CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40303

CORRESPONDENCE

ANDA 40-303

Endo Pharmaceuticals Inc.
Attention: Andrew G. Clair, Ph.D.
500 Endo Blvd.
Garden City, NY 11530

MAR 30 1998

Dear Sir:

We acknowledge the receipt of your abbreviated new drug application submitted pursuant to Section 505(j) of the Federal Food, Drug and Cosmetic Act.

Reference is also made to the telephone conversation dated March 18, 1998 and your correspondence dated March 18, 1998.

NAME OF DRUG: Oxycodone and Acetaminophen Capsules USP, 5 mg/500 mg

DATE OF APPLICATION: March 12, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: March 13, 1998

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 ANDA number shown above.

Should you have questions concerning this application, contact:

Tim Ames
Project Manager
(301) 827-5849

Sincerely yours,

/S/

Jerry Phillips
Director
Division of Labeling and Program Support
Office of Generic Drugs
Center for Drug Evaluation and Research

Endo

Endo Pharmaceuticals Inc.

March 12, 1998

505(j)(2)(A) OK
3/19/98

Douglas Sporn
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

Re: Original Abbreviated New Drug Application
Oxycodone HCl/Acetaminophen Capsule, 5/500mg, USP

Dear Mr. Sporn:

Pursuant to 21 CFR 314.94 and Section 505(j) of the Federal Food, Drug and Cosmetic Act, Endo Pharmaceuticals Inc. hereby submits this original Abbreviated New Drug Application (ANDA) for the above-referenced drug product.

Please note that this drug product and strength (ANDA , was previously submitted on August 8, 1997 and withdrawn

Withdrawal of ANDA was based on the Agency's September 3, 1997 letter (see Section XVII - Prior Correspondence) which noted the ANDA would not be filed because "the quantity of Docusate Sodium/Sodium Benzoate as an inactive ingredient in your proposed drug product is greater than previously approved in a solid oral dosage form".

We have reformulated our product with a quantity of Docusate Sodium mg/capsule) which is within the limit of the Inactive Ingredient Guide. This resubmitted ANDA includes a finished product formulation with the revised quantity of Docusate Sodium.

The ANDA consists of four volumes submitted in duplicate as archival and technical review copies as follows:

Archival Copy	Vol. 1.1 to 1.4	(CMC & Bioequivalence Waiver in blue jackets)
Review Copy	Vol 1.1 to 1.3	(CMC in red jackets)
Review Copy	Vol. 1.4	(Bioequivalence Waiver in orange jackets)

Duplicate copies of the Methods Validation package are submitted in black binders.

500 ENDO BOULEVARD GARDEN CITY, NY 11530 FAX (516) 832-2291

To assist your review, preceding each volume is the Cover Letter, Table of Contents, ANDA Checklist for Completeness and Acceptability for Filing and signed Form FDA 3439.

Oxycodone HCl/Acetaminophen Capsules, USP, 5 mg/500 mg is "AA" rated to the reference listed drug (Tylox® 5 mg/500 mg , manufactured by McNeil Pharmaceutical), as per the Approved Drug Products with Therapeutic Equivalence Evaluations ("Orange Book"). Based on this, we have requested a waiver of *in-vivo* bioequivalence studies in this application.

To support this waiver request we are providing test results including dissolution testing of the finished product and comparative dissolution data of Endo's product versus the Reference Listed Drug which indicate that this product meets *in-vitro* dissolution requirements.

Endo Pharmaceuticals Inc. certifies that a copy of the chemistry, manufacturing and controls section of the ANDA (Volumes 1.1 - 1.3) and field copy certification (see Section XVII) has concurrently been sent to the New York District Office.

For your information, Endo Pharmaceuticals Inc. is an independent, stand-alone company formed from the recent business divestiture of Endo® Laboratories, L.L.C. (formerly a subsidiary of The DuPont Merck Pharmaceutical Company) from DuPont Merck. functions as a contract firm for the manufacturing, processing, packaging, labeling and quality control testing for Endo. This information is outlined in the Form FDA 3439 located in Section I. Oxycodone Acetaminophen Capsules, USP, 5 mg/500 mg will be manufactured at

Please be advised that the material and data contained in this submission are confidential. The legal protection of such confidential material is hereby claimed under the application provision of 18 U.S.C. Section 331(j).

Any questions regarding this application may be directed to me at (516) 522-3305. Any written communications may be faxed to me at (516) 832-2291.

Sincerely,

Carol Patterson
Manager, Regulatory Affairs

attachments
FDA-1998.doc

Endo Pharmaceuticals Inc.

May 6, 1999

NDA ORIG AMENDMENT
N/Ac

Douglas Sporn
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

Re: ANDA 40-303; Oxycodone and Acetaminophen Capsules, USP
5 mg/500 mg
Major Amendment

Dear Mr. Sporn:

Reference is made to your March 30, 1999 major deficiency letter which contains chemistry and manufacturing control comments for our original application dated March 12, 1998 for the subject product.

