CONFIDENTIAL

PARKE-DAVIS PHARMACEUTICAL RESEARCH
DIVISION OF WARNER-LAMBERT COMPANY
ANN ARBOR, MICHIGAN

RESEARCH REPORT NO.: RR 744-00249

DATE ISSUED: February 04, 1997

CLINICAL INVESTIGATOR(S):

PERIODS COVERED: 04/17/95 to 04/28/95

GABAPENTIN (CI-945) ANALYST(S)

DEPARTMENT: Pharmacokinetics/Drug Metabolism and Clinical Pharmacology

COMPOUND NUMBERS (PD,WL,GOE,CI):
CI-945, PD 087842-0000

LOT NUMBER(S):
CM 0190295, CF 0390793

PHASE:
1

PROTOCOL NUMBER:
945-189-0

NOTEBOOK (OR OTHER REFS):

SUGGESTED KEY WORDS:
Gabapentin, Neurontin, Single Dose, Bioequivalence, Anticonvulsant, Human

TITLE: A Single-Dose Bioequivalence Study Comparing 600-mg CI-945 Tablets to 300-mg Gabapentin Capsules (Protocol 945-189-0)

TABLE 4.1. Individual Gabapentin Pharmacokinetic Parameters Following Administration of One 600-mg Gabapentin Tablet (Test) (Protocol 945-189)

Subject	Sequence	Cmax (µg/mL)	tmax (hr)	AUC(0-tldc) (µg•hr/mL)	AUC(0-∞) (µg•hr/mL)	AUC_{extrap} (%)	λz (1/hr)	t½ (hr)	Ae% (%)
1	B								
2	B								
3	A								
4	A								
5	B								
6	B								
7	A								
8	A								
9	B								
10	B								
11	A								
12	A								
13	A								
14	A								
15	B								
16	B								
17	A								
18	B								
19	A								
20	B								
Mean		4.65	4.1	50.1	51.0	1.7	0.0834	8.5	47.7
SD		1.15	1.2	13.0	13.3	0.7	0.0140	1.6	12.2
%RSD		24.8	29.4	25.9	26.0	43.9	16.7	18.4	25.5
N		20	20	20	20	20	20	20	20

AUC_{extrap} = Portion of AUC(0-∞) due to extrapolation, expressed as a percentage of AUC(0-∞).
%RSD = Relative standard deviation (% of mean value).
N = Number of observations (subjects).
Sequence = Treatment sequence; A= one 600-mg gabapentin tablet/two 300-mg gabapentin capsules; B = two 300-mg gabapentin) capsules/one gabapentin 600-mg tablet.
Other parameters are as defined in Section 5.6.

TABLE 4.2. Individual Gabapentin Pharmacokinetic Parameters Following Administration of Two 300-mg Gabapentin Capsules (Reference) (Protocol 945-189)

Subject	Sequence	Cmax (µg/mL)	tmax (hr)	AUC(0-tldc) (µg•hr/mL)	AUC(0-∞) (µg•hr/mL)	AUC_{extrap} (%)	λz (1/hr)	t½ (hr)	Ae% (%)
1	B								
2	B								
3	A								
4	A								
5	B								
6	B								
7	A								
8	A								
9	B								
10	B								
11	A								
12	A								
13	A								
14	A								
15	B								
16	B								
17	A								
18	B								
19	A								
20	B								
Mean		4.19	3.4	45.6	46.6	2.2	0.0835	9.1	43.6
SD		1.05	1.2	12.6	12.7	2.7	0.0208	3.6	12.1
%RSD		25.1	36.3	27.7	27.3	123	24.9	39.9	27.8
N		20	20	20	20	20	20	20	20

AUC_{extrap} = Portion of AUC(0-∞) due to extrapolation, expressed as a percentage of AUC(0-∞).
%RSD = Relative standard deviation (% of mean value).
N = Number of observations (subjects).
Sequence = Treatment sequence; A = one 600-mg gabapentin tablet/two 300-mg gabapentin capsules; B = two 300-mg gabapentin capsules/one gabapentin 600-mg tablet.
Other parameters are as defined in Section 5.6.

