CENTER FOR DRUG EVALUATION AND RESEARCH

APPROVAL PACKAGE FOR:

APPLICATION NUMBER

21-168

Chemistry Review(s)

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120
REVIEW OF CHEMISTRY, MANUFACTURING, AND CONTROLS

AUG - 4 2000

NDA 21-168

CHEM. REVIEW #	2	**REVIEW DATE**	03-AUG-00

SUBMISSION TYPE	**DOCUMENT DATE**	**CDER DATE**	**ASSIGNED DATE**
Original	30-SEP-99	04-OCT-99	13-OCT-99
NC	02-AUG-99	03-AUG-99	03-AUG-99

NAME AND ADDRESS OF APPLICANT

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-3500

DRUG PRODUCT NAME

Proprietary:	Depakote ER Tablets
Nonproprietary/USAN:	Divalproex Sodium
Code Name/Number:	A-50711
Chem. Type/Ther. Class:	6S / 2011110
PHARMACOLOGICAL CATEGORY/INDICATION	Migraine
DOSAGE FORM	Tablets
STRENGTHS	500 mg
ROUTE OF ADMINISTRATION	Oral
DISPENSED	XXX RX ___ OTC
SPECIAL PRODUCTS	___YES XX NO

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA
Sodium hydrogen bis(2-propylvalerate), oligomer

$(C_{16}H_{31}NaO_4)_n$

F.W. 310.41

CAS Registry # [76584-70-8]

SUPPORTING DOCUMENTS: NDA 18-723 (Depakote Tablets, provides CMC for drug substance) NDA 20-782 (NA)(Depakote ER Tablets, provides CMC for drug product) IND — DMF — (all Type 3)
RELATED DOCUMENTS: NDA 19-680 (Depakote Sprinkle Capsules), 19-794 (Depakote Dispertab CP Tablets), 20-320 (Depakote Tablets), — IND —
CONSULTS: See NDA 20-782 for consult regarding the trademark name, Depakote® ER

REMARKS/COMMENTS: Insert labeling was reviewed and found acceptable as amended. Packaging labeling was reviewed. The format was found acceptable and requisite information was found in the packaging. Objectionable provisions were found with labeling of the sample packaging. The objectionable items were statements of clinical indication and promotional statements of the dosage form. After discussions among the review division, DDMAC and the sponsor, provisions were made to accept the provisions of note.

CONCLUSIONS & RECOMMENDATIONS: Recommend APPROVAL of NDA 21-168. The product insert labeling and the packaging labeling are ADEQUATE.

/S/

T. Broadbent, Ph.D., Chemist

cc: Orig. NDA 21-168
HFD-120/Division File
HFD-120/TBroadbent
HF-120/LChen
HFD-120/MGuzewska
R/D Init by: MEG

8/4/00

Filename: N21168A.000.DOC

Redacted 6

pages of trade

secret and/or

confidential

commercial

information

DIVISION OF NEUROPHARMACOLOGICAL DRUG PRODUCTS, HFD-120 JUL 21 2000
REVIEW OF CHEMISTRY, MANUFACTURING, AND CONTROLS

NDA 21-168

CHEM. REVIEW # 1		**REVIEW DATE**	20-JUL-00
SUBMISSION TYPE Original	**DOCUMENT DATE** 30-SEP-99	**CDER DATE** 04-OCT-99	**ASSIGNED DATE** 13-OCT-99

NAME AND ADDRESS OF APPLICANT

Abbott Laboratories
100 Abbott Park Road
D-491, AP6B-1SW
Abbott Park, Illinois 60064-3500

DRUG PRODUCT NAME

Proprietary:	Depakote ER Tablets
Nonproprietary/USAN:	Divalproex Sodium
Code Name/Number:	A-50711
Chem. Type/Ther. Class:	6S / 2011110
PHARMACOLOGICAL CATEGORY/INDICATION	Migraine
DOSAGE FORM	Tablets
STRENGTHS	500 mg
ROUTE OF ADMINISTRATION	Oral
DISPENSED	XXX RX ___ OTC
SPECIAL PRODUCTS	___YES XX NO

CHEMICAL NAME, STRUCTURAL FORMULA, MOLECULAR FORMULA
Sodium hydrogen bis(2-propylvalerate), oligomer

$(C_{16}H_{31}NaO_4)_n$

F.W. 310.41

CAS Registry # [76584-70-8]

SUPPORTING DOCUMENTS: NDA 18-723 (Depakote Tablets, provides CMC for drug substance) NDA 20-782 (NA)(Depakote ER Tablets, provides CMC for drug product) IND ___
DMF ___ (all Type 3)
RELATED DOCUMENTS: NDA 19-680 (Depakote Sprinkle Capsules), 19-794 (Depakote Dispertab CP Tablets), 20-320 (Depakote Tablets), ___ IND ___
CONSULTS: See NDA 20-782 for consult regarding the trademark name, Depakote® ER

REMARKS/COMMENTS: This NDA is for the product provided by NDA 20-782. The basis for this application is the new clinical indication, prophylaxis of migraine. ___ ___ CMC review #1 ___ (reviewer: Dr. Klein) recommended the application was not approvable because of various deficiencies. The deficiencies were addressed and CMC review # 2 recommended the amended application was approvable based upon an acceptable EER. OC issued an acceptable recommendation on 28 June 2000. The summary EER is attached. The methods validation reports are pending.

CONCLUSIONS & RECOMMENDATIONS: Recommend APPROVAL of NDA 21-168.

/S/

T. Broadbent, Ph.D., Chemist

cc: Orig. NDA 21-168
HFD-120/Division File
HFD-120/TBroadbent
HF-120/LChen
HFD-120/MGuzewska
R/D Init by: MEG /S/ 7/21/00

Filename: N21168.000.DOC

Redacted 8

pages of trade

secret and/or

confidential

commercial

information