VOLUME 3. 1

NEW DRUG APPLICATION

NDA No. 88596

NAME OF APPLICANT

CAMALL

NAME OF NEW DRUG

Phentermine HCl

37.5 mg Tab.

ARCHIVAL COPY

FORM FDA 2626 (7/84)

THIS SUBMISSION: VOL. _____ OF _____ VOLS.

VOLUME

1/1

NEW DRUG APPLICATION

NDA No. 88-596

NAME OF APPLICANT

NAME OF NEW DRUG

Camall Company
70945 Van Dyke Avenue
Romeo, MI 48065

Phentermine HCL
37.5 mg. White with
Blue Specks
Tablets

THIS SUBMISSION: VOL. _____ OF _____ VOL.

FORM FD 2626 (7/75)

VOLUME 2 of 4

NEW DRUG APPLICATION

NDA No. 88-596

NAME OF APPLICANT

CAMALL Co

NAME OF NEW DRUG

Phentermine HCl

37.5 mg Tablets

(White w/ Blue Specks)

THIS SUBMISSION: VOL. _____ OF _____ VOLS.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

ANDA 88-596/S-006

Camall Company
Attention: Eugene Schmall
P.O. Box 218
Washington, Michigan 48094

Dear Sir:

Reference is made to your supplemental new drug application submitted pursuant to Section 314.70 of the Regulations, dated July 7, 1987, regarding your abbreviated new drug application for Phentermine Hydrochloride, 37.5 mg, White/Blue Specks Tablets.

We acknowledge your amendment dated August 1, 1987.

The supplemental application provides for an alternate analytical laboratory facility:

We have reviewed the material submitted and have the following comments:

1. Clarify how samples will be obtained and transferred to this facility. Describe all tests to be conducted for raw materials, in-process controls, and the drug product at the "alternate Laboratory Facility." Explain the procedures to track and control the flow of samples.

2. Clarify if all instruments, gauges and recording devices are calibrated to demonstrate accuracy prior to use.

3. Please submit Certificates of Analysis on the same lot of the drug product comparing test results obtained by your laboratory at Michigan with that supplied by
of

4. Clarify water testing at this site.

Please let us have your response promptly.

Sincerely yours,

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

05

APR 4 1984

NDA 88-596

Camall Company
Attention: Eugene M. Schmall
Post Office Box 218
Washington, Michigan 48094

Dear Mr. Schmall:

Reference is made to your abbreviated new drug application dated November 23, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Phentermine Hydrochloride Tablets, 37.5 mg (White/Blue Specks).

Reference is also made to your amendments dated February 29, 1984, and February 2, 1984.

We refer also to our letter dated February 16, 1984.

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

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

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

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

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). Also, please do not use Form FD-2253 for this submission.

For Subsequent Campaigns: We call your attention to Regulation 21 CFR 310.300(b)(3) which requires that all material for any subsequent advertising or promotional campaigns 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 application.

Sincerely yours,

Marvin Seife 4/4/84

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: DET-DO
HFN-530
HFN-616
HFN-534 (HCZell)
LDavidson/HCZell/4/2/84
HCZell/MSeife/4/3/84
gp/4/3/84
1625A APPROVAL

4/3/84

4/3/84

NOTICE OF APPROVAL
NEW DRUG APPLICATION OR SUPPLEMENT

NDA NUMBER: 88-596

DATE APPROVAL LETTER ISSUED: APR 4 1984

TO: Press Relations Staff (HFI-40)

FROM:
- [X] 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
- [X] ABBREVIATED ORIGINAL NDA
- [ ] SUPPLEMENT TO ANDA

CATEGORY
- [X] HUMAN
- [ ] VETERINARY

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

Phentermine Hydrochloride Tablets, 37.5 mg (White with Blue Specks)

