

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

Approval Package for:

APPLICATION NUMBER:

89-557/S-004

Generic Name: Hydrocodone bitartrate and
Acetaminophen Elixir
7.5mg/500mg per mL

Sponsor: Mikart, Inc.

Approval Date: July 31, 1998

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

89-557/S-004

CONTENTS

Reviews / Information Included in this ANDA Review.

Approval Letter(s)	X
Tentative Approval Letter(s)	
Final Printed Labeling	
CSO Labeling Review(s)	
Medical Officer Review(s)	
Chemistry Review(s)	X
Microbiology Review(s)	
Bioequivalence Review(s)	
Administrative Document(s)	X
Correspondence	X

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-557/S-004

APPROVAL LETTER

ANDA

DRUG PRODUCT

74-028/008	Amanatadine Hydrochloride Syrup USP, 50 mg/5 mL
40-062/002	Methazolamide Tablets USP, 25 mg, 50 mg
40-085/011	Butalbital, Acetaminophen, and Caffeine Capsules, 50 mg/500 mg/40 mg
89-987/006	Butalbital and Acetaminophen Tablets, 50 mg/325 mg
89-988/005	Butalbital and Acetaminophen Tablets, 50 mg/650 mg
89-451/031	Butalbital, Acetaminophen and Caffeine Tablets, USP 50 mg/500 mg/40 mg
89-007/035	Butalbital, Acetaminophen and Caffeine Capsules, 50 mg/325 mg/40 mg
89-175/031	Butalbital, Acetaminophen and Caffeine Tablets, USP 50 mg/325 mg/40 mg
81-319/017	Pyrazinamide Tablets, USP 500 mg
40-109/002	Acetaminophen, Caffeine and Dihydrocodeine Bitartrate Capsules, 356.4 mg/30 mg/16 mg
81-226/004	Hydrocodone Bitartrate and Acetaminophen Elixir, 5 mg/500 mg per 15 mL
89-557/004	Hydrocodone Bitartrate and Acetaminophen Elixir, 5 mg/500 mg per 5 mL
81-118/001	Isoniazid Syrup, USP 50 mg/5 mL
81-051/015	Hydrocodone Bitartrate and Acetaminophen Elixir, 7.5 mg/500 mg per 15 mL
40-090/001	Isoniazid Tablets, USP 100 mg & 300 mg
89-008/046	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg
89-271/037	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 5 mg/500 mg
89-699/026	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 7.5 mg/500 mg
89-697/003	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 5 mg/500 mg (blue)
89-689/038	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 7.5 mg/650 mg
81-223/017	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 10 mg/650 mg
81-070/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (gray/black)
81-067/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (gray/lavender)
81-068/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (yellow/orange)
81-096/004	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/30 mg
89-698/015	Hydrocodone Bitartrate and Acetaminophen Tablets USP, 2.5 mg/500 mg
81-069/005	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (blue/aqua)

81-095/004	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/15 mg
89-450/008	Acetaminophen and Codeine Phosphate Oral Solution USP, 120 mg/12 mg per 5 mL
81-097/005	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/60 mg
89-363/004	Acetaminophen and Codeine Phosphate Tablets USP, 650 mg/60 mg
89-231/025	Acetaminophen and Codeine Phosphate Tablets USP, 650 mg/30 mg
89-238/013	Acetaminophen and Codeine Phosphate Tablets USP, 300 mg/30 mg
89-244/018	Acetaminophen and Codeine Phosphate Tablets USP, 300 mg/60 mg

cc: ANDA #s Attached List
 Division Files
 Field Copy
 HFD-82
 HFD-210/B.Poole

Endorsements:

HFD-647/ MPSelvam/ 6/12/1998 — *[Signature]* 7/31/98
 HFD-647/ UVVenkataram/6/12/98
 HFD-647/TAmes/6/14/98 *[Signature]* H.V. Venkataram
 FT/njg/6/15/98 *[Signature]* 7/31/98
 X:\wpfile\branch7\Selvam\40109s02.LMS
 x:\new\firmam\mikart\ltrs&rev\40109s02.apf
 APPROVED

APPEARS THIS WAY
 ON ORIGINAL

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-557/S-004

CHEMISTRY REVIEW(S)

OFFICE OF GENERIC DRUGS
REVIEW OF SUPPLEMENT TO
ABBREVIATED NEW DRUG APPLICATION

5004

1. ANDA NUMBER

40-109 and attached list of Mikart Supplements

2. NAME AND ADDRESS OF APPLICANT

Mikart, Inc.,
1750, Chattahoochee Ave, NW
Atlanta, GA-30318

3. PURPOSE OF AMENDMENT/SUPPLEMENT

These (Global) Supplements provide for an additional

4. DATE(S) OF SUBMISSION(S)

January 6, 1998- Original submissions

5. PHARMACOLOGICAL CATEGORY

See the attachment

6. TRADE NAME

See the attachment

7. NONPROPRIETARY NAME

See the attachment

8. DOSAGE FORM

See the attachment

9. POTENCY

See the attachment

10. RX OR OTC

See the attachment

11. RELATED IND/NDA/DMF

N/A

12. STERILIZATION

N/A

13. LABELING

Review Status: N/A

14. BIOEQUIVALENCY STATUS

Review Status: N/A

15. ESTABLISHMENT INSPECTION

Review Status: Acceptable; CDER Establishment Evaluation Report, 6/11/1998 based on profile.

16. COMPONENTS, COMPOSITION, MANUFACTURING & CONTROLS

No changes in Components, Composition, manufacturing or Controls proposed.

