CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

74944

CHEMISTRY REVIEW(S)

DIVISION REVIEW SUMMARY

ANDA #: 74-944 **DRUG PRODUCT:** Atracurium Besylate Injection, Unpreserved

FIRM: Marsam Pharmaceuticals Inc.

DOSAGE: Injection

STRENGTH: 10 mg/mL, 5 mL vials

cGMP STATEMENT/EIR UPDATE STATUS:
cGMP: GMP Certification is enclosed. (Pages 189-191).
EER: Pending.

BIO STUDY(ies)/BIOEQUIVALENCE STATUS:
On 12/23/96 the Division of Bioequivalence issued a no comments letter to the firm.

METHODS VALIDATION (Including dosage form description):
The methods were verified by Philadelphia field laboratories for drug substance and product. The methods are found adequate after incorporation of the comments from the Field labs.

STABILITY(Conditions, Containers, methods):
Bio batch

Evaluation of stability indicating methods:

Stability Assays

Test	**Specifications**
Appearance	Clear, colorless liquid.
Assay (active)	%
Particulate matter	
pH	

Degradation products Total Cp 7110 trans Laudanosine Unknown/unspecified 7113 7114 7115 + 7116 7110 cis CP 7185 CP 7149 Unidentified RRT 0.11	 NMT % NMT % NMT % NMT % NMT % NMT % NMT % NMT % NMT % NMT % NMT %
Sterility	Complies
Bacterial Endotoxin	EU/MG

Stability studies were done on the bio batch. Containers are the same those listed in the container section. Stability studies are in conformance with the FDA Guidelines.

LABELING REVIEW STATUS: Satisfactory dated 7/31/97.

STERILIZATION VALIDATION (If Applicable): Acceptable (dated June 10, 1997).

BATCH SIZES:

BIO BATCH: Lot # M96020 L size)
NDS source:
STABILITY BATCHES (different from BIO BATCH, manuf. site, process)
Stability batch is the same as the bio-batch

PROPOSED PRODUCTION BATCH
L is the proposed production batch size.

Process is the same as the demonstration batch.

COMMENTS: Approvable

CHEMISTRY REVIEWER: **DATE:**

Radhika Rajagopalan April 7, 1998

Reviewer is on extended leave; letter needs to issue [signature] 7/8/98

1. CHEMISTRY REVIEW NO. 5

2. ANDA # 74-944

3. NAME AND ADDRESS OF APPLICANT
Marsam Pharmaceuticals Inc.
Attention: Steven W. Brown R.Ph.
Building 31, 24 Olney Avenue
Cherry Hill, NJ 08034

4. LEGAL BASIS FOR SUBMISSION
US Patent No. 4,179,507 for the listed drug will expire on December 18, 1996. Exclusivity I-108 (Expanded Use - For ICU patients undergoing long-term infusion during mechanical ventilation) expired on June 6, 1997.

5. SUPPLEMENT
N/A

6. PROPRIETARY NAME
N/A

7. NONPROPRIETARY NAME
Atracurium Besylate

8. SUPPLEMENT PROVIDE FOR:
N/A

9. AMENDMENTS AND OTHER DATES:

August 21, 1996--	ANDA Original Submission.
September 20, 1996--	FDA acknowledgment letter.
December 23, 1996--	Division of Bioequivalence issued Bio acceptance letter
January 27, 1997--	FDA major deficiency letter (chemistry, micro and labeling)
February 24, 1997--	ANDA amendment by firm
May 8, 1997--	FDA Minor deficiency letter by fax (chemistry, micro and labeling)
May 21, 1997--	ANDA minor amendment by firm
May 23, 1997--	New correspondence by firm
June 10, 1997--	Micro review acceptable
July 1, 1997--	Labeling review #3 deficient
July 16, 1997--	T-conference initiated by chemist
July 18, 1997--	Amendment by firm (chemistry issues)
July 23,1997	Amendment by firm
September 22, 1997--	Not approvable letter by FDA
February 5, 1998--	Minor amendment by firm
March 2, 1998--	Minor deficiencies to firm (review #4)

March 30, 1998-- Amendment by firm

10. PHARMACOLOGICAL CATEGORY
Neuromuscular Blocking Agent

11. Rx or OTC
Rx

12. RELATED DMF #

13. DOSAGE FORM
Injectable, IV
single dose

14. POTENCY
10 mg/mL; 5 mL
(Unpreserved)

15. CHEMICAL NAME AND STRUCTURE
2,2-(pentamethylenebis(oxycaronylethylene))bis(1,2,3,4-tetrahydro-6,7-dimethoxy-2-methyl-1-veratrylisoquinolinium) dibenzenesulfonate

16. RECORDS AND REPORTS
N/A

17. COMMENTS
Awaiting satisfactory EER.
Final acceptable label review satisfactory (7/30/97).
Minor amendment (3/30/98) addresses all the deficiencies from the method verification. The firm has also updated drug substance specifications as per USP PF Monograph.
Adminstrative review on this application is already completed. Hence, ANDA can be approved.
Bio waiver granted on 12/23/96.

18. CONCLUSIONS AND RECOMMENDATIONS
Chemistry is approved.

19. REVIEWER: DATE COMPLETED:

Radhika Rajagopalan, Ph.D. 4/7/98