ml.) would be found in the 8, 12, and 24-hour samples. This assumption was implemented by arbitrary use of respective 2 ml. and 5 ml. aliquots and standard curves. In review, it is apparent that such pattern was not the case in many instances, and that said system was inappropriate to all RCH, and all but two MSD, 1-hour samples, inter alia. This system resulted in strong negative bias re RCH data, especially in "outlier" cases where good urinary output is not paralleled by apparent HCT concentration.

Consider the extreme maximum sensitivity levels thusfar entertained -- the original 10 mcg./ml. and 0.0 mcg./ml. Summary non-0-Hour HCT concentration data reveal that there were the following instances of levels reported at less than:

- 10 mcg./ml.: RCH-59; MSD-42; Total-101 (almost 1/2 of all data); and
- 0.01 mcg./ml.: RCH-14; MSD-4; Total-18 (almost 1/11 of all data).

In both cases, RCH data (instances) were far more affected than were MSD data (factors of 1.3 and 3.5, respectively).

Thus the outlier data are clearly the least reliable -- due to highest incidence of sub-maximum sensitivity levels coupled with relatively high urinary output, as well as to use of inappropriate aliquot volumes and standard curves. Any non-0-Hour value falling below a maximum sensitivity level (MSL) is, by definition, unreliable. One could argue for arbitrary replacement of all such sub-MSL values with "m" (MSL-0.01) values. One could propose replacement with "n" (MSL/2) values. In any case, one cannot reasonably accept a "0.00" value for HCT concentration which, when multiplied by urinary volume (no matter how high), results in a "0.00" value for HCT excretion.

Obviously, any recalculation with "m" or "n" values will provide significant, and justifiable, improvement in the relative mean bioavailability (RCH/MSD) ratios of the outliers. Just as one conservative example, replacement with "n" (MSL/2) values, where MSL = 10 mcg./ml., results in an outlier RCH/MSD shift as follows:

--

-- Mean = 59.6%

which correlates far more closely with the most conservative (0-8 hrs.) values given in

Generic Drug Staff -- HFD-107 (continued)

Table I under "New Analytic Approach Proposals". Cursory projection indicates that "m" (MSL-0.01) replacement, where MSL = 10 mcg./ml., would provide still higher RCH/MSD values and still closer correlation with Table I values.

New Analytic Approach Proposals

Regarding an alternative analysis, we suggest the following. Merck's HydroDiuril<sup>R</sup> is FDA-recognized as an effective diuretic. Its FDA-approved labeling claims action onset at 2 hours, peak at 4 hours, and persistence from 6 to 12 hours. Our test protocol controlled water intake only up through Hour 8 (120 ml. p.o. per collection; and lib thereafter). Since diuretics are employed to enhance urinary output volume (and not to remedy urinary deficiencies of, inter-alia, hydrochlorothiazide), it seems reasonable to consider urinary output volume responses to test and reference drugs. We agreed that a clinician would expect discernable diuresis from even a single 50 mg. dose of this drug. We propose that, in such context, if urinary response to RCH is comparable to that of MSD, the question of bioavailability is best answered in terms of bioeffectiveness. Exhibit C presents such data, scanned at 3 time frames: 0-8 hr. (end of water intake control), 0-12 (end of MSD's claimed action-persistence), and 0-24 (total study). Our conclusions are:

- true diuresis obtained in all cases. Following pre-dose fast of 10 hours, fluid intake was limited to 120 ml. of water each at Hours 0,1,2,3,4, and 6 -- a total of 720 ml. available in the 0-8 hr. urine collection time frame. The lowest output in this frame was 982 ml. (1/3 greater than intake); the average output, either drug, in that frame was about 1360 ml. (almost double the intake).
- essential iso-bioeffectiveness (bioequivalency), no matter how analyzed (time frame, drug sequence group, or collective).
- the only mild trend distinguished is that the first drug administered seems to produce slightly better results.
- all group averages at all time frames show that MSD sets the extremes (both highs and lows)--RCH response is more centralized.
- in this analysis, the erstwhile 4-outlier level and pattern is considerably changed as may be seen in the table below.

Table I. Comparison of Urinary Excretion Volume Data, Hydrochlorothiazide Study

| Collection Period (hr.) | URINARY VOLUME |      |            |
|-------------------------|----------------|------|------------|
|                         | DATA (ml.)     |      | R/M (as %) |
|                         | RCH            | MSD  |            |
| 0-8                     | 984            | 1284 | 76.6%      |
| 0-12                    | 1142           | 1434 | 79.6%      |
| 0-24                    | 1684           | 1640 | 102.7%     |
| 0-8                     | 1058           | 1337 | 79.1%      |
| 0-12                    | 1356           | 1573 | 86.2%      |
| 0-24                    | 1638           | 1725 | 95.0%      |
| 0-8                     | 1400           | 1722 | 81.3%      |
| 0-12                    | 1762           | 1962 | 89.8%      |
| 0-24                    | 2458           | 2860 | 85.9%      |
| 0-8                     | 982            | 1904 | 51.6%      |
| 0-12                    | 1264           | 2372 | 53.3%      |
| 0-24                    | 1806           | 2954 | 61.1%      |

**RICHLYN  
LABORATORIES  
INC.**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

**Generic Drug Staff -- HFD-107 (continued)**

Note that the outlier range has gone from 5 (0-12 hr.), and % up to (0-8 hrs.), 24 hr.). Furthermore, is now the least dramatic of the outliers (he was previously the extreme -- having exchanged positions with . Still more impressive, the mean outlier R/M value for the 0-8 hr. frame is 72.2%. This should be acceptable, since no objection was raised to s R/M value of 131.6% (see Exhibit A).

In short, this analysis demonstrates that our product is bioequivalent (isobioavailable) to Merck's. It also demonstrates that both products affect urinary excretion volume more predictably than they affect certain optical absorbance characteristics of samples from said urine.

Additional Information

Our Product's Disintegration and Dissolution Characteristics. Since initial submission of this ANDA, we have received only one request for technical data on the test lot. Per 4/25/73 letter (page 2, point 9), Dr. Seife relayed DCR's request for "potency and content uniformity" data on both test and reference product. Said data were supplied FDA per our 5/14/73 letter covering submission of HRC's initial report dated May, 1973.

DCR's concern re test product's analytic in-vitro characteristics should be adequately answered by our Exhibit D. These data, which we gladly would have supplied DCR upon their request, profile excellent homogeneity of active ingredient dispersion among tablets with narrow weight variation and content uniformity ranges. There is excellent agreement among assays obtained in pre-compression sampling, tablet content uniformity, and composite (tablet) testing. The tablets disintegrate in 1/2 minute -- 60 times faster than the usual requirement for such compressed products, and provide an average dissolution of 100.5% (vs. the usual 60% requirement) at 30 minutes. We project that they provide complete active-ingredient dissolution well before the standard 30-minute test-time. Even assuming rapid gastric emptying time, we project at least 85% active ingredient dissolution (and presumed availability for transmucosal absorption) at the ileal level. In short, we cannot envision a significantly more favorable in-vitro profile for such a product.