17. PACKAGING

Review Status: N/A

18. STABILITY

Review Status: N/A

19. REMARKS AND CONCLUSION

Supplements are Approved

20. ORDER OF REVIEW:

The application submissions covered by this review were taken in the date order of receipt

If no, explain reason(s) below:

New reviewer in training

SPOT? ~~_____~~

If yes, complete form

21. REVIEWER AND DATE COMPLETED :

Mouna P.Selvam, Ph.D., / 12, June 1998

CC:
Mikart ANDA Supplements (34 Applications) [Global]
Division Files (x34)
Field Copy
HFD-600/Reading File

22. Endorsements

HFD-647/M.Selvam
HFD-647/U.Venkataram

 7/31/98
U.V. Venkataram 7/31/98

**APPEARS THIS WAY
ON ORIGINAL**

ANDA

DRUG PRODUCT

74-028/008	Amanatadine Hydrochloride Syrup USP, 50 mg/5 mL
40-062/002	Methazolamide Tablets USP, 25 mg, 50 mg
40-085/011	Butalbital, Acetaminophen, and Caffeine Capsules, 50 mg/500 mg/40 mg
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89-988/005	Butalbital and Acetaminophen Tablets, 50 mg/650 mg
89-451/031	Butalbital, Acetaminophen and Caffeine Tablets, USP 50 mg/500 mg/40 mg
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89-175/031	Butalbital, Acetaminophen and Caffeine Tablets, USP 50 mg/325 mg/40 mg
81-319/017	Pyrazinamide Tablets, USP 500 mg
40-109/002	Acetaminophen, Caffeine and Dihydrocodeine Bitartrate Capsules, 356.4 mg/30 mg/16 mg
81-226/004	Hydrocodone Bitartrate and Acetaminophen Elixir, 5 mg/500 mg per 15 mL
89-557/004	Hydrocodone Bitartrate and Acetaminophen Elixir, 5 mg/500 mg per 5 mL
81-118/001	Isoniazid Syrup, USP 50 mg/5 mL
81-051/015	Hydrocodone Bitartrate and Acetaminophen Elixir, 7.5 mg/500 mg per 15 mL
40-090/001	Isoniazid Tablets, USP 100 mg & 300 mg
89-008/046	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg
89-271/037	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 5 mg/500 mg
89-699/026	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 7.5 mg/500 mg
89-697/003	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 5 mg/500 mg (blue)
89-689/038	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 7.5 mg/650 mg
81-223/017	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 10 mg/650 mg
81-070/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (gray/black)
81-067/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (gray/lavender)
81-068/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (yellow/orange)
81-096/004	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/30 mg
89-698/015	Hydrocodone Bitartrate and Acetaminophen Tablets USP, 2.5 mg/500 mg
81-069/005	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (blue/aqua)

81-095/004	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/15 mg
89-450/008	Acetaminophen and Codeine Phosphate Oral Solution USP, 120 mg/12 mg per 5 mL
81-097/005	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/60 mg
89-363/004	Acetaminophen and Codeine Phosphate Tablets USP, 650 mg/60 mg
89-231/025	Acetaminophen and Codeine Phosphate Tablets USP, 650 mg/30 mg
89-238/013	Acetaminophen and Codeine Phosphate Tablets USP, 300 mg/30 mg
89-244/018	Acetaminophen and Codeine Phosphate Tablets USP, 300 mg/60 mg

APPEARS THIS WAY
ON ORIGINAL

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-557/S-004

**ADMINISTRATIVE
DOCUMENTS**

CDER Establishment Evaluation Report
for June 11, 1998

Application: **ANDA 89557/004**
Stamp: **13-JAN-1998** Regulatory Due:
Applicant: **MIKART**
2090 MARIETTA BLVD NORTHWEST
ATLANTA, GA 30318

Priority:
Action Goal:
Brand Name: **LORTAB**
Established Name: **ACETAMINOPHEN;HYDROCODON**
E BITARTRATE
Generic Name:
Dosage Form: **ELX (ELIXIR)**
Strength: **500 MG/5 MG PER 15 ML**

Org Code: **600**

District Goal: **13-JUN-1998**

FDA Contacts: **T. AMES (HFD-617)**
U. VENKATARAM (HFD-647)

301-827-5849 , Project Manager
301-827-5849 , Team Leader

Overall Recommendation:

ACCEPTABLE on 10-JUN-1998 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment: _____

DMF No:
AADA No:

Profile: **CTL** OAI Status: **NONE**
Last Milestone: **OC RECOMMENDATION**
Milestone Date: **10-JUN-1998**
Decision: **ACCEPTABLE**
Reason: **BASED ON PROFILE**

Responsibilities: _____

**APPEARS THIS WAY
ON ORIGINAL**

5-004

89.557

ELECTRONIC MAIL MESSAGE

Date: 16-Jan-1998 03:57pm EST
From: Kassandra Sherrod
SHERRODK
Dept: HFD-617 MPN2 113
Tel No: 301-827-5849 FAX 301-594-3839

8 addressees

C: 9 addressees

Subject: Mikart, Inc. Submits Multiple Supplements

On January 6, 1998, Mikart Inc. submitted 34 supplements to multiple applications to provide for an additional

These supplements may be reviewed as a "GLOBAL". The applications affected are as follows:

Table with 3 columns: ANDA, DRUG PRODUCT, CHEMIST. Includes sub-sections for BRANCH 3, BRANCH 5, and BRANCH 6. Lists various drug products like Amanatadine Hydrochloride Syrup USP, Methazolamide Tablets USP, and Butalbital, Acetaminophen, and Caffeine formulations.

