

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

Approval Package for:

APPLICATION NUMBER:

76-200/S-002;S-003;S-004

Generic Name: Acetaminophen Extended Release
Tablets 650mg

Sponsor: Corepharma, LLC

Approval Date: December 3, 2002

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

76-200/S-002;S-003;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:

76-200/S-002;S-003;S-004

APPROVAL LETTER

ANDA 76-200/S-002, S-003, S-004

Corepharma LLC
Attention: Mukteeshwar Gande, M.S., R.Ph.
215 Wood Avenue
Middlesex, NJ 08846

DEC 3 2002

Dear Madam:

This is in reference to your supplemental new drug applications, dated May 17, 2002, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug applications for Acetaminophen Extended Release Tablets 650 mg.

Reference is also made to your amendment dated September 18, 2002.

These supplemental applications, submitted as "Changes Being Effected in 30 days", provide for the following changes:

S-002

S-003

S-004 The addition of a bulk packaging configuration.

We have completed the review of these supplemental applications and they are approved.

We remind you that you must comply with the requirements for an approved abbreviated new drug application described in 21 CFR 314.80-81.

**APPEARS THIS WAY
ON ORIGINAL**

The material submitted is being retained in our files.

Sincerely yours,

for



12/2/02

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

APPEARS THIS WAY
ON ORIGINAL

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-200/S-002;S-003;S-004

CHEMISTRY REVIEW(S)

ANDA 76-200/S-002, S-003, S-004

REVIEW #2

NAME AND ADDRESS OF APPLICANT:

Corepharma LLC
Attention: Mukteeshwar Gande, M.S., R.Ph.
215 Wood Avenue
Middlesex, NJ 08846

PURPOSE OF AMENDMENT/SUPPLEMENT

The CBE-30 supplement provides for:

S-002

S-003

S-004 The addition of a bulk packaging configuration.

DATE(S) OF SUBMISSION(S)

May 17, 2002 Original submission
September 18, 2002 Minor amendment (Subject of this review)

<u>PHARMACOLOGICAL CATEGORY</u>	<u>TRADE NAME</u>	<u>NONPROPRIETARY NAME</u>
Analgesic	N/A	Acetaminophen Extended Release Tablets 650 mg

<u>DOSAGE FORM</u>	<u>POTENCY</u>	<u>RX OR OTC</u>
Tablet, oral	650 mg	Rx

<u>SAMPLES</u>	<u>RELATED IND/NDA/DMF</u>	<u>STERILIZATION</u>
N/A	N/A	N/A

LABELING

A copy of the bulk shipment label intended for re-packaging only is included (p. 52). All drug facts are obtained from the approved labels.

BIOEQUIVALENCY STATUS

N/A

ESTABLISHMENT INSPECTION

Acceptable on 6/5/02 for:

COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS

The applicant proposes to use the following



Repackaging will be done using approved containers, closures, and labels within a period of three months. Certificates of cGMP are included for both (p. 7, 10). The packaging components' specification sheets from _____ are included (p. 14-45).

PACKAGING

Bulk container/closure will be as follows:

Corrugated boxes lined with two plastic bags and tied with a tie.

Corrugated box: _____ No direct contact with the product.

Liner: Clear poly bags _____ Letters from the _____ from _____ and materials that are _____ and in compliance with the pertinent regulations are included (p. 47-48).

Comment:

Please indicate if the bulk packaging used for shipping the drug product is tamper resistant.

Response (Am: 9/18/02):

The applicant acknowledges that the bulk packaging is tamper resistant.

STABILITY

A repackaging period of three months is established based on acceptable three months RT stability data generated for lot

#CPA223 packaged in the bulk container (p. 49-51). All results are in compliance with the approved specifications.

Comment:

Please provide a commitment to place the first lot packaged in each of the proposed packaging sites on long term stability according to the stability protocol as approved in the original application.

Response (Am: 9/18/02):

The applicant commits to place on stability the first lot package at _____ whenever they start using this facility. The first lot packaged at _____ is no longer available. The current lot has been placed on stability upon receipt of the deficiency letter. The stability protocols are included.

Comment:

Please acknowledge that the expiration dating of the repackaged product will be calculated starting from the date of the pre-mix operation as approved in the original application.

Response (Am: 9/18/02)

The applicant acknowledges the comment above.

REMARKS AND CONCLUSION

Recommend approval.

RECALLS

N/A

Reviewer

M. Piñeiro-Sánchez, Ph.D.

Date Completed

November 19, 2002

ORDER OF REVIEW:

The application submission(s) covered by this review was taken in the date order of receipt Yes_____ No X

If no, explain reason(s) below.

Minor.

ANDA 76-200/S-002, S-003, S-004

NAME AND ADDRESS OF APPLICANT:

Corepharma LLC
Attention: Mukteeshwar Gande, M.S., R.Ph.
215 Wood Avenue
Middlesex, NJ 08846

PURPOSE OF AMENDMENT/SUPPLEMENT

The CBE-0 supplement provides for:

S-002

S-003

S-004 The addition of a bulk packaging configuration.