Let even Exhibit D data be considered too thin, we enclose Exhibit E, based on 20 lots of subject product, and involving disintegration time (av.: 1/2 min.), dissolution (av.: 97.6%/tablet at 30 min.), content uniformity (av.: 100.3%/tablet), and composite assay (av.: 99.4%/tablet) values obtained on a total of 840 tablets tested.

Our Request for Review and Approval of Study

1. Employing the original HCT excretion data (unadjusted re MSL) and DCR's most critical analysis, our product still passes DCR's minimum acceptance limit of 80% for mean cumulative relative bioavailability with an R/M value of 81.3% (DCR's calculation) or 86.1% (our calculation).
2. The question re HCT excretion outliers -- presumably defined by DCR as about  $\pm$  40% deviation from analog values (their 4/15/74 letter and acceptance of an R/M value of 131.6%) is resolvable in three ways:

**RICHLYN  
LABORATORIES  
INC.**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

Generic Drug Staff -- HFD-107 (continued)

-- employing conservative adjustment ("n" = 5; MSL = 10 mcg./ml.) of the HCT excretion data, the erstwhile outlier group's mean cumulative relative bioavailability (unadjusted value: 44%) is recalculated to an R/M value of 60%, thus passing DCR's minimum acceptance limit; or

-- employing the most conservative (0-8 hr.) analysis of urinary excretion volume data, the mean cumulative relative bioavailability for the "outlier" group is calculated to an R/M value of 72% (well above DCR's lower limit); or,

-- comparison of the last 3 cited R/M values indicates far closer agreement between the excretion volume values and the adjusted HCT excretion values than between the former and the unadjusted HCT excretion values. It is hard to see how a 44% "available" drug can produce a 72% diuretic effect. Although it is easier to accept the 60% "availability"-72% diuresis spread, we frankly have more confidence in the much simpler and more clinically pertinent measurement of urinary excretion volume. DCR has apparently regained its original respect for the latter approach. FDA's 8/16/74 letter re our Trichlormethiazide Tablets, 4 mg. (ANDA #83-967), recommends use of the diuresis (bioeffectiveness) study approach in support of isobioavailability claim.

3. When all subjects' average urinary excretion volume data in the most conservative (0-8 hr.) time frame are compared -- RCH:1358 ml.; MSD:1368 ml. -- the overall mean cumulative relative bioavailability is calculated to an R/M value of 99.3% (virtual identity).

4. Part of the HCT excretion analytic methodology and calculations have been shown to be inadvertently fallacious, resulting in significant, selective, negative bias re RCH "outliers". The latter cease to be outliers when conservative and justifiable adjustment of HCT excretion data is applied. This equalizing trend is carried to RCH-MSD parity when urinary excretion volume data are compared (i.e., isobioeffectiveness = isobioequivalency = isobioavailability).

5. The probability of isobioavailability is further supported by extensive and detailed presentation of pertinent in vitro data on more than 800 subject tablets manufactured and tested by Richlyn.

\* \* \* \* \*

In answer to your specific inquiry (7/18/74 letter), the hydrochlorothiazide (active ingredient) used in producing this study's clinical supply of Richlyn product (Lot #25785) was our control #20357, control #5062, and was manufactured by . All this is as stated and certificate-evidenced in our 5/14/74 (FDA-received 5/16/74) and 5/16/74 (FDA-received 5/20/74) submissions in response to your prior inquiries.

\* \* \* \* \*

We request that this response be accepted, by reference, as reply to your 6/12/74 inquiry re our 25 mg. strength tablet of the same item (ANDA #84-029) since the subject is identical.

**RICHLYN  
LABORATORIES  
INC.**

Cable Address "RICHLYN"

PHARMACEUTICALS      ANTIBIOTICS      GENERICS

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

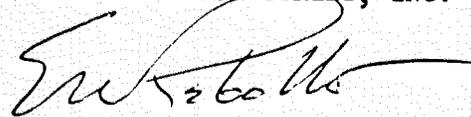
Generic Drug Staff -- HFD-107 (continued)

\* \* \* \* \*

We appreciate this opportunity to respond (delay occasioned by regulatory agency inspections and by the time needed to fully review the subject). In summary, we respectfully submit that this study does demonstrate isobioavailability and accordingly should be approved.

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo  
Vice President

Enc.: Exhibits A-E

EWR:tp



NDA 83-607

AF 28-724

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

AUG 09 1974

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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communications dated May 23 and May 30, 1974, pertaining to distributors.

The application 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 distributors to be:

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:

That requested in our letter of July 18, 1974, pertaining to the bioavailability of your formulation.

It is also suggested that further amendments to provide for additional distributors not be submitted until the bioavailability status of your application is clarified.

The material submitted (for distributors) is being retained in our files with its review deferred.

Marvin Seife, M.D.  
Director  
Genaris Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

1-1-74

RICHLYN  
LABORATORIES  
INC.

NDA ORIGINAL AMENDMENT

Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

May 30, 1974

FPL

Generic Drug Staff - HFD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, USP.  
50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

PACKAGING UNIT

100s



Sincerely,

RICHLYN LABORATORIES, Inc.

*L. P. Cecchini*

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

LPC/  
Encl.  
AL-F01  
6-72

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS

ANTIBIOTICS

GENERICS

**FPO**

Cable Address "RICHLYN"

ORIG

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

May 23, 1974

Generic Drug Staff -- HFD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, USP  
50 mg. C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

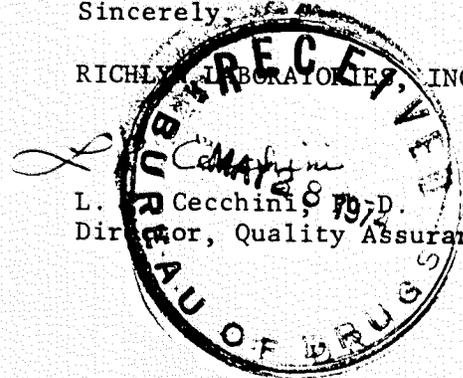
50 mg.

100s

Sincerely,

RICHLYN LABORATORIES, INC.

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



LPC/  
Encl.  
AL-F01  
6-72

**NDA 83-607**

**AF 28-724**

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

**JUL 18 1974**

**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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communication dated May 16, 1974.

This communication:

- A. In regard to distributors (1) withdraws material pertaining to C with the option of resubmission and (2) clarifies your intentions re labeling for others, including the proposal to separate for different potencies of the drug.
- B. In regard to testing, notes (1) your revision of the certification to be used on your behalf by outside testing labs as per section 314.1(f) of the regulations (21CFR) and (2) your commitment to yourself to perform full compendial testing, as per USP XVIII for both the active ingredient and drug dosage form.
- C. In regard to bioavailability, notes (1) your proposal to provide for hydrochlorothiazide from two manufacturers and (2) request a conference between representatives of the Division of Clinical Research and those from (responsible for your bioavailability study).

