CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40308

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA: 40-308

FIRM: Barr Laboratories, Inc.
2 Quaker Road
P.O. Box 2900
Pomona, NY 10970-5019

DOSAGE FORM: Tablet STRENGTH: 5 mg/500 mg, 7.5 mg/750 mg

DRUG: Hydrocodone Bitartrate and Acetaminophen

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable 11/16/98

BIO STUDY INFORMATION: Bio waiver granted. In-vitro dissolution data found acceptable per H. Nguyen on 8-4-98.

METHODS VALIDATION:

Active drug substance and drug dosage forms are both compendial items per USP 24.

STABILITY:

The containers used in the stability study are of the same size and material as those described in the container section. The firm submitted accelerated stability data for the product packaged in all container sizes.

The firm requests an expiration date of 24 months based on the data submitted.

The stability tests and specifications are as follows:

Product description and physical characteristics:

5 mg/500 mg:

Description: White, capsule-shaped, scored tablets. Debossed with b/915 on one side and plain on the other side.

7.5 mg/750 mg:

Description: Light yellow, capsule-shaped, scored tablets. Debossed with b/736 on one side and plain on the other side.

Dissolution:

a. Hydrocodone Bitartrate:
pH 5.8 buffer, 900 mL, USP 2, 50 rpm, assay, NLT __% dissolved in 30 mins.

b. Acetaminophen:
pH 5.8 buffer, 900 mL, USP 2, 50 rpm, assay, NLT __% dissolved in 30 mins.

Assay:

Impurities/degradants:

LABELING: Acceptable 11/10/99.

STERILIZATION VALIDATION: N/A

SIZE OF BIO BATCH:

Bio-waiver was granted based on in-vitro dissolution data obtained on the exhibit batch.

SIZE OF STABILITY BATCHES:

The executed batch records can be found on the following pages:

5 mg/500 mg:

a. (executed batch #7T91501), p.12-0005-12-00110)
b. (blank batch record), p. 11-00010-11-00083

7.5 mg/750 mg:

a. (executed batch #7T73601) p.12-00123-12-00281
b. (blank batch record), p.11-00084-11-000165

PROPOSED PRODUCTION BATCH:

The proposed production batch sizes for the strengths indicated above are[ ]and[ ]respectively.

RECOMMENDATION: Approve.

SIGNATURE: DATE:

/S/ 7/25/00

/S/ 7/25/00

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Manufacturing Controls

1. CHEMISTRY REVIEW NO. 3

2. ANDA # 40-308

3. NAME AND ADDRESS OF APPLICANT
Barr Laboratories, Inc.
Attention: Christine Mundkur
2 Quaker Road
P.O. Box 2900
Pomona, NY 10970-5019

4. LEGAL BASIS FOR SUBMISSION
The RLD is Vicodin & Vicodin ES 5 mg/500 mg, 7.5 mg/750 mg

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Hydrocodone Bitartrate and Acetaminophen Tablets USP

9. AMENDMENTS AND OTHER DATES:
Firm:
4-14-98: Original application
7-13-99: Amendment
4-12-00: Amendment
7-11-00: tele-amendment

FDA:
5-21-98: acknowledgement

10. PHARMACOLOGICAL CATEGORY
Analgesic and Antitussive

11. Rx or OTC
Rx

12. RELATED IND/NDA/DMF(s)
DMF
DMF
See Review Element# 37 for DMFs and see Review Elements# 22 and 26 for LOAs.

13. DOSAGE FORM
Tablet

14. POTENCY
5 mg/500 mg, 7.5 mg/750 mg

15. CHEMICAL NAME AND STRUCTURE
Acetaminophen:
C8H9NO2 M.W. 151.16
Chemical name: Acetamide, N-(4hydroxyphenyl)-4'-Hydroxyacetanilide

Hydrocodone Bitartrate:
C18H21NO3.C4H6O6.22H2O M.W. 494.5
Morphinan-6-one, 4,5-epoxy-3-methoxy-17-methyl,(5a)-,[R-(R*,*)]-2,3-dihydroxybutanedioate(1:1), hydrate(2:5).
4,5a-Epoxy-3methoxy-17-methylmorphinan-6-one tartrate(1:1) hydrate (2:5).
Anhydrous 449.46

17. COMMENTS

a. **EER**: Acceptable.

Requested for Barr Laboratories Inc. (Forest, VA, Northvale, NJ and Pomona, NY), [ ] by T, Ames on 5/21/98. AC 11/16/98.

Note: A summary of the findings from the initial inspection were submitted in a memo from Compliance dated November 17, 1998. The investigator included a note to the chemist expressing concern over the lack of validation for determination of impurities in the The review chemist has determined that the applicant conducts testing for the the major known impurities in both the and final drug product. Method descriptions and validation data have been provided.

b. **MV** (method validation): **Acceptable**

Active drug substance and drug dosage forms are both compendial items per USP 23. Samples will not be requested for testing by FDA labs.

c. **Bio-Review: Acceptable**

Acceptable per Z. Wahba reviewed on 8-6-98.

d. **Labeling review: Satisfactory**

Acceptable per review dated 11/10/99.

e. **DMFs: satisfactory**

DMF [ ] for Acetaminophen, USP was reviewed by A.Langowski and found satisfactory on 4/27/00.

DMF [ ] for Hydrocodone Bitartrate was reviewed by Langowski and found satisfactory on 07/24/00.

18. CONCLUSIONS AND RECOMMENDATIONS
Approval.

19. REVIEWER:	DATE COMPLETED:
Andrew J. Langowski	6/09/00;07/19/00

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