DOSAGE FORM: Tablets ORIGINAL ABBREVIATED

HOW DISPENSED
- [X] 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.)*

Phentermine Hydrochloride, 37.5 mg

NAME OF APPLICANT *(Include City and State)*

Camall Company
Post Office Box 218
Washington, Michigan 48094

PRINCIPAL INDICATION OR PHARMACOLOGICAL CATEGORY

Anorectic

COMPLETE FOR VETERINARY ONLY

ANIMAL SPECIES FOR WHICH APPROVED

COMPLETE FOR SUPPLEMENT ONLY

CHANGE APPROVED TO PROVIDE FOR

FORM PREPARED BY

NAME: L. Davidson — DATE: March 30, 1984

4/3/84

FORM APPROVED BY

NAME: H. C. Zell, Ph.D. — DATE: April 2, 1984

4/3/84

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

CHEMIST'S REVIEW NDA 88-596

3. NAME AND ADDRESS OF APPLICANT
Camall Company
Romeo, Michigan 48065

4. AF NUMBER
DESI 5378
FR 8/8/70, 7/19/74

5. SUPPLEMENT(s)
Original (11/23/83)

6. NAME OF DRUG
Phentermine Hydrochloride

8. SUPPLEMENT(s) PROVIDE(s) FOR:
Original Submission (amended)

9. AMENDMENTS AND OTHER DATES:
Correspondence History
FIRM
3/1/84 Amendment dated 2/29/84 - FPL, Reply to 2/16/84 letter.

FDA
2/22/84 Memo from HFN-322 (Hartley) - in CGMP compliance
2/15/84 Review (Davidson) - Not Approvable
2/16/84 Letter sent (Davidson) - Not Approvable, Request facilities for CGMP from container info., stability protocol revisions, labeling revisions.

10. PHARMACOLOGICAL CATEGORY
Anorectic

11. HOW DISPENSED
RX

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM(s)
Tablet

14. POTENCY
37.5 mg (White with Blue Specks)

15. CHEMICAL NAME AND STRUCTURE
$C_{10}H_{15}N \cdot HCl$, MW 185.7

17. COMMENTS
Deficiencies noted:
Remaining deficiencies satisfactorily answered 2/29/84.

18. CONCLUSIONS AND RECOMMENDATIONS
Approval letter should issue. Methods validation is not required since this is a compendial product and not the first ANDA. Dissolution has been approved by BIO. Full manufacturing and controls are required as per Federal Register Notice of 7/19/74.

19. REVIEWER: LDavidson HCZell
DATE COMPLETED: 3/30/84 4/2/84
4/3/84 4/3/84

20. COMPONENTS AND COMPOSITION
Satisfactory (See 2/15/84 Review)

21. FACILITIES AND PERSONNEL
Satisfactory (2/15/84)

22. SYNTHESIS
N/A

23. RAW MATERIAL CONTROLS
A. NEW DRUG SUBSTANCE
Satisfactory (2/15/84)

B. OTHER INGREDIENTS
Satisfactory (2/15/84)

24. OTHER FIRM(s)
Satisfactory

A signed statement certifying CGMP compliance and a brief description of the duties to be performed was submitted for 2/29/84.
is an alternate testing lab for

A brief description of the facilities and equipment for was provided 2/29/84.

25. MANUFACTURING AND PROCESSING
Satisfactory (2/15/84)

26. CONTAINER
Satisfactory
A corrected page 20 was submitted 2/29/84 which lists a plastic cap rather than a white metal cap. Specifications for the white plastic cap were previously submitted and are satisfactory.

27. PACKAGING AND LABELING
Satisfactory (2/15/84)

28. LABORATORY CONTROLS (IN-PROCESS AND FINISHED DOSAGE FORM)
Satisfactory (2/15/84)

29. STABILITY
Satisfactory
A commitment was made 2/29/84 to perform and promptly report the results of complete stability tests on the first three (3) production lots after any changes in packaging, etc., as well as formulation changes made.

The stability protocol for accelerated studies on pages 239, 371D and 373A were revised to be consistent in including test stations at 30 and 60 days as well as 90 days. The stability program on page 371D was further revised to delete the statement that 'The accelerated study will permit 24 months additional expiry dating on top of the ambient data generated'.

The proposed expiration date of two years is tentatively satisfactory based on challenge data for Lot #9-2983 in 100's (with and without cap) at 0, 1, 2, and 3 months at 37°C/75% RH.

30. CONTROL NUMBERS
Satisfactory (2/15/84)

31. SAMPLES AND RESULTS
Satisfactory (2/15/84)

32. LABELING
Satisfactory
As per medical review of 3/30/84 (Johnson), the FPL container and insert labeling submitted 2/29/84 is satisfactory.

33. ESTABLISHMENT INSPECTION
Satisfactory
Memo dated 2/22/84 from HFN-322 (Hartley) states that
is in CGMP compliance, Memo dated 12/13/83 from HFN-322 (Hartley)
states tht are all in CGMP
compliance.