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:

Re C(1) above, clarification regarding the source of the hydrochlorothiazide used in the bioavailability study.

Please let us have your response promptly.

11/21  
Herta Saife, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

18/74

**RICHLYN  
LABORATORIES  
INC.**

**RESUBMISSION**  
**NDA ORIG AMENDMENT**  
PHARMACEUTICALS    ANTIBIOTICS    GENERICS

Cable Address "RICHLYN"

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

May 16, 1974

Generic Drug Staff -- HFD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

*Orig*

Ref.: Hydrochlorothiazide Tablets, 50 mg.  
ANDA #83-607  
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 4/5/74 and 5/9/74 requests for additional information.

(Additional Distributor). Said proposed distributor improperly submitted their statement to you and their labeling specimens to us. We have been holding their labeling, pending receipt of statement, so that both might be reviewed and properly co-submitted. We have requested them to re-execute said statement and send it to us so that normal procedure may ensue.

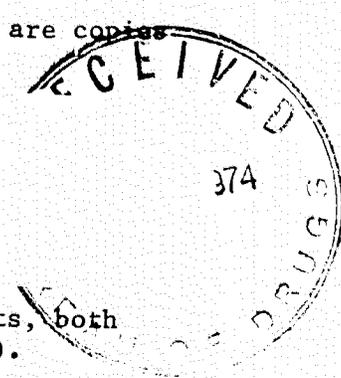
Certification Statements, Outside Testing Facilities. We confirm your 4/5/74 acknowledgement that this point is now moot in view of our full and employed context analytic capability. However, since said statement format apparently disturbs FDA, we have reviewed it for the third time in the hope of reconciliation applicable to other ANDAs. We enclose a copy of the statement, marked to indicate that the bracketed sections provide verbatim or essential transcription of 21 CFR 130.4 (f)(1)(iv) -- (now recodified as section 314.1). The replacement of the phrase "...the manufacture, processing, packing, and holding of the drug..." with the phrase "...our testing of (:Product Name) to determine whether it meets the requirements currently stipulated by (:Identity of Analytic Reference)" is in complete accord with FD-356H Form's terminal admonition re a willfully false statement. Such contracting laboratories can certify CGMP compliance only re their context involvement which is specified in detail in the latter half of the statement. Our review of this matter indicates that a full verbatim recitation of subject CFR section for such a laboratory service would be irrelevant, improper, and illegal. We believe our form complies with the full letter and spirit of reference section and CGMP. We await your response.

Suppliers' (Manufacturers') Certificates of Analysis. Enclosed are copies of said certificates for subject raw material as follows:

Supplier  
Supplier's Control No.  
Manufacturer  
Manufacturer's Control No.  
Richlyn's Control No.

\*Supplier's identification of manufacturer also enclosed.

Please note prior submission of our laboratory's analytic results, both above lots, as "Exhibit A" (page 3 of our 2/11/74 communication).



Additional Distributors' Statements. Per our original (10/8/73) general agreement to "strength-split" certain ANDAs, we have been requesting and submitting new labeling and statements per such split-offs upon receipt of your letters assigning new NDA numbers to same. Some such amendments have already been submitted for this Application. As previously noted to you, our transition system is geared to time of true next printing and/or next customer order. The resultant time lag will be minimized by us wherever possible.

Bioavailability. We acknowledge 4/19/74 receipt of Dr. Seife's 4/15/74 letter relaying DCR's long-awaited comments on this study. Their conclusion ("un-acceptable and unapproved"), aside from being disappointing, is surprising when one considers that the entire protocol was pre-approved by DCR (per one set of specifications which were understood and met).

One year after study report submission, DCR appears to reject its own contract-validated analytic methodology (our study, incidently, was performed by the same laboratory employed by DCR for said validation), ignores the satisfactory results of the ANOVAR that they stipulated, cites "erratic" results unilaterally, and now claims that a new criterion of "20% detectable differences at a 'p' level of 0.05 and a test power of 0.80" can be achieved only by increasing the size of the subject population.

Basically, we and the contract laboratory not agree with DCR's calculations, new criteria, interpretations, conclusion, and recommendation. The most serious problem is DCR's latest claim that the maximum analytic sensitivity is 10 mcg./ml. Conservative in vitro calculations (based on 50 mg. stat dose, 2000 ml. urine output per day, 5 ml. urine aliquot, and 13 ml. of final sample solvent) indicate:

$$\frac{50000 \text{ mcg.} \times 5 \text{ ml.}}{2000 \text{ ml.} \times 13 \text{ ml.}} = 9.6 \text{ mcg./ml.}$$

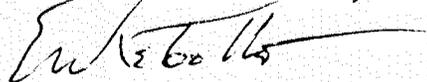
--"clearly" less than the 10 mcg./ml. minimum. This would surely affect the reliability of at least the 0,1, 2, 8, 12, and 24-hour sample data.

Thus, if DCR is correct re the maximum sensitivity (we dispute same), then DCR never should have approved the analytic methodology that they themselves had validated. Still more important, if the test is inadequately sensitive, how can more unreliable data from more subjects provide ultimate reliability?

Representatives of \_\_\_\_\_ an imminent meeting with DCR personnel to discuss (and, hopefully, satisfactorily reconcile) this matter. Naturally, we will advise you of the results of such discussion.

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo,  
Vice President

**NBA 89-807**

AF 28-724

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

MAY 09 1974

**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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communications dated (1) March 25, 1974, amending the application (2) an undated bioavailability statement (received on March 20, 1974)---submitted on your behalf by (3) March 15, 1974, pertaining to a distributor.

The application 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 distributor to be:

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. Adequate data to assure the bioavailability of your preparation, since we note that the part of your material pertaining to bioavailability was disapproved in a letter of April 15, 1974.
2. That previously requested.

Please let us have your response promptly.

74 / MARVIN Seife, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

246 5/8/74

T-19/74

**RICHLYN  
LABORATORIES  
INC.**

**ORIG NEW CORRES**

Cable Address "RICHLYN"

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

ORIG

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

MAR 25 1974

Generic Drug Staff -- HFD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref.: Hydrochlorothiazide Tablets, U.S.P.  
50 mg., C.T. Peach Scored  
ANDA #83-607  
Additional Information Requested

Gentlemen:

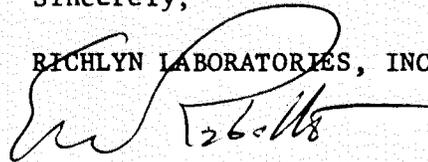
This triplicate submission is in response to your 3/11/74 request for additional information. Your requests re the 25 mg. strength (NDA #84-029) are answered under separate cover, referenced per latter designation.

To our best knowledge, all additional information requested to date has been supplied. This includes our 3/4/74 response to your 2/26/74 letter re, inter alia, the wholesaler distributor (not repackager/ relabeler) status of [redacted] Laboratory, Inc. in context of this Application.