	Dihydrocodeine Bitartrate Capsules, 356.4 mg/30 mg/16 mg	
81-226/004	Hydrocodone Bitartrate and Acetaminophen Elixir, 5 mg/500 mg per 15 mL	"
89-557/004	Hydrocodone Bitartrate and Acetaminophen Elixir, 5 mg/500 mg per 5 mL	"
81-118/001	Isoniazid Syrup, USP 50 mg/5 mL	"
81-051/015	Hydrocodone Bitartrate and Acetaminophen Elixir, 7.5 mg/500 mg per 15 mL	"
40-090/001	Isoniazid Tablets, USP 100 mg & 300 mg	Basaran
89-008/046	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg	Tang
89-271/037	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 5 mg/500 mg	"
89-699/026	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 7.5 mg/500 mg	"
89-697/003	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 5 mg/500 mg (blue)	"
89-689/038	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 7.5 mg/650 mg	"
81-223/017	Hydrocodone Bitartrate and Acetaminophen Tablets, USP 10 mg/650 mg	"
81-070/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (gray/black)	"
81-067/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (gray/lavender)	"
81-068/006	Hydrocodone Bitartrate and Acetaminophen Capsules, 5 mg/500 mg (yellow/orange)	"
81-096/004	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/30 mg	"
89-698/015	Hydrocodone Bitartrate and Acetaminophen Tablets USP, 2.5 mg/500 mg	"
81-069/005	Hydrocodone Bitartrate and Acetaminophen Shostak Capsules, 5 mg/500 mg (blue/aqua)	"
81-095/004	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/15 mg	"
89-450/008	Acetaminophen and Codeine Phosphate Oral Solution USP, 120 mg/12 mg per 5 mL	"
81-097/005	Acetaminophen, Aspirin and Codeine Phosphate Capsules, 150 mg/180 mg/60 mg	"
89-363/004	Acetaminophen and Codeine Phosphate Tablets" USP, 650 mg/60 mg	"
89-231/025	Acetaminophen and Codeine Phosphate Tablets" USP, 650 mg/30 mg	"
89-238/013	Acetaminophen and Codeine Phosphate Tablets" USP, 300 mg/30 mg	"
89-244/018	Acetaminophen and Codeine Phosphate Tablets" USP, 300 mg/60 mg	"

The majority of these supplements are assigned to branch 6. Therefore, they should be reviewed by a chemist in that branch as they appear on the queue.



Ruby

DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

DATE: 10/6/86

TO : Division of Manufacturing & Product Quality (HFN-320)

FROM: Division of Generic Drugs HFN- 232

Requester's Name DAVID ROSEN Phone 443-0193

ESTABLISHMENT EVALUATION REQUEST

Sterile Product Non Sterile Product [check]

Application and Supplement No. 89-557

Brand Name (if any) LORTAB

Establishment Name, Dosage Form and Strength Hydrocodone Bitartrate 5mg/15mL and Acetaminophen 500mg/15mL

Profile Class Code: LIQ

Priority Classification: (See SMG BD-4820.3)

Applicant's Name: Russ Pharmaceuticals, Inc

Address: 2256 Rocky Ridge Rd, Birmingham Alabama 35216

Facilities to be Evaluated: PO BOX 20507 (Name, full Address, DMF No., and responsibility)

For HFN-320 Use Status & Date of Inspection:

- 1. Applicant - DISTRIBUTOR above address
2. MKART Inc 2040 Marietta Blvd NW DMF ATLANTA, GEORGIA 30318 MANUF finished AC 4/10/87

Other Information or Special Requests: Inspection Requested 11/5/86 for MKART

For HFN-320 Use Only: Date Received 10/10/86

CGMP Compliance Status of Facilities Evaluated: acceptable

CSO: Duane Sylvia Date Completed August 11, 1987

Distribution: Original and First Copy: HFN-320 Remaining Copies: Requesting Office Use

Russ - label distributor
mkart manufactures product



DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

DATE: 10/6/86

TO : Division of Manufacturing & Product Quality (HFN-320)

FROM: Division of Generic Drugs HFN- 232

Requester's Name DAVID L ROSEN Phone 443-0193

ESTABLISHMENT EVALUATION REQUEST

Sterile Product Non Sterile Product [checked]

Application and Supplement No. 89-557

Brand Name (if any) Lortab

Establishment Name, Dosage Form and Strength Hydrocodone Bitartrate 5mg/15mL AND

Acetaminophen 500mg/15mL Profile Class Code: LIQ

Priority Classification: (See SMG BD-4820.3)

Applicant's Name: Russ Pharmaceuticals Inc

Address: 2256 Rocky Ridge Rd Birmingham Alabama 35216 PO Box 20507

Facilities to be Evaluated: (Name, full Address, DMF No., and responsibility)

For HFN-320 Use Status & Date of Inspection:

Table with 2 columns: Facility Name/Address, Status & Date of Inspection. Row 1: St. Louis MO 63147. Rows 2-5 are empty.

APPEARS THIS WAY ON ORIGINAL

Other Information or Special Requests:

For HFN-320 Use Only: Date Received

CGMP Compliance Status of Facilities Evaluated: acceptable

CSO: Duane Sylvia Date Completed August 11, 1987

Distribution: Original and First Copy: HFN-320 Remaining Copies: Requesting Office Use

Memorandum

10/15/86

Director HFN-230
Division of Generic Drugs

BChen OT

89432

Request for Review

09/586

Division of Bioequivalence (HFN-227)

ANDA/ #: 89-557

COMPANY NAME: Russ Pharmaceuticals

NAME OF DRUG: Hydrocodone Bitartrate 5mg/15ml &
Acetaminophen 500mg/15ml syrup

Please review the request for waiver of in-vivo bioequivalence study requirements for the above referenced drug.