Comment 12 in this letter noted that a number of pages were missing from the original application. These pages constituted an entire volume and portions of another volume. In the attached March 31, 1999 letter to the FDA, Endo Pharmaceuticals Inc. requested the agency to recheck its files in light of an "Acceptance for filing letter" dated March 20, 1998 which we had received. In an April 5th conversation with Mr. Tim Ames, Project Manager, Endo was informed that the files, which we had submitted with our original application, were found at the FDA. Endo feels that the comment on the missing files significantly contributed to the FDA's classification of our deficiency letter as a "Major Deficiency". We would appreciate, if in light of the fact that the missing files were actually submitted by Endo in our original application, the FDA would please change the status of our deficiency letter from a "Major" to a "Minor".

We are amending this application with our responses to the Agency's comments. Included in this amendment are the following:

- Completed FDA Form 356h and Addendum
- Field Copy Certification
- A copy of FDA's March 30, 1999 Facsimile Letter
- CMC Responses 1 - 12

RECEIVED
MAY 07 1999
CDER/ONDC

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It is our understanding that the following has been completed:

Bioequivalence Study:	March 30, 1999 letter indicates no further comments at this time.
Preapproval Inspection:	March 25, 1998 FDA District letter indicates the application is approvable from a field standpoint.
Method Verification:	Samples were submitted to the Brooklyn Regional Laboratory on April 6, 1998. As per Mr. Tim Ames, Project Manager, Method Validation is not necessary since the product is USP
CMC:	This amendment completes all outstanding issues.
Labeling:	September 30, 1998 Facsimile Amendment resolved labeling comments and provided Final Printed Labeling. As per Mr. Adolph Vezza, Project Manager, Labeling Division, the labeling is satisfactory.

If there are any questions regarding this amendment, or any further issues, please contact me at (516) 522-3305.

Sincerely,

Carol Patterson, MS
Manager, Regulatory Affairs

attachments
CAP.wj
DefResp/OxyAPAP5-500mg

Endo®

Endo Pharmaceuticals Inc.

October 26, 1998

labeling review
draft 10/28/98
ABJr

Douglas Sporn
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation and Research
Food and Drug Administration
Document Control Room, Metro Park North II
7500 Standish Place, Room 150
Rockville, MD 20855

Re: ANDA 40-303; Oxycodone and Acetaminophen Capsules USP, 5 mg/500 mg
TELEPHONE AMENDMENT

Dear Mr. Sporn:

References made to the teleconference on October 22, 1998 between Carol Patterson, Endo Pharmaceuticals and Adolph Vezza, Food and Drug Administration for the above subject product. As requested, the Oxycodone and Acetaminophen blister cell final printed labeling has been revised to appear in actual size.

Enclosed are twelve copies (one additional copy is enclosed in the FDA archival copy) of final printed blister cell labels. In addition, a side-by-side comparison of the previous blister cell label submitted on September 30, 1998 vs. the proposed label is included in accordance with 21 CFR 314.94 (a)(8) (iv).

If there are any questions, please contact me at (516) 522-3305.

Sincerely,

Carol Patterson

OCT 27 1998

Carol A. Patterson, M.S.
Manager, Regulatory Affairs

Enclosures

500 ENDO BOULEVARD GARDEN CITY, NY 11530 FAX (516) 832-2291

Archival Copy
CMC Submission

Endo®

Endo Pharmaceuticals Inc.

November 11, 1999

NEW CORRESP
No to
Fax

Douglas Sporn
Director
Office of Generic Drugs, HFD-600
Center for Drug Evaluation & Research
Food and Drug Administration
Metro Park North II, Room 150
7500 Standish Place
Rockville, MD 20855

Re: ANDA 40-303; Oxycodone and Acetaminophen Capsules, USP
5 mg/500 mg
Facsimile Amendment

Dear Mr. Sporn:

Reference is made to the November 3, 1999 facsimile correspondence from the Agency which describes chemistry comments on the subject file.

We are amending this application with our responses to the Agency's comments. Included in this amendment are the following:

- Completed FDA Form 356h and Addendum
- Field Copy Certification
- A copy of FDA's November 3, 1999 Facsimile Letter
- CMC Responses

It is our understanding that this amendment resolves all outstanding issues, and we look forward to approval of this application.

If there are any questions regarding this amendment, please contact me at (516) 522-3305.

Sincerely,

Carol Patterson, MS
Manager, Regulatory Affairs

attachments
Submiss/FDADefResponseOxyCaps11-10-99

500 ENDO BOULEVARD GARDEN CITY, NY 11530 FAX (516) 832-2291