34. RECALLS
Satisfactory (2/15/84)

DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

TO :Manufacturing Review Branch (HFN-322)
Division of Drug Quality Compliance

DATE: February 14, 1984

FROM :Division of Generic Drugs HFN-534
Requester's Name Lynn A. Davidson PHONE: 443-1390

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 88-596

DRUG TRADE MARK (if any) —

DRUG NONPROPRIETARY NAME: Phentermine Hydrochloride

DOSAGE FORM AND STRENGTH(S): 37.5 mg TCM White with Blue Spec-

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

APPLICANT'S NAME: Canall Company
ADDRESS: P.O. Box 218, Washington, MI 48094

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

Testing Lab:

OK 9/82

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

Reason: ____

****

FOR HFN-322 USE ONLY:

Request Rec'd: ____ Inspection Requested: ____ (if applicable)

Firm(s) are in Compliance With GMPs: Approved 3/22/84
Basis for Decision: Above
Reviewing CSO:

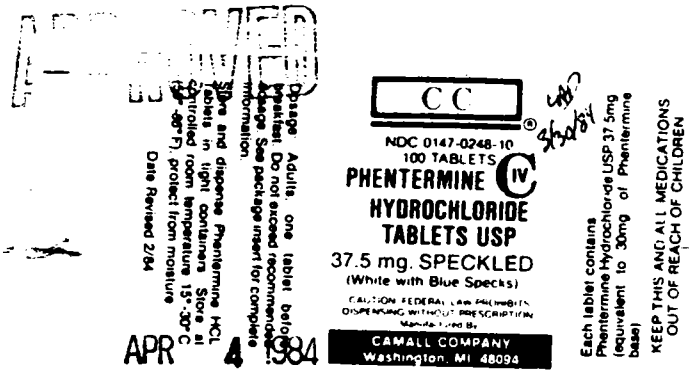
cc: HFN-530
HFN-534
HFN-322

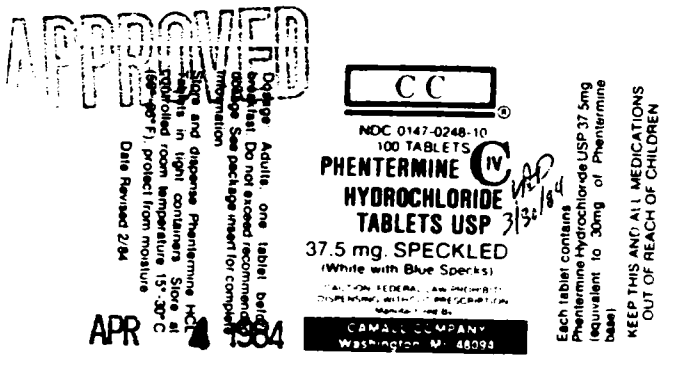
(1/83)

Labeling: ORIGINAL

NDA No: 88596 Rec'd. 3/1/84

Reviewed by: _____





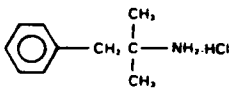
APP

APPROVED 3/30/84

APR 4 1984

PHENTERMINE Ⓒ IV HYDROCHLORIDE TABLETS USP, 37.5mg.

DESCRIPTION: Each tablet contains Phentermine Hydrochloride USP 37.5mg (equivalent to 30mg phentermine base). Phentermine hydrochloride is designated chemically as α, α-Dimethylphenethylamine hydrochloride. It is a white, odorless, hygroscopic crystalline powder which is soluble in water and lower alcohols.



ACTIONS: Phentermine hydrochloride is a sympathomimetic amine with pharmacologic activity similar to the prototype drugs of this class used in obesity, the amphetamines. Actions include central nervous system stimulation and elevation of blood pressure. Tachyphylaxis and tolerance have been demonstrated with all drugs of this class in which these phenomena have been looked for.

Drugs of this class used in obesity are commonly known as "anorectics" or "anorexigenics." It has been established, however, that the action of such drugs in treating obesity is primarily one of appetite suppression. Other central nervous system actions, or metabolic effects, may be involved, for example.

Adult obese subjects instructed in dietary management and treated with "anorectic" drugs, lose more weight on the average than those treated with placebo and diet, as determined in relatively short-term clinical trials. The magnitude of increased weight loss of drug-treated patients over placebo-treated patients is only a fraction of a pound a week. The rate of weight loss is greatest in the first weeks of therapy for both drug and placebo subjects and tends to decrease in succeeding weeks. The possible origins of the increased weight loss due to the various drug effects are not established. The amount of weight loss associated with the use of an "anorectic" drug varies from trial to trial, and the increased weight loss appears to be related in part to variables other than the drug prescribed, such as the physician-investigator, the population treated, and the diet prescribed. Studies do not permit conclusions as to the relative importance of the drug and non-drug factors on weight loss.

