CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

40265

CHEMISTRY REVIEW(S)

ANDA Number: 40-265

FIRM: Bigmar Inc.

DOSAGE FORM: Methotrexate Injection USP (Non-Preserved).

STRENGTH 25mg/mL, of 4 mL, 8 mL and 10 mL fills in a 10 mL vial.

CGMP STATEMENT/EER UPDATE STATEMENT:

EER pending. Acceptable 2/24/99 RW.

BIO STUDY: Waiver granted 12/31/97

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

Not applicable. Both drug substance and drug product are USP.

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

Yes. Container section describes a 10 mL clear glass vial with rubber cap and aluminum seal.

Tentative Expiration date is 24 months (2 years).

LABELING:

FPL found adequate on 1/13/99.

STERILIZATION VALIDATION (IF APPLICABLE):

Sterilization validation found adequate on 2/2/99.

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

No bio batch (waiver granted 12/29/97).

ANDA 40-265 also covers 2mL fill in 10mL vial See CR #2,3,4.
M Smela 2/24/99

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

Two batches were manufactured at Liters each.

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

Liters (Manufactured in the same manner as stability batch).

/S/ 2/10/99

Prepared by Stephen Sherken on 2/10/99.

/S/ 2/18/99

1. CHEMISTRY REVIEW NO. 5

2. ANDA # 40-265

3. NAME AND ADDRESS OF APPLICANT

Bigmar Inc.
Johnstown, OH 43031-9141

4. LEGAL BASIS FOR SUBMISSION

505(j), 21 CFR 314.94

5. SUPPLEMENT(s)	6. PROPRIETARY NAME
N/A	N/A

7. NONPROPRIETARY NAME	8. SUPPLEMENT(s) PROVIDE(s) FOR:
Methotrexate Injection USP	N/A

9. AMENDMENTS AND OTHER DATES:

DOA 7/30/97; Amend 9/17/97; Amend 11/3/97; Amend (Chemistry-Vol 2.1 (Micro-Vol 2.2) 12/20/97; NA (Chem Major) 1/29/98; NA (Micro) 6/11/98; Amend 2/9/98; Amend (Major) 2/16/98; Amend (Micro) 5/29/98; Amend (Chem) 6/11/98; NA Chem & Micro, (FAX) 8/19/98; Amend (FAX) 9/16/98; FAX NA with Micro deficiencies 10/23/98; Label FAX 11/4/98; FAX Amend 11/20/98; Micro Review 12/17/98; Revised Labeling Amend 11/25/98; NA (Fax) 12/24/98; FPL Amend 1/8/99; Label rev (adequate) 1/13/99; Amend 1/21/99; New Corresp 1/27/99; Micro review (adequate) 2/2/99.

10. PHARMACOLOGICAL CATEGORY	11. Rx or OTC
Neoplastic Diseases	Rx

12. RELATED IND/NDA/DMF(s)

NDA 11-719, DMF-

13. DOSAGE FORM	14. POTENCY
Clear colorless solution.	25 mg/mL in 4 mL, 8 mL and 10 mL fills in a 10 mL vial, (non-preserved).

15. CHEMICAL NAME AND STRUCTURE

See review #1.

16. RECORDS AND REPORTS N/A

17. COMMENTS

No further chemistry deficiencies found.

ANDA 40-265 also covers 2 mL fill. See CR # 2, 3, 4.

/S/
2/24/99

Sterility assurance review completed for the 1/21/99 & 1/27/99 amendments on 2/2/99. They were found adequate.

Bio-waiver was granted in review dated 12/31/97.

EER recommends withhold by M.Egas on 6/3/98. FUR pending Labeling review of 1/8/99 amendment found adequate on 1/13/99.

18. CONCLUSIONS AND RECOMMENDATIONS

Approve ANDA 40-265 pending acceptable EER.

19. REVIEWER: DATE COMPLETED:

Stephen Sherken 2/10/99

cc: ANDA 40-265
Division File
Field Copy

Endorsements:

HFD-625/SSherken/2/9/99
HFD-625/Msmela/2/10/99
V:\FIRMSAM\BIGMAR\LTRS&REV\40265.RV5.DOC
F/t by: gp/2/16/99

/S/ 2/17/99

/S/ 2/18/99

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Chemistry Review #5