

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 020936

CHEMISTRY REVIEW(S)

JAN 27 1999

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS

REVIEW OF CHEMISTRY AND MANUFACTURING CONTROLS

NDA 20-936

	<u>letterdate</u>	<u>stampdate</u>	<u>rec'd by chemist</u>	<u>completed</u>
INITIAL SUBMISSION:	19-DEC-97	19-DEC-97	30-DEC-97	27-APR-98
AMENDMENTS:	19-NOV-98	20-NOV-98	23-NOV-98	20-JAN-99
	18-DEC-98	21-DEC-98	28-DEC-98	20-JAN-99

CHEMIST REVIEW: # 2 **SPONSOR:** SMITHKLINE BEECHAM PHARMACUETICALS

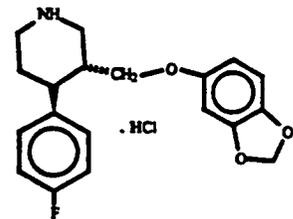
REVIEW CHEMIST: M.Zarifa, Ph.D **ADDRESS:** 1250 South Collegeville Road
P.O.Box 5089
Collegeville, PA 19426-0989

PRODUCT NAME:
Proprietary: Paxil®
USAN [1997]: Paroxetine Hydrochloride
Code Name: BRL-029060

DOSAGE FORM/ROUTE OF ADMINISTRATION: 12.5, 25 mg CR Tablets/Oral

PHARMACOL.CATEGORY/PRINCIPAL INDICATION: Depression

STRUCTURAL FORMULA & CHEMICAL NAME:



(-)-(3S,4R)-4-(p-Fluorophenyl)-3-[(3,4-methylene-dioxyphenoxy)methyl]piperidine hydrochloride hemihydrate

$C_{19}H_{20}NO_3F \cdot HCl \cdot \frac{1}{2} H_2O$ Mol. Wt. 374.8 (329.4 free base)

REMARKS: In response to the CMC deficiency letter dated August 12, 1998, SKB provides description and validation data for the newly developed stability-indicating degradation method and the chiral method for the drug product. SKB submits an amended method validation package in triplicate. The new package includes the new degradation and chiral methods with their respective validation reports. The list of drug product specifications is amended to include chiral limits/test. The sponsor updates the stability data up to the 18-month time point.

CONCLUSIONS & RECOMMENDATIONS: Recommend NDA 20-936 to be APPROVED. Site Inspections are complete and Office of Compliance recommendation is satisfactory

SKB's dissolution limits in the pH 7.5 buffer include a limit dissolved in hours using USP apparatus II at 150 rpm. The Biopharmaceutical Division agreed on this specification for the 12.5 mg and 25 mg strengths. The sponsor will not market the 37.5 mg and 50 mg strengths. The available stability data at the present time support an expiry date not to exceed 18 months for the 12.5 mg and 25 mg tablets.

cc: ORIG: NDA
HFD-120/Div. File
HFD-120/ [redacted]
HFD-810/CHolberg
HFD-120/RLostritto/RSeever
HFD-120/MGuzewska/MZarifa
INIT: RS/

/S/ 1/27/99

/S/
Mona Zarifa, Ph.D., Chemist