We have reviewed this subject jacket and conclude that prior (through 3/4/74) submissions, as supplemented by this response, provide more than adequate basis for approval of this Application which was originally submitted as a collective ANDA one year ago (3/22/73).

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo  
Vice President

EWR:tp



*Drug*

NDA ORIG AMENDMENT

*e*

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    **FPL**    GENERICS

Cable Address "RICHLYN"

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

March 15, 1974

Generic Drug Staff -- HFD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

158

(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

50 mg.

1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*L. Cecchini*  
L. Cecchini, M.D.  
Director, Quality Assurance



LPC/mes  
Encl.  
AL-F01  
6-72

NDA 83-607

NDA 83-607 (25 mg)

AY 28-724

**Richlys Laboratories, Inc.**  
**Attention: Mr. E. W. Rabellie**  
**Castor & Kensington Avenues**  
**Philadelphia, PA 19124**

APR 05 1974

**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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of (1) your communications dated February 11 and March 4, 1974, amending the application and (2) an undated distributor's statement (received on March 12, 1974)—submitted on your behalf by Geneva Generics of Detroit, MI.

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. Additional information—including labeling et al—from the above distributor.
2. Certification statements, in the language previously transmitted to you—from outside testing facilities—although we note your commitment to perform the requisite procedures yourself.
3. Supplier(s) certificates of analysis, as per the reference in your communication of February 11; and your own results for these lots.

Please let us have your response promptly.

Sincerely yours,

/S/

**Marvin Seife, M.D.**  
**Director**  
**Generic Drug Staff**  
**Office of Scientific Evaluation**  
**Bureau of Drugs**

4/4/74

NDA 83-607

~~NDA 83-607~~ (25 wgs)

AF 28-724

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

APR 05 1974

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 Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of (1) your communications dated February 11 and March 4, 1974, amending the application and (2) an undated distributor's statement (received on March 12, 1974)—submitted on your behalf by

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. Additional information—including labeling et al—from the above distributor.
2. Certification statements, in the language previously transmitted to you—from outside testing facilities—although we note your commitment to perform the requisite procedures yourself.
3. Supplier(s) certificates of analysis, as per the reference in your communication of February 11; and your own results for these lots.

Please let us have your response promptly.

Sincerely yours,

/S/

Marvin Seife, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

'1/74

/74

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Re: Hydrochlorothiazide Tablets, U.S.P.  
50 mg. C.T. Peach Scored  
ANDA #83-607

Gentlemen:

The undersigned, regularly and lawfully engaged (IN CONTEXT OF THIS APPLICATION ONLY) as a repacker\*, relabeler\*, X wholesaler, retail pharmacist, other (specify): \_\_\_\_\_, in the handling, distribution, or dispensing of prescription drugs, hereby agrees to use only the labeling upon which ANDA #83-607 has been or will be approved in connection with the distribution of Hydrochlorothiazide Tablets, U.S.P., 50 mg., C.T. Peach Scored purchased from Richlyn Laboratories, Inc., Castor & Kensington Ave., Phila., Pa. 19124.

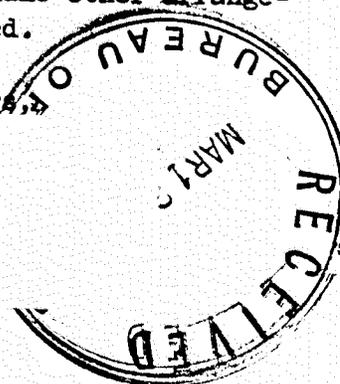
\*We hereby certify that the methods used in, and the facilities and controls used for, the processing, packaging, and holding of the drug are in conformity with current good manufacturing practice in accord with 21 CFR Part 133 of the regulations.

We further agree that no changes will be made in such labeling or any other printed material used in the connection with the distribution of the drug other than that set forth in such new drug application, as approved. In the event that any changes are proposed in such labeling, they will first be submitted as an amendment and/or supplement to the said new drug application and will not be used or otherwise distributed until or unless the amendment shall have been approved.

We understand that the right to distribution of this drug, a "new drug" under the Federal Food, Drug and Cosmetic Act, by the undersigned, is permitted only as an amendment to the new drug application when and as approved. In the event that we should market the drug supplied by any other source, we understand that we cannot rely on the said new drug application, but must in that event make other arrangements as far as the new drug provisions of the Act are concerned.

Very truly yours,

/S/



RICHLYN  
LABORATORIES  
INC.

*Original*

*Kew.W.H.*

RESUBMISSION

Cable Address "RICHLYN"

PHARMACEUTICALS

ANTIBIOTICS

GENERIC

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

ANDA URGENT AMENDMENT

MAR 4 1974

Generic Drug Staff -- HFD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Ref: Hydrochlorothiazide Tablets, U.S.P.  
ANDA #83-607  
Additional Information Requested

Gentlemen:

This triplicate submission is in response to your 2/26/74 request for additional information.

Please note that the distribution-statement dated 1/18/74 for Robinson Laboratory, Inc. references the latter solely as a wholesaler distributor (not as a repackager/relabeler). Thus, no separate ANDA for same is required.

Re "additional information previously requested", please see our:  
2/11/74 submission (all answers re 50 mg. strength); and,  
2/13/74 submission (full separate ANDA re 25 mg. strength).

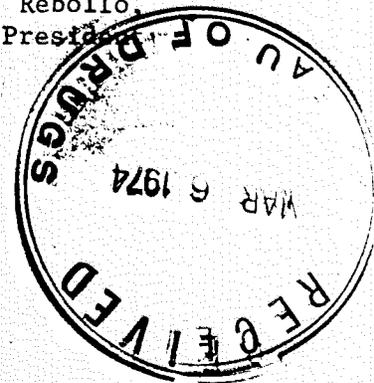
We respectfully submit that both ANDAs are now approvable.

Sincerely,

RICHLYN LABORATORIES, INC.

*E. W. Rebollo*  
E. W. Rebollo,  
Vice President

EWR:rb





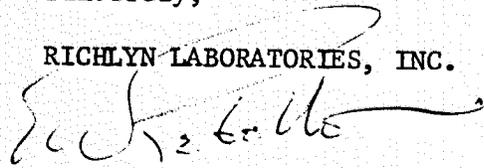
Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
February 11, 1974  
Page 2

We now possess a \_\_\_\_\_ and have validated our ability to employ same in context analysis. Accordingly, we can and do agree to complete U.S.P. testing of the drug dosage form. Use of the alternative (content uniformity) methodology will be limited henceforth to optional, additional testing.

We await with interest DCR's evaluation of subject bioavailability study (latest re-analysis submitted 10/11/73, receipted 10/18/73). We trust it will be favorable, permitting approval of this application which was originally submitted 3/22/73.

Sincerely,

RICHLYN LABORATORIES, INC.



E. W. Rebollo,  
Vice President

EWR:rb  
Enc. Exhibit A

NDA 83-607  
84-029

MAR 11 1974

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

Gentlemen:

Reference is made to your abbreviated new drug application submitted pursuant to Section 305(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

We acknowledge receipt of your communication dated February 6, 1974, amending the application with information pertaining to a distributor.