The natural history of obesity is measured in years, whereas, the studies cited are restricted to a few weeks duration; thus, the total impact of drug-induced weight loss over that of diet alone must be considered clinically limited.

INDICATIONS: Phentermine hydrochloride is indicated in the management of exogenous obesity as a short term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction.

The limited usefulness of agents of this class (see ACTIONS) should be measured against possible risk factors in their use such as those described below.

CONTRAINDICATIONS: Advanced arteriosclerosis, symptomatic cardiovascular disease, moderate to severe hypertension, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma.

Agitated states.

Patients with a history of drug abuse.

During or within 14 days following the administration of monoamine oxidase inhibitors (hypertensive crisis may result).

WARNINGS: Tolerance to the anorectic effect usually develops within a few weeks. When this occurs, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Phentermine hydrochloride may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly.

Drug Dependence: Phentermine hydrochloride is related chemically and pharmacologically to the amphetamines. Amphetamines and related stimulant drugs have been extensively abused, and the possibility of abuse of phentermine hydrochloride should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with intense psychological dependence and severe social dysfunction. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia.

APPROVED 3/30/84

APR 4 1984

Usage in Pregnancy: No reproduction studies or teratology studies of phentermine hydrochloride, in animals or humans, have been published. Therefore, use of phentermine hydrochloride by women who are or may become pregnant, requires that the potential benefit be weighed against the possible hazard to mother and infant.

Usage in Children: Phentermine hydrochloride is not recommended for use in children under 12 years of age.

PRECAUTIONS: Caution is to be exercised in prescribing phentermine hydrochloride for patients with even mild hypertension.

Insulin requirements in diabetes mellitus may be altered in association with the use of phentermine hydrochloride and the concomitant dietary regimen.

Phentermine hydrochloride may decrease the hypotensive effect of guanethidine.

The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage.

Phentermine Hydrochloride 37.5mg. White with Green Specks oblong tablets contain FD&C Yellow #5 (tartrazine) which may cause allergic-type reactions (including bronchial asthma) in certain susceptible persons. Although the overall incidence of FD&C Yellow #5 (tartrazine) sensitivity in the general population is low, it is frequently seen in patients who also have aspirin hypersensitivity.

ADVERSE REACTIONS:
Cardiovascular: Palpitation, tachycardia, elevation of blood pressure.
Central Nervous System: Overstimulation, restlessness, dizziness, insomnia, euphoria, dysphoria, tremor, headache; rarely psychotic episodes at recommended doses.
Gastrointestinal: Dryness of the mouth, unpleasant taste, diarrhea, constipation, other gastrointestinal disturbances.
Allergic: Urticaria.
Endocrine: Impotence, changes in libido.

OVERDOSAGE: Manifestations of acute overdosage with phentermine hydrochloride include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultive behavior, hallucinations, panic states.

Fatigue and depression usually follow the central stimulation.

Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. In fatal poisoning, death is usually preceded by convulsions and coma.

Management of acute phentermine hydrochloride intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Acidification of the urine increases phentermine hydrochloride excretion. Intravenous phentolamine (Regitine) has been suggested for possible acute, severe hypertension, if this complicates phentermine hydrochloride overdosage.

DOSAGE AND ADMINISTRATION: The usual adult dose is one tablet daily, administered before breakfast. Dosage may be adjusted to the patient's need. For some patients, ½ tablet daily may be adequate, while in some cases it may be desirable to give ½ tablet two times a day. Do not exceed this recommended dosage.

Phentermine hydrochloride is not recommended for use in children under 12 years of age.

HOW SUPPLIED:

YELLOW TABLETS Bottles of 100, 500, and 1000 tablets.
Each Phentermine Hydrochloride 37.5mg yellow oblong tablet (equivalent to 30mg phentermine base) is 0.225 X 0.550, scored, with CC 232 logo imprinting.

WHITE WITH BLUE SPECKS TABLETS Bottles of 100 tablets.
Each Phentermine Hydrochloride 37.5mg White with Blue Specks tablets (equivalent to 30mg phentermine base) is 0.200 X 0.400 scored, with CC 248 logo imprinting.

