CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40249

CHEMISTRY REVIEW(S)

ANDA NUMBER 40-249

FIRM: Kiel Laboratories, Inc.

DOSAGE FORM: Tablet Extended Release

STRENGTH: 100 mg

DRUG: Orphenadrine Citrate

CGMP STATEMENT/EIR UPDATE STATUS: Acceptable 6/30/98.

BIO STUDY: From bioequivalence point of view, the firm has met the requirements of *in vivo* bioequivalency and *in vitro* dissolution testing, and the application is acceptable. Review concur date 10/10/98 by Director of the Division of Bioequivalence.

METHODS VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S):

MV is pending.

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION? Yes

100s: 60 cc round white HDPE bottles manufactured by HDPE.

Cap: 33 mm white polypropylene cap (lined with by and seal by manufactured by

250s: 150 cc round white HDPE bottles manufactured by Resin:

Cap: 45 mm white polypropylene cap (lined with by and seal by manufactured by

Void filler for each container: Rayon Fiber, USP manufactured by

Studies: 6 month accelerated (40°C/75% RH with testing at 0, 1, 3 and 6 months) data and 24 months room temperature data are provided for test batch GA185. Data support a 24 month expiry date.

LABELING:

Satisfactory. Approval Summary dated 11/19/98 per TWatkins. Post-approval revisions requested.

STERILIZATION VALIDATION (IF APPLICABLE):

N/A

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?):

GA185 - tablets (theoretical yield)

Batch yield for total tablets packaged is %.

Active ingredient by DMF is acceptable.

SIZE OF STABILITY BATCHES - (IF DIFFERENT FROM BIO BATCH, WERE THEY MANUFACTURED VIA SAME PROCESS):

Same as bio batch.

PROPOSED PRODUCTION BATCH - MANUFACTURING PROCESS THE SAME AS BIO/STABILITY? Yes

Proposed production batch size - tablets.

Review Chemist: Shirley S. Brown /S/ 12/14/98
Supervisor: Michael Smela
Date: December 14, 1998

/S/ 12/15/98

1. CHEMISTRY REVIEW NO. 3

2. ANDA# 40-249

3. NAME AND ADDRESS OF APPLICANT

Kiel Laboratories, Inc.
2225 Centennial Drive
Gainsville, GA 30504

4. BASIS OF SUBMISSION

Accepted by OGD

5. SUPPLEMENT(s)

N/A

6. PROPRIETARY NAME

N/A

7. NONPROPRIETARY NAME

Orphenadrine Citrate

8. SUPPLEMENT(s) PROVIDE(s) FOR:

N/A

9. AMENDMENTS AND OTHER DATES:

2/17/97	Original submission
5/1/97	FDA's letter of refusal to file the ANDA
5/7/97	Amendment responding to FDA's letter of 5/1/97
3/26/98	Amendment responding to Bioequivalence's 9/15/97 correspondence
4/16/98	Amendment responding to Chemistry's NAL of 11/10/97
*11/10/98	Amendment responding to Chemistry's NAL of 10/22/98
*11/25/98	Amendment responding to telecon of 11/24/98
*12/14/98	Amendment responding to telecon of 12/14/98

*subject of this review

10. PHARMACOLOGICAL CATEGORY

Relaxant (skeletal muscle)
Antihistaminic

11. Rx or OTC

Rx

12. RELATED IND/NDA/DMF(s)

DMF

DMF

DMF
DMF

13. DOSAGE FORM

Tablet, Extended Release

14. POTENCY

100 mg

15. CHEMICAL NAME AND STRUCTURE

See USP XXIII, page 1116.

16. RECORDS AND REPORTS

N/A

17. COMMENTS

November 10, 1998 amendment responding to the October 22, 1998 NAL:

1. **Review of the bioequivalency amendment dated March 26, 1998 is pending.**

   Response: The review of the bioequivalency amendment has been completed. The release specifications were revised as requested (widen the lower limit for the 1 hour point to %, delete the 2nd and 6nd hour time points and add a 12 hour time point with a limit of NLT %).

2. **As the subject drug product is not an official article in the United States Pharmacopeia (USP), we require a satisfactory methods validation for the finished dosage form to support the ANDA. The study will be scheduled with a FDA servicing laboratory once the specifications have been revised satisfactorily and a dissolution test and specification have been accepted by our Division of Bioequivalence. It would be helpful if you would include a copy of the current methods for the drug product in a separate section of your amendment.**

   Response: Copies of the finished product analytical methods are provided.

3. **Your response must also address the labeling deficiencies.**

Response: Labeling deficiencies are addressed.

4. Please provide any additional stability data that may be available.

Response: Twenty-four month RT stability data are provided. Future tables will include the revised DP release and impurities specifications (page 38).

18. CONCLUSIONS AND RECOMMENDATIONS

Prepare Approval package.

MV will be requested.

19. REVIEWER: /S/ DATE COMPLETED: 12/31/98

Shirley S. Brown November 24, 1998 (11/10/98 amendment)
December 9, 1998 (11/25/98 amendment)
December 14, 1998 (12/14/98 amendment)

/S/
12/21/98