Reference is also made to our letters through February 26, 1974.

It also provides for the repackager/relabeler to be:

and the trade name to be

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:

That previously requested.

We call to your attention our comments of February 26, 1974, regarding the suitability of including information pertaining to \_\_\_\_\_ in this application.

We also note your submission of a separate new drug application—with the reference number 84-029—for the 25 mg. potency; and request that labeling originally submitted herein for that potency be resubmitted in connection with that application.

Please let us have your response promptly.

ISI

Te 3/4/74

✓ Marvin Seife, M.D.  
Director  
Generic Drug Staff  
Office of Scientific Evaluation  
Bureau of Drugs

RESUBMISSION

SR18 ←

Cable Address "RICHLYN"

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS

NDA ORIG AMENDMENT  
ANTIBIOTICS GENERICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

February 6, 1974

FPL

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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.

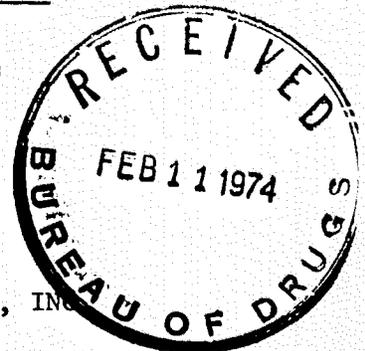
Labeling submission is  original  revised.

DOSE STRENGTH

PACKAGING UNIT

50 mg.

100's



Sincerely,

RICHLYN LABORATORIES, INC.

*L. P. Cecchini*

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

LPC/ mes  
Encl.  
AL-F01  
6-72

**NDA 83-607**

**AF 28-724**

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

**FEB 26 1974**

**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 Hydrochlorothiazide Tablets.

We acknowledge receipt of your communications dated January 22 (three) and January 28, 1974, amending the application with information pertaining to distributors.

Reference is also made to our letters through February 6, 1974.

The application 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 distributors to be:

It also provides for the repackager/relabeler to be:

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:

**Rishlyn Laboratories, Inc.**  
**NDA 83-607**

**-2-**

**That previously requested.**

**We have also reviewed that part pertaining to the repackager/relabeler and recommend that the proposed repackager/relabeler file a separate abbreviated new drug application for his part of the operation - using your application as a manufacturing cross-reference.**

**Please let us have your response promptly.**

**/S/**

**Marvin Sella, M.D.**  
**Director**  
**Generic Drug Staff**  
**Office of Scientific Evaluation**  
**Bureau of Drugs**

**2/74**



RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

FPL

January 22, 1974

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

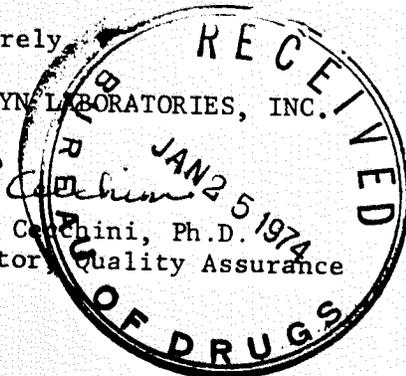
50 mg.

100's

Sincerely

RICHLYN LABORATORIES, INC.

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



LPC/ mes  
Encl.  
AL-F01  
6-72

NDA ORIG AMENDMENT

ORIG E

RICHLYN  
LABORATORIES  
INC.

PHARMACEUTICALS

ANTIBIOTICS

FPL  
GENERIC

Cable Address "RICHLYN"

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

January 22, 1974

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

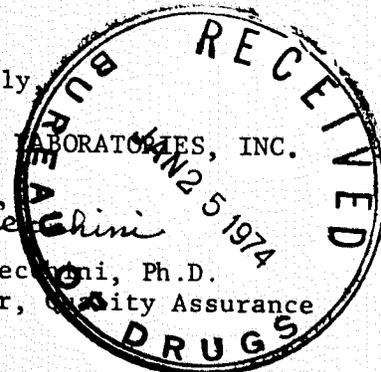
1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*L. P. Cecchini*

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



LPC/ mes  
Encl.  
AL-F01  
6-72

NDA ORIG AMENDMENT

0216 E

RICHLYN  
LABORATORIES  
INC.

Cable Address "RICHLYN"

PHARMACEUTICALS

ANTIBIOTICS

FPL  
GENERIC

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

January 22, 1974

Generic Drug Staff -- BD-69  
Office of Scientific Evaluation  
Bureau of Drugs  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

Reference: Hydrochlorothiazide Tablets, U.S.P.,  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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.

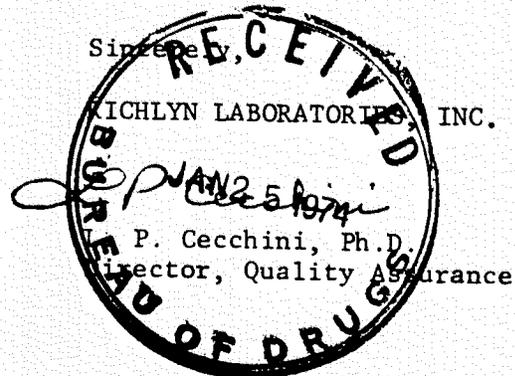
DOSE STRENGTH

PACKAGING UNIT

50 mg.

1000's

LPC/ mes  
Encl.  
AL-F01  
6-72



AUG 19 1977

NDA B3-607/S-001

Richlyn Laboratories, Inc.  
Attention: Mr. Louis P. Cecchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated June 16, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 100 (but not 1000) tablet containers with a label showing the distributor to be:

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

IS/ 9/77  
Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

Barany 8-10-77

**RICHLYN  
LABORATORIES  
INC.**

*Orig*  
Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

JUN 16 1977

83607 REF. NO. *5/006*  
*Dist*  
NDA SUPPL FOR *David A. Brown, Inc*

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(ii) Applicant will conform.  
(iii) Distributor's Statement:

previously submitted.  
 herewith submitted.

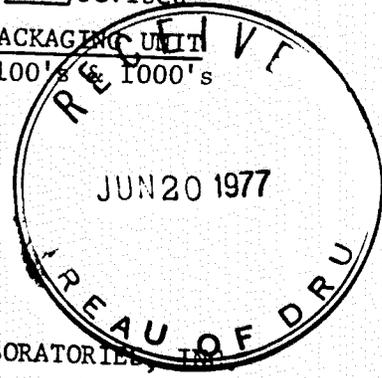
(iv) Labeling (12 copies) herewith submitted thus:

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

Labeling submission is  original  revised

DOSE STRENGTH  
50 mg.