TABLE 5.1. Comparison of Individual Gabapentin Cmax Values Following Administration of One 600-mg Gabapentin Tablet to Two 300-mg Gabapentin Capsules (Protocol 945-189)

Subject	Sequence	Cmax Values by Formulation		Difference	Ratio	ln(Ratio/100)
		One 600-mg Tablet	Two 300-mg Capsules			
1	B					
2	B					
3	A					
4	A					
5	B					
6	B					
7	A					
8	A					
9	B					
10	B					
11	A					
12	A					
13	A					
14	A					
15	B					
16	B					
17	A					
18	B					
19	A					
20	B					
Mean		4.65	4.19	0.46	113	0.108
SD		1.15	1.05	0.77	21.8	0.183
%RSD		24.8	25.1	165	19.2	170
N		20	20	20	20	20

Sequence = Treatment sequence; A = one 600-mg gabapentin tablet/two 300-mg gabapentin capsules; B = two 300-mg gabapentin capsules/one 600-mg gabapentin tablet.
Cmax = Maximum observed plasma gabapentin concentration (µg/mL).
Difference = Difference (tablet capsules) in Cmax values (µg/mL).
Ratio = Ratio (tablet capsules) of Cmax values expressed as a percentage.
ln(Ratio/100) = Natural logarithm of the ratio of Cmax values.
%RSD = Relative standard deviation (% of mean value).
N = Number of observations (subjects).

TABLE 5.2. Comparison of Individual Gabapentin AUC(0-∞) Values Following Administration of One 600-mg Gabapentin Tablet to Two 300-mg Gabapentin Capsules (Protocol 945-189)

Subject	Sequence	AUC(0-∞) Values by Formulation		Difference	Ratio	ln(Ratio/100)
		One 600-mg Tablet	Two 300-mg Capsules			
1	B					
2	B					
3	A					
4	A					
5	B					
6	B					
7	A					
8	A					
9	B					
10	B					
11	A					
12	A					
13	A					
14	A					
15	B					
16	B					
17	A					
18	B					
19	A					
20	B					
Mean		51.0	46.6	4.41	111	0.0931
SD		13.3	12.7	7.40	17.2	0.16
%RSD		26.0	27.3	168	15.5	167
N		20	20	20	20	20

Sequence = Treatment sequence; A = one 600-mg gabapentin tablet/two 300-mg gabapentin capsules; B = two 300-mg gabapentin capsules/one 600-mg gabapentin tablet.
AUC(0-∞) = Area under the plasma concentration-time curve from time zero to infinite time (µg•hr/mL).
Difference = Difference (tablet - capsules) in AUC(0-∞) values (µg•hr/mL).
Ratio = Ratio (tablet/ capsules) of AUC(0-∞) values expressed as a percentage.
ln(Ratio/100) = Natural logarithm of the ratio of AUC(0-∞) values.
%RSD = Relative standard deviation (% of mean value).
N = Number of observations (subjects).

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PARKE-DAVIS PHARMACEUTICAL RESEARCH
DIVISION OF WARNER-LAMBERT COMPANY
ANN ARBOR, MICHIGAN

RESEARCH REPORT NO.: RR 744-00337

DATE ISSUED: June 9, 1997

INVESTIGATOR(S):

PERIODS COVERED: 12/10/96 to 02/10/97

CI-945 ANALYST(S):

DEPARTMENT: Pharmacokinetics/Drug Metabolism and Clinical Pharmacology

COMPOUND NUMBERS (PD,WL,GOE,CI):
CI-945, PD 087842-0000

LOT NUMBER(S):
CV1771196, 02166VA

PHASE:
4

PROTOCOL NUMBER:
945-205-0

NOTEBOOK (OR OTHER REFS):

SUGGESTED KEY WORDS:
Gabapentin, Neurontin®, Single Dose, Bioequivalence, Anticonvulsant, Human

TITLE: A Single-Dose Bioequivalence Study Comparing 600-mg Gabapentin Tablets Manufactured in to 300-mg Gabapentin Capsules

TABLE D.3.1. Individual and Mean Gabapentin Pharmacokinetic Parameter Values Following Administration of Two 300-mg Gabapentin Capsule (Reference) (Protocol 945-205)