Thank you,

J. J. Sturm
Marvin Seife, M.D.

APPEARS THIS WAY
ON ORIGINAL



REUPDATE FOR APPROVAL
This is noncompendial drug product.

Memorandum

Date January 18, 1991
From Division of Chemistry I
Generic Drugs
Requestor's Name Lucia C. Tang
Subject ESTABLISHMENT EVALUATION REQUEST

HFD- 837
Phone 295-8305

To Division of Manufacturing & Product Quality (HFD-320)

Sterile Product _____ Non Sterile Product x

Application and Supplement No. 89-557

Brand Name (if any) _____

Establishment Name, Dosage Form and Strength Hydrocodone Bitartrate, 5 mg/15 mL
and Acetaminophen 500 mg/15 mL
Profile Class Code: LIQ

Priority Classification: _____ (See SMG BD-4820.3)

Applicant's Name: Mikart, Inc.
Address: 2090 Marietta BLVD., N.W. Atlanta, GA 30318

Facilities to be Evaluated: (Name, full Address, DMF No., and responsibility)

For HFD 320 Use
Status & Date of Inspection:

- 1. Applicant, Manuf. finished product
- 2. [_____
- 3. [_____
- 4. C _____
- 5. [_____

Other Information or Special Requests: Method validation for finished product. Please make

6. For testing

For HFD-320 Use Only: Date Received: _____

CGMP Compliance Status of Facilities Evaluated: _____

CSO: _____ Date Completed: _____

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

DATE: JUL 27 1987

Best Available Copy

FROM: Chief, Prescription Drug Compliance Branch (HFN-313)

SUBJECT: Rachel S. Silk's Memo Regarding Proprietary Name Change
To T-TAB for Clorazepate Dipotassium Now Marketed Under
an Approved NDA as Tranxene - Reference Drug Product Problem
Report #73141TO: Charles S. Kunkhian, Ph.D.
Office of Drug Research & Review (HFN-102)

The question of the requirement for an NDA supplement for a new proprietary name has been the subject of discussions at the Center level.

It has been determined that a name change for an approved drug product does not require prior supplemental approval.

This is consistent with the FDA's policy not requiring resubmission of repackaged drugs which have been previously approved. Name changes by the repacker for these NDA products are often a part of the repackaging process and the FDA has never objected to this.

This position is also consistent with the change of ownership requirements for an application regulation 21 CFR 314.71, which states that the change of a product's brand name by the new owner may be submitted in the next annual report.

With respect to the referenced DPPR we do not believe we can insist on name changes for either T-TABS or K-TABS based on a potential for confusion in writing of prescriptions, since these are clearly different names of drugs and if there were any doubt as to the prescription it should be clarified with the doctor prior to dispensing.

Richard J. Chastonay

cc:
HFN-310 (Apodaca)
HFA-224
DDLC File
HFN-310 R/F
RJChastonay:crj/07/23/87:nd:7/27/87
2424G - 310-7-8

*File in jacket 89-557, see comment 111. in review
dated 5/3/90 which references this. (ymille)
FOR THE RECORD*

MEMORANDUM

DEPARTMENT OF HEALTH AND HUMAN SERVICES
PUBLIC HEALTH SERVICE
FOOD AND DRUG ADMINISTRATION
CENTER FOR DRUG EVALUATION AND RESEARCH

DATE: APR - 6 1990

FROM: Director, Division of Drug Labeling Compliance, HFD-310

SUBJECT: Hydrocodone Bitartrate Acetaminophen Tablets, ANDA 89-689/R-07 vol 5.1

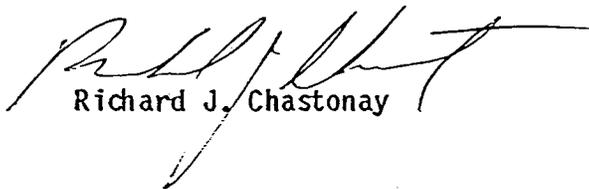
TO: Yana Mille
Division of Generic Drugs, HFD-238

This is in response to your memo of October 26, 1989. As demonstrated by the attached memo of July 27, 1987, we have previously determined that a name change for an approved product does not require prior supplemental approval. However, this does not mean that we can not object to a misleading trade name under the misbranding division of the Act.

In this regard, we agree that Mikart's use of the name _____ a name which you previously formally objected to, is inappropriate.

In this case, since the article is covered by an NDA, we suggest that you write to Mikart and request the reason why they made the change in spite of our previous objection, and inform them that if they intend to continue using the name _____ the matter will be referred to the Office of Compliance since we continue to regard the proposed name of _____ to be misleading for the reasons stated in your March 29, 1988 letter.

Please advise us of the firm's response so that we can make a determination if regulatory action is warranted.


Richard J. Chastonay

Attachment



DEPARTMENT OF HEALTH & HUMAN SERVICES

Memorandum

Date June 13, 1991
From Eric S. Weilage
Subject Method validation sample collection request for ANDA #89-697 and #89-557
To Lucia C. Tang, ANDA Chemist Office of Generic Drugs
thru Dawn L. Todd, Supervisory Investigator ATL-DO

Firm: Mikart, Inc.
2090 Marietta Blvd., NW
Atlanta, GA 30318
CFN 1050658

A FDA team (Robert C. Coleman, Eric S. Weilage, Kimberly L. Jackson, Edith P. Scott) conducted an inspection of Mikart Inc. and covered pre-approval ANDA assignments for ANDA 89-363, 89-223, and 89-452. This inspection also extended coverage to include ANDA 89-987, 89-988, 89-450, and 89-697. We also received assignments from Lucia C. Tang, ANDA Chemist to collect method validation samples for ANDA 89-697 (Hydrocodone Bitartrate and Acetaminophen Tablets, 5mg/500mg blue) and ANDA 89-557 (Hydrocodone Bitartrate and Acetaminophen Elixir, 5mg/500mg per 15ml).