PACKAGING UNIT  
100's & 1000's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.  
AL-F01  
6-72

NDA 83-607/S-002

AUG 19 1977

Richlyn Laboratories, Inc.  
Attn: Mr. Louis P. Cecchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated June 16, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 1000 tablet containers with a label showing the distributor to be:

and the trade name to be:

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

ar

( )  
1  
)  
( )

/S/

177

Marvin Sette, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

**RICHLYN  
LABORATORIES  
INC.**

*Orig*  
Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

JUN 16 1977

NDA NO 83-607 REF. NO. 51003  
NDA SUPPL FOR J. Pharm, Co

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

PACKAGING UNIT  
1000's

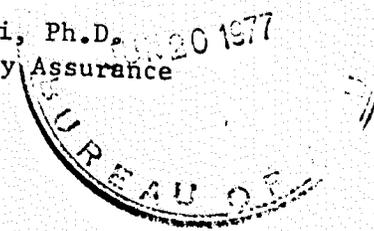
Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.  
AL-F01  
6-72



AUG 19 1977

MDA 83-607/S-003

Richlyn Laboratories, Inc.  
Attn: Mr. Louis P. Cecchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated June 16, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 1000 tablet containers of the drug with a label showing the distributor to be:

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

1/S/

77

MARVIN SALTER, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

1 2/77

ation

**RICHLYN  
LABORATORIES  
INC.**

*Orig*  
Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

JUN 16 1977  
NDA NO. 83-607 REF. NO. 51003  
*list*  
NDA SUPPL FOR Medco Supply Co

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

PACKAGING UNIT

1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*  
Louis P. Cecchini, Ph.D.  
Director, Quality Assurance

JUN 20 1977

Encl.  
AL-F01  
6-72

AUG 19 1977

NDA 83-607/S-004

Richlyn Laboratories, Inc.  
Attn: Mr. Louis P. Cacchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated June 16, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 1000 tablet containers with a label showing the distributor to be:

and the trade name to be:

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

8-18-77  
Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

19/77

ation

**RICHLYN  
LABORATORIES  
INC.**

*Orig*  
Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Attn.: Document Control Room #16-72  
Bureau of Drugs-- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

JUN 16 1977  
NDA NO. 83-607 REF. NO. 5100  
NDA SUPPL FOR Verical Pharm. Co.

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

PACKAGING UNIT

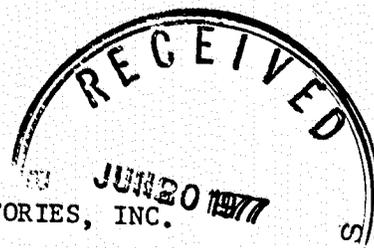
1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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



Encl.  
AL-F01  
6-72

AUG 19 1977

NDA 83-607/S-005

Richlyn Laboratories, Inc.  
Attn: Mr. Louis P. Cecchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated June 16, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 1000 tablet containers with a label showing the distributor to be:

and the trade name to be:

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

/S/ 177  
MARVIN SETTE, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

*Orig*  
Cable Address "RICHLYN"

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

CASTOR & KENSINGTON AVENUES    PHILADELPHIA, PENNSYLVANIA 19124    215 CU 9-2270

JUN 16 1977

Attention: Document Control Room #16-72  
Bureau of Drugs - HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

ANDA NO. 83-607    51005  
*Robinson*

Ref.: Hydrochlorothiazide Tablets 50 mg  
C.T. Peach, Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor  
Amendment

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg

PACKAGING UNIT

1000s



Sincerely,

RICHLYN LABORATORIES, Inc.

*Louis P. Cecchini*

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

Encl.

405 19 1977

**NDA 83-607/S-006**

**Richlyn Laboratories, Inc.  
Attn: Mr. Louis P. Cacchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124**

**Gentlemen:**

Reference is made to your supplement dated June 16, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

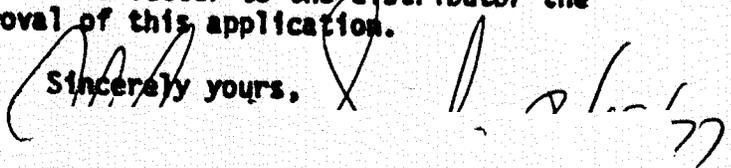
The supplemental application provides for you to label 100 & 1000 tablet containers with a label showing the distributor to be:

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

ar

Sincerely yours, 

**Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs**

ation

**RICHLYN  
LABORATORIES  
INC.**

*Craig*  
Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

NDN NO. 83-607  
*Cost*  
NDA SUPPL FOR *Hydrochlorothiazide*

JUN 16 1977

Reference: Hydrochlorothiazide Tablets  
50 mg., C.T. Peach Scored  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

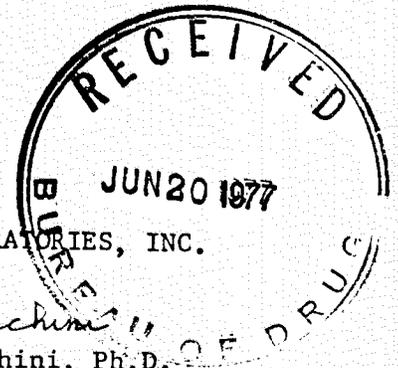
PACKAGING UNIT

100's & 1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*  
Louis P. Cecchini, Ph.D.  
Director, Quality Assurance



Encl.  
AL-F01  
6-72

AUG 19 1977

**NDA 83-607/S-007**

**Richlyn Laboratories, Inc.  
Attention: Mr. Louis P. Cacchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124**

**Gentlemen:**

Reference is made to your supplement dated July 12, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 100 & 1000 tablet containers with a label showing "actual" your own line logo; with the qualification manufactured by Richlyn Laboratories, Inc.

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

U U

( /S/ )

77

**Harvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs**

Orig  
Cable Address "RICHLYN"

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

July 12, 1977

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

NDA NO. 83-607 NO. 51002  
NDA SUPPL. *Richlyn Lab. Inc.*

FPL

Ref.: Hydrochlorothiazide Tablets  
50 mg. C.T. Peach  
NDA #83-607

Supplemental Application  
Additional Distributor:

Gentlemen:

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

- (i) Designated Distributor: Richlyn Laboratories, Inc.  
Castor & Kensington Aves.  
Philadelphia, Pa. 19124
- (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     resubmission

DOSE STRENGTH

PACKAGING UNIT

50 mg.

100's & 1000's

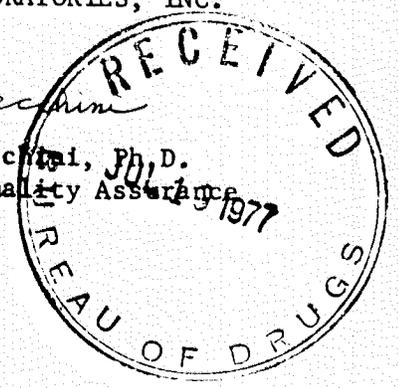
"Mutual" is a Richlyn line logo.

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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



Encl.

AUG 19 1977

**NDA 83-607/S-008**

**Richlyn Laboratories, Inc.  
Attn: Mr. Louis P. Cacchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124**

**Gentlemen:**

Reference is made to your supplement dated July 12, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 100 tablet containers with a label showing the distributor to be:

**R.A. McNeil Co.  
4713 Briarwood Drive  
Chattanooga, TN 37416**

and the trade name to be: M-Zide.