Subject	Day	Cmax (µg/mL)	tmax (hr)	AUC(0-tldc) (µg•hr/mL)	AUC(0-∞) (µg•hr/mL)	AUCextrap (%)	λz (1/hr)	t½ (hr)
1	1							
2	8							
3	8							
4	1							
5	8							
6	8							
7	1							
8	1							
9	1							
10	8							
11	8							
12	1							
13	1							
14	1							
15	8							
16	8							
17	1							
18	1							
19	8							
20	8							
Mean		4.48	3.5	46.8	47.7	2.3	0.0718	15.4
SD		1.16	1.2	13.3	12.9	3.3	0.0387	13.9
%RSD		25.9	34.1	28.4	27.1	139.4	53.9	90.5
N		20	20	20	20	20	20	20
Median		4.63	3.5	43.6	44.1	1.2	0.0730	9.5
Minimum								
Maximum								

Cmax = Maximum plasma concentration (µg/mL).
tmax = Time (hr) for Cmax.
AUC(0-tldc) = Area under plasma concentration-time curve from time 0 to time of the last detectable concentration (µg•hr/mL).
AUC(0-∞) = Area under plasma concentration-time curve from time 0 extrapolated to infinite time (µg•hr/mL).
λz = Elimination rate constant (1/hr).
t½ = Elimination half-life (hr).

TABLE D.3.2. Individual and Mean Gabapentin Pharmacokinetic Parameter Values Following Administration of One 600-mg Gabapentin Tablet (Test) (Protocol 945-205)

Subject	Day	Cmax (µg/mL)	tmax (hr)	AUC(0-tldc) (µg•hr/mL)	AUC(0-∞) (µg•hr/mL)	AUCextrap (%)	λz (1/hr)	t½ (hr)
1	8							
2	1							
3	1							
4	8							
5	1							
6	1							
7	8							
8	8							
9	8							
10	1							
11	1							
12	8							
13	8							
14	8							
15	1							
16	1							
17	8							
18	8							
19	1							
20	1							
Mean		4.94	3.2	51.3	52.5	2.7	0.0736	15.6
SD		1.52	0.9	16.3	15.8	3.8	0.0437	13.7
%RSD		30.9	27.3	31.8	30.2	140.5	59.3	88.2
N		20	20	20	20	20	20	20
Median		4.61	3	48.2	49.8	1.5	0.0661	10.6
Minimum								
Maximum								

Cmax = Maximum plasma concentration (µg/mL).
tmax = Time (hr) for Cmax.
AUC(0-tldc) = Area under plasma concentration-time curve from time 0 to time of the last detectable concentration (µg•hr/mL).
AUC(0-∞) = Area under plasma concentration-time curve from time 0 extrapolated to infinite time (µg•hr/mL).
λz = Elimination rate constant (1/hr).
t½ = Elimination half-life (hr).

TABLE D.4.1. Comparison of Individual Gabapentin Cmax Values Following Administration of One 600-mg Gabapentin Tablet to Two 300-mg Gabapentin Capsules (Protocol 945-205)

Subject	Sequence	Cmax Values by Formulation		Difference	Ratio	ln(Ratio)
		One 600-mg Tablet	Two 300-mg Capsules			
1	A					
2	B					
3	B					
4	A					
5	B					
6	B					
7	A					
8	A					
9	A					
10	B					
11	B					
12	A					
13	A					
14	A					
15	B					
16	B					
17	A					
18	A					
19	B					
20	B					
Mean		4.94	4.48	0.46	1.13	0.0885
SD		1.52	1.16	1.38	0.33	0.2786
%RSD		30.9	25.9	303.62	28.6	314.8
N		20	20	20	20	20

Sequence = Treatment sequence; A = two 300-mg gabapentin capsules/one 600-mg gabapentin tablet; B = one 600-mg gabapentin tablet/two 300-mg gabapentin capsules.
Cmax = Maximum observed plasma gabapentin concentration (µg/mL).
Difference = Difference (tablet - capsules) in Cmax values (µg/mL).
Ratio = Ratio (tablet/ capsules) of Cmax values.
ln(Ratio) = Natural logarithm of the ratio of Cmax values.
SD = Standard deviation.
%RSD = Relative standard deviation (% of mean value).
N = Number of observations.

