CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

ANDA 088602

Name: Corphed (Triprolidine HCl and Pseudoephedrine HCl) Tablets USP 2.5 mg/60 mg

Sponsor: Cord Laboratories, Inc.

Approval Date: April 11, 1985

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 088602

CONTENTS

Reviews / Information Included in this Review	
Approval Letter	X
Tentative Approval Letter	
Labeling	X
Labeling Review(s)	X
Medical Review(s)	
Chemistry Review(s)	X
Bioequivalence Review(s)	X
Statistical Review(s)	
Microbiology Review(s)	
Administrative & Correspondence Documents	X

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 088602

APPROVAL LETTER

NDA 88-602

Cord Laboratories, Inc.
Attention: Roger Schwede
2555 W. Midway Boulevard
Broomfield, Colorado 80020

APR 11 1985

Dear Mr. Schwede:

Reference is made to your abbreviated new drug application dated March 7, 1984, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Corphed (Triprolidine and Pseudoephedrine Hydrochlorides) Tablets, USP (2.5 mg/60 mg).

Also referenced is your ANDA original amendment resubmission dated March 29, 1985.

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

Any significant change in the conditions outlined in this abbreviated application requires an approved supplemental application before the change may be made, except for changes made in conformance with other provisions of Section 314.8 of the new drug regulations.

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

For Initial Campaigns: We request that you submit, in duplicate, any proposed advertising or promotional copy which you intend to use in your immediate advertising or promotional campaigns. Please submit all proposed materials in draft or mock-up form, not final print. Submit both copies together with a copy of the proposed or final printed labeling to the Division of Drug Advertising and Labeling (HFN-240). Please do not use Form FD-2253 for this initial submission.

For Subsequent Campaigns: We call your attention to Regulation 21 CFR 310.300 (b)(3) which requires that materials for any subsequent advertising or promotional campaign, at the time of their initial use, be submitted to our Division of Drug Advertising and Labeling (HFN-240) with a completed Form FD-2253. A copy of Form FD-2253 is enclosed for your convenience.

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

Sincerely yours,

Marvin Seife 4/11/85

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

Enclosures:
Conditions of Approval of a New Drug Application
Records & Reports Requirements
Form FD 2253

cc: DEN-DO
HFN-83
HFN-10
HFN-313
HFN-230
HFN-234
TPoux/HCZell/KJFurnkranz
R/D INITIALED BY HCZell/MSeife
mstephens: 4/10/85 (0594B)
Approve
Kenneth J. Furnkranz
April 11, 1985

4/11/85

HCZell 4/11/85

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 088602

LABELING

NDA 88-602
CORPHED TABLETS

Cord Laboratories

APPROVED

APR 11 1985

Labeling: ORIGINAL

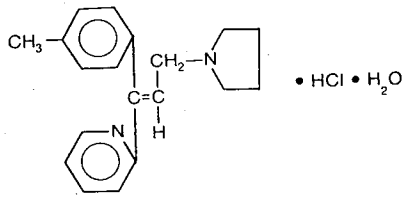
NDA No: 88602 Re'd. APR 2 1985

Reviewed by: _____

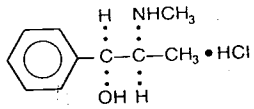
TRIPROLIDINE AND PSEUDOEPHEDRINE HYDROCHLORIDES TABLETS, USP

DESCRIPTION: Each tablet for oral administration contains Triprolidine Hydrochloride, USP 2.5mg. and Pseudoephedrine Hydrochloride, USP 60mg.
Triprolidine hydrochloride is Pyridine, 2-[1-(4-methylphenyl)-3-(1-pyrrolidinyl)-1-propenyl]-, monohydrochloride, monohydrate, (E)-, a potent antihistamine. It is virtually tasteless and lacking in topical anesthetic effect.
Pseudoephedrine hydrochloride is Benzenemethanol, α -[1-(methylamino)ethyl]-, [S- (R*,R*)]-, hydrochloride, a naturally occurring dextrostereoisomer of ephedrine. The compound is classified as a sympathomimetic amine.

The structural formulas are as follows:



Triprolidine HCl
$C_{19}H_{22}N_2 \cdot HCl \cdot H_2O$ M.W. 332.87



Pseudoephedrine HCl
$C_{10}H_{15}NO \cdot HCl$ M.W. 201.70

CLINICAL PHARMACOLOGY: Triprolidine hydrochloride acts as an antagonist of the H_1 histamine receptor. Consequently, it prevents histamine from eliciting typical immediate hypersensitivity responses in the nose, eyes, lungs and skin.
Pseudoephedrine acts as an indirect sympathomimetic agent by stimulating sympathetic (adrenergic) nerve endings to release norepinephrine. Norepinephrine in turn stimulates alpha and beta receptors throughout the body. The action of pseudoephedrine hydrochloride is apparently more specific on the blood vessels of the upper respiratory tract and less specific for the blood vessels of the systemic circulation. The vasoconstriction elicited at these sites results in the shrinkage of tissues in the sinuses and nasal passages.
INDICATIONS AND USAGE: For the treatment of the symptoms of seasonal and perennial allergic rhinitis, and vasomotor rhinitis, including nasal obstruction (congestion).
CONTRAINDICATIONS:
Use in Newborn and Premature Infants: Triprolidine and pseudoephedrine should not be used in newborn or premature infants.
Use in Lower Respiratory Disease: This drug is contraindicated for the treatment of lower respiratory symptoms including asthma.

Cord Laboratories

APPROVED

APR 11 1985

Labeling: ORIGINAL

NDA No: 88602 Re'd. APR 2 1985

Reviewed by: _____

Also contraindicated in the following conditions: Hypersensitivity to: 1) triprolidine hydrochloride and other antihistamines of similar chemical structure; and/or 2) sympathomimetic amines including pseudoephedrine.
Monoamine oxidase (MAO) inhibitor therapy (see Drug Interactions section).
WARNINGS: Triprolidine and pseudoephedrine should be used with considerable caution in patients with: Increased intraocular pressure (narrow angle glaucoma); stenosing peptic ulcer; pyloroduodenal obstruction; symptomatic prostatic hypertrophy; bladder neck obstruction; hypertension; diabetes mellitus; ischemic heart disease and hyperthyroidism.
Use in the Elderly (approximately 60 years or older): Antihistamines are more likely to cause dizziness, sedation and hypotension in elderly patients. This age group is also more likely to have adverse reactions to sympathomimetics.
PRECAUTIONS:
General: Triprolidine and pseudoephedrine should be used with caution in patients with a history of bronchial asthma.
Information to Patients: Patients should be cautious about engaging in activities requiring mental alertness such as driving a car or operating appliances, machinery, etc. Triprolidine has additive effects with alcohol and other Central Nervous System (CNS) depressants (hypnotics, sedatives, tranquilizers, etc.).
Drug Interactions: MAO inhibitors prolong and intensify the anticholinergic (drying) effects of antihistamines and overall effects of sympathomimetics.
Triprolidine has additive effects with alcohol and other CNS depressants (hypnotics, sedatives, tranquilizers, etc.).
Sympathomimetics may reduce the antihypertensive effects of methyldopa, guanethidine, reserpine, decamylamine, and veratrum alkaloids.
Carcinogenesis, Mutagenesis, Impairment of Fertility: Long term studies in animals have not been performed to evaluate carcinogenic potential of the active ingredients of triprolidine and pseudoephedrine.
Pregnancy: Teratogenic Effects: Pregnancy Category B. Reproduction studies consisting of teratology studies have been performed in rats and rabbits at doses up to 70 times the human dose and have revealed no evidence of impaired fertility or harm to the fetus due to the combination of triprolidine and pseudoephedrine. There are, however, no adequate and well-controlled studies in pregnant women. Because animal reproduction studies are not always predictive of human response, this drug should be used during pregnancy only if clearly needed.
Nursing Mothers: Because of the higher risk of antihistamines and sympathomimetic amines for infants generally and for newborn and premature infants in particular, therapy with triprolidine and pseudoephedrine is contraindicated in nursing mothers.
Pediatric Use: See "CONTRAINDICATIONS" section.
ADVERSE REACTIONS: The most frequent adverse reactions are underlined:

1. GENERAL: Dryness of mouth, dryness of nose and dryness of throat, urticaria, drug rash, anaphylactic shock, photosensitivity, excessive perspiration, chills.
2. CARDIOVASCULAR SYSTEM: Hypotension, headache, palpitations, tachycardia, extrasystoles.
3. HEMATOLOGIC SYSTEM: Hemolytic anemia, thrombocytopenia, agranulocytosis.
4. NERVOUS SYSTEM: Sedation, sleepiness, dizziness, disturbed coordination, fatigue, confusion, restlessness, excitation, nervousness, tremor, irritability, insomnia, euphoria, paresthesia, blurred vision, diplopia, vertigo, tinnitus, acute labyrinthitis, hysteria, neuritis, convulsions, CNS depression, hallucination.
5. G.I. SYSTEM: Epigastric distress, anorexia, nausea, vomiting, diarrhea, constipation.
6. G.U. SYSTEM: Urinary frequency, difficult urination, urinary retention, early menses.
7. RESPIRATORY SYSTEM: Thickening of bronchial secretions, tightness of chest and wheezing, nasal stuffiness.

OVERDOSAGE: Since triprolidine and pseudoephedrine is comprised of two pharmacologically different components, it is difficult to predict how an overdose will be manifested in a given individual. Reaction to an overdose may vary from CNS depression to stimulation. Stimulation is particularly likely in children. A detailed description of symptoms which are likely to appear after ingestion of an excess of the individual components follows:

NDA 88-602
CORPHED TABLETS

Cord Laboratories

APPROVED

APR 11 1985

ORIGINAL

Labeling:

NDA No: 88602 Re'd. APR 2 1985

Reviewed by:

Overdosage with pseudoephedrine can cause CNS stimulation resulting in such manifestations as excitement, nervousness, anxiety, tremor, restlessness and insomnia. Other effects include tachycardia, hypertension, pallor, mydriasis, hyperglycemia and urinary retention. Severe overdosage may cause tachypnea or hyperpnea, hallucinations, convulsions, or delirium, but in some individuals, there may be CNS depression, with somnolence, stupor or respiratory depression. Arrhythmias (including ventricular fibrillation) may lead to hypotension and circulatory collapse. Severe hypokalemia can occur, probably due to compartmental shift rather than depletion of potassium.

Overdosage of triprolidine may produce reactions varying from depression to stimulation of the CNS; the latter is particularly likely in children. Atropine-like signs and symptoms, dry mouth, fixed dilated pupils, flushing, tachycardia, hallucinations, convulsions, urinary retention, cardiac arrhythmias and coma may occur.

The mean LD_{50} (single, oral dose) of pseudoephedrine is 726 mg./kg. in the mouse, 2206 mg./kg. in the rat, and 1177 mg./kg. in the rabbit. The toxic and lethal concentrations in human biologic fluids are not known. Excretion rates increase with acidification of urine and decrease with alkalinization.

The mean LD_{50} (single, oral dose) of triprolidine is 163 to 308 mg./kg. in the mouse (depending on strain) and 840 mg./kg. in the rat.

Insufficient data are available to estimate the toxic and lethal doses of either compound in man. Few reports of toxicity due to pseudoephedrine have been published, and no case of fatal overdosage is known. No reports of acute poisoning with triprolidine have appeared.

Adrenergic-receptor blocking agents are antidotes to pseudoephedrine. In practice, the most useful is the beta-blocker propranolol, which is indicated when there are signs of cardiac toxicity. There is no specific antidote to triprolidine. Histamine should not be given. Administration of activated charcoal will help reduce the absorption of triprolidine if given within 1 hour of ingestion. If instituted within 4 hours of overdosage, therapy is initially aimed at reducing further absorption of the drugs. If vomiting has not occurred spontaneously, the patient should be induced to vomit. This is best done by having him drink a glass of water or milk, then making him gag. Centrally-acting emetics are likely to be less effective than usual in view of the anti-emetic action of antihistamines. Gastric aspiration and lavage may be carried out up to 4 hours after ingestion if large amounts of milk were given beforehand. Either isotonic or half isotonic saline may be used for lavage.

