CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: NDA 20582/S001

CHEMISTRY REVIEW(S)

NOV 10 1998

CHEMIST'S REVIEW	1. ORGANIZATION	2. NDA NUMBER
	DMEDP, HFD-510	20-582

3. NAME AND ADDRESS OF APPLICANT	4. SUPPLEMENT NUMBER, DATE
Organon Inc. 375 Mt. Pleasant Avenue West Orange, New Jersey 07052	S-001 5/18/98 USER FEE DATE: 11/19/98

5. NAME OF THE DRUG	6. NONPROPRIETARY NAME	8. AMENDMENTS/REPORT, DATE
Follistim	Follitropin beta for injection	Amendment 11/4/98

7. SUPPLEMENT PROVIDES FOR:	11. RELATED IND/NDA/DMF
changing the diluent from 0.45% sodium chloride to sterile water for injection, USP	DMF

9. PHARMACOLOGICAL CATEGORY	10 HOW DISPENSED
Hormone , follicle stimulating hormone	Rx

12. DOSAGE FORM	13. POTENCY
Lyophilized Powder for injection	75 IU or 150 IU/vial

14. CHEMICAL NAME AND STRUCTURE.

See Chemistry Review #1

15. COMMENTS

The amendment dated 11/4/98 contains additional information requested over the phone by the reviewer and a request for wavier of bioequivalence study made by the applicant, regarding the use of a new diluent. During the telephone inquiry on 10/22/98, Organon was asked to revise the tonicity limit for the reconstituted solution and provide the test and stability results for the new diluent. Firm indicated in this amendment that the tonicity limit will be revised, however, the value was not provided. Also, the firm also referred to the DMF for the tests and specifications and the stability data for the new diluent. Although the chemistry information for the new diluent provided in DMF has been reviewed and found adequate, Organon still needs to provide acceptance tests to be performed on the diluent received from the suppliers. In a second telephone inquiry made on 11/16/98, Mr. Mayo of the Organon indicated that Organon performs acceptance tests for all materials received from outside suppliers. Also the revised tonicity has been set as -0.25 to -0.35°C (freezing point depression). The information was provided in a fax on the same day and according to Mr. Mayo, a formal submission will follow(see attached). In addition, Dr. Jarugula, the Biopharm reviewer co-located with HFD-580, also indicated that the request for wavier of bioequivalence study included in this amendment is acceptable, based on the previous data provide in the original NDA. At this point, there is no more outstanding issue concerning the approval of this supplement. **This chemistry review now supersedes the previous review dated 10/23/98, in which an approvable letter with information requests was recommended.**

16. CONCLUSION AND RECOMMENDATION

Adequate information has been provided. The supplement can now be approved. Issue an approval letter.

17. NAME	REVIEWER SIGNATURE	DATE COMPLETED
Duu-Gong Wu, Ph.D. Team Leader, DNDCII	/S/	11/16/98

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CC: HFD-580/MJ Rhee;HFD-510/DG Wu

OCT 23 1998

CHEMIST'S REVIEW	1. ORGANIZATION	2. NDA NUMBER
	DMEDP, HFD-510	20-582

3. NAME AND ADDRESS OF APPLICANT	4. SUPPLEMENT NUMBER, DATE
Organon Inc. 375 Mt. Pleasant Avenue West Orange, New Jersey 07052	S-001 5/18/98 USER FEE DATE: 11/19/98
5. NAME OF THE DRUG: Follistism 6. NONPROPRIETARY NAME: Follitropin beta for injection	8. AMENDMENTS/REPORT, DATE
7. SUPPLEMENT PROVIDES FOR: changing the diluent from 0.45% sodium chloride to sterile water for injection, USP	
9. PHARMACOLOGICAL CATEGORY: Hormone , follicle stimulating hormone 10 HOW DISPENSED: Rx	11. RELATED IND/NDA/DMF
12. DOSAGE FORM: Lyophilized Powder for injection 13. POTENCY: 75 IU or 150 IU/vial	
14. CHEMICAL NAME AND STRUCTURE. See Chemistry Review #1	

15. COMMENTS

This is a consult review for HFD-580. This supplement provides for change of the current diluent, 0.45% sodium chloride, to sterile water for injection, USP. The change was submitted, according the applicant, to enhance patient comfort during dose administration. The supporting documents include 1) authorization letter from the manufacturer of the new diluent to reference DMF for the CMC information of the new diluent, 2) a comparability study report for the drug product reconstituted with water for injection, and 3) revised labeling to reflect the change of diluent. The submission, however, did not provide the revised tests and specifications as well as the stability protocol for the diluent. Also, the tonicity specification for the reconstituted solution should be revised to reflect the change of diluent

16. CONCLUSION AND RECOMMENDATION

The supplement is approvable, pending a satisfactory response to chemistry deficiencies and issues related to bioequivalence. Issue an approvable letter.

17. NAME	REVIEWER SIGNATURE	DATE COMPLETED
Duu-Gong Wu, Ph.D. Team Leader, DNDCII	/S/	10/23/98

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R/D INITIATED BY:

FILE NAME:20582.s01