TABLE D.4.2. Comparison of Individual Gabapentin AUC(0-∞) Values Following Administration of One 600-mg Gabapentin Tablet to Two 300-mg Gabapentin Capsules (Protocol 945-205)

Subject	Sequence	AUC(0-∞) Values by Formulation		Difference	Ratio	ln(Ratio)
		One 600-mg Tablet	Two 300-mg Capsules			
1	A					
2	B					
3	B					
4	A					
5	B					
6	B					
7	A					
8	A					
9	A					
10	B					
11	B					
12	A					
13	A					
14	A					
15	B					
16	B					
17	A					
18	A					
19	B					
20	B					
Mean		52.5	47.7	4.8	1.13	0.0884
SD		15.8	12.9	12.9	0.286	0.2491
%RSD		30.2	27.1	271.2	25.4	281.8
N		20	20	20	20	20

Sequence = Treatment sequence; A = two 300-mg gabapentin capsules/one 600-mg gabapentin tablet; B = one 600-mg gabapentin tablet/two 300-mg gabapentin capsules.
AUC(0-∞) = Maximum observed plasma gabapentin concentration (µg/mL).
Difference = Difference (tablet - capsules) in AUC(0-∞) values (µg/mL).
Ratio = Ratio (tablet capsules) of AUC(0-∞) values.
ln(Ratio) = Natural logarithm of the ratio of AUC(0-∞) values.
SD = Standard deviation.
%RSD = Relative standard deviation (% of mean value).
N = Number of observations.

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PARKE-DAVIS PHARMACEUTICAL RESEARCH
DIVISION OF WARNER-LAMBERT COMPANY
ANN ARBOR, MICHIGAN

RESEARCH REPORT NO.: RR 744-00328

DATE ISSUED: June 9, 1997

INVESTIGATOR(S):

PERIODS COVERED: 03/05/96 to 03/28/96

CI-945 ANALYST(S):

DEPARTMENT: Pharmacokinetics/Drug Metabolism and Clinical Pharmacology

COMPOUND NUMBERS (PD,WL,GOE,CI):
CI-945, PD 087842-0000

LOT NUMBER(S):
CM 1731095
01905V

PHASE:
4

PROTOCOL NUMBER:
945-208-0

NOTEBOOK (OR OTHER REFS):

SUGGESTED KEY WORDS:
Gabapentin, Neurontin, Single Dose, Bioequivalence, Anticonvulsant, Human

TITLE: A Single-Dose Bioavailability Study Comparing 800-mg CI-945 Tablets to 400-mg Gabapentin Capsules (Protocol 945-208-0)

Name of Company: **Warner-Lambert**	INDIVIDUAL STUDY TABLE	(For National Authority Use Only)
Name of Finished Product: **Neurontin**	Referring to Part of the Dossier	
Name of Active Ingredient: **Gabapentin**	Volume: Page:	

Protocol 945-208-0 (Page 3)

Bioequivalence criteria for Cmax and AUC(0-∞) values were met. Ratios of formulation least-squares mean values for secondary parameters [untransformed Cmax, untransformed and log-transformed AUC(0-tldc), and untransformed AUC(0-∞)] and corresponding 90% confidence intervals further support the bioequivalence of 800-mg gabapentin tablets to 400-mg gabapentin capsules.

Conclusions Eight-hundred milligram gabapentin tablets are bioequivalent to 2 × 400-mg gabapentin capsules.

TABLE D.4.1. Individual and Mean Gabapentin Pharmacokinetic Parameter Values Following Administration of One 800-mg Gabapentin Tablet (Test) (Protocol 945-208)

Subject	Day	Cmax (µg/mL)	tmax (hr)	AUC(0-tldc) (µg•hr/mL)	AUC(0-∞) (µg•hr/mL)	AUC_{extrap} (%)	λz (1/hr)	t½ (hr)	Ae% (%)
1	1								
2	8								
4	8								
5	8								
6	8								
7	1								
8	1								
9	1								
10	8								
11	8								
12	1								
13	8								
14	8								
15	1								
16	1								
17	1								
18	8								
19	1								
20	8								
Mean		4.60	3.0	46.4	47.2	2.1	0.0627	14.3	34.8
SD		1.78	1.0	16.4	16.3	2.0	0.031	8.0	10.8
%RSD		38.8	32.8	35.4	34.4	95.0	49.5	55.9	31.1
N		19	19	19.0	19.0	19	19	19	19
Median		4.36	3.0	43.1	43.8	1.5	0.0577	12.0	36.4
Minimum									
Maximum									