Saline cathartics such as Milk of Magnesia, by drawing water into the gut, help to dilute the concentration of the drug in the bowel and hasten its elimination.

In severe cases of overdosage, it is essential to monitor both the heart (by electrocardiography) and plasma electrolytes and to give intravenous potassium as indicated by these continuous controls. Vasopressors may be used to treat hypotension, and excessive CNS stimulation may be counteracted with parenteral diazepam. Stimulants should not be used.

DOSAGE AND ADMINISTRATION: DOSAGE SHOULD BE INDIVIDUALIZED ACCORDING TO THE NEEDS AND THE RESPONSE OF THE PATIENT.

Usual Dose: Adults and children 12 years and older — 1 tablet 3 or 4 times a day. Children 6 to 12 years — 1/2 tablet 3 or 4 times a day. For children under 6 years, Triprolidine and Pseudoephedrine Syrup should be used for greater ease and flexibility in administering doses smaller than 1/2 tablet.

HOW SUPPLIED: Tablets — round, white, scored, in bottles of 100, 250, and 1000. Store at controlled room temperature 15-30°C (59-86°F). Protect from moisture.

CAUTION: Federal law prohibits dispensing without prescription.

Rev. 85-1B
1120

C85/1

Manufactured By
Cord Laboratories, Inc.
Broomfield, CO 80020

NDA 88-602
CORPHED TABLETS

Labeling: ORIGINAL

NDA No: 88602 Rc'd. APR 2 1985

Reviewed by: _____

Cord Laboratories

APPROVED

APR 11 1985

NDC 0117-1120-02

CORPHED

(Triprolidine and Pseudoephedrine Hydrochlorides Tablets, USP)

Caution: Federal law prohibits dispensing without prescription.

100 TABLETS

CORD LABORATORIES, INC.
Broomfield, CO 80020

Each tablet contains:
Triprolidine HCl., USP 2.5mg.
Pseudoephedrine HCl., USP 60mg.
Dosage and Administration: Consult accompanying professional literature.
Rev. 85-1B C85/3

Store at controlled room temperature 15-30°C (59-86°F). Protect from moisture. Preserve and dispense in containers which are tight, light-resistant as defined in the USP.
KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

Lot No.:

Exp.:

NDC 0117-1120-03

CORPHED

(Triprolidine and Pseudoephedrine Hydrochlorides Tablets, USP)

Caution: Federal law prohibits dispensing without prescription.

250 TABLETS

CORD LABORATORIES, INC.
Broomfield, CO 80020

Each tablet contains:
Triprolidine HCl., USP 2.5mg.
Pseudoephedrine HCl., USP 60mg.
Dosage and Administration: Consult accompanying professional literature.
Rev. 85-1B C85/3

Store at controlled room temperature 15-30°C (59-86°F). Protect from moisture. Preserve and dispense in containers which are tight, light-resistant as defined in the USP.
KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

Lot No.:

Exp.:

NDC 0117-1120-05

CORPHED

(Triprolidine and Pseudoephedrine Hydrochlorides Tablets, USP)

Caution: Federal law prohibits dispensing without prescription.

1000 TABLETS

CORD LABORATORIES, INC.
Broomfield, CO 80020

Each tablet contains:
Triprolidine HCl., USP 2.5mg.
Pseudoephedrine HCl., USP 60mg.
Dosage and Administration: Consult accompanying professional literature.
Rev. 85-1B C85/3

Store at controlled room temperature 15-30°C (59-86°F). Protect from moisture. Preserve and dispense in containers which are tight, light-resistant as defined in the USP.
KEEP THIS AND ALL DRUGS OUT OF THE REACH OF CHILDREN.

Lot No.:

Exp.:

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 088602

LABELING REVIEWS

REVIEW OF PROFESSIONAL LABELING

ANDA - DRAFT

DATE OF REVIEW: 12-30-83

NAME OF FIRM: Cord Labs.

ANDA #: 88-602

NAME OF DRUG: Trade: Corphed

Generic: Triprolidine HCl and Pseudoephedrine HCl

DATE OF SUBMISSION: (rec'd) 12-8-83

COMMENTS:

Container: Not satisfactory (100s, 250s, 1000s)

Center panel: Note quantitative information as required by 21 CFR 201.10(h)(1).

Left panel: D & A must not be different from insert labeling.

Insert: Not satisfactory

a) DOSAGE AND ADMINISTRATION: (add) For children under 6 years, Triprolidine and Pseudoephedrine Syrup should be used for greater ease and flexibility in administering doses smaller than 1/2 tablet.

b) HOW SUPPLIED: (add) imprinting or debossing) (if any).

c) Add: Month-Year of revision.

RECOMMENDATIONS:

1. Revise labels and labeling, then prepare and submit FPL.

Kent T. Johnson

cc:
dup
KTJ/cl/1-4-84

REVIEW OF PROFESSIONAL LABELING

ORIGINAL AMENDMENT - FPL

DATE OF REVIEW: 8-31-84

ANDA #: 88-602 NAME OF FIRM: Cord Laboratories, Inc.

NAME OF DRUG: Trade: Corphed
Generic: Triprolidine and Pseudoephedrine Hydrochlorides Tablets

DATE OF SUBMISSION: 8-27-84

Container: Not Satisfactory

1. We believe that the expression for the established name for this combination product is not correct as presented. The established name is: Triprolidine and Pseudoephedrine Hydrochlorides Tablets, USP.

   Quantitative information should not be a part of the established name, and should be presented on the main panel if there is room, otherwise it may appear on the side panel.

Insert: Not Satisfactory
Must be revised to follow our Guideline which provides updated information. The established name is now: Triprolidine and Pseudoephedrine Hydrochlorides Tablets, USP.

RECOMMENDATIONS:

1. Inform firm of the above comments.
2. Send current labeling guideline.
3. Request that they revise labels and labeling as recommended, then prepare and submit FPL.

Kent T. Johnson

cc: Dup.
KJohnson/mk/8/31/84
5194A

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 088602

CHEMISTRY REVIEWS

CHEMIST'S REVIEW NDA 88-602

3. NAME AND ADDRESS OF APPLICANT
Cord Laboratories
2555 W. Midway Boulevard
Broomfield, CO 80020

4. AF NUMBER
DESI #11935

5. SUPPLEMENT(s)

6. NAME OF DRUG
Corphed

7. NONPROPRIETARY NAME
Pseudoephedrine HCl, 60 mg and
Triprolidine HCl, 25 mg

8. SUPPLEMENT(s) PROVIDE(s) FOR:

9. AMENDMENTS AND OTHER DATES:

10. PHARMACOLOGICAL CATEGORY
Antihistamine/decongestant

11. HOW DISPENSED
Rx

12. RELATED IND/NDA/DMF(s)
DMF 2416 - Cord Type I DMF - General facilities and mfg. and controls information.
DMF [redacted] (b) (4)

13. DOSAGE FORM(s)
Tablet

14. POTENCY
See (7)

15. CHEMICAL NAME AND STRUCTURE
Chemical Names and Structures in insert are satisfactory.

16. RECORDS AND REPORTS

17. COMMENTS
a) [redacted] (b) (4) must submit proper DMF reference (DMF [redacted] (b) (4) does not belong to [redacted] (b) (4)).
b) Must submit a batch formula and batch instructions.
c) Stability Protocol, Data and Commitment need revision.
d) Methods validation must be performed.
e) Labeling must be revised.

18. CONCLUSIONS AND RECOMMENDATIONS
Not Approvable

19. REVIEWER:
Kenneth Furnkranz
Mar. 6, 1984

DATE COMPLETED:
Feb. 27, 1984

Following this page, 4 pages withheld in full (b)(4)-CCI/TS

NDA 88-602 CHEMIST'S REVIEW FOR ANDA OR SUPPLEMENT

NAME AND ADDRESS OF APPLICANT:
Cord Laboratories
Broomfield, Colorado

PURPOSE OF AMENDMENT/SUPPLEMENT
Methods Validation

DATE(S) OF SUBMISSION(S)
O-ANDA 11/1/83
R-O ANDA 3/26/84

PHARMACOLOGICAL CATEGORY	NAME OF DRUG
Antihistamine/Decongestant	Pseudoephedrine HCl, 60 mg Triprolidine HCl, 25 mg

HOW DISPENSED
RX

DOSAGE FORM
Tablet

COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS
Methods Validation Information submitted. Not required, since a monograph for the drug product was published in USP XX, Supplement 5.

REMARKS AND CONCLUSION
Response to Points 1, 2, 3, 4, and 6 of our Not Approvable letter of 3/7/84 have not been received.

Not Approvable

Kenneth J. Furnkranz
April 20, 1984

HC Zell 4/20/84

CHEMIST'S REVIEW NDA 88-602

3. NAME AND ADDRESS OF APPLICANT
Cord Laboratories
Broomfield, Colorado

4. AF NUMBER
DESI

7. NONPROPRIETARY NAME
Triprolidine HCl, 2.5 mg, and Pseudoephedrine HCl, 60 mg

9. AMENDMENTS AND OTHER DATES:
ANDA Original Amendment Resubmission 3/26/84
ANDA Original Amendment Resubmission 8/27/84

10. PHARMACOLOGICAL CATEGORY
Antihistamine/Decongestant

11. HOW DISPENSED
RX

13. DOSAGE FORM(s)
Tablet

15. CHEMICAL NAME AND STRUCTURE
Satisfactory

17. COMMENTS
Labeling must be revised
BIO review is acceptable. Firm has incorporated dissolution testing into the finished product and stability protocols.

19. REVIEWER: DATE COMPLETED:

Kenneth J. Turnbach Dec 10, 1984

RC Zell 12/10/84

Following this page, 1 page withheld in full (b)(4)-CCI/TS

28. LABORATORY CONTROLS (IN-PROCESS AND FINISHED DOSAGE FORM)
Satisfactory. Finished Product Controls are as per recently included USP XX Monograph.

29. STABILITY
Protocol: Satisfactory
Commitment: Satisfactory
Data: Supports a tentative 2 year expiration date

30. CONTROL NUMBERS Satisfactory

31. SAMPLES AND RESULTS Not necessary: USP Monograph Drug

32. LABELING See Kent Johnson's label review dated 8/31/84.

33. ESTABLISHMENT INSPECTION
Satisfactory - See Establishment Evaluation Report in ANDA.

NDA 88-602 CHEMIST'S REVIEW FOR ANDA OR SUPPLEMENT

NAME AND ADDRESS OF APPLICANT:
Cord Laboratories, Inc.
Broomfield, Colorado 80020

PURPOSE OF AMENDMENT/SUPPLEMENT
FPL

DATE(S) OF SUBMISSION(S)
O-ANDA 3/7/84
R-O-ANDA 3/29/85

PHARMACOLOGICAL CATEGORY	NAME OF DRUG	HOW DISPENSED
Antihistamine/ Decongestant	Corphed	RX

DOSAGE FORM	POTENCY
Tablets	Triprolidine HCl 2.5 mg Pseudoephedrine HCl 60 mg

LABELING
Labels and labeling satisfactory as per T. Poux 4/8/85.

BIOLOGIC AVAILABILITY
BIO is acceptable (see 3/2/84 review)

ESTABLISHMENT INSPECTION Satisfactory
See EIR dated 12/8/83. Approved nds manufacturers are:
(b)(4) - Pseudoephedrine HCl
(b)(4) - Pseudoephedrine HCl
(b)(4) - Triprolidine HCl manufacturer

COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS
Batch formula for (b)(4) tablets is satisfactory (See attached batch formula).

PACKAGING
100, 250, and 1000 tablet package sizes approved (see 3/7/84 review)

STABILITY
PROTOCOL: Satisfactory
EXP.DATE: Tentative 2 year expiration date.

REMARKS AND CONCLUSION
Approve

Kenneth J. Furnkranz
Kenneth J. Furnkranz
April 11, 1985
HCZell 4/11/85

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 088602

BIOEQUIVALENCE REVIEWS

JAN 12 1984

Pseudoephedrine HCl, 60 mg and
Triprolidine HCl, 2.5 mg
[Corphed Tablets]
ANDA 88-602
Reviewer: T.E. Mary Ong-Chen
Wang #3025e

Cord Laboratories
Broomfield, Colorado
Submission Dated:
November 1, 1983
Document No.: Wang # 3025e

REVIEW OF DISSOLUTION & STABILITY TEST DATA

The firm has submitted dissolution test results and dissolution specification in support of bioavailability/bioequivalence requirement for its combination product containing pseudoephedrine hydrochloride, 60 mg and triprolidine hydrochloride, 2.5 mg.