DATE(S) OF SUBMISSION(S)

May 17, 2002: Original

May 29, 2002: New Correspondence

PHARMACOLOGICAL CATEGORY

Analgesic

TRADE NAME

N/A

NONPROPRIETARY NAME

Acetaminophen
Extended Release
Tablets 650 mg

DOSAGE FORM

Tablet, oral

POTENCY

650 mg

RX OR OTC

Rx

SAMPLES

N/A

RELATED IND/NDA/DMF

N/A

STERILIZATION

N/A

LABELING

A copy of the bulk shipment label intended for re-packaging only is included (p. 52). All drug facts are obtained from the approved labels.

BIOEQUIVALENCY STATUS

N/A

ESTABLISHMENT INSPECTION

N/A

COMPONENTS, COMPOSITION, MANUFACTURING, CONTROLS

The applicant proposes to use the following

PACKAGING

Bulk container/closure will be as follows:

Corrugated boxes lined with two plastic bags and tied with a tie.

Corrugated box: _____ No direct contact with the product.

Liner: Clear poly bags _____ Letters from the _____
from _____ and materials that are food grade and in compliance with the pertinent regulations are included (p. 47-48).

Comment:

Please indicate if the bulk packaging used for shipping the drug product is tamper resistant.

STABILITY

A repackaging period of three months is established based on acceptable three months RT stability data generated for lot #CPA223 packaged in the bulk container (p. 49-51). All results are in compliance with the approved specifications.

Comment:

1. Please provide a commitment to place the first lot packaged in each of the proposed packaging sites on long term stability according to the stability protocol as approved in the original application.

2. Please acknowledge that the expiration dating of the repackaged product will be calculated starting from the date of the pre-mix operation as approved in the original application.

REMARKS AND CONCLUSION

Do not recommend approval. Minor

RECALLS

N/A

Reviewer

M. Piñeiro-Sánchez, Ph.D.

Date Completed

August 12, 2002

ORDER OF REVIEW:

The application submission(s) covered by this review was taken in the date order of receipt Yes X

No _____

If no, explain reason(s) below.

**APPEARS THIS WAY
ON ORIGINAL**

**CENTER FOR DRUG
EVALUATION AND
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APPLICATION NUMBER:

76-200/S-002;S-003;S-004

**ADMINISTRATIVE
DOCUMENT(S)**

FDA CDER EES
ESTABLISHMENT EVALUATION REQUEST
SUMMARY REPORT

Application : ANDA 76200/002 Sponsor: COREPHARMA -
Org Code : 600 215 WOOD AVE
Priority : MIDDLESEX, NJ 08846

Stamp Date : 20-MAY-2002 Brand Name :
PDUFA Date : Estab. Name: ACETAMINOPHEN
Action Goal : Generic Name:
District Goal: 20-OCT-2002 Dosage Form: (EXTENDED-RELEASE TABLET)
Strength : 650 MG

FDA Contacts: J. MIN Project Manager (HFD-617) 301-827-5761

Overall Recommendation: ACCEPTABLE on 05-JUN-2002 by J. D AMBROGIO (HFD-324) 301-827-0062

Establishment : CFN : [REDACTED] FEI : [REDACTED]

DMF No: AADA:

Responsibilities: [REDACTED]

Profile : TTR OAI Status: NONE
Last Milestone: OC RECOMMENDATION
Milestone Date: 05-JUN-02
Decision : ACCEPTABLE
Reason : BASED ON PROFILE

**APPEARS THIS WAY
ON ORIGINAL**

**CENTER FOR DRUG
EVALUATION AND
RESEARCH**

APPLICATION NUMBER:

76-200/S-002;S-003;S-004

CORRESPONDENCE

September 18, 2002

Office of Generic Drugs
CDER, Food and Drug Administration
Metro Park North
7500 Standish Place, Room 150
Rockville, MD 20855

NDA SUPPL AMENDMENT
SCPO04 AM
SCD-003-AM
SCD-002-AM

MINOR
AMENDMENT

Re: Acetaminophen Extended Release Tablets 650 mg, ANDA # 76-200

Dear Director:

Reference is made to the above; ANDA for Acetaminophen Extended Release Tablets 650 mg. Reference is also made to the Agency's minor deficiency letter dated August 29, 2002.

The deficiency questions are attached and responded to in the same order as they appear on the minor deficiency letter.

Field Copy: We certify that a true copy of the technical section described in 21 CFR 314.94(d)(5) of this submission has been provided to the Food and Drug Administration, New Jersey District Office.

If you have any questions or comments regarding this submission, please call me at (732) 868 1090 or fax at (732) 868 1091.

Sincerely,



Mukteeshwar Gande, M.S., R.Ph.
Vice President

RECEIVED

SEP 19 2002

OGD / CDER

AUG 29 2002

Corepharma LLC
Attention: Mukteeshwar Gande, M.S., R.Ph.
215 Wood Avenue
Middlesex, NJ 08846

Dear Madam:

This is in reference to your supplemental new drug applications dated May 17, 2002, submitted under section 505(j) of the Federal Food, Drug, and Cosmetic Act, regarding your abbreviated new drug application for Acetaminophen Extended Release Tablets 650 mg.