These samples could not be collected because the batch(E8159)supporting the ANDA 89-697 was manufactured 5/19/88 and was not within it's tentative expiration date-2 years. No other batches were made. Sample handling procedures under CP 7346.842 state samples should not be collected if the product is not with it's expiration date.

DATE: 6/14/91

TO: Lucia C. Tang (HFD-637)

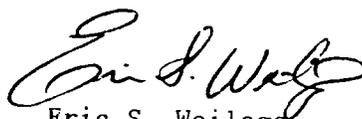
Per your sample request, no samples could be collected for either ANDA 89-697 or ANDA 89-557 as indicated above.

DAWN L. TODD
Supervisory Investigator
ATL-DO

O: ATL-DO
cc: HFD-637 (Lucia Tang)
cc: DLT
cc: REK

A sample was not collected for ANDA-557 because Mikart has committed to make a new batch to support this application using new equipment and new procedures. Previous inspections dated 11/5-8/90 and 1/15-18/91 found significant objectionable conditions which withheld similar liquid ANDAs. As of this date, this new batch has not been made.

Attached are copies of the assignments and applicable pages from CP 7346.832.



Eric S. Weilage
Investigator #307 ATL-DO

**APPEARS THIS WAY
ON ORIGINAL**

Redacted 4

Page(s) of trade

secret and /or

confidential

commercial

information

Please File

Note to: M. Beatrice

From: F. Fang

Jr 1/17/92

cc: R. Pollock
J. Mastronardy
F. Holcombe
L. Tang

Date: Jan. 16, 1992

Subject: Addendum to Note Re: ANDA 89-450 (1/8/92)

I pursue further the subject of incomplete amendments and the following is a summary of my findings:

It is our policy that only complete amendments (to original ANDAs and supplements) in response to OGD deficiency letters will activate the review clock. Refer to the statement in the end paragraph of all not-approvable letters: "A partial reply will not be considered for review nor will the review clock be reactivated until all the deficiencies have been addressed."

However, in actual practice, an incomplete amendment still activates the review clock when it is logged into the system. EVEN IF it is caught upon receipt at the Document Room level or the applications examiner level, there is an increase of a cycle when the Program Support Staff issues the Not Approvable letter without the chemist review. That is how our document handling system functions at the present time. An INCOMPLETE submission causes the "review" cycle to increase by one.

In addition to Lucy's 89-450 partial amendment, at this time there are three other amendments which are incomplete (all Mikart's):

89-450	27-AUG-91 amendment	Current Cycle #8	(Tang)
81-051	17-JUL-91 amendment	Current Cycle #4	(Holcombe)
81-226	17-JUL-91 amendment	Current Cycle #3	(Holcombe)
89-557	16-OCT-91 amendment	Current Cycle #9	(Tang)

I would like to make a **SUGGESTION**:

While we cannot prevent firms from submitting incomplete submissions, our "accounting" system should accurately document these as such. These amendments should be logged into the MIS system WITHOUT activating the review clock. And if an inaccurate entry is made (an incomplete submission is entered as a complete amendment) there should be a mechanism to reverse the entry without adding a cycle to the review process.

IMMEDIATE ACTIONS FOR US:

Joe Mastronardy has called Mikart to inform the firm that in the future, incomplete submissions will not be reviewed.

We will issue the letters as prepared for 89-450 and 81-051.

Note: The MIS (January 2, 1992 printout) indicates 89-450 at cycle 8, Lucy's accounting indicates Review # 6.

The discrepancy is that the chemist has only written 6 reviews. The MIS system added one cycle for the Jan. 31, 1989 labeling amendment and another cycle for June 6, 1990 incomplete submission.

APPEARS THIS WAY
ON ORIGINAL

Note to: Mike

From: Florence



1/8/92

Re: ANDA 89-450 (6 cycles)

Review # 5 Firm is using a new container/closure system. Product stability data in the new system is requested.

Amendment (9/20/91) to NA letter (Review # 5) is incomplete. Firm stated that a new test batch will be manufactured and stability data generated. The amendment should NOT have been accepted.

Review # 6 Await the data, calling for major amendment.

Recommendation:

Perhaps we should not issue the letter but call the firm to advise that the amendment of 8/20/91 will not be reviewed and the review clock will not be reactivated until a full response is received. (Also convey the other two minor requests in the letter to the firm). In the meantime, we should correct the MIS listing.

APPEARS THIS WAY
ON ORIGINAL



872

Memorandum

Top 200

This is noncompensial drug product.

Date January 18, 1991
From Division of Chemistry I
Requestor's Name Lucia C. Tang
Subject ESTABLISHMENT EVALUATION REQUEST

HFD- 637
Phone 295-8305

To Division of Manufacturing & Product Quality (HFD-320)

Sterile Product Non Sterile Product x

Application and Supplement No. 89-557

Brand Name (if any)

Establishment Name, Dosage Form and Strength Hydrocodone Bitartrate, 5 mg/15 mL
and Acetaminophen 500 mg/15 mL
Profile Class Code: LIQ

Priority Classification: (See SMG BD-4820.3)

Applicant's Name: Mikart, Inc.
Address: 2090 Marietta BLVD., N.W. Atlanta, GA 30318

Facilities to be Evaluated: (Name, full Address, DMF No., and responsibility)

For HFD 320 Use
Status & Date of Inspection:

1. MIKA Applicant, Manuf. finished product

AC-2/25/92

5. [Redacted] AC-11/7/90
AC-11/8/90

Other Information or Special Requests: "This is non-compensial drug product. Please make Method validation for finished product."