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

Sincerely yours,

*[Signature]*  
/S/  
**Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs**

*Orig*  
Cable Address "RICHLYN"

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

July 12, 1977

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

NDA NO. 83-607 REF. NO. 51008  
NDA SUPPL FOR R.A. McNeil Co.

Ref.: Hydrochlorothiazide Tablets  
50 mg. C.T. Peach  
ANDA #83-607

**EPLU**

**Supplemental Application  
Additional Distributor**

Gentlemen:

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

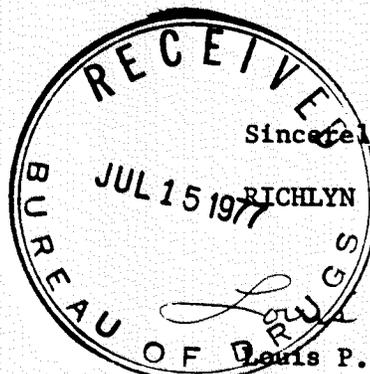
- (i) Designated Distributor R. A. McNeil Co.  
4713 Briarwood Dr.  
Chattanooga, Tennessee 37416
  - (ii) Applicant will conform.
  - (iii) Distributor's statement:  previously submitted  
 herewith submitted.
  - (iv) Labeling (12 copies) herewith submitted thus:  
 Label(s) only -- approved neutral (Richlyn) insert will be used.  
 Label(s) & insert.
- Labeling submission is  original     revised     resubmission

DOSE STRENGTH

50 mg.

PACKAGING UNIT

100's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.

NDA 83-607/S-009

AUG 19 1977

Richlyn Laboratories, Inc.  
Attn: Mr. Louis P. Cecchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated July 12, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 100 & 1000 tablet containers with a label showing the distributor to be:

Interstate Drug Exchange, Inc.  
Engineers Hill - Skyline Drive  
Plainview, NY 11803

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

Sincerely yours,

*[Signature]*  
/S/  
Marvin Seife, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

215 CU 9-2220

*Orig*  
Cable Address: "RICHLYN"

July 12, 1977

Attn.: Document Control Room #16-72  
Bureau of Drugs --HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

NDA NO. 83-607 REF. NO. 5/10/77  
NDA SUPPL FOR Interstate Drug  
Exchange, Inc

Ref.: Hydrochlorothiazide Tablets,  
50 mg. C.T. Peach  
ANDA #83-607

Supplemental Application  
Additional Distributor

EPL

Gentlemen:

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

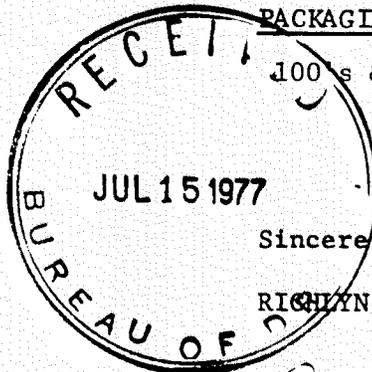
- (i) Designated Distributor: Interstate Drug Exchange, Inc.  
Engineers Hill - Skyline Drive  
Plainview, L.I. New York 11803
- (ii) Applicant will conform.
- (iii) Distributor's statement:  previously submitted  
 herewith submitted.
- (iv) Labeling (12 copies) herewith submitted thus:  
 Label(s) only -- approved neutral (Richlyn) insert will be used.  
 Label(s) & insert.  
Labeling submission is  original     revised     resubmission

DOSE STRENGTH

50 mg.

PACKAGING UNIT

100's & 1000's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.

AUG 19 1977

NDA 83-607/S-010

Richlyn Laboratories, Inc.  
Attention: Mr. Louis P. Cecchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated July 12, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 100 & 1000 tablet containers with a label showing the distributor to be:

Spencer-Mead, Inc.  
270 West Merrick Road  
Valley Stream, NY 11582

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

Sincerely yours,

*[Handwritten signature]*  
*[Handwritten initials]*  
*[Handwritten date: 3/19/77]*

Marvin Sette, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

*[Handwritten note: primary 8-18-77]*

ug Application

*Orig*  
Cable Address "RICHLYN"

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

July 12, 1977

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

NDA NO. 13607 REF. NO. 5/010  
*Disc*  
NDA SUPPL FOR Spencer Mead Inc

Ref.: Hydrochlorothiazide Tablets  
50 mg. C.T. Peach  
NDA #83-607

**FPI**

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor: Spencer Mead Inc.  
270 West Merrick Rd.  
Valley Stream, N.Y. 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.

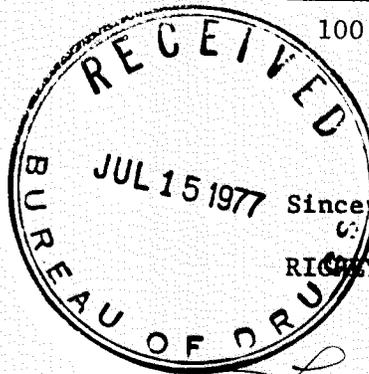
Labeling submission is  original     revised     Resubmission

DOSE STRENGTH

50 mg.

PACKAGING UNIT

100's & 1000's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.

AUG 19 1977

NDA 83-607/S-011

Richlyn Laboratories, Inc.  
Attn: Mr. Louis P. Cecchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated June 30, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 100 & 5000 tablet containers with a label showing the distributor to be:

Molins Pharmacal Corp.  
78 Marcus Drive  
Melville, NY 11746

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

*[Handwritten signature]*  
Marvin Seitz, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

cation

*Crig*  
Cable Address "RICHLYN"

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

June 30, 1977

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

NDA NO. 322 REF. NO. Slott  
NDA SUPPL FOR Wolins Pharm Corp

Ref.: Hydrochlorothiazide Tablets  
50 mg. C.T. Peach  
ANDA #83-607 **FPU**

**Supplemental Application  
Additional Distributor**

Gentlemen:

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

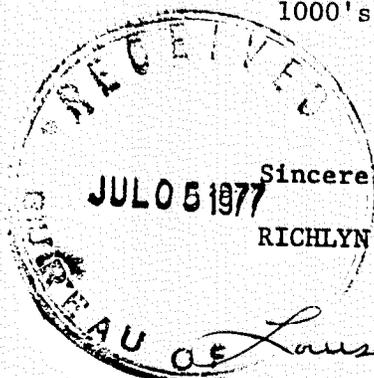
- (i) Designated Distributor: Wolins Pharmacal Corp.  
75 Marcus Drive  
Melville, N.Y. 11746
- (ii) Applicant will conform.
- (iii) Distributor's statement:  previously submitted  
 herewith submitted.
- (iv) Labeling (12 copies) herewith submitted thus:  
 Label(s) only -- approved neutral (Richlyn) insert will be used.  
 Label(s) & insert.  
Labeling submission is  original     revised     Resubmission

DOSE STRENGTH

50 mg

PACKAGING UNIT

1000's & 5000's



Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.