Cmax = Maximum plasma concentration.
tmax = Time for Cmax.
AUC(0-tldc) = Area under plasma concentration-time curve from time 0 to time of the last detectable concentration.
AUC(0-∞) = Area under plasma concentration-time curve from time 0 extrapolated to infinite time.
λz = Elimination rate constant.
t½ = Elimination half-life.
Ae% = Percent of Dose excreted in Urine (%).

APPEARS THIS WAY
ON ORIGINAL

TABLE D.4.2. Individual and Mean Gabapentin Pharmacokinetic Parameter Values Following Administration of Two 400-mg Gabapentin Capsule (Reference) (Protocol 945-208)

Subject	Day	Cmax (µg/mL)	tmax (hr)	AUC(0-tldc) (µg•hr/mL)	AUC(0-∞) (µg•hr/mL)	AUC_{extrap} (%)	λz (1/hr)	t½ (hr)	Ae% (%)
1	1								
2	8								
4	8								
5	8								
6	8								
7	1								
8	1								
9	1								
10	8								
11	8								
12	1								
13	8								
14	8								
15	1								
16	1								
17	1								
18	8								
19	1								
20	8								
Mean		4.77	3.2	49.0	49.9	2.0	0.0710	14.5	37.1
SD		0.91	0.9	12.3	11.9	2.6	0.0393	11.5	9.09
%RSD		19.1	26.4	25.0	23.8	124.9	55.4	79.3	24.5
N		19	19	19	19	19	19	19	19
Median		4.86	3	49.5	50.5	1	0.0646	10.7	40.5
Minimum									
Maximum									

Cmax = Maximum plasma concentration.
tmax = Time for Cmax.
AUC(0-tldc) = Area under plasma concentration-time curve from time 0 to time of the last detectable concentration.
AUC(0-∞) = Area under plasma concentration-time curve from time 0 extrapolated to infinite time.
λz = Elimination rate constant.
t½ = Elimination half-life.
Ae% = Percent of dose excreted in urine.

TABLE D.5.1. Comparison of Individual Gabapentin Cmax Values Following Administration of One 800-mg Gabapentin Tablet to Two 400-mg Gabapentin Capsules (Protocol 945-208)

Subject	Sequence	Cmax Values by Formulation		Difference	Ratio	ln(Ratio)
		One 800-mg Tablet	Two 400-mg Capsules			
1	B					
2	A					
4	A					
5	A					
6	A					
7	B					
8	B					
9	B					
10	A					
11	A					
12	B					
13	A					
14	A					
15	B					
16	B					
17	B					
18	A					
19	B					
20	A					
Mean		4.60	4.77	-0.17	0.97	-0.0915
SD		1.78	0.91	1.52	0.33	0.3703
%RSD		38.8	19.1	914.69	33.99	
N		19	19	19	19	19

Sequence	=	Treatment sequence; A = Two 400-mg gabapentin capsules/one 800-mg gabapentin tablet; B = One 800-mg gabapentin tablet/two 400-mg gabapentin capsules.
Cmax	=	Maximum observed plasma gabapentin concentration (µg/mL).
Difference	=	Difference (tablet/ capsules) in Cmax values (µg/mL).
Ratio	=	Ratio (tablet/ capsules) of Cmax values.
ln(Ratio)	=	Natural logarithm of the ratio of Cmax values.
SD	=	Standard deviation.
%RSD	=	Relative standard deviation (% of mean value).
N	=	Number of observations.

TABLE D.5.2. Comparison of Individual Gabapentin AUC(0-∞) Values Following Administration of One 800-mg Gabapentin Tablet to Two 400-mg Gabapentin Capsules (Protocol 945-208)

Subject	Sequence	AUC(0-∞) Values by Formulation		Difference	Ratio	ln(Ratio)
		One 800-mg Tablet	Two 400-mg Capsules			
1	B					
2	A					
4	A					
5	A					
6	A					
7	B					
8	B					
9	B					
10	A					
11	A					
12	B					
13	A					
14	A					
15	B					
16	B					
17	B					
18	A					
19	B					
20	A					
Mean		47.2	49.9	-2.7	0.95	-0.0866
SD		16.3	11.9	12.4	0.26	0.2920
%RSD		34.4	23.8	464.3	27.7	
N		19	19	19	19	19

Sequence = Treatment sequence; A = Two 400-mg gabapentin capsules/one 800-mg gabapentin tablet; B = One 800-mg gabapentin tablet/two 400-mg gabapentin capsules.

