CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER _____

CORRESPONDENCE

Review Copy

Endo®

Endo Pharmaceuticals Inc.

FPL
NEW CONCEPT
NC

December 23, 1998

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 75-351; Butalbital, Aspirin, Caffeine and Codeine Phosphate Capsules, USP, 50 mg/325 mg /40 mg/30 mg
Facsimile Amendment

Dear Mr. Sporn:

Reference is made to your December 1, 1998 facsimile correspondence which describes chemistry, manufacturing and controls and labeling deficiencies in connection with our original application dated March 31, 1998 for the subject product.

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 December 1, 1998 Facsimile Letter
- CMC Responses
- Labeling Responses

RECEIVED
DEC 24 1998

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It is our understanding that the following has been completed:

Bioequivalence Study: December 1, 1998 letter indicates no further comments at this time.
Preapproval Inspection: April 24, 1998 FDA District letter indicates the application is approvable
Method Verification: samples were submitted to the Brooklyn Regional Laboratory on April 21, 1998
CMC & Labeling: this amendment (12/23/98) completes all outstanding issues.

If there are any questions regarding this information, please contact me at (516) 522-3306.

Sincerely,

Jeanne Stelter

Jeanne Stelter
Regulatory Associate

attachments

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Endo Pharmaceuticals Inc.

March 31, 1998

Labeling review drafted 8/17/98

Douglas Sporn
Director
Office of Generic Drugs
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
Butalbital, Aspirin, Caffeine and Codeine Phosphate Capsules, USP
50 mg/325 mg/40 mg/30 mg

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.

This ANDA consists of nine volumes submitted in duplicate as archival and technical review copies.

The Archival copy of the application consists of nine volumes in blue jackets designated as Volumes 1.1 to 1.9. The technical review copy of this application consists of Volumes 1.1 - 1.3 in red jackets (Chemistry, Manufacturing and Controls information and Labeling) and Volume 1.4 - 1.9 (Bioequivalence Study Report and associated product information) in orange jackets. In addition, the Methods Validation Package (Section XVIII) has been submitted, in duplicate, in separate black binders.

This application includes the results of the following *in vivo* bioequivalence study comparing the Endo product to Fiorinal® w/Codeine manufactured by Sandoz Pharmaceuticals:

- "A Single-dose Crossover Study in Healthy Volunteers to Evaluate the *In Vivo* Bioequivalence of Butalbital/Codeine/Caffeine/Aspirin Test and Reference Capsules" (Study No. 3179-001, Volume 1.5 - Volume 1.9). The data diskette for this study is located in Volume 1.5 of the Review copy.

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Plasma concentrations of butalbital and codeine were assayed. These were found to be equivalent based upon meeting the 90% confidence interval criteria of 80-125% for the log-transformed AUCs and Cmax, between the test and reference product.

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.

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. As a result, The DuPont Merck Pharmaceutical Company functions as a [redacted] the manufacturing, processing, packaging, labeling and quality control testing for Endo. This information is outlined throughout this application. Butalbital, Aspirin, Caffeine and Codeine Phosphate Capsules, USP, 50 mg/325 mg/40 mg/30 mg will be manufactured at DuPont Merck's cGMP facility in [redacted]

Endo Pharmaceuticals Inc. certifies that, concurrent with the filing of this application, a true copy of the technical section of the ANDA has been sent to the local District office.

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) 522-3306. Any written communications may be faxed to me at (516) 832-2291.

Sincerely,

Jeanne Stelter

Jeanne Stelter
Regulatory Associate

attachments

ANDA 75-351

APR 10 1998

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

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.

NAME OF DRUG: Aspirin, Butalbital, Caffeine and Codeine Phosphate Capsules USP, 325 mg/50 mg/40 mg/30 mg

DATE OF APPLICATION: March 31, 1998

DATE (RECEIVED) ACCEPTABLE FOR FILING: April 1, 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,

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