6. *****

For HFD-320 Use Only: Date Received:

CGMP Compliance Status of Facilities Evaluated: All Acceptable

CSO: [Signature] Date Completed: 4/29/92

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

M E M O R A N D U M

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

DATE: January 28, 1991

TO: Atlanta District Office (HFR-SE100)
Attention: Mr. John H. Turner
60 Eighth Street
Atlanta, GA. 30309

FROM: Lucia C. Tang, ANDA Chemist
Division of Chemistry I
Office of Generic Drugs

SUBJECT: Method Validation for ANDA # 89-557

Product: Hydrocodone Bitartrate and Acetaminophen
Elixir, 5 mg/500 mg per 15 mL

Applicant:
Mikart, Inc.
Attention: Ms. Cerie B. McDonald
2090 Marietta Blvd., N.W.
Atlanta, GA 30318

We request methods validation :

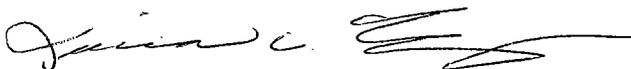
_____ for the drug substance(s)
 x for the finished dosage form

be conducted by the servicing laboratory as described in the attached methods validation request and reporting sheet, Form FD2671a.

The firm has been advised that samples of the active, and inactive components, and the finished dosage form will be picked up by FDA district/laboratory staff. Since the drug product is not an article in the USP, all analytical methods will be validated.

Also, if you have any questions or problems, please advise Ms. Lucia Tang (FTS-295-8305).

Sincerely Yours,



Lucia C. Tang

M E M O R A N D U M

DEPARTMENT OF HEALTH & HUMAN SERVICES
Public Health Service
Food and Drug Administration
Center for Drug Evaluation and Research

DATE: March 27, 1991

TO: Atlanta District Office (HFR-SE150)
Attention: Mr. Roger E. Kline, Dir. Invest. Branch
60 Eighth Street, N. E.
Atlanta, GA. 30309

FROM: Lucia C. Tang, ANDA Chemist
Division of Chemistry I
Office of Generic Drugs

SUBJECT: Method Validation for ANDA # 89-557

Product: Hydrocodone Bitartrate and Acetaminophen
Elixir, 5 mg/500 mg per 15 mL

Applicant:
Mikart, Inc.
Attention: Ms. Cerie B. McDonald
2090 Marietta Blvd., N.W.
Atlanta, GA 30318

We request methods validation :

_____ for the drug substance(s)
 x for the finished dosage form

be conducted by the servicing laboratory as described in the attached methods validation request and reporting sheet, Form FD2671a.

The firm has been advised that samples of the active, and inactive components, and the finished dosage form will be picked up by FDA district/laboratory staff. Since the drug product is not an article in the USP, all analytical methods will be validated.

Also, if you have any questions or problems, please advise Ms. Lucia Tang (FTS-295-8305).

Sincerely Yours,



Lucia C. Tang

89577MAL.LLT/3-27-91

FFang/LTang

Roger E. Kline's Telephone: 404-347-3151 or 8-257-3151

**APPEARS THIS WAY
ON ORIGINAL**

SEP 30 1991

Lucia Tang
HFD-632

TO: Director, Atlanta District, HFR-SE100
FROM: Acting Chief
Investigations & Compliance Evaluation Branch, HFD-324

SUBJ: Inspection Request
~~ANDA 89-55~~
Hydrocodone Bitartrate,
5 mg/15 mL and
Acetaminophen, 500
mg/15 ml

Applicant:
Mikart Inc.
2090 Marietta Blvd., N.W.
Atlanta, GA 30318

Establishment:
Mikart Inc.
2090 Marietta Blvd., N.W.
Atlanta, GA 30318

PROFILE: LIQ

CFN#: 1050658

In connection with FDA's review of ANDA 89-557, please conduct a CGMP inspection of the referenced establishment. The application provides for this establishment to manufacture the drug product Hydrocodone Bitartrate 5mg/15mL and Acetaminophen, 500mg/15mL. This is a Top 200 Drug Product, requiring a product specific inspection regardless of the last GMP EI covering the profile class LIQ. **This is a non-compendial product. Please evaluate method validation for finished product.** For guidance, refer to CP 7346.832, Pre-Approval Inspections.

This application cannot be acted upon until the inspection is completed and your findings are reported to this office. Please call well in advance if you are unable to meet the time frame, whether due to priorities or the lack of readiness on the part of the firm.

Upon completion of this assignment, please provide this office with a copy of the EIR endorsement (FDA 481(E)-(CG)). If this inspection is classified OAI, include a recommendation to withhold application approval and full documentation of CGMP violations. If the district expects delays in completing a non-violative EIR, notify this office of the inspection findings by EMS.

