CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

75-138

ADMINISTRATIVE DOCUMENTS

DIVISION REVIEW SUMMARY

ANDA: 75-138

FIRM: Mylan Pharmaceuticals, Inc.

DOSAGE FORM: Extended-release Capsules

STRENGTHS: 120 mg, 180 mg & 240 mg

DRUG: Verapamil Hydrochloride

CGMP STATEMENT/EIR UPDATE STATUS:
Acceptable dated 12/22/98.

BIO STUDY INFORMATION:
Mylan submitted an amendment on December 31, 1997 providing for the 120 mg and 180 mg strengths. The Division of Bioequivalence reviewed them in conjunction with the firm's response to the Bio deficiencies.

The Division of Bioequivalence has no further questions at this time (September 19, 1998). The approval includes the 240 mg, 180 mg and 120 mg strengths.

The following dissolution testing was incorporated into the firm's stability testing and quality control program:

Conduct the test in 900 mL of 0.1N HCl at 37EC using USP XXIII apparatus II (paddle) at 100 rpm. The following tentative specifications are recommended:

2 hours
4 hours
8 hours
24 hours

METHODS VALIDATION - (DESCRIPTION OF DOSAGE FORM SAME AS FIRM'S)
Acceptable dated 1/13/98.

STABILITY - ARE CONTAINERS USED IN STUDY IDENTICAL TO THOSE IN CONTAINER SECTION?
Fully described in the container/closure section of the application for the 100's and 500's.

A revised post-approval stability protocol for the 120 mg (p. 17), 180 mg (p. 18) and 240 mg (p. 19) strengths are appended. The following test and limits are common for all strengths:

Test	Limit
Assay	90.0% - 110.0%
Dissolution (drug release)	2 hours 4 hours 8 hours 24 hours
Related compounds	Individual: Total:
Moisture content	
Appearance	Visual observation

LABELING
Acceptable dated 1/22/99.

STERILIZATION VALIDATION (IF APPLICABLE)
N/A

SIZE OF BIO BATCH - (FIRM'S SOURCE OF NDS O.K.?)
capsules for the 120 mg and 180 mg dosage forms and
capsules for the 240 mg dosage form.

The source of the NDS was found acceptable, and DMF Verapamil HCl was found adequate on 10/22/98. It is noted that the drug substance is compendial. The firm has added a test and specifications for particle size.

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

All batches manufactured via same process: 240 mg lot No. 2C004J, 180 mg lot No. 2D002J, and 120 mg lot No. 2001J.

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

Blank batch records for capsules (240 mg) and capsules (120 mg & 180 mg) are included. The manufacturing process is the same.

RECOMMENDATION: Recommend approval letter to issue.

SIGNATURE:
A. Croitoru
Edwin Ramos
(revised)

DATE:
January 26, 1999
February 5, 1999

2/8/99