WHITE WITH GREEN SPECKS TABLETS: Bottles of 100 tablets.
Each Phentermine Hydrochloride 37.5mg White with Green Specks tablets (equivalent to 30mg phentermine base) is 0.200 X 0.400, scored, with CC 248 logo imprinting.

Special Handling and Storage Conditions: Package and store in accordance with DEA regulations pertaining to Schedule IV controlled substances. Keep this and all medication out of the reach of children. **CAUTION:** Federal law prohibits dispensing without prescription. Manufactured by Camall Company, Inc — Washington, MI 48094. Revised 2/84

Labeling: ORIGINAL
NDA No: 86-504
Reviewed by: Bo'd. 3/30/84

NDA 88-596

FEB 10 84

Camall Company
Attention: Eugene M. Schmall
P.O. Box 218
Washington, Michigan 48094

Dear Mr. Schmall:

Please refer to your abbreviated new drug application dated November 23, 1983, submitted pursuant to Section 505(b) of the Federal Food, Drug, and Cosmetic Act for Phentermine Hydrochloride Tablets, 37.5 mg (White/Blue Specks).

Reference is also made to your amendment dated February 2, 1984.

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

1. It fails to provide a brief description of the facilities and equipment for either directly or by appropriate DMF reference. Full manufacturing and controls are required for this application in accord with the Federal Register notice dated July 19, 1974.

2. It fails to include a signed statement from certifying that the methods used in, and the facilities and controls used for, the manufacture, processing, packing, and holding of the drug are in conformity with current good manufacturing practice in accord with Parts 210 and 211 of 21 CFR.

   Clarification of the duties to be performed by the is also requested.

3. It fails to provide specifications for the white metal closure system listed on page 20. We note that specifications provided refer only to a white plastic (CRC) closure system. Please correct page 20 if a white metal closure is not used for the product in this application.

4. It fails to include a commitment to perform and promptly report the results of complete stability tests on the first three (3) production lots after any future change in packaging, etc., as well as formulation changes. The commitment on pages 240 and 369 refers only to changes in formulas.

5. It fails to be consistent in the description of the protocol for accelerated studies on pages 239, 371D and 373A. The testing schedule for accelerated studies should in all references include test stations at 30 and 60 days as well as 90 days. The stability program on page 371D must be revised to delete the statement that 'The accelerated study will permit 24 months additional expiry dating on top of the ambient data generated'. Accelerated data may not be combined with room temperature data to extend the expiration dating beyond 24 months. The storage conditions used for a given stability study should not be altered in the middle of the study for any reason.

6. It fails to provide twelve (12) copies of final printed labeling (FPL) which incorporate the following revisions:

I. Container Labeling:
   a) Title: Phentermine Hydrochloride Tablets USP
   b) Right Panel:
      1) Add.... (equivalent to 30 mg of phentermine base)
      2) Delete.... Store below 30°C (86°F). (Note - this statement is in conflict with the left panel recommendations).
   c) Left Panel:
      1) Replace packaging and dispensing instructions with:
         Store and dispense Phentermine HCl Tablets in tight containers. Store at controlled room temperature 15° - 30°C (59° - 86° F), protect from moisture.

II. Insert Labeling:
   a) DESCRIPTION:
      1) .... Dimethyl .... (capital D) .... It is a white, odorless, hygroscopic, crystalline powder which is soluble in water and lower alcohols.
   b) HOW SUPPLIED:
      1) Describe if tablets are scored or unscored.
      2) We note that white tablets with green specks are also manufactured. They should therefore be added to the HOW SUPPLIED section to be consistent with the draft insert labeling for 88-600.

3) We believe the 'readability' of this section could be greatly improved by constructing a Table for the information presented. In its present form, the information is very difficult to find.
4) The firm is responsible for only including package sizes which have approved package/labels.