COMMENT:

1. The firm has conducted dissolution testing of its Corphed tablets according to the proposed USP specification that is described in the Nov.-Dec., 1982 issue of Pharmacopeial Forum. A summary of test results is as follow:

	Corphed Tablets (Cord)	
	Pseudoephedrine HCl	Triprolidine HCl
Mean (%)	111	93
RSD (%)	2.4	5.3
Range (%)	(b) (4)	(b) (4)

2. In the stability testing of the combination drug product, the firm failed to submit individual tablet data. The firm should be advised that, in future submissions of dissolution & stability test results, all raw data as well as summary data (i.e., to include mean, range, coefficient of variation) should be included.

RECOMMENDATION:

1. The dissolution testing conducted by Cord Laboratories, Inc. on its Corphed Tablets (pseudoephedrine hydrochloride, 60 mg and triprolidine hydrochloride, 2.5 mg) is acceptable. In the future, for product approval, the firm is required to submit comparative dissolution data (i.e., to use Actifed^{R} tablets as the reference drug: pseudoephedrine HCl, 60 mg and triprolidine HCl, 2.5 mg).

2. The dissolution specification and testing should be incorporated into firm's manufacturing controls and stability program. Testing should be conducted in 900 ml of deaerated water at 37^{o}C using USP XX Apparatus 2 at 50 rpm. The test product should meet the following specification: Not less than 75% of the labeled amount of each of the active components in dosage forms is dissolved in 45 minutes.

3. From the biopharmaceutics point of view, the application is incomplete.

The above recommendations and comment #2 should be conveyed to the firm.

Teo Eng Ong Chen 1/10/84
T.E. Mary Ong Chen, Biochemist

INITIALED BY CMISE C.M.L.

cc: ANDA 88-602 Orig., HFN-530 (4), Review File, Drug File, Chron File, Division File, HFN-522 (Chen, Ise-2), HFN-503 (Hare)

TEOCHEN/dea/3025e

Table I

Stability Profiles of the Combined Test Product (Batch # 83-023)

ENVIRONMENTAL STORAGE CONDITION (Period, Temp., Humidity)	LABELED AMOUNT DISSOLVED IN 45 MINUTES Mean % (Range) Pseudoephedrine HCl	Triprolidine HCl
Initial	105	99
4 wks @ 37°C	104	102
4 wks @ 45°C	106	99
4 wks, 37°C, 75% R.H.	103	99
12 wks @ 37°C	108	99
12 wks @ 45°C	108	96
12 wks, 37°C, 75% R.H.	109	96
Retainer Samples	112	93

(b) (4)

(b) (4)

* USP XX Paddle, 50 rpm; 900 ml H_2O, 37°C; HPLC assay; n= ? tablets; Q = NLT 75%/45' (triprolidine HCl & pseudoephedrine HCl)

FEB 29 1984

Pseudoephedrine Hydrochloride, 60 mg with
Triprolidine Hydrochloride, 2.5mg
[Corphed Tablet]
ANDA 88-602
Reviewer: T.E. Mary Ong-Chen

Cord Laboratories
Broomfield, Colorado
Submission Dated:
February 9, 1983
Document No.: Wang # 3216e

REVIEW OF COMPARATIVE DISSOLUTION DATA

As advised by the Division of Biopharmaceutics, the firm provided individual tablet data in the comparative dissolution study of the combination test (Corphed) and reference (B-W's Actifed^{R}) drug products. The summary of dissolution results for each of the two active drug components of the combination tablet products are outlined below.

	LABELED AMOUNT DISSOLVED IN 45 MINUTES* Mean % (Range) C.V.,%	
COMPONENT	Cord's Corphed Tablets (Lot # 83-023)	B-W's Actifed^{R} Tablets (Lot # 1G2292)
Pseudoephedrine.HCl	111 (b) (4) 2	96 (b) (4) 6
Triprolidone.HCl	93 5	83 9

* USP Paddle, 50 rpm; 0.9L Deaerated H_2O; n= 12 tablets; Q = NLT 75%/45'

COMMENT

1. The firm has committed in this submission to incorporate the dissolution testing of the test combination tablet product into the quality control and stability testing programs.

RECOMMENDATION:

1. The dissolution testing conducted by Cord Laboratories on its Corphed^{R} test tablet product (Lot #83-023) is acceptable.

2. The dissolution testing should be incorporated into firm's manufacturing controls and stability program. Testing should be conducted in 900 ml of deaerated water at 37°C, using USP XX apparatus 2 (paddle) at 50 rpm. The test product should meet the specifications in that not less than 75% of the labeled amount of each of the active drug ingredients in the dosage form is dissolved in 45 minutes.

3. From the biopharmaceutics point of view, the application is approvable.

Teo Ong Ong Chen 2/27/84
T.E. Mary Ong Chen, Biochemist

INITIALED BY CMISE C M Ise

cc: ANDA 88-602 Orig., HFN-530 (4), HFN-522 (Chen, Ise-2), HFN-503 (Hare), Review File, Drug File, Chron File, Division File

TEOCHEN/02/22/84(3216e)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

ANDA 088602

ADMINISTRATIVE and CORRESPONDENCE DOCUMENTS

for administrative determination, all issues relating to the legal status of a drug product named above and of all identical, related or similar drug products.

An applicant or any other person subject to this notice under 21 CFR 310.6 who decides to seek a hearing shall file (1) on or before June 24, 1982, a written notice of appearance and request for hearing, and (2) on or before July 26, 1982, the data, information, and analyses relied on to justify a hearing, as specified in 21 CFR 314.200. Any other interested person may also submit comments on this notice. The procedures and requirements governing this notice of opportunity for hearing, a notice of appearance and request for hearing, a submission of data, information, and analyses to justify a hearing, other comments, and a grant or denial of hearing, are contained in 21 CFR 314.200.

The failure of the applicant or any other person subject to this notice under 21 CFR 310.6 to file timely written notice of appearance and request for hearing as required by 21 CFR 314.200 constitutes an election by the person not to make use of the opportunity for a hearing concerning the action proposed with respect to the product and constitutes a waiver of any contentions concerning the legal status of any such drug product. Any such drug product may not thereafter lawfully be marketed, and the Food and Drug Administration will initiate appropriate regulatory action to remove such drug products from the market. Any new drug product marketed without an approved NDA is subject to regulatory action at any time.

A request for a hearing may not rest upon mere allegations for denials, but must set forth specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for hearing that there is no genuine and substantial issue of fact which precludes the withdrawal of approval of the application, or when a request for hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person(s) who requests the hearing, making findings and conclusions, and denying a hearing.

All submissions pursuant to this notice shall be filed in four copies. Such submissions except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

(Federal Food, Drug, and Cosmetic Act (sec. 505, 52 Stat. 1052–1053, as amended (21 U.S.C. 355)), and under the authority delegated to the Director of the Bureau of Drugs (21 CFR 5.82))

Dated: April 30, 1982.

J. Richard Crout,

Director, Bureau of Drugs.

[FR Doc. 82-14147 Filed 5-24-82; 8:45 am]

BILLING CODE 4160-01-M

[Docket No. 82N-0095; DESI 6514 and 11935]

Drugs for Human Use; Drug Efficacy Study Implementation; Revocation of Exemption for Two Oral Prescription Drugs Offered for Relief of Symptoms of Cough, Cold, or Allergy ("Paragraph XIV/Category 15"); Followup Notice and Opportunity for Hearing

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) revokes the temporary exemption for two oral prescription drug products offered for relief of symptoms of cough, cold, or allergy. The exemption has permitted the products to remain on the market beyond the time limit scheduled for implementatin of the Drug Efficacy Study. FDA reclassifies the products to lacking substantial evidence of effectiveness, proposes to withdraw approval of the new drug applications, and offers an opportunity for a hearing on the proposal.

DATES: Revocation of exemption effective May 25, 1982. Hearing requests due on or before June 24, 1982.

ADDRESSES: Communications in response to this notice should be identified with Docket No. 82N-0095, directed to the attention of the appropriate office named below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Requests for opinion of the applicability of this notice to a specific product: Division of Drug Labeling Compliance (HFD-310), Bureau of Drugs.

Requests for the report of the National Academy of Sciences-National Research Council: Public Records and Document Center (HFI-35), Rm. 12A-12.

Requests for hearing, supporting data, and other comments: Dockets Management Branch (HFA-305), Rm. 4-62.

Other communications regarding this notice: Drug Efficacy Study Implementation Project Manager (HFD-501), Bureau of Drugs.

FOR FURTHER INFORMATION CONTACT: David T. Read, Bureau of Drugs (HFD-32), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301-443-3650.

SUPPLEMENTARY INFORMATION: In notices published in the Federal Register (DESI 6514, February 9, 1973 (38 FR 4006), formerly Docket No. FDC-D-537, and DESI 11935, July 27, 1972 (37 FR 15022)), FDA classified the drug products described below as less than effective for their labeled indications. The 1973 notice also offered an opportunity for a hearing on a proposal to withdraw approval of the new drug applications (NDA's).

Subsequently, in a notice published in the Federal Register of December 14, 1973 (38 FR 34481), FDA granted a temporary exemption from the time limits established for completing certain phases of the drug efficacy study (DESI) program, for certain oral prescription drugs offered for relief of cough, cold, allergy, and related symptons. That exemption covered the drugs that are the subject of this notice and superseded the earlier February 1973 notice. The exemption was granted because of the close relationship between drugs sold over the counter (OTC)—and thus subject to the ongoing OTC drug review (21 CFR Part 330)—and prescription drugs offered for relief of cough, cold, allergies, and related symptoms. Postponement of final evaluations on the DESI prescription products enabled the agency to consider the recommendations of the OTC drug review panel in addition to any evidence submitted by NDA holders in response to various DESI notices covering relevant products. Those recommendations and a proposed monograph for over-the-counter cold, cough, allergy, bronchodilator, and antiasthmatic (CCABA) drugs were published in the Federal Register of September 9, 1976 (41 FR 38312).

This notice revokes the temporary exemption announced in the Federal Register of December 14, 1973. It also proposes to withdraw approval of the new drug applications listed below and offers an opportunity for hearing on the proposal. Persons who wish to request a hearing may do so on or before June 24, 1982.

1. NDA 9-319: Ambenyl Expectorant containing codeine sulfate, bromodiphenhydramine hydrochloride, diphenhydramine hydrochloride, ammonium chloride, potassium guaiacolsulfonate, and menthol; Marion

Laboratories, Inc., Pharmaceutical Division, Marion Industrial Park, 10236 Bunker Ridge Rd., Kansas City, MO 64137. (DESI 6514). NDA was previously owned by Parke-Davis, Division of Warner-Lambert Co.

2. NDA 5-814: As it pertains to Pyribenzamine and Ephedrine Tablets containing tripelennamine hydrochloride and 12 mg ephedrine sulfate; Ciba Pharmaceuticals Co., 556 Morris Ave., Summit, NJ 07901 (DESI 11935).

The OTC drug review panel for CCABA drugs reached the following conclusions which are relevant to Ambenyl Expectorant:

1. There is no evidence to support the effectiveness of ammonium chloride as an expectorant. (41 FR 38359)

2. There are no well-controlled studies documenting the effectiveness of potassium guaiacolsulfonate as an expectorant. (41 FR 38367)

3. Combinations containing an antihistamine and an expectorant are irrational because an expectorant promotes the production of secretions whereas the anticholinergic activity of an antihistamine produces an opposite effect. (41 FR 38326 at paragraph II.C.9.e.(3)).

4. The combination of pharmacologic groups represented by the product was not found to be a safe and effective combination. (41 FR 38326 at paragraph II.C.6.).

The OTC drug review panel for CCABA also reached the following conclusion which is relevant to Pyribenzamine and Ephedrine Tablets, which contains 12 mg ephedrine sulfate: No conclusive data were found to support claims of effectiveness of ephedrine sulfate for doses of 8 to 12 mg. (41 FR 38408).