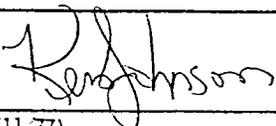
In communicating with this office (FTS 295-8098), reference should be made to the above ANDA number. Please direct your written response to the Investigations & Compliance Evaluation Branch, HFD-324.

for Melissa Garcia
Michael F. Karpers

Priority: ANDA Pending
Target Completion: NOV 11 1991

cc:
HFD-324 ICEB R/F
HFD-Lucia Tang
JANINE'S DISK

HFD-324 EER File
9/23/91:jmd
1723.200:September 23,1991

RECORD OF TELEPHONE CONVERSATION/MEETING	DATE 89-557	
Cerrie McDonald Mikart	NDA NUMBER	
	IND NUMBER	
09 March 92 10:00 a.m.	TELECON/MEETING	
<p>Kent Johnson (KJ) returned a call (to Peter Rickman) from Cerrie McDonald of Mikart. KJ chose to make this call because the issue was "tradename" of this proposed product. CMcD summarized the issue. She recognized that FDA was opposed to the name Lortab Elixir. However the distributor, Whitby, is also intent upon using this tradename. They have been using this tradename and say "there has been no problem". KJ summarized the reasons for OGD opposition, and the support from non OGD groups for our position. CMcD suggested that KJ call Rob Falconer and discuss the issue directly with him. Mikert simply wants to gain the approval and allow the distributor to market the product. MCD gave authority to make this direct contact.</p> <p>Falconer # 804-254-4261</p> <p style="text-align: center;">APPEARS THIS WAY ON ORIGINAL</p>	INITIATED BY <input type="checkbox"/> APPLICANT/ SPONSCR <input type="checkbox"/> FDA	MADE <input type="checkbox"/> BY TELE- PHONE <input type="checkbox"/> IN PERSON
	PRODUCT NAME Hydrocodone bitart & APAP Elix	
	FIRM NAME Mikart	
	NAME AND TITLE OF PERSON WITH WHOM CONVERSATION WAS HELD	
<p style="text-align: center;">APPEARS THIS WAY ON ORIGINAL</p>	TELEPHONE NO.	
	DIVISION	
SIGNATURE 		



Pre-Approval Update

Memorandum

Date: April 15, 1992
From: Division of Chemistry II, Office of Generic Drugs
Requestor's Name: Lucia C. Tang
Subject: ESTABLISHMENT EVALUATION REQUEST

HFD- 637
Phone 295-8305

To: Division of Manufacturing & Product Quality (HFD-320)

Sterile Product Non Sterile Product x

Application and Supplement No. 89-557

Brand Name (if any)

Establishment Name, Dosage Form and Strength Hydrocodone Bitartrate and Acetaminophen

Elixir, 5 mg/500 mg per 15 mL

Profile Class Code: LIQ

Priority Classification: Pre-approval (See SMG BD-4820.3)

Applicant's Name: Mikart Inc.

Address: 2090 Marietta Blvd., N.W., Atlanta, GA 30318

Facilities to be Evaluated: (Name, full Address, DMF No., and responsibility) For HFD 320 Use Status & Date of Inspection:

Applicant; address is same as above, manuf. finished product

Other Information or Special Requests: Updated EER was OK on 1-18-91

For HFD-320 Use Only:

Date Received:

CGMP Compliance Status of Facilities Evaluated:

CSO:

Date Completed:

Distribution: Original and First Copy: HFD-320
Remaining Copies: Requesting Office Use

[DESI 7289]

**CODEINE WITH ACETAMINOPHEN,
ASPIRIN, AND CAFFEINE FOR ORAL USE**
Drugs for Human Use; Drug Efficacy Study
Implementation

The Food and Drug Administration has evaluated a report received from the National Academy of Sciences—National Research Council, Drug Efficacy Study Group, on trigesic with codeine tablets (NDA 7-289) containing codeine, acetaminophen, aspirin, and caffeine; E. R. Squibb & Sons, Division Olin Mathieson Chemical Corp., 745 Fifth Avenue, New York, N.Y. 10022.

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

A. Effectiveness classification. 1. The Food and Drug Administration has considered the Academy's report, as well as other available evidence, and concludes that combination drugs containing codeine with acetaminophen, aspirin, and caffeine are effective for the relief of mild to moderate pain.

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

1. **Form of drug.** Preparations containing codeine, acetaminophen, aspirin, and caffeine are in 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(s). The indication for use is: For the relief of mild to moderate pain.

3. **Marketing status.** Marketing of such drugs may be continued under the conditions described in the notice entitled Conditions for Marketing New Drugs Evaluated in Drug Efficacy Study, published in the FEDERAL REGISTER July 14, 1970 (35 FR 11273), as follows:

a. For holders of "deemed approved" new drug applications (i.e., an application which became effective on the basis of safety prior to October 10, 1962), the submission of a supplement for revised labeling and an abbreviated supplement for updating information as described in paragraph (a) (1) (i) and (iii) of the notice of July 14, 1970.

b. For any person who does not hold an approved or effective new drug application, the submission of an abbreviated new drug application as described in paragraph (a) (3) (i) of that notice.

c. For any distributor of the drug, the use of labeling in accord with this announcement for any such drug shipped within the jurisdiction of the Act as described in paragraph (b) of that notice.

A copy of the Academy's report has been furnished to the firm referred to above. Communications forwarded in response to this announcement should be identified with the reference number DESI 7289, directed to the attention of the appropriate office listed below, and addressed to the Food and Drug Administration, 5500 Fishers Lane, Rockville, MD 20852.

Supplements (Identify with NDA number):
Office of Scientific Evaluation (BD-100),
Bureau of Drugs.

Requests for the Academy's report: Drug
Efficacy Study Information Control (BB-
66), Bureau of Drugs.

All other communications regarding this announcement: Drug Efficacy Study Implementation Project Office (ED-60), Bureau of Drugs.

All identical, related, or similar products, not the subject of an approved new drug application, are covered by the new drug application reviewed and are subject to this notice. See 21 CFR 130.40 (37 FR 23185, October 31, 1972). Any person who wishes to determine whether a specific product is covered by this notice should write to the Food and Drug Administration, Bureau of Drugs, Office of Compliance (BD-300), 5600 Fishers Lane, Rockville, MD 20852.