AUC(0-∞) = Area under plasma concentration-time curve from time 0 extrapolated to infinite time (μg·hr/mL).

Difference = Difference (tablet capsules) in AUC(0-∞) values.

Ratio = Ratio (tablet capsules) of AUC(0-∞) values.

ln(Ratio) = Natural logarithm of the ratio of AUC(0-∞) values.

SD = Standard deviation.

%RSD = Relative standard deviation (% of mean value).

N = Number of observations.

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER: 20882

ADMINISTRATIVE DOCUMENTS/CORRESPONDENCE

Division of Neuropharmacological Drug Products

PROJECT MANAGER REVIEW

Application Number: NDA 20-882: Response to Not Approvable N(AZ)

Name of Drug: Neurontin (Gabapentin) Tablets

Sponsor: Parke-Davis

Material Reviewed

Submission Date(s): August 12, 1998

Receipt Date(s): August 13, 1998

Background and Summary Description:

Response to Not Approvable Letter was submitted August 12, 1998. The NDA was not approved

The Response to Not Approvable Letter submission addresses the deficiencies and is expected to be approved by October 12, 1998. This labeling will be approved on draft in the Approval letter.

Draft labeling submitted by Sponsor on August 12, 1998 for Neurontin (Gabapentin Capsules and Gabapentin Tablets) was compared to the last approved labeling for Neurontin (Gabapentin Capsules) of September 29, 1998.

Review

A line-by-line comparison was done to compare Neurontin (Gabapentin Capsules and Gabapentin Tablets) Labeling submitted August 12, 1998 with draft labeling for Neurontin (Gabapentin Capsules) approved September 29, 1998. No changes were made outside the approval letter of September 29, 1998 except:

1. In the **DESCRIPTION** section, the Sponsor has added a description of the tablets to the first paragraph (in **bold** below):

   "Neurontin (gabapentin capsules and gabapentin tablets) is supplied as imprinted hard shell capsules containing 100 mg, 300 mg, and 400 mg **or elliptical film-coated tablets containing 600 mg and 800 mg of gabapentin."**

2. In the **DESCRIPTION** section, the Sponsor has added a description of the inactive ingredients for the tablets as the 3rd paragraph (in **bold** below):

"The inactive ingredients for the tablets are poloxamer 407 NF, copolyvidonum, cornstarch, magnesium stearate, hydroxypropyl cellulose, talc, candelilla wax and purified water. The imprinting ink for the 600 mg tablets contains synthetic black iron oxide, pharmaceutical shellac, pharmaceutical glaze, propylene glycol, ammonium hydroxide, isopropyl alcohol and n-butyl alcohol. The imprinting ink for the 800 mg tablets contains synthetic yellow iron oxide, synthetic red iron oxide, hydroxypropyl methylcellulose, propylene glycol, methanol, isopropyl alcohol and deionized water."

3. In the **DOSAGE AND ADMINISTRATION** section, third paragraph,

   a. the Sponsor has added the tablet strengths (in **bold** below):

   "The effective dose of Neurontin is 900 to 1800 mg/day and given in divided doses (three times a day) using 300- or 400-mg capsules **or 600- or 800-mg tablets**.....If necessary, the dose may be increased using 300- 400-mg capsules **or 600- or 800-mg tablets** three times a day up to 1800 mg/day."

   b. As per SE2-011 and the approval letter of September 29, 1998, the following sentences have been deleted (in **bold** below):

   "Titration to an effective dose can take place rapidly, over a few days, giving 300 mg on Day 1, 300 mg twice a day on Day 2, and 300 mg three times a day on Day 3. To minimize potential side effects, especially somnolence, dizziness, fatigue, and ataxia, the first dose on Day 1 may be administered at bedtime."

   To replace the above sentences, the following sentence has been added (in **bold** below):
   "The starting dose is 300 mg three times a day."

4. In the **HOW SUPPLIED** section, the Sponsor has added the following (in **bold** below):

600 mg tablets:

White elliptical film-coated tablet printed in black ink with "Neurontin 600" on one side; available in :
Bottles of 100: N 0071-0416-24
Bottles of 500: N 0071-0416-30
Unit dose 50's: N 0071-0416-40

800 mg tablets:

White elliptical film-coated tablet printed in orange with "Neurontin 800" on one side; available in :
Bottles of 100: N 0071-0426-24
Bottles of 500: N 0071-0426-30
Unit dose 50's: N 0071-0426-40

Storage (Tablets)
Store at controlled room temperature 20-25°C (68°-77°F) (see USP).

Conclusions

The changes noted above are acceptable except for the following:

1. In the **DESCRIPTION** section, "**NF**" should be deleted from the first line of the 3rd paragraph.

2. In the **HOW SUPPLIED** section, the following sentence shall replace the current one under **Storage (Tablets)**:
Store at 25°C (77°F)

An Approval letter should issue including draft labeling.

/S/

Project Manager

Supervisory Comment/Concurrence:

/S/

Supervisor, Project Management Staff 9/30/98

cc:
Original
HFD-120/Div. Files
HFD-120/Leber/Katz
HFD-120/Guzewska/Rzeszotarski
HFD-120/Chen
draft: September 28, 1998 lyc
final:
C:/wpfiles/neuronti.tab/lbl_rev.cso

CSO REVIEW

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 20-882

JUL 1 1998

Parke-Davis Pharmaceutical Research
Division of Warner-Lambert Company
Attention: Sean Brennan, Ph.D.
2800 Plymouth Road
Ann Arbor, MI 48105

Dear Dr. Brennan:

Please refer to your new drug application dated July 1, 1997, received July 2, 1997, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Neurontin (gabapentin) Tablets, 600mg and 800mg.

We acknowledge receipt of your additional correspondence and amendments dated:

January 9, 1998	March 12, 1998	April 14, 1998
February 10, 1998	April 2, 1998	

The User Fee goal date for this application is July 2, 1998.

This original new drug application provides for a tablet formulation of gabapentin for use as adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults with epilepsy.

We have completed our review and find the information presented is inadequate, and the application is not approvable under section 505(d) of the Act and 21 CFR 314.125(b). Our reasons are as follows.

Although we agree that you have presented evidence of acceptable biopharmaceutic performance of your proposed 600mg and 800mg gabapentin tablets, we consider your proposal

Your proposed

Consequently, this impurity must be "qualified". Although you have submitted evidence to qualify this impurity, we do not find this information acceptable.

Upon review of your preclinical data, we note that you have performed a one month rat toxicology study and an Ames test However, under current ICH guidelines, these studies would Specifically, the rat toxicology study is too short, the doses administered are too low, and no reproductive or developmental toxicology studies have been conducted.

Additionally, we consider o be considerably more toxic than the parent gabapentin, as judged by LD50 (200 - 500 mg/kg vs. greater than 8000mg/kg in mice and rats). This toxicity raises a clinical safety concern regarding human exposure to this level of impurity. However, there was no clinical data submitted which would address in humans. Specifically, no data addressing the issue humans have been exposed to (and how this would relate to the exposure that would result if is adopted) and what adverse events occurred in these patients was submitted for review.

While it is probably true that there was little if anything known about to which humans had been exposed prior to the approval of gabapentin capsules for the approved capsule formulations , no such rules regarding qualification of impurities were in place at the time of approval of the gabapentin NDA.

We note that the data you have submitted would support expiration dating of 18 months and 6 months for the 600 and 800 mg tablets, respectively

In addition to the issues noted above, we have the following comments and requests. Although these issues were not reasons for our not approvable action, we would ask that you address them in your response to this letter.

Nomenclature

We note that you have proposed one package insert be developed to include both Neurontin formulations, i.e. capsules and tablets. In your proposed package insert in this NDA, you represent the established name as "gabapentin capsules and tablets". We have been advised by the CDER Labeling and Nomenclature Committee that this convention is unacceptable.