No person has submitted additional data on the drugs listed above. The Director of the Bureau of Drugs concludes that the holder of the NDA has not shown, for each of the products listed above, that each component makes a contribution to the claimed effects and that the dosage of each component is such that the combination is safe and effective for a significant patient population. 21 CFR 300.50. Therefore each of the products is reclassified to lacking substantial evidence of effectiveness.

In addition to the holders of the new drug applications specifically named above, this notice applies to any person who manufactures or distributes a drug product that is not the subject of an approved new drug application and that is identical, related, or similar to a drug product named above, as defined in 21 CFR 310.6. (This notice does not apply to OTC drugs. 21 CFR 310.6(f). It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product that the person manufactures or distributes. Any person may request an opinion of the applicability of this notice to a specific drug product by writing to the Division of Drug Labeling Compliance (address given above).

On the basis of all the data and information available to him, the Director of the Bureau of Drugs is unaware of any adequate and well-controlled clinical investigation, conducted by experts who are qualified by scientific training and experience, that meets the requirements of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and 21 CFR 314.111(a)(5) and 300.50, and demonstrates the effectiveness of the drug products referred to in this notice.

Notice is given to the holders of the new drug applications, and to all other interested persons, that the Director of the Bureau of Drugs proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)), withdrawing approval of the new drug applications and all amendments and supplements thereto providing for the drug products referred to in this notice on the ground that new information before him with respect to the drug products, evaluated together with the evidence available to him when the applications were approved, shows there is a lack of substantial evidence that the drug products will have any of the effects they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in the labeling.

This notice of opportunity for hearing encompasses all issues relating to the legal status of the drug products subject to it (including identical, related, or similar drug products as defined in 21 CFR 310.6), e.g., any contention that any such product is not a new drug because it is generally recognized as safe and effective within the meaning of section 201(p) of the act of because it is exempt from part or all of the new drug provisions of the act under the exemption for products marketed before June 25, 1938, in section 201(p) of the act, or under section 107(c) of the Drug Amendments of 1962, or for any other reason.

In accordance with section 505 of the act (21 U.S.C. 355) and the regulations promulgated under it (21 CFR Parts 310, 314), the applicants and all other persons who manufacture or distribute a drug product that is identical, related, or similar to a drug product named above (21 CFR 310.6) and not the subject of a new drug application, are hereby given an opportunity for a hearing to show why approval of the new drug applications should not be withdrawn and an opportunity to raise, for administrative determination, all issues relating to the legal status of a drug product named above and all identical, related, or similar drug products not the subject of a new drug application.

Any applicant or other person subject to this notice under 21 CFR 310.6 who decides to seek a hearing shall file (1) on or before June 24, 1982, a written notice of appearance and request for hearing, and (2) on or before July 26, 1982, the data, information, and analyses relied on to justify a hearing, as specified in 21 CFR 314.200. Any other interested person may also submit comments on this proposal to withdraw approval. The procedures and requirements governing this notice of opportunity for hearing, a notice of appearance and request for hearing, a submission of data, information, and analyses to justify a hearing, other comments, and a grant or denial of hearing, are contained in 21 CFR 314.200.

The failure of the applicants or any other person subject to this notice under 21 CFR 310.6 to file a timely written notice of appearance and request for hearing as required by 21 CFR 314.200 constitutes an election by the person not to make use of the opportunity for a hearing concerning the action proposed, and a waiver of any contentions concerning the legal status of the relevant drug product. Any such drug product may not thereafter lawfully be marketed, and the Food and Drug Administration will initiate appropriate regulatory action to remove such drug product from the market. Any new drug product marketed without an approved NDA is subject to regulatory action at any time.

A request for a hearing may not rest upon mere allegations or denials, but must present specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for hearing that there is no genuine and substantial issue of fact which precludes the withdrawal of approval of the application, or when a request for hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person(s) who requests the hearing, making findings and conclusions, and denying a hearing.

All submissions pursuant to this notice are to be filed in four copies. Except for data and information prohibited from pubic disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, the submissions may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

(Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050–1053 as amended (21 U.S.C. 352, 355)) and under the authority delegated to the Director of the Bureau of Drugs (21 CFR 5.70 and 5.82))

Dated April 22, 1982.

J. Richard Crout,

Director, Bureau of Drugs.

[FR Doc. 82-14144 Filed 5-24-82; 8:45 am]

BILLING CODE 4160-01-M

[Docket No. 81N–0391; DESI 6514]

Drugs for Human Use; Drug Efficacy Study Implementation; Revocation of Exemption for Certain Oral Prescription Drugs Offered for Relief of Symptoms of Cough, Cold, or Allergy ("Paragraph XIV/Category 15"); Followup Notice and Opportunity for Hearing.

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) revokes the temporary exemption for three oral prescription drug products offered for relief of symptoms of cough, cold, or allergy. The exemption has permitted the products to remain on the market beyond the time limit scheduled for implementation of Drug Efficacy Study. FDA reclassifies the products to lacking substantial evcidence of effectiveness, proposes to withdraw approval of the new drug applications, and offers an opportunity for a hearing on the proposal. These products are labeled as antitussives.

DATE: Revocation of exemption effective May 25, 1982. Hearing requests due on the before June 24, 1982.

ADDRESSES: Communications in response to this notice should be identified with Docket No. 81N–0391, directed to the attention of the appropriate office named below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Requests for opinion of the applicability of this notice to a specific product: Division of Drug Labeling Compliance (HFD–310), Bureau of Drugs.

Other communications regarding this notice: Drug Efficacy Study Implementation Project Manager (HFD–501), Bureau of Drugs.

Requests for the report of the National Academy fo Sciences-National Research Council: Public Records and Document Center (HFI–35), Rm. 12A–12.

Requests for hearing, supporting data, and other comments: Dockets Management Branch (HFA–305), Rm. 4–62.

FOR FURTHER INFORMATION CONTACT: David T. Read, Bureau of Drugs (HFD–32), Food and Drug Administration, 5600 Fisher Lane, Rockville, MD 20857, 301–443–3650.

SUPPLEMENTARY INFORMATION: In a notice (formerly Docket No. FDC–D–537) published in the Federal Register of February 9, 1973 (38 FR 4006), FDA classified the drug products described below as lacking substantial evidence of effectiveness for their labeled indications. The notice also offered an opportunity for a hearing on the proposal to withdraw approval of the new drug application (NDA) for each product.

Subsequently, in a notice published in the Federal Register of December 14, 1973 (38 FR 34481), FDA granted a temporary exemption from the time limits established for completing certain phases of the drug efficacy study (DESI) program, for certain oral prescription drugs offered for relief of cough, cold, allergy, and related symptoms. That exemption covered the drugs that are the subject of this notice and superseded the February 1973 notice. The exemption was granted because of the close relationship between drugs sold over the counter (OTC)—and thus subject to the ongoing OTC drug review (21 CFR Part 330)—and prescription drugs offered for relief of cough, cold, allergies, and related symptoms. Postponement of final evaluations on the DESI prescription products enabled the agency to consider the recommendations of the OTC review panel in addition to any evidence submitted by NDA holders in response to various DESI notice covering relevant products. Those recommendations and a proposed monograph for over-the-counter cold, cough, allergy, bronchodilator, and antiasthmatic (CCABA) drugs were published in the Federal Register of September 9, 1976 (41 FR 38312).

The OTC reached the following conclusions which are relevant to Omni-Tuss Suspension:

1. Combinations containing an antihistamine and an expectorant are irrational because an expectorant promotes the production of secretions whereas the anticholinergic activity of an antihistamine produces an opposite effect. (41 FR 38326 at paragraph II.C.9.e.(3)). Omni-Tuss Suspension contains the antihistamines phenyltoloxamine and chlorpheniramine maleate, and the expectorant guaiacol carbonate.

2. The combination of an antihistamine, an expectorant, an antitussive, and a bronchodilator was not found to be a safe and effective combination. (41 FR 38326 at paragraph II.C.8.).

No person has submitted additional data on the three drugs listed below. The Director of the Bureau of Drugs concludes that the holder of the new drug applications has not shown, for each of the products listed below, that each component makes a contribution to the claimed effects and that the dosage of each component is such that the combination is safe and effective for a significant patient population 21 CFR 300.50. Therefore each of the products is reclassified to lacking substantial evidence of effectiveness.

This notice revokes the temporary exemption announced in the Federal Register of December 14, 1973. It also proposes to withdraw approval of the new drug applications listed below, and offers an opportunity for hearing on the proposal. Persons who wish to request a hearing may do so on or before June 24, 1982.

1. NDA 10–768: Tussionex Tablets and Suspension, each containing dihydrocodeinone and phenyltoloxamine dihydrogen sulfate (both as cation exchange resin complexes of sulfonated polystyrene); Pennwalt Corporation, Pharmaceutical Division, 755 Jefferson Rd., Rochester, NY 14623.

2. NDA 12–666: Omni-Tuss Suspension, containing codeine sulfate, phenyltoloxamine dihydrogen sulfate, chlorpheniramine maleate, ephedrine sulfate (all as cation exchange resin complexes of sulfonated polystyrene), and guaiacol carbonate: Pennwalt Corp.

In addition to the holder of the new drug applications specifically named above, this notice applies to any person who manufactures or distributes a drug product that is not the subject of an approved new drug application and that is identical, related, or similar to a drug product named above, as defined in 21 CFR 310.6. (This notice does not apply to OTC drugs. 21 CFR 310.6(f).) It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product that the person manufactures or distributes. Any person may request an opinion of the applicability of this notice to a specific drug product by writing to the Division

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the following consumer exchange meeting: Philadelphia District Office, chaired by the Philadelphia District Director.

DATE: Thursday, November 4, 1982, 1 p.m.

ADDRESS: Federal Bldg., Rm. 3207, 844 King St., Wilmington, DE.

FOR FURTHER INFORMATION CONTACT: Theresa A. Young, Consumer Affairs Technician, Food and Drug Administration, 2d & Chestnut Sts., Philadelphia, PA 19106, 215–597–0837.

SUPPLEMENTARY INFORMATION: The purpose of this meeting is to encourage dialogue between consumers and FDA officials, to identify and set priorities for current and future health concerns, to enhance understanding and exchange information between local consumers and FDA's District Offices, and to contribute to the agency's policymaking decisions on vital issues.

Dated: October 18, 1982.

William F. Randolph,

Acting Associate Commissioner for Regulatory Affairs.

[FR Doc. 82-29027 Filed 10-19-82; 11:22 am]

BILLING CODE 4160-01-M

[Docket No. 82N-0311; DESI No. 11935]

Drugs for Human Use; Drug Efficacy Study Implementation; Revocation of Exemption for Certain Effective Oral Prescription Drugs Offered for Relief of Symptoms of Cough, Cold, or Allergy ("Paragraph XIV/Category 15"); Followup Notice and Opportunity for Hearing

AGENCY: Food and Drug Administration (FDA), HHS.

ACTION: Notice.

SUMMARY: FDA revokes the temporary exemption for Actifed Syrup and Tablets, two drug products offered for relief of symptoms of cough, cold, or allergy. The exemption has permitted the products to remain on the market beyond the time limit scheduled for implementation of the Drug Efficacy Study. FDA announces the conditions for marketing these products for the indication for which they are now regarded as effective and offers an opportunity for a hearing concerning indications reclassified to lacking substantial evidence of effectiveness.

DATES: Revocation of exemption effective October 22, 1982. Hearing requests due on or before November 22, 1982; supplements to approved new drug applications and data in support of hearing requests due on or before December 21, 1982.

ADDRESSES: Communications in response to this notice should be identified with Docket No. 82N–0311, directed to the attention of the appropriate office named below, and addressed to the Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

Supplements to full new drug applications (identify with NDA number): Division of Surgical-Dental Drug Products (HFN–160), Rm. 18B–08, National Center for Drugs and Biologics.

Original abbreviated new drug applications and supplements thereto (identify as such): Division of Generic Drug Monographs (HFN–530), National Center for Drugs and Biologics.

Requests for opinion of the applicability of this notice to a specific product: Division of Drug Labeling Compliance (HFN–310), National center for Drugs and Biologics.

Requests for the report of the National Academy of Sciences-National Research Council: Public Records and Document Center (HFI–35), Rm. 12A–12.