This notice is issued pursuant to provisions of the Federal Food, Drug, and Cosmetic Act (secs. 502, 505, 52 Stat. 1050-53, as amended; 21 U.S.C. 352, 355) and the Administrative Procedure Act (5 U.S.C. 554) and under the authority delegated to the Commissioner of Food and Drugs (21 CFR 2.120).

Dated: January 26, 1973.

SAM D. FITZ,
Associate Commissioner
for Compliance,

(FR Doc. 73-2017 Filed 2-1-73; 8:45 am)

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

89-557/S-004

CORRESPONDENCE



January 6, 1998

Mr. Douglas Sporn, Director
Office of Generic Drugs
Document Control Room
Center for Drug Evaluation and Research
Food and Drug Administration
Metro Park North II (MPN II)
Room 150
7500 Standish Place
Rockville, MD 20855-2773

NDA NO. _____
NDA SUB. _____

Scovf
Facility Add.

Re: Multiple supplements for an additional _____

ANDAs included in this submission:

ANDA #	Product Name
40-062	Methazolamide Tablets USP 25mg & 50mg
40-085	Esgic Plus (Butalbital, Acetaminophen, and Caffeine Capsules 50mg/500mg/40mg)
40-090	Isoniazid Tablets USP 100mg & 300mg
40-109	Acetaminophen, Caffeine, and Dihydrocodeine Bitartrate Capsules 356.4 mg / 30mg / 16mg
74-028	Amantadine Hydrocodone Syrup USP 50mg per 5mL
81-051	Hydrocodone Bitartrate and Acetaminophen Elixir 7.5mg / 500mg per 15mL
81-067	Hydrocodone Bitartrate and Acetaminophen Capsules 5mg / 500mg (gray / lavender)
81-068	Hydrocodone Bitartrate and Acetaminophen Capsules 5mg / 500mg (yellow / orange)
81-069	Hydrocodone Bitartrate and Acetaminophen Capsules 5mg / 500mg (blue / aqua)
81-070	Hydrocodone Bitartrate and Acetaminophen Capsules 5mg / 500mg (gray / black)
81-095	Acetaminophen, Aspirin, and Codeine Phosphate Capsules 150mg / 180mg / 15mg
81-096	Acetaminophen, Aspirin, and Codeine Phosphate Capsules 150mg / 180mg / 30mg
81-097	Acetaminophen, Aspirin, and Codeine Phosphate Capsules 150mg / 180mg / 60mg
81-118	Isoniazid Syrup USP 50mg / 5mL
81-223	Hydrocodone Bitartrate and Acetaminophen Tablets USP 10mg / 650mg
81-226	Hydrocodone Bitartrate and Acetaminophen Elixir 5mg / 500mg per 15mL
81-319	Pyrazinamide Tablets USP 500mg
89-007	Butalbital, Acetaminophen, and Caffeine Capsules 50mg / 325mg / 40mg
89-008	Hydrocodone Bitartrate and Acetaminophen Capsules 5mg / 500mg (white / white)
89-175	Butalbital, Acetaminophen, and Caffeine Tablets USP 50mg / 325mg / 40mg
89-231	Acetaminophen and Codeine Phosphate Tablets USP 650mg / 30mg
89-238	Acetaminophen and Codeine Phosphate Tablets USP 300mg / 30mg
89-244	Acetaminophen and Codeine Phosphate Tablets USP 300mg / 60mg
89-271	Hydrocodone Bitartrate and Acetaminophen Tablets USP 5mg / 500mg
89-363	Acetaminophen and Codein Phosphate Tablets USP 650 mg / 60mg
89-450	Acetaminophen and Codein Phosphate Oral Solution USP 120mg / 12mg per 5mL
89-451	Butalbital, Acetaminophen, and Caffeine Tablets USP 50mg / 500mg / 40mg
89-557	Hydrocodone Bitartrate and Acetaminophen Elixir 5mg / 500mg per 5mL
89-689	Hydrocodone Bitartrate and Acetaminophen Tablets USP 7.5mg / 650mg
89-697	Hydrocodone Bitartrate and Acetaminophen Tablets USP 5mg / 500mg
89-698	Hydrocodone Bitartrate and Acetaminophen Tablets USP 2.5mg / 500mg

RECEIVED

JAN 13 1998

GENERIC DRUGS

Mr. Douglas Sporn
January, 1998
Page 2

89-699	Hydrocodone Bitartrate and Acetaminophen Tablets USP 7.5mg / 500mg
89-987	Butapap Tablets 50mg / 325mg (Butalbital and Acetaminophen Tablets)
89-988	Butapap Tablets 50mg / 650mg (Butalbital and Acetaminophen Tablets)

Dear Mr. Sporn:

Mikart would like to supplement the above applications to add an additional ~~_____~~. Currently, Mikart and ~~_____~~ are the designated facilities for ~~_____~~. Mikart performs methods I & V, and ~~_____~~. At this time, Mikart would like to designate ~~_____~~ to also, if necessary, be able to ~~_____~~ requiring such testing.

We are aware that this change requires prior approval by the FDA in order to be implemented, in accordance with 21 CFR 314.70 (b) (2) (vi). Following approval of these applications, Mikart will add ~~_____~~ as a designated ~~_____~~ specification sheet. The revised specification sheets will be submitted in the annual report.

Thank you for your cooperation in the review of these supplements.

Sincerely,



Cerie B. McDonald
Executive Vice-President

CBM/lac