CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20-415/S-003

CHEMISTRY REVIEW

FEB 1 5 1997

CHEMIST REVIEW OF SUPPLEMENT

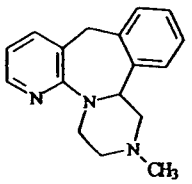
1. ORGANIZATION: HFD-120
2. NDA NUMBER: *20-415*
4. SUPPLEMENT NUMBERS/DATES: **S-003**
LETTERDATE 18-NOV-96
STAMPDATE 19-NOV-96

5. AMENDMENTS/REPORTS/DATES:
LETTERDATE 02-JAN-97
STAMPDATE 03-JAN-97

6. REC'D BY CHM: 25-NOV-96
07-JAN-97

7. APPLICANT NAME AND ADDRESS:
Organon Inc.
375 Mt. pleasant Avenue
West Orange
NJ 07052

8. NAME OF DRUG: **REMERON®**
9. NONPROPRIETARY NAME: Mirtazapine
10. CHEMICAL NAME/STRUCTURE: 1,2,3,4,10,14b-hexahydro-2-methylpyrazino [2,1-a]pyrido[2,3-c]benzazepine



11. DOSAGE FORM(S): Tablets
12. POTENCY(IES): 15 mg, 30 mg, and 45 mg (this Suppl.)
13. PHARM. CATEGORY: Depression
14. HOW DISPENSED: XXX (Rx) ___ (OTC)
15. RECORDS AND REPORTS CURRENT: XXX (YES) ___ (NO)
16. RELATED IND/NDA/DMF(S): IND 20,522; DMF ———

17. SUPPLEMENT PROVIDES FOR: An additional tablet strength, the 45-mg tablet.

18. COMMENTS: The sponsor provides adequate CMC data to support the new strength. The new strength production scale tablets will be made from a ——— with the other strengths approved in the NDA. The sponsor provides executed batch records for one stability batch ——— of 45-mg strength and one ——— NDA batch of 30-mg strength. A facility inspection has already been conducted for the original NDA and is not deemed necessary for this supplement. **See CMC Review Notes.**

19. CONCLUSIONS AND RECOMMENDATIONS: Recommend **APPROVAL** of NDA 20,415 SUPPLEMENT 003 contingent upon Biopharmaceutics approval. No facility inspection is needed for this supplement since a recent inspection was conducted for the NDA.

20. REVIEWER NAME	***SIGNATURE***	***DATE COMPLETED***
Mona Zarifa, Ph.D.		**09-JAN-97**

Copies:
ORIG. NDA
HFD-120
HFD-120/PDavid
HFD-120/MZarifa/

Filename: **N20451.S03**

INIT: SWB/

2/15/97

ATTACHMENT WITH TRADE SECRET PAGES.

3 page(s) have been removed because it contains trade secret and/or confidential information that is not disclosable.

The samples will be tested for appearance, assay, dissolution, hardness, and related substances with the same test methods described in the supplement (same as in original NDA).

Expiry Date

The expiry date approved for the original NDA is 24 months.

10. PLACEBO N/A for NDA

C. INVESTIGATIONAL FORMULATIONS

None provided in this supplement.

D. ENVIRONMENTAL ASSESSMENT

This supplement application is categorically excluded under 21 CFR 25.24© since the drug product will not be administered at higher dosage levels or for a longer duration.

E. METHODS VALIDATION

Methods were validated in the original NDA.

F. LABELING

Copies of revised draft package insert is provided and includes the 45-mg strength. Packaging labels are provided for the bottles and blister packs for the 45-mg tablets in all configurations. All required information is on the labels and the labels are clear and easy to read.

G. ESTABLISHMENT INSPECTION

A facility inspection has already been conducted for the original NDA and is not deemed necessary for this supplement.