Request for hearing, supporting data, and other comments: Dockets Management Branch (HFA–305), Rm. 4–62.

Other communications regarding this notice: Drug Efficacy Study Implementation Project Manager (HFN–501), National Center for Drugs and Biologics.

FOR FURTHER INFORMATION CONTACT: David T. Read, National Center for Drugs and Biologics (HFN–8), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3650.

SUPPLEMENTARY INFORMATION: In a notice published in the Federal Register of July 27, 1972 (37 FR 15022), FDA classified Actifed Syrup and Tablets as less than effective for their labeled indications (probably effective, possibly effective, and lacking substantial evidence of effectiveness).

Subsequently, in a notice published in the Federal Register of December 14, 1973 (38 FR 34481), FDA granted a temporary exemption from the time limits established for completing certain phases of the drug efficacy study (DESI) program, for certain oral prescription drugs offered for relief of cough, cold, allergy, and related symptoms. That exemption covered Actifed Syrup and Tablets and superseded the notice published earlier. The exemption was granted because of the close relationship between drugs sold over the counter (OTC)— and thus subject to the ongoing OTC drug review (21 CFR Part 330)—and prescription drugs offered for relief of cough, cold, allergies, and related symptoms. Postponement of final evaluations on the DESI prescription products enabled the agency to consider the recommendations of the OTC drug review panel in addition to any evidence submitted by NDA holders in response to various DESI notices covering relevant products. Those recommendations and a proposed monograph for over-the-counter cold, cough, allergy, bronchodilator, and antiasthmatic (CCABA) drugs were published in the Federal Register of September 9, 1976 (41 FR 38312).

The OTC drug review panel classified pseudoephedrine hydrochloride as a generally recognized as safe and effective nasal decongestant (41 FR 38402). Triprolidine hydrochloride, which was not reviewed by the OTC drug review panel, was classified by the FDA as an effective antihistamine on March 19, 1973 (DESI 6303; 38 FR 7285). In addition to the conclusion of the OTC drug review panel for CCABA drugs that combinations containing an antihistamine and a nasal decongestant, each present in amounts within the effective dosage range, are safe and effective (41 FR 38328). Burroughs-Wellcome Co. submitted two adequate and well-controlled clinical studies, in accord with 21 CFR 314.111 and 21 CFR 300.50, demonstrating the effectiveness of the combination products.

Therefore, on the basis of additional data and information, and the recommendations of the OTC drug review panel, the Director of the National Center for Drugs and Biologics has reclassified the following drug products:

NDA's 11–835 and 11–836; Actified Syrup and Tablets, respectively, containing triprolidine hydrochloride and pseudoephedrine hydrochloride; Burroughs-Wellcome Co., 3030 Cornwallis Rd., Research Triangle Park, NC 27709.

The temporary exemption announced in the December 14, 1973 notice, as it pertains to these drug products, is hereby revoked. These drugs are regarded as new drugs (21 U.S.C. 321(p)) and an approved new drug application is required for marketing them. Supplemental new drug applications are now required to revise the labeling in and to update previously approved applications providing for these drugs. This notice does not prevent the FDA, in any future OTC drug monograph, from including either of the ingredients listed above, and requiring labeling different from that approved for prescription use.

In addition to the holder of the new drug applications specifically named

above, this notice applies to any person who manufactures or distributes a drug product that is not the subject of an approved new drug application and that is identical to a drug product named ib . It may also be applicable, under 21 R 310.6, to a related or similar drug product that is not the subject of an approved new drug application. (This notice does not apply to OTC drugs. 21 CFR 310.6(f).) It is the responsibility of every drug manufacturer or distributor to review this notice to determine whether it covers any drug product that he person manufactures or distributes. Any person may request an opinion of he applicability of this notice to a specific drug product by writing to the Divison of Drug Labeling Compliance address given above).

A. *Effectiveness classification.* The Food and Drug Administration has reviewed all available evidence and concludes that the drugs are effective for the indication listed in the labeling conditions below. The drugs lack substantial evidence of effectiveness for their other labeled indications.

B. *Conditions for approval and marketing.* The Food and Drug Administration is prepared to approve abbreviated new drug applications and supplements to previously approved new drug applications under conditions described herein.

1. *Form of drug.* The preparation is in a syrup or tablet form suitable for oral administration.

2. *Labeling conditions.* a. The label bears the statement, "Caution: Federal law prohibits dispensing without prescription."

b. The drug is labeled to comply with all requirements of the act and regulations, and the labeling bears adequate information for safe and effective use of the drug. The Indication is as follows:

For the treatment of the symptoms of seasonal and perennial allergic rhinitis and vasomotor rhinitis, including nasal obstruction (congestion).

3. *Marketing Status.* a. Marketing of such drug products that are now the subject of an approved or effective new drug application may be continued provided that, on or before December 21, 1982, the holder of the application has submitted (i) a supplement for revised labeling as needed to be in accord with the labeling conditions described in this notice, and complete container labeling if current container labeling has not been submitted, and (ii) a supplement to provide updating information with respect to items 6 (components), 7 (composition), and 8 (methods, facilities, and controls) of new drug application form FD-356H (21 CFR 314.1(c)) to the extent required in abbreviated new drug applications (21 CFR 314.1(f)).

b. Approval of an abbreviated new drug application (21 CFR 314.1(f)) must be obtained before marketing such products. The bioavailability regulations (21 CFR 320.21) require any person submitting a full or abbreviated new drug application after July 7, 1977, to include either evidence demonstrating the in vivo bioavailability of the drug or information to permit waiver of the requirement. Marketing drug products before approval of a new drug application will subject those products, and those persons who caused the products to be marketed, to regulatory action.

C. *Notice of opportunity for hearing.* On the basis of all the data and information available to him, the Director of the National Center for Drugs and Biologics is unaware of any adequate and well-controlled clinical investigation, conducted by experts qualified by scientific training and experience, that meets the requirements of section 505 of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355) and 21 CFR 314.111(a)(5) and 21 CFR 300.50, and demonstrates the effectiveness of the drug products in indications for prescription use not referred to in paragraph B.2.b., above.

Notice is given to the holder of the new drug applications, and to all other interested persons, that the Director of the National Center for Drugs and Biologics proposes to issue an order under section 505(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)), withdrawing approval of the new drug applications and all amendments and supplements thereto providing for the indications lacking substantial evidence of effectiveness on the ground that new information before him with respect to the drug products, evaluated together with the evidence available to him when the applications were approved, shows there is a lack of substantial evidence that the drug products will have all the effects they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in the labeling. An order withdrawing approval will not issue with respect to any application supplemented, in accord with this notice, to delete the claims lacking substantial evidence of effectiveness.

This notice of opportunity for hearing encompasses all issues relating to the legal status of the drug products subject to it (including identical, related, or similar drug products as defined in 21 CFR 310.6), e.g., any contention that any such product is not a new drug because it is generally recognized as safe and effective within the meaning of section 201(p) of the act or because it is exempt from part or all of the new drug provisions of the act under the exemption for products marketed before June 25, 1938, in section 201(p) of the act, or under section 107(c) of the Drug Amendments of 1962, or for any other reason.

In accordance with section 505 of the act (21 U.S.C. 355) and the regulations promulgated under it (21 CFR Parts 310, 314), the applicant and all other persons who manufacture or distribute a drug product that is identical, related, or similar to a drug product named above (21 CFR 310.6), are hereby given an opportunity for a hearing to show why approval of the new drug applications should not be withdrawn, and an opportunity to raise, for adminstrative determination, all issues relating to the legal status of a drug product named above and of all identical, relted, or similar drug products not the subject of a new drug application.

An applicant or any other person subject to this notice under 21 CFR 310.6 who decides to seek a hearing, shall file (1) on or before November 22, 1982, a written notice of appearance and request for hearing, and (2) on or before December 21, 1982, the data, information, and analyses relied on to justify a hearing, as specified in 21 CFR 314.200. Any other interested person may also submit comments on this proposal to withdraw approval. The procedures and requirements governing this notice of opportunity for hearing, a notice of appearance and request for hearing, a submission of data, information, and analyses to justify a hearing, other comments, and a granting or denial of a hearing, are contained in 21 CFR 314.200.

The failure of the applicant or any other person subject to this notice under 21 CFR 310.6 to file a timely written notice of appearance and request for hearing as required by 21 CFR 314.200 constitutes an election by the person not to make use of the opportunity for a hearing concerning the action proposed, and a waiver of any contentions concerning the legal status of the relevant drug product. Any such drug product labeled for the indications referred to in this notice as lacking substantial evidence of effectiveness may not thereafter lawfully be marketed, and the Food and Drug Administration will initiate appropriate regulatory action to remove such a drug product from the market. Any new drug product marketed without an approved

new drug application is subject to regulatory action at any time.

A request for a hearing may not rest upon mere allegations or denials, but must present specific facts showing that there is a genuine and substantial issue of fact that requires a hearing. If it conclusively appears from the face of the data, information, and factual analyses in the request for hearing that there is no genuine and substantial issue of fact which precludes the withdrawal of approval of the application, or when a request for hearing is not made in the required format or with the required analyses, the Commissioner of Food and Drugs will enter summary judgment against the person(s) who requests the hearing, making findings and conclusions, and denying a hearing.

All submissions pursuant to this notice are to be filed in four copies. Except for data and information prohibited from public disclosure under 21 U.S.C. 331(j) or 18 U.S.C. 1905, the submissions may be seen in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

This notice is issued under the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050–10–1053, as amended (21 U.S.C. 352, 356)), and under the authority delegated to the Director of the National Center for Drugs and Biologics (see 21 CFR 5.70, 5.82 and 47 FR 28813 published in the Federal Register of June 22, 1982).

Dated: October 14, 1982.

Harry M. Meyer, Jr.,

Director, National Center for Drugs and Biologics.

[FR Doc. 82-29888 Filed 10-21-82; 8:45 am]

BILLING CODE 4110-01-M

Office of the Secretary

Agency Forms Submitted to the Office of Management and Budget for Clearance

Each Friday the Department of Health and Human Services (HHS) publishes a list of information collection packages it has submitted to the Office of Management and Budget (OMB) for clearance in compliance with the Paperwork Reduction Act (44 U.S.C. Chapter 35). The following are those packages submitted to OMB since the last list was published on October 15.

Public Health Service

Centers for Disease Control

Subject: VD Control Program Grant Requirements (0920–0112)—Revision
Respondents: State or local governments/businesses
OMB Desk Officer: Richard Eisinger

Health Care Financing Administration

Subject: Request for Certification and the Survey Process for Certifying Ambulatory Surgical Centers for Medicare and Medicaid (HCFA–377 and R7)—New
Respondents: Ambulatory surgical centers
Subject: Medicare/Medicaid Skilled Nursing Facility Certification Survey (HCFA–1569)—Revised
Respondents: Skilled nursing facilities
OMB Desk Officer: Fay S. Iudicello

Copies of the above information collection clearance packages can be obtained by calling the HHS Reports Clearance Officer on 202–245–6511.

Written comments and recommendations for the proposed information collections should be sent directly to both the HHS Reports Clearance Officer and the appropriate OMB Desk Officer designated above at the following addresses:

J. J. Strnad, HHS Reports Clearance Officer, Hubert H. Humphrey Building, Room 524–F, Washington, D.C. 20201
and
OMB Reports Management Branch, New Executive Office Building, Room 3208, Washington, D.C. 20503, Attn: (name of OMB Desk Officer)

Dated: October 15, 1982.

Dale W. Sopper,

Assistant Secretary for Management and Budget.

[FR Doc. 82-29889 Filed 10-21-82; 8:45 am]

BILLING CODE 4110-01-M

DEPARTMENT OF THE INTERIOR

Fish and Wildlife Service

Information Collection Submitted for Review

The proposal for the collection of information listed below has been submitted to the Office of Management and Budget for approval under the provisions of the Paperwork Reduction Act (44 U.S.C. Chapter 35). Copies of the proposed information collection requirement and related forms and explanatory material may be obtained by contacting the Service's clearance officer at the phone number listed below. Comments and suggestions on the requirement should be made directly to the Service clearance officer and the Office of Management and Budget reviewing official, Mr. Rick Otis, at 202–395–7340.