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 2/16/84

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

cc: DET-DO
HFN-530
HFN-534 (H.C. Zell)
KJohnson/HCZell/LDavidson
R/D INITIALED BY HCZell/MSeife
mstephens: 2/14/84 (0402A
Not Approvable

2-16-84
2/15/84

2/15/84

CHEMIST'S REVIEW NDA 88-596

3. NAME AND ADDRESS OF APPLICANT
Camall Company
Romeo, Michigan 48065

4. AF NUMBER
DESI 5378
FR 8/8/70, 7/19/74

5. SUPPLEMENT(s)
Original (11/23/83)

6. NAME OF DRUG
Phentermine Hydrochloride

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

9. AMENDMENTS AND OTHER DATES:
Correspondence History

FIRM

11/30/83 Original ANDA submission dated 11/23/83
2/6/84 Amendment dated 2/2/84 - Stability

FDA

12/1/83 Inspection Request (Rosen)

12/2/83 Acknowledgement of ANDA submission
12/7/83 Memo from Seife requesting BIO review
12/13/83 Memo from HFN-322 (Hartley) - and
are all in CGMP compliance
12/15/83 BIO Review (Chen, Ise) - Application approvable
12/20/83 Letter sent (Seife) - BIO recommendations
1/10/84 Medical Review (Johnson) - Labeling requires revision

10. PHARMACOLOGICAL CATEGORY
Anorectic

11. HOW DISPENSED
RX

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM(s)
Tablet

14. POTENCY
37.5 mg\White with Blue Specks

15. CHEMICAL NAME AND STRUCTURE
$C_{10}H_{15}N \cdot HCl$, M.W. 185.7

17. COMMENTS

Deficiencies noted:

a) A brief description of the facilities and equipment for is required.

b) A statement certifying CGMP compliance and a description of tests performed by re required.

c) Commitment is required to perform and promptly report the results of complete stability tests on the first 3 production lots after any future change in packaging, etc., as well as formulation changes.

d) The statement that 'the accelerated study will permit 24 months additional expiry dating on top of the ambient data generated'. (Page 371D).

e) The stability data protocol on p. 239 and 373A should be revised to include test stations at 30, 60, and 90 days for accelerated studies.

f) Labeling revision required in accord with 1/10/84 medical review.

g) Clarification is requested of white metal cap listed on page 20 for which the specifications were not provided.

18. CONCLUSIONS AND RECOMMENDATIONS

A not approvable letter should issue describing the deficiencies as detailed in review section 17 above. Methods validation is not required since this is a compendial product and not the first ANDA. Dissolution has been approved by BIO. Full manufacturing and controls are required as per the Federal Register Notice of 7/19/74.

19. REVIEWER: DATE COMPLETED: 2/15/84

2/15/84

REVIEW OF PROFESSIONAL LABELING

ANDA - FPL

DATE OF REVIEW: 1-10-84

ANDA #: 88-593 (white with blue specks)
88-600 (white with green specks) NAME OF FIRM: Camall Co.

NAME OF DRUG: Generic: Phentermine Hydrochloride Tablets

DATE OF SUBMISSION: 11-30-83

COMMENTS:

Container: Not satisfactory

a) Title)

Phentermine
Hydrochloride Tablets
USP

b) Right Panel: (add)

(equivalent to phentermine base.....30 mg)

c) (delete) Store below 30°C (86°F). (Note - this statement is in conflict with the left panel recommendations)

d) Left panel: Store and dispense Phentermine HCl Tablets in tight containers. Store at controlled room temperature 15°-30°C (59°-86°F), protect from moisture.

Insert: NOT satisfactory. Describe if tablets are scored or unscored, in the HOW SUPPLIED SECTION.

RECOMMENDATIONS:

1. Inform firm of the above comments.

2. Request that they revise labeling as recommended, then prepare and submit revised container labels.

Kent T. Johnson

cc:
dup
KTJ/cl/1-11-84

DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

TO :Manufacturing Review Branch (HFN-322) DATE: February 14, 1984
Division of Drug Quality Compliance

FROM :Division of Generic Drugs HFN-534
Requester's Name Lynn A Davidson PHONE: 443-1390

SUBJECT: ESTABLISHMENT EVALUATION REQUEST

NDA, ANDA, AND SUPPLEMENT NUMBER: 88-596

DRUG TRADE MARK (if any) _____

DRUG NONPROPRIETARY NAME: Phentermine Hydrochloride

DOSAGE FORM AND STRENGTH(S): 37.5 mg TCM white with Blue Specks

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

APPLICANT'S NAME: Carall Company
ADDRESS: P.O. Box 218, Washington, MI 48094

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

Testing lab:

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

Reason: _____

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FOR HFN-322 USE ONLY:

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

Firm(s) are in Compliance With GMPs: _____
Basis for Decision: _____
Reviewing CSO: _____ Concurrance: _____

cc: HFN-530
HFN-~~534~~
HFN-322

FORM FDA 3274 (1/83)