**RICHLYN  
LABORATORIES  
INC.**

*Orig*  
Cable Address "RICHLYN"

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

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

June 30, 1977

Attn.: Document Control Room #16-72  
Bureau of Drugs -- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

NDA NO. 83-657 REF. NO. S/012  
NDA SUPPL FOR Wesley Hamilton, Inc.

Ref.: Hydrochlorothiazide Tablets  
50 mg. C.T. Peach  
ANDA #89-607

*FPL*

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

1000's

Sincerely,

RICHLYN LABORATORIES, INC.



*Louis P. Cecchini*  
Louis P. Cecchini, Ph.D.  
Director, Quality Assurance

Encl.

NDA 83-607/S-013

Richlyn Laboratories, Inc.  
Attention: Mr. Louis P. Cecchini  
Castor & Kensington Avenues  
Philadelphia, PA 19124

Gentlemen:

Reference is made to your supplement dated August 1, 1977 regarding your abbreviated new drug application submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Hydrochlorothiazide Tablets, 50 mg.

The supplemental application provides for you to label 100 & 1000 tablet containers with a label showing the distributor to be:

We have completed the review of this supplemental application and it is approved. Our letter of June 6, 1977 detailed the conditions relating to the approval of this application.

Promotion of a product marketed under an abbreviated new drug application must not convey the impression that the product is a new entity.

We are enclosing with the copy of this letter to the distributor the conditions relating to the approval of this application.

Sincerely yours,

*[Handwritten signature]*  
/S/  
Marvin Wolfe, M.D.  
Director  
Division of Generic Drug Monographs  
Office of Drug Monographs  
Bureau of Drugs

*[Handwritten initials]*

**RICHLYN  
LABORATORIES  
INC.**

PHARMACEUTICALS    ANTIBIOTICS    GENERICS

CASTOR & KENSINGTON AVENUES

PHILADELPHIA, PENNSYLVANIA 19124

Cable Address: ...

August 1, 1977

Attn.: Document Control Room #16-72  
Bureau of Drugs-- HFD-530  
Food & Drug Administration  
5600 Fishers Lane  
Rockville, Maryland 20852

NDA NO. 83607 REF. NO. 5/013  
DIST. STERI-MED, INC.  
NDA SUPPLEMENT

Ref.: Hydrochlorothiazide Tablets  
50 mg. C.T. Peach  
ANDA #83-607

Supplemental Application  
Additional Distributor

Gentlemen:

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

(i) Designated Distributor:

(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

50 mg.

PACKAGING UNIT

100's & 1000's

Sincerely,

RICHLYN LABORATORIES, INC.

*Louis P. Cecchini*

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

Encl.

**TRANSMITTAL OF PERIODIC REPORTS FOR DRUGS FOR HUMAN USE**  
(21 CFR 310.300, 310.302, and 431.60)

DATE SUBMITTED

November, 1977

Form Approved  
OMB 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 (HFD-106), 5600 Fishers Lane, Rockville, Maryland 20852.

| 1. NDA OR ANDA NUMBER |   |   |   |   |   |
|-----------------------|---|---|---|---|---|
| 1                     | 2 | 3 | 4 | 5 | 6 |
| N                     | 8 | 3 | 6 | 0 | 7 |

| 2. REPORT NO. (FDA Complete) |   |   |  |
|------------------------------|---|---|--|
| R                            | 8 | 9 |  |
|                              | Q | A |  |

**APPLICANT NOTE**  
Reference NDA and R numbers (entered on Acknowledgment Copy) in any subsequent correspondence regarding report.

3. CFR SECTION NUMBER (Antibiotic only)

6. TYPE OF REPORT (Check one (10))  
 QUARTERLY  SEMIANNUAL  
 ANNUAL  OTHER

| 8. PERIOD COVERED BY REPORT |       |            |       |
|-----------------------------|-------|------------|-------|
| FROM (11-14)                |       | TO (15-18) |       |
| YEAR                        | MONTH | YEAR       | MONTH |
| 75                          | 7     | 77         | 7     |

4. APPLICANT  
**Richlyn Laboratories, Inc.**

5. DRUG NAME  
**Hydrochlorothiazide 50 mg Tablets**

7. OTHER NDA/ANTIBIOTIC APPLICATION NUMBERS (List all numbers if any part of report applies to more than one number.)

9. REPORT INFORMATION REQUIRED (See §§ 310.300(a) or 431.60(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    | B   | C   |
| (19) | a. CLINICAL DATA  | Renewed; NAE  |
| X    | b. ADVERSE REACTION(S)  | Dizziness (5-22-78)                                     |
| X    | c. ANIMAL DATA  |   |
| (22) | d. CHEMICAL OR PHYSICAL DRUG PROPERTIES                           | Stability Report Attached                               |
| X    | e. MANUFACTURING OR CONTROL CHANGES (§§ 314.8 (a) (5))            |   |
|      | f. CURRENT PACKAGE LABELING (Whether or not previously submitted) | Attached  |
|      | g. QUANTITY DISTRIBUTED (in-000's)                                | 7/75-7/76: ; 7/76-7/77:                                 |

TYPED NAME AND TITLE OF RESPONSIBLE OFFICIAL OR AGENT

**E. W. Rebollo, Vice President**

SIGNATURE  
*E. W. Rebollo*

APPLICANTS RETURN ADDRESS (Type within the window envelope tic marks)

**Richlyn Laboratories, Inc.  
Castor & Kensington Avenues  
Philadelphia, Pa. 19124**

| FDA USE ONLY        |    |    |    |    |    |
|---------------------|----|----|----|----|----|
| 10. DATE OF RECEIPT |    |    |    |    |    |
| 24                  | 25 | 26 | 27 | 28 | 29 |
|                     | 28 | 25 | 17 |    |    |

| 11. REPORT FILED IN NDA NO. |    |    |    |    |    |
|-----------------------------|----|----|----|----|----|
| 30                          | 31 | 32 | 33 | 34 | 35 |
| N                           | 8  | 3  | 6  | 0  | 7  |

12. DIVISION (18) 13. TYPE CARD (20)

14. FDA ACKNOWLEDGMENT  
**MAY 17 1978**  
**GENERIC DRUGS**

OMG

FROM: gerry millar (thru Jack L. Meyer) OFFICE 07/10/73  
Mr. B.T. Loftus, Gen. Dir. Office of Compliance DIVISION CD-69  
CD-300

SUBJECT: collaborative draft(s)

SUMMARY : In connection with NDA 83-607 for hydrochlorothiazide tablets  
The applicant: richlyn labs  
phila, pa 19124  
AF 28-724

We acknowledge receipt on 3/27/73 + of abbr NDA  
dated 3/22/73 +  
for

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

The above firms are to do testing of the Tablets---  
as per USP XVIII monograph

PLEASE EXPEDITE

SIGNATURE DOCUMENT NUMBER 83-607