- Title: Hunter Surveys, to monitor the size and effects of hunting harvests on national wildlife refuges.
- Bureau Form Number: N/A
- Frequency: On occasion
- Description of Respondents: Selected hunters on national wildlife refuges
- Annual Responses: 100,000
- Annual Burden Hours: 5,000
- Service Clearance Officer: Arthur J. Ferguson, 202–653–8770

Walter R. McAllester,

Acting Associate Director–Wildlife Resources.

October 14, 1982.

[FR Doc. 82-29878 Filed 10-21-82; 8:45 am]

BILLING CODE 4310-55-M

Bureau of Land Management

Casper District, Wyoming; Proposed Coal Exchange

AGENCY: Bureau of Land Management, Interior.

ACTION: Notice of Environmental Assessment on Proposed Exchange of Coal Leases in Campbell County, Wyoming (I–90 exchange).

SUMMARY: The Bureau of Land Management proposes to accept portions of coal lease W–5035 from Exxon Coal Resources, USA, Inc., in exchange for other Federal Coal in the same county. Part of the coal offered for exchange is under Interstate Highway 90. Notice of this exchange proposal is required under 43 CFR 3435.3–5.

FOR FURTHER INFORMATION CONTACT: Charles F. Wilkie, Special Projects Team Leader, Casper District Office, Bureau of land management 951 Rancho Road, Casper, Wyoming 82601 (307–261–5597).

SUPPLEMENTARY INFORMATION: The Carter Mining Company, a division of Exxon Coal USA, Inc., wants to exchange 396 million tons of coal under its current lease for 293 million tons of Federal coal adjacent to 2 of the company's existing mines. The Bureau of Land Management proposes to authorize this exchange. Such an exchange was made possible in 1978 by Pub. L. 95–554, which amended the Minerals Leasing Act of 1920: Bureau of land management Environmental Assessment WY–061–2–72 covers this proposal. Copies are available from the Casper District Office on request.

The proposed exchange is in the public interest because the only effect of mining the selected areas would be to increase the life of 2 existing mines by 5 and 7 years, respectively. If the exchange did not take place, noise and air pollution from mining of the offered areas would affect Gillette, Wyoming, and an area containing 390 housing units would be scheduled for mining. In addition, the coal covered by Interstate 90 would not be recovered. Therefore,

[Docket Nos. 81N–0391 and 82N–0095; DESI 6514 AND 11935]

Drugs for Human Use; Drug Efficacy Study Implementation; Oral Prescription Drugs Offered for Relief of Symptoms of Cough, Cold, or Allergy; Withdrawal of Approval

AGENCY: Food and Drug Administration.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is withdrawing approval of the new drug application for Omni-Tuss Suspension and those parts of another application that pertain to Pyribenzamine and Ephedrine Tablets. The basis of the withdrawal is that there is a lack of substantial evidence that the fixed-combination drugs are effective in the relief of symptoms that the fixed-combination drugs are effective in the level of symptoms of cough, cold, or allergy.

EFFECTIVE DATE: June 23, 1983.

ADDRESS: Requests for an opinion of the applicability of this notice to a specific product should be identifed with the appropriate docket number and directed to the Division of Drug Labeling Compliance (HFN–310), National Center for Drugs and Biologics, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857.

FOR FURTHER INFORMATION CONTACT: David T. Read, National Center for Drugs and Biologics (HFN–8), Food and Drug Administration, 5600 Fishers Lane, Rockville, MD 20857, 301–443–3650.

SUPPLEMENTARY INFORMATION: In notices published in the Federal Register of May 25, 1982 (47 FR 22606 and 22604), the Director of the then Bureau of Drugs revoked the temporary exemption for the two drug products described below which permitted these products to remain on the market beyond the time limit scheduled for the implementation of the Drug Efficacy Study. Those notices also proposed to issue orders withdrawing approval of the new drug applications, or parts thereof, that provide for these drug products. The proposal was based on the lack of substantial evidence of effectiveness that each ingredient in the combination products contributes to the claimed effects or is present in an amount considered to be effective, as required by section 305(e) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(e)) and 21 CFR 314.111(a)(5) and 300.50. The two products are:

1. NDA 12–666: Omni-Tuss Suspension, containing codeine sulfate, phenyltoloxamine dihydrogen sulfate, chloropheniramine maleate, ephedrine sulfate (all as cation exchange resin complexes of sulfonated polystyrene), and guaiacol carbonate; Pennwalt Corp., Pharmaceutical Division, 755 Jefferson Rd., Rochester, NY 14623 (DESI 6514; Docket No. 81N–0391).

2. NDA 5–914: As it pertains to Pyribenzamine and Ephedrine Tablets containing tripelennamine hydrochloride and ephedrine sulfate; Ciba Pharmaceuticals Co., 556 Morris Ave., Summit, NJ 07901 (DESI 11935; Docket No. 82N–0095).

Neither Pennwalt Corp. nor Ciba Pharmaceuticals requested a hearing on the two products listed above. Failure to file an appearance and request a hearing constitutes a waiver of the opportunity for a hearing.

The three other products listed in the two May 25, 1982, notices—Ambenyl Expectorant (47 FR 22604; see also 47 FR 50344), and Tussionex Tablets and Suspension (47 FR 22606—and a product related to Omni-Tuss Suspension called Ru-Tuss Expectorant, manufactured by Boots Pharmaceuticals, Inc., are not affected by this notice. The manufacturers of these products have requested hearings; the products will be the subject of future Federal Register notices.

Any drug product that is identical, related, or similar to Omni-Tuss Suspension and Pyribenzamine and Ephedrine Tablets and is not the subject of a pending hearing request or an approved new drug application is covered by the new drug applications reviewed and is subject to this notice (21 CFR 310.6). Any person who wishes to determine whether a specific product is covered by this notice should write to the Division of Drug Labeling Compliance (address given above).

The Director of the National Center for Drug and Biologics, under the Federal Food, Drug, and Cosmetic Act (sec. 505, 52 Stat. 1052–1053 as amended (21 U.S.C. 355)), and under the authority delegated to him (see 21 CFR 5.82 and 47 26913 published in the Federal Register of June 22, 1982) finds that, on the basis of new information before him with respect to the products, evaluated together with the evidence available to him when the applications were approved, there is lack of substantial evidence that the two drug products will have the effects they purport or are represented to have under the conditions of use prescribed, recommended, or suggested in their labeling.

Therefore, pursuant to the foregoing finding, approval of those parts of NDA 5–914 that provide for Pyribenzamine and Ephedrine Tablets, and approval of NDA 12–666, and all amendments and supplements thereto, are withdrawn effective June 23, 1983.

Shipment in interstate commerce of the above products, or any identical, related, or similar product that is not the subject of a pending hearing request or an approved new drug application, will then be unlawful.

Dated: May 18, 1983.

Harry M. Meyer, Jr.,

Director, National Center for Drugs and Biologics.

[FR Doc. 83–13857 Filed 5–23–83; 8:45 am]

BILLING CODE 4160–01–M

Health Resources and Services Administration

Home Health Services; Section 339 of the Public Health Service Act; Delegation of Authority

Notice is hereby given that the following delegations have been made regarding home health services under section 339 of the Public Health Service Act (42 U.S.C. 255), as amended.

1. Delegation from the Administrator, Health Resources and Services Administration, to the Regional Health Administrators, Regions I–X, with authority to redelegate, of the following authorities under Section 339 of the Public Health Service Act (42 U.S.C. 255) within their respective regions (for projects that are not multiregional or national in scope):

(a) Under section 339(a), to make grants to public and nonprofit private entities and loans to proprietary entities to meet the initial costs of establishing and operating home health programs;

(b) Under section 339(b), to make grants to public and private entities to assist them in developing appropriate training programs for paraprofessionals (including homemaker home health aides) to provide home health services.

2. Delegation from the Administrator, Health Resources and Services Administration, to the Director, Bureau of Health Care Delivery and Assistance, with authority to redelegate, of all the authorities under section 339 of the Public Health Service Act except those authorities specifically delegated to the Regional Health Administrators, excluding the authorities to submit reports to Congress or a Congressional committee and to issue regulations.

Previous delegations and redelegations made to officials within the Public Health Service of authorities under Title III of the Public Health Service Act may continue in effect provided they are consistent with this delegation.

Cord Laboratories
2555 W. Midway Blvd. • Broomfield, CO 80020 • [303] 469-2131

Orig

November 1, 1983

Marvin Seife, M.D., Director
Division of Generic Drugs
Office of Drug Standards HFN 530
National Center for Drugs and Biologics
5600 Fishers Lane
Rockville, Maryland 20857

ABBREVIATED
NEW DRUG APPLICATION

DRAFT LABELING

RE: Abbreviated New Drug Application for Corphed Tablets
(Pseudoephedrine HCl 60 mg. and Triprolidine HCl 2.5 mg.)
DESI 11935 (Docket No. 82N-0311)
FEDERAL REGISTER Announcement Dated October 22, 1982

Dear Dr. Seife:

Cord Laboratories is hereby submitting a New Drug Application for Corphed Tablets as required by Section 505(b) of the Federal Food, Drug, and Cosmetic Act.

In view of the prior marketing history of this compound and the publicly expressed views of experts, we believe that this product is an "old drug" which does not require approval of a new drug application prior to marketing. We are, nevertheless, submitting this application in order to avoid unnecessary legal confrontations.

We understand that the in vivo bioavailability/bioequivalence requirement for this combination product has been deferred at this time. We are enclosing dissolution data and a dissolution specification for the finished product (see Sections 18 & 5).

While the information enclosed in this Abbreviated New Drug Application should be sufficient, you may refer to our Drug Master File 2416 for additional information concerning our manufacturing and quality control procedures.

Sincerely,

CORD LABORATORIES, INC.

Raj K. Matkari

Raj K. Matkari, Ph.D.
Vice President, Regulatory Affairs

RECEIVED
DEC 8 1983
GENERIC DRUGS

RKM:cs

Enclosures

DEPARTMENT OF HEALTH & HUMAN SERVICES

143

Fumkaoy

Memorandum

TO :Manufacturing Review Branch (HFN-322) DATE: 12-8-83
Division of Drug Quality Compliance

FROM :Division of Generic Drugs
Requester's Name David Rosen PHONE: 443-4080

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 88-602

DRUG TRADE MARK (if any) CORPHED Tablets

DRUG NONPROPRIETARY NAME: Pseudoephedrine HCl 60 mg and Triprolidine H(2.!

DOSAGE FORM AND STRENGTH(S): TCM

DRUG CLASSIFICATION: PROFILE CLASS CODE:
(Priority) ____ A or B____ 1C____Other____ ____

APPLICANT'S NAME: Cord Laboratories, Inc. 5/82
ADDRESS: 2555 West Midway Blvd., Broomfield, CO 80020

FACILITIES TO BE EVALUATED: (Name, Full Address, DMF# (if any), and Responsibility)

ok 1. applicant 5/82

2. [redacted] (b) (4)

ok 3.

ok 4.

5.

Comments: ( ) See Attached.
( ) Actual on-site inspection requested.

Reason: _____

cc: DDarrow 12-87 HFO-503

****

FOR HFN-322 USE ONLY:

Request Rec'd: 12/12 Inspection Requested: update for [redacted] (b) (4)
(if applicable)

Firm(s) are in Compliance With GMPs: Approved 11/84
Basis for Decision: Re Office EIS and District update
Reviewing CSO: Lee Hartley Concurrance: _____

cc: HFN-____
HFN-____
HFN-322 update Keyser [redacted] (b) (4) cf

FORM FDA 3274 (1/83)

DEPARTMENT OF HEALTH & HUMAN SERVICES

(147)

Funkranz

Memorandum

TO :Manufacturing Review Branch (HFN-322) DATE: 12-8-83
Division of Drug Quality Compliance

FROM :Division of Generic Drugs
Requester's Name David Rosen PHONE: 443-4080

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 88-602

DRUG TRADE MARK (if any) CORPHED Tablets

DRUG NONPROPRIETARY NAME: Pseudoephedrine HCl 60 mg and Triprolidine HCl 2.5 mg

DOSAGE FORM AND STRENGTH(S): TCM

DRUG CLASSIFICATION: PROFILE CLASS CODE:
(Priority) _____ A or B _____ 1C _____ Other _____ _____

APPLICANT'S NAME: Cord Laboratories, Inc.
ADDRESS: 2555 West Midway Blvd., Broomfield, CO 80020

FACILITIES TO BE EVALUATED: (Name, Full Address, DMF# (if any), and Responsibility)

1. applicant 9/81
2. (b) (4)
3.
4.
5.