Reference is also made to your new correspondence dated May 29, 2002.

These supplemental applications, submitted as "Changes Being Effected", provide for the following changes:

S-002 ~~_____~~

S-003 ~~_____~~

S-004 The addition of a bulk packaging configuration.

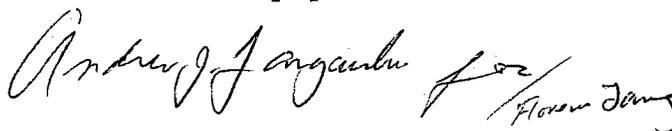
The supplemental applications are deficient and, therefore, not approvable under Section 505 of the Act for the following reasons:

Chemistry Deficiencies:

1. Please indicate if the bulk packaging used for shipping the drug product is tamper resistant
2. Please provide a commitment to place the first lot packaged in each of the proposed packaging sites on long term stability according to the stability protocol as approved in the original application.
3. Please acknowledge that the expiration dating of the repackaged product will be calculated starting from the date of the pre-mix operation as approved in the original application.

The file on these supplemental applications is now closed. You are required to take an action described under 21 CFR 314.120 which will either amend or withdraw these supplemental applications. Your amendment should respond to all the deficiencies listed. A partial reply will not be considered for review, nor will the review clock be reactivated until all deficiencies have been addressed. The response to this letter will be considered a MINOR amendment and should be so designated in your cover letter. If you have substantial disagreement with our reasons for not approving these supplemental applications, you may request an opportunity for a hearing.

Sincerely yours,

A handwritten signature in cursive script, appearing to read "Andrew J. Fong for Florence S. Fang". The signature is written in dark ink and is positioned above the typed name of the signatory.

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

May 29, 2002

NEW CORRESP

SCD-002 NC

Office of Generic Drugs
CDER, Food and Drug Administration
Metro Park North
7500 Standish Place, Room 150
Rockville, MD 20855

Re: **Acetaminophen Extended Release Tablets 650 mg, ANDA # 76-200**
New Correspondence to CBE 30 Supplement, Dated May 17, 2002

Dear Director:

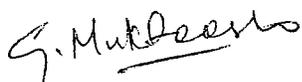
This is the new correspondence to CBE 30 supplement submitted on May 17, 2002 for our approved ANDA, Acetaminophen Extended Release Tablets 650 mg, ANDA # 76-200. We included OGD's recommendations as follows:

1. Please be advised that ~~_____~~ are operating under cGMP regulations and they are suitable for the packaging of Solid Oral Dosage Forms including Extended Release Dosage Forms.
2. Corepharma commits to place the first batch packaged at each ~~_____~~ on long term stability and conduct stability testing as described in the approved stability protocol. Results of the stability testing will be submitted as part of the routine annual reports, or as specified by FDA.

This also certifies that a True Copy of this submission (including a copy of the 356h form) was sent to our local New Jersey district office.

Please direct any written communication regarding this submission to me at the above address. If you need to call or fax me, my telephone number is (732) 868 1090 and (732) 868 1091 (fax).

Sincerely,



Mukteeshwar Gande, M.S., R.Ph.
Vice President

RECEIVED

MAY 30 2002

OGD / CDER



May 17, 2002

Office of Generic Drugs
CDER, Food and Drug Administration
Metro Park North
7500 Standish Place, Room 150
Rockville, MD 20855

NDA NO. 76 200 REF. NO. SCD 002 AT
NDA SUPPL FOR Pack addⁿ

**CHANGES BEING
EFFECTED - 30 DAYS**

NDA NO. 76200 REF. NO. SCD 003 AT
NDA SUPPL FOR Pack Addⁿ

Re: **Acetaminophen Extended Release Tablets 650 mg, ANDA # 76-200
Alternate Packaging Site**

NDA NO. 76-200 REF NO. SCD-002
NDA SUPPL FOR Pack. change AT

Dear Director:

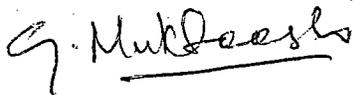
Please find enclosed a "Changes Being Effected - 30 Days Supplement" to our approved ANDA for Acetaminophen Extended Release Tablets 650 mg, ANDA # 76-200.

This supplement includes _____ for the finished product. The finished product (film coated tablets) will be shipped in bulk containers to the new site for packaging into final containers (bottles).

Corepharma has submitted an additional copy of this supplemental application, as required under 314.71(b), to the Food and Drug Administration, New Jersey District Office. We hereby certify that this additional copy (field copy) is a true copy of the supplemental application.

Please direct any written communication regarding this submission to me at the above address. If you need to call or fax me, my telephone number is (732) 868 1090 and (732) 868 1091 (fax).

Sincerely,



Mukteeshwar Gande, M.S., R.Ph.
Vice President

RECEIVED

MAY 20 2002

OGD / CDER