CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40-424

ADMINISTRATIVE DOCUMENTS

APPROVAL SUMMARY

ANDA: 40-424

DRUG PRODUCT: Spironolactone Tablets USP

FIRM: Mylan Pharmaceuticals Inc.

DOSAGE FORM: Oral Tablets

STRENGTH: 25 mg, 50 mg, and 100 mg

cGMP STATEMENT/EER UPDATE STATUS: Acceptable *(1/02/01, J.D. Ambrogio)*

BIO STUDY: Acceptable (*2/19/01, M. Makary*).
The recommended dissolution specifications and conditions are as follows:

1000 mL of 0.1 N HCl containing 0.1% sodium lauryl sulfate at 37 °C using USP Apparatus 2 (Paddles) at 75 rpm.

NLT of the labeled amount of Spironolactone is dissolved in 60 minutes.

VALIDATION: N/A

STABILITY: The container/closure system used for the stability study (HDPE bottles of 100 and 500 units for all strengths) is equivalent to the system proposed for commercial use. All reported data are within specifications as listed. A 24-month expiration date is proposed.

Stability tests and specifications are as follows:

Appearance (Visual): Meets Requirements
Assay 95%-105% of Label Claim
Dissolution in 60 min
Related Compounds
NMT
NMT
NMT Unidentified Impurities
NMT
Loss on Drying:

LABELING: Acceptable (*7/11/01, J. Barlow*).

STERILIZATION VALIDATION: (IF APPLICABLE): N/A

SIZE OF BIO Batch:
Mylan manufactured three ANDA batches, one for each strength. The batch size and lot numbers are as follows:

Strength	Lot Number	Batch size	Purpose
25 mg	R1H0634		stability
50 mg	R1H0635		stability
100 mg	R1H0636		bioequivalence/stability

SIZE OF STABILITY BATCHES: See above

PROPOSED PRODUCTION BATCHES:
The batch sizes for the proposed production batches are as follows:

Strength	Proposed Production Batch size
25 mg	tablets
50 mg	tablets
100 mg	tablets

Review Chemist: André Raw **DATE:** 8/14/01
Andre Raw, Ph.D.

Team Leader: A J Mueller **DATE:** 8-14-01
Albert Mueller, Ph.D.

Telephone Conversation Memorandum

ANDA: 40-424

DRUG: Spironolactone Tablets USP, 25 mg, 50 mg and 100 mg

FIRM: Mylan Pharmaceuticals Inc.

PERSONS INVOLVED: Vince Mancinelli, Mylan
Tim Ames, FDA

PHONE NUMBER: 304-599-2595

DATE: June 18, 2001

Following related to firm as a Telephone Amendment request:

1. Your room temperature stability data (3, 6, 9, 12 months) indicates a significant trend toward Spironolactone degradation, based upon diminishing assay values. Furthermore, after 12 months, the observed assay values for Spironolactone approach the lower limit of your acceptance criteria (95-105%). Based upon these observations, we feel that a tentative 24-month expiry period is not justified. Therefore we request that the expiry period for Spironolactone Tablets USP be based upon real time room temperature stability data.

2. Based upon your room temperature stability data (3, 6, 9, 12 months), it is noted that while the assay values for Spironolactone consistently diminished for all strengths tested (as much as degradation is observed), that the level for related compounds remained constant. Please explain and clarify whether any potential degradants are retained on the column, elute close to the beginning of the run, or are not adequately quantified by your analytical method.

Timothy W. Ames, R.Ph., M.P.H.
Project Manager, Div Chem. I, Team 1, OGD