Comments: ( ) See Attached.
( ) Actual on-site inspection requested.

Reason: _____

****

FOR HFN-322 USE ONLY:

Request Rec'd: 12/13 Inspection Requested: _____
(if applicable)

Firm(s) are in Compliance With GMPs [redacted] Approved 1/4/8
Basis for Decision: Re above ES
Reviewing CSO: Lillian Hartling Concurrance: _____

cc: HFN-____
HFN-____
HFN-322

FORM FDA 3274 (1/83)

ANDA ADMINISTRATIVE CONTROL RECORD

Applicant Card Laboratories ANDA # 88-602

Date Recd. 12-8-83

Trade Name Corphed Tablets RX___ OTC___

Generic Name/Dosage Form/Strength: Pseudoephedrine Hydrochloride 60 mg and Triprolidine Hydrochloride Hcl 2.5 mg

DESI Drug ✓

Similar or Related ___

Applicant Manufacturer: Yes ✓ No ___

If No: Name of Manufacturer ___

ANDA # ___ Approved: ___ Pending ___ Same Formulation ___

Application Complete YES ✓ NO ___
Application Acceptable: YES ✓ NO ___

Letter to Firm: Acknowledgement: ✓ Not-acceptable ___ Date 12/13-83

CSO/CST: Margo Bennett Date 12-8-83

BIO Review Required: YES ___ NO ✓ IN VITRO ___ IN VIVO ___

Medical Officer SELFE

Chemist K. Fuhrhranz

Inspection Request to HFD 320 (Date): 12-8-83

7899e/mlb

88-602

1. Completeness of Submission

	Yes	No
Cover Letter	✓	
356h Signed	✓	
Table of Contents	✓	
Labeling	draft	
Statement re Rx/OTC Status	✓	
Components & Composition (Unit Composition)	✓	
Manufacturing Controls	✓	
Batch Formulation	✓	
Certification of GMP	✓	
Description of Facilities	✓	
Manufacturing Procedures (Batch Records)	✓ DMF 2416	
Specs & Tests for Active Ingredient and Finished Dosage Form	✓	
Stability Profile Including Stability Data (Use of Stability indicating method)	✓	
Samples Statement Plus Data		
Bio Protocol (If Applicable)	—	
Dissolution Data (If Applicable)	✓	
Environmental Impact Analysis	✓	

Bio Data protocol_____

Study: IN VIVO_____ IN VITRO_____

Reviewed Date_____ Approved_____

Deficiency Letter Sent, Date_____

JCMorrison/mlb/6-10-80
5218P

DEC 13 1983

NDA 88-602

Cord Laboratories, Inc.
Attention: Raj K. Matkari, Ph.D.
2555 W. Midway Blvd.
Broomfield, CO 80020

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: Corphed Tablets (Pseudoephedrine Hydrochloride 60 mg and Triprolidine Hydrochloride 2.5 mg)

DATE OF APPLICATION: November 1, 1983

DATE OF RECEIPT: December 8, 1983

We will correspond with you further after we have had the opportunity to review the application.

Please identify any communications concerning this application with the NDA number shown above.

Sincerely yours,

Kent T. Johnson for 12-13-83

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics

DEN-DO DUP HFN-530 HFN-534
HCZell/mlb/12-9-83 HCZell 12/12/83
ack

MSKF

NDA 88-502

Cord Laboratories, Inc.
Attention: Seymour Hyden
2555 W. Midway Blvd.
Broomfield, CO 80020

Gentlemen:

Reference is made to the dissolution data you submitted on November 1, 1983 for Corphed (pseudoephedrine hydrochloride, 60 mg and triprolidine hydrochloride, 2.5 mg) Tablets.

The data have been reviewed by our Division of Biopharmaceutics and they have the following comments:

> "In the stability testing of the combination drug product, the firm failed to submit individual tablet data. The firm is advised that, in future submissions of dissolution & stability test results, all raw data as well as summary data (i.e., to include mean, range, coefficient of variation) should be included.

RECOMMENDATIONS:

1. The dissolution testing conducted by Cord Laboratories, Inc. on its Corphed Tablets (pseudoephedrine hydrochloride, 60 mg and triprolidine hydrochloride, 2.5 mg) is acceptable. In the future, for product approval, the firm is required to submit comparative dissolution data (i.e., to use Actifed® tablets as the reference drug: pseudoephedrine HCl, 60 mg and triprolidine HCl, 2.5 mg).

2. The dissolution specification and testing should be incorporated into firm's manufacturing controls and stability program. Testing should be conducted in 900 ml of deaerated water at 37°C using USP XX Apparatus 2 at 50 rpm. The test product should meet the following specification: Not less than 75% of the labeled amount of each of the active components in dosage forms is dissolved in 45 minutes.

3. From the biopharmaceutics point of view, the application is incomplete."

Sincerely yours,

Marvin Seife 1/18/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs & Biologics

cc:
DEN-DO
HFN-530/DUP
HFN-522 (Rm 15-42)
MSeife/cjl:1-17-84
BIO

Dup to Bio Drug

Cord Laboratories
2555 W. Midway Blvd. • Broomfield, CO 80020 • [303] 469-2131

February 9, 1984

ORIG NEW CORRES

Marvin Seife, M.D., Director
Division of Generic Drugs
Office of Drug Standards HFN 530
National Center for Drugs and Biologics
5600 Fishers Lane
Rockville, Maryland 20857

BIOAVAILABILITY MATERIAL

RE: NDA 88-602 Corphed Tablets (Pseudoephedrine HCl 60 mg. and Triprolidine HCl 2.5 mg. Tablets)
Amendment (Controls)

Dear Dr. Seife:

We are submitting an amendment to our unapproved New Drug Application for Corphed (Pseudoephedrine HCl 60 mg. and Triprolidine HCl 2.5 mg.) Tablets in accord with Section 505(b) of the Federal Food, Drug, and Cosmetic Act.

In response to your communication dated January 18, 1984 which included the Division of Biopharmaceutics' evaluation of our data, I am submitting dissolution results for the brand name product Actifed. In order to facilitate direct comparison of these results, I have also included the dissolution data for Cord Laboratories' product.

Additionally, Cord Laboratories does commit to incorporate the dissolution testing of finished product into our quality control and stability testing programs. The testing will be conducted in 900 ml of deaerated water at 37°C using USP XX Apparatus 2 at 50 rpm. The specifications will be Not Less Than 75% of the labeled amount of each active component will be dissolved in 45 minutes.

This information is submitted for your review and approval of the NDA.

Sincerely,

CORD LABORATORIES, INC.

Roger Schwede
Manager, Drug Regulatory Affairs

RS:cs

RECEIVED
FEB 15 1984
GENERIC DRUGS

MAR 2

NDA 88-502

Cord Laboratories
Attention: Roger Schwede
2555 W. Midway Boulevard
Broomfield, Colorado 80020

Gentlemen:

Reference is made to the dissolution data you submitted on February 9, 1984 for Corphed Tablets (triprolidine hydrochloride 2.5 mg and pseudoephedrine hydrochloride 60 mg).

The data have been reviewed by our Division of Biopharmaceutics and they have the following comments:

"1. The dissolution testing conducted by Cord Laboratories on its Corphed® test tablet product (Lot #83-023) is acceptable.

2. The dissolution testing should be incorporated into firm's manufacturing controls and stability program. Testing should be conducted in 900 ml of deaerated water at 37°C, using USP XX apparatus 2 (paddle) at 50 rpm. The test product should meet the specifications in that not less than 75% of the labeled amount of each of the active drug ingredients in the dosage form is dissolved in 45 minutes."

Sincerely yours,

Marvin Seife 3/2/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics

cc: DEN-DO
HFN-530
HFN-525
HFN-616
MSeife/gp/3/1/84
0783A

MAR - 7 1984

NDA 88-602

Cord Laboratories
Attention: Roger Schwede
2555 W. Midway Boulevard
Broomfield, CO 80020

Gentlemen:

Please refer to your abbreviated new drug application dated November 1, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation Corphed (triprolidine HCl, 2.5 mg and pseudoephedrine HCl, 60 mg) Tablets.

The application is deficient and therefore not approvable under Section 505(b) of the Act as follows:

1. It fails to contain sufficient information from [redacted] (b)(4) one of the manufacturers of the Triprolidine Hydrochloride nds.

   Full manufacturing and controls information, including a complete synthesis of the nds, must be submitted. [redacted] (b)(4) submitted an authorization to view DMF [redacted] (b)(4) for this information, however, the cited DMF does not belong to [redacted] (b)(4). Please request that [redacted] (b)(4) provide us with proper authorization.

2. It fails to include a batch formula representative of that to be employed for the manufacture of the finished dosage form, or batch instructions for the complete manufacturing, processing, packaging, labeling and control operations performed.

3. It fails to include the following information on the active nds(s):

   A. Cord Laboratories raw material specification sheets for Triprolidine HCl and Pseudoephedrine HCl.

   B. Cord Laboratories certificates of analysis for Triprolidine HCl and Pseudoephedrine HCl.

   Please submit this information.

4. It fails to contain acceptable stability information.

   A. The stability protocol must be revised as follows:

      1) The smallest and largest package size must be placed into your stability program (100's and 1000's).

      2) Test stations should be as follows:

         a) Accelerated Stability: At least 1 pilot batch with 0, 4, 8, and 12 week test stations (for a tentative expiration date).

         b) First 3 production batches: 0, 3, 6, 9, 12, 18, and 24 months and yearly thereafter, until the desired expiration date is reached.

         c) Annual Check Batches: Yearly test stations (provided that at least 3 production lots have been carried through the full protocol ((b) above).

   B. The stability data is insufficient:

      1) 100's - Data is satisfactory for a tentative 2 year date (based on accelerated data).

      2) 250's and 1000's - You must submit accelerated data for the 1000's to justify an expiration date for the 250's and 1000's.

   C. Please commit to:

      1) Perform post-approved stability studies as outlined in the ANDA and approved by this Agency.

      2) Report the results of stability studies, as they become available, in the periodic reports.

      3) Withdraw from the market any batch which falls out of specifications.

5. It is necessary that the finished product control methods be validated.

We recommend that you prepare and submit, under separate cover, a methods validation packet, which should include:

A. A list of the components, and composition of the finished drug product (p. 3 of the ANDA submission).

B. Specifications and methods for the finished product.

C. Results of determinations (certificate of analysis) for the lot of drug product you will submit for validation of the methods. Please include method validation information performed in your laboratories (pp. 208-212 of the ANDA), and System Suitability criteria for the GC method.

At such time as we receive this information and assign a laboratory, we will contact you concerning the submission of samples directly to the district laboratory.

6. It fails to include acceptable labeling for the drug product:

Container (100's, 250's, and 1000's): Not Satisfactory.

Center Panel: Note quantitative information as required by 21 CFR 201.10(h)(1).

Left Panel: Dosage and Administration must not differ from insert labeling.

Insert: Not Satisfactory.

DOSAGE AND ADMINISTRATION: (add) For children under 6 years, Triprolidine and Pseudoephedrine Syrup should be used for greater ease and flexibility in administering doses smaller than 1/2 tablet.

HOW SUPPLIED: Include the presence of any debossing or imprinting (if any).

Add Month and Year of revision.

We recommend that you revise the labels and labeling, and prepare and submit FPL for our review and comment.

The file is now closed. If you wish to reopen it, the submission should be in the form of an amendment to this application, adequately organized, which represents the information necessary to remove all deficiencies we have outlined.

If you do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.110(d). If you do so, the application shall be re-evaluated and within 90 days of the date of receipt of such request (or additional period as we may agree upon), the application shall be approved or you shall be given a written notice of opportunity for a hearing on the question of whether the application is approvable.

Sincerely yours,

3/7/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
National Center for Drugs and Biologics

cc: DEN-DO
HFN-530
HFN-534 (HZell)
K.Johnson HZell/KFurnkranz 3/7/84
R/D INITIAL HZell/MSeife HZell 3/6/84
mm:3/5/84 (0885A)
Not Approvable
Kenneth F. Furnkranz
Mar 6, 1984

Cord Laboratories
2555 W. Midway Blvd. • Broomfield, CO 80020 • [303] 469-2131

Drug

March 26, 1984

RESUBMISSION

NDA ORIG AMENDMENT

Marvin Seife, M.D., Director
Division of Generic Drugs
Office of Drug Standards HFN 530
National Center for Drugs and Biologics
5600 Fishers Lane
Rockville, Maryland 20857

RE: NDA 88-602 Corphed (Triprolidine Hydrochloride 2.5 mg. and Pseudoephedrine Hydrochloride 60 mg.) Tablets
Amended Supplement - Re-opening of File; Methods Validation Packet

Dear Dr. Seife:

We are submitting an amendment to an earlier supplement to our unapproved NDA for Corphed Tablets in accord with Section 505(b) of the Federal Food, Drug, and Cosmetic Act. This amendment is for the purpose of re-opening the file for this drug product.

Reference is made to your communication dated March 7, 1984. Cord Laboratories is hereby providing the information requested as part of a methods validation packet. The following information is enclosed with this amended supplement.

1. List of product components and finished drug product composition.

2. Specifications and methods for the finished drug product.

3. A Certificate of Analysis for lot. #83-023. Method validation information performed by Cord Laboratories including the system suitability criteria for the G.C. Methodology is also enclosed.

This information is submitted with our understanding that NDA approval may be granted prior to completion of the methods validation. Information in response to remaining issues identified in your letter of March 7, 1984 will be provided under a separate amended supplement.

RECEIVED
APR 3 1984
GENERIC DRUGS

Sincerely,

CORD LABORATORIES, INC.

Roger Schwede
Manager, Drug Regulatory Affairs

RS:cs
Enclosures

3 1984

NDA 88-602

Cord Laboratories
Attention: Roger Schwede
2555 W. Midway Boulevard
Broomfield, Colorado 80020

Dear Mr. Schwede:

Please refer to your abbreviated new drug application dated November 1, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for the preparation Corphed (Triprolidine HCl, 2.5 mg, and Pseudoephedrine HCl, 60 mg).

Also referenced is your original ANDA resubmission dated March 26, 1984.

The application is deficient and therefore not approvable under Section 505(b) of the Act as follows:

Points 1, 2, 3, 4, and 6 of our letter of March 7, 1984 have not been answered.

In response to our request for methods validation information (Point #5), a methods validation packet was submitted to the Agency. Subsequent to our request, a monograph for the above referenced drug product was published in the USP (XX, Supplement 5, effective 5/1/84). It is, therefore, no longer necessary for the method to be evaluated in our laboratory. Your GC method may be used as the finished product and stability assay method. Please be advised, however, that for regulatory purposes, your drug product must meet USP specifications using the USP methods.

The file is now closed. If you wish to reopen it, the submission should be in the form of an amendment to this application, adequately organized, which represents the information necessary to remove all deficiencies we have outlined.

If you do not agree with our conclusions, you may make a written request to file the application over protest, as authorized by 21 CFR 314.110(d). If you do so, the application shall be re-evaluated and

within 90 days of the date of receipt of such request (or additional period as we may agree upon), the application shall be approved or you shall be given a written notice of opportunity for a hearing on the question of whether the application is approvable.

Sincerely yours,

Marvin Seife 4/23/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

cc: DEN-DO
HFN-230
HFN-234 (H.C. Zell)
HCZell/KJFurnkranz
R/D INITIALED BY HCZell/MSeife HC Zell 4/20/84
mstephens: 4/19/84 (2145A)
Not approvable
Kenneth J. Furnkranz
April 20, 1984

Cord Laboratories
2555 W. Midway Blvd. • Broomfield, CO 80020 • [303] 469-2131

Orig

August 27, 1984

RESUBMISSION

NDA ORIG AMENDMENT

FPL

Marvin Seife, M.D., Director
Division of Generic Drugs
HFN 230, Room 16-70
Office of Drug Standards
Center for Drugs and Biologics
5600 Fishers Lane
Rockville, Maryland 20857

RE: NDA 88-602 Corphed Tablets (Pseudoephedrine HCl 60 mg. and Triprolidine HCl 2.5 mg.)
Amendment (Reopening the File)

Dear Dr. Seife:

We are submitting an amendment to our unapproved New Drug Application for Corphed Tablets (Pseudoephedrine HCl 60 mg. and Triprolidine HCl, 2.5 mg.) in accord with Section 505(b) of the Federal Food, Drug, and Cosmetic Act. The purpose of this amendment is for reopening the file.

This information is submitted in response to the deficiencies cited in your letter dated March 7, 1984. In order to facilitate review of the information being provided, this amendment is tabulated to correlate to the numbered deficiencies cited in your letter.

Section 1: Suppliers of the Drug Substance - Triprolidine

At the time of our original application (b)(4) a wholly owned subsidiary of (b)(4), filed for a DMF for the manufacture of Triprolidine Hydrochloride. DMF (b)(4) which they referred to is held by (b)(4) and was the subject of an agreement between these two companies.

Since that time (b)(4) has discontinued pursuing their own DMF and they will not be supplying Triprolidine Hydrochloride drug substance to Cord Laboratories. In this respect, we hereby withdraw the portion of (b)(4). We will not use any material manufactured by them in the Corphed product and will source this material from the second supplier identified in our original application, (b)(4), for which the necessary DMF reference was provided.

Section 2: Manufacturing Records

Included in Section 2 are complete composition and manufacturing summaries, along with the representative master batch record for the processing and manufacturing of the Corphed product. Packaging, labeling and control information is provided in latter sections of this amendment.

Section 3: Raw Material Control Specifications

A complete list of control specifications and methods for both actives, Triprolidine Hydrochloride and Pseudoephedrine Hydrochloride are provided. A Cord Laboratories' analysis of a typical receipt of each of these materials is also included.

Section 4: A. Stability Protocol

A revised stability protocol has been prepared. This revision addresses the responsibility to incorporate both the largest and smallest container/closure systems used into the program. The required test stations and intervals are also included.

B. Stability Data

Additional stability data generated on both the largest and smallest container/closure systems is divided. This accelerated data is used as justification for the two year expiration date for the package sizes used. A listing of the packaging specifications is also enclosed.

C. Stability Commitment

A signed stability commitment is provided as requested.

Section 5: Methods Validation Package

A methods validation package was provided on 3-26-84 as requested. Subsequently with the publication of the monograph for the Corphed product in USP XX Supplement 5, it was concluded that validation work was not necessary. The Cord methodology was accepted as the alternative to the official methods. A listing of complete finished product control specifications is provided. Based on this information we consider the deficiencies in Section 5 resolved.

Section 6: Finished Product Labeling

Revised finished product labeling and inserts are provided with the required changes having been made. Please note that the revision dates, for all Cord labeling, are coded in the lower left hand corner. Rev. 84-5 reflects the text which was established in the fifth month of 1984.

Information provided in this amendment, reopening the file, is provided towards the approval of the NDA for Corphed Tablets.

Sincerely,

CORD LABORATORIES, INC.

Roger Schwede, Manager
Drug Regulatory Affairs

RS:cs

Enclosures

NDA 88-602

DEC 11 1984

Cord Laboratories
Attention: Roger Schwede
2555 W. Midway Boulevard
Broomfield, Colorado 80020

Dear Mr. Schwede:

Please refer to your abbreviated new drug application dated March 7, 1984, submitted pursuant to Section 505(j) of the Federal Food, Drug, and Cosmetic Act for Corphen (Triprolidine and Pseudoephedrine Hydrochlorides) Tablets, USP (2.5 mg/60 mg).

Also referenced are your ANDA Original Amendment Resubmissions dated March 26, 1984, and August 27, 1984.

We have completed the review of this abbreviated application as submitted. However, before the application may be approved, it will be necessary for you to submit revised final printed labeling. The labeling should be identical in content to the submitted copy, but incorporating the revisions as outlined below:

General Comments:	A)	The established name for this combination product is not correct as presented in the submitted labels and labeling. The established name is "Triprolidine and Pseudoephedrine Hydrochlorides Tablets."
Container Label:		Quantitative information should not be part of the established name. This information should, however, be presented on the main panel if room is available. Otherwise, it may appear on the side panel.
Insert Labeling:		The insert labeling must be revised to follow our Guideline, which provides updated information. A copy of the revised Guideline is enclosed. Also the newly established name should appear on the insert labeling.

If additional information relating to the safety or effectiveness of this drug becomes available before we receive the final printed labeling, revision of that labeling may be required.

Please submit twelve copies of the final printed labels and other labeling.

In addition, we would appreciate your submitting, in duplicate, the advertising copy which you intend to use in your immediate or proposed promotional or advertising campaign. Please submit this information to the Division of Drug Advertising and Labeling (HFN-240).

The drug may not be legally marketed until you have been notified in writing that the application is approved.

Sincerely yours,

Marvin Seife 12/11/84

Marvin Seife, M.D.
Director
Division of Generic Drugs
Office of Drug Standards
Center for Drugs and Biologics

Enclosure: Labeling Guidelines

cc: DEN-DO
HFN-83
HFN-230
HFN-234 12-11-84
KJohnson/HCZell/KJFurnkranz
R/D INITIALED BY HCZell/MSeife HCZell 12/10/84
mstephens: 12/6/84 (7469A)
Approvable
Kenneth J Furnkranz
Dec 10, 1984

Orig

Cord Laboratories
2555 W. Midway Blvd. • Broomfield, CO 80020 • [303] 469-2131

FPL contains labels and package insert labeling satisfactory 4/8/85 Conf

March 29, 1985

RESUBMISSION
NDA ORIG AMENDMENT
FPL

Marvin Seife, M.D., Director
Division of Generic Drugs
HFN 230, Room 16-70
Office of Drug Standards
Center for Drugs and Biologics
5600 Fishers Lane
Rockville, Maryland 20857

RE: NDA 88-602 Corphed (Triprolidine and Pseudoephedrine Hydrochlo Tablets, USP (2.5 mg/60 mg.)
Amendment

Dear Dr. Seife:

Reference is made to your communication dated December 11, 1984. Enclosed please find printed finished labeling for the container and insert which have been revised per your recommendations.

This information is submitted toward the approval of the Abbreviated New Drug Application.

Sincerely,

CORD LABORATORIES, INC.

Roger Schwede, Manager
Drug Regulatory Affairs

RS:cs

Enclosures

RECEIVED
APR 2 1985
GENERIC DRUGS

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 88-602

DATE APPROVAL LETTER ISSUED:

TO: Press Relations Staff (HFI-40)

FROM: [XX] Bureau of Drugs [ ] Bureau of Veterinary Medicine

ATTENTION

Forward original of this form for publication only after approval letter has been issued and the date of approval has been entered above.

TYPE OF APPLICATION: [ ] ORIGINAL NDA [ ] SUPPLEMENT TO NDA [XX] ABBREVIATED ORIGINAL NDA [ ] SUPPLEMENT TO ANDA

CATEGORY: [XX] HUMAN [ ] VETERINA

TRADE NAME (or other designated name) AND ESTABLISHED OR NONPROPRIETARY NAME (if any) OF DRUG:
Corphed (Triprolidine and Pseudoephedrine Hydrochlorides)

DOSAGE FORM: Tablets

HOW DISPENSED: [XX] RX [ ] OTC

ACTIVE INGREDIENT(S) (as declared on label. List by established or nonproprietary name(s) and include amount(s), if amount is declared on label.)

Triprolidine HCl, USP - 2.5 mg
Pseudoephedrine HCl, USP - 60 mg

NAME OF APPLICANT (Include City and State)

Cord Laboratories, Inc.
Broomfield, Colorado 80020

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

Antihistamine/Decongestant

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME: Kenneth J. Furnkranz — Kenneth J. Furnkranz — DATE: April 11, 1985

FORM APPROVED BY

NAME: Howard C. Zell, Ph.D. — Howard C. Zell — DATE: 4/11/85

FORM FD 1642 (2/75) PREVIOUS EDITION MAY BE USED UNTIL SUPPLY IS EXHAUSTED.