CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 75-684

CHEMISTRY REVIEW(S)

ADDENDUM

1. CHEMISTRY REVIEW NO. 5

2. ANDA # 75-684

3. NAME AND ADDRESS OF APPLICANT
Bedford Laboratories
300 Northfield Road
Bedford, OH 44146

4. LEGAL BASIS FOR SUBMISSION
Innovator Product: PEPCID® AC (famotidine) Injection
Innovator Company: Merck & Co., Inc. (NDA #19-510)
Patent Certification and Exclusivity Statement are provided (p. 007)
Patent Expiration Date: 10/15/00
U.S. Patent No. 4,283,408

5. SUPPLEMENT(s)
N/A

6. PROPRIETARY NAME
Famotidine Injection

7. NONPROPRIETARY NAME
Famotidine Injection

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

9. AMENDMENTS AND OTHER DATES:

Firm			FDA	
Orig. submission		7/30/99	Acknowledgement letter	9/24/99
			Bio review	11/16/99
			Labeling review	1/28/00
			Deficiency letter	2/2/00
Amendment		2/28/00	Labeling review	5/3/00
Amendment		6/13/00	Deficiency letter	8/10/00
Amendment	(minor)	11/3/00	Telephone call	11/30/00
Amendment	(telephone)	12/1/00	Tentatively approved	1/24/01
Amendment	(minor)	2/16/01		
Amendment	(FAX)	3/26/01		

This review covers submission dated 3/26/01.

10. PHARMACOLOGICAL CATEGORY
An inhibitor of histamine) H2-receptor and gastric secretion

11. Rx or OTC
℞

12. RELATED IND/NDA/DMF(s)

13. DOSAGE FORM
Injection

14. POTENCY
10 mg/mL (50 mL per vials)

15. CHEMICAL NAME AND STRUCTURE

[1-Amin0-3-[[[2-(diaminomethylene)amino]-4-thiazoly]methyl]thio]propylidene]sulfamide

Molecular weight: 337.43 Formula: $C_8H_{15}N_7O_3S_3$

16. RECORDS AND REPORTS None -

17. COMMENTS
The analytical method BNCH3721-025 has been revised with respect to the calculation of the impurities. Previously, the method required preparation and analysis of each individual known impurity reference standard in order to quantitative any known impurities found in the sample of the drug substance. This method of calculation required significant amounts of impurity reference standards, which are not readily available from the API manufacturer. Therefore, the method has been revised with the relative response factors of each of these known impurities. The RRF is used in the calculation of sample impurities instead of comparison to the actual preparation of each individual standard. Either method of calculation yields the same results and has no impact on the reporting of impurity values. A report is provided which outlines the determination of the Relative Response Factors of the impurities. Also included is the revised analytical method, BNCH3721-025.

Process impurity ——— is not monitored in the drug product.

[ ]

Applicant has revised the bioload specification for the drug substance for clarification purposes. It has been revised to read NMT (Not More Than) as opposed to the greater than symbol (>) that was used previously. No changes to the actual values have been made. The revised specifications are provided in Attachment VI.

18. CONCLUSIONS AND RECOMMENDATIONS
APPROVED

19. REVIEWER:
Raymond Brown

DATE COMPLETED:
April 5, 2001

38. CHEMISTRY COMMENTS TO BE PROVIDED TO THE APPLICANT

ANDA: 75-684 APPLICANT: **Bedford Laboratories**

DRUG PRODUCT: **Famotidine Injection, 10 mg/mL (50 mL per vial)**

The deficiencies presented below represent MINOR deficiencies.

Drug Master File —— remains deficient and the DMF holder has been advised of the deficiencies. A satisfactory resolution of the DMF deficiencies is required by the holder prior to the approval of the application.

Please submit a comparative impurity profile of your drug product and the RLD.

Sincerely yours,

/S/

Florence S. Fang
Director
Division of Chemistry II
Office of Generic Drugs
Center for Drug Evaluation and Research

2 pages have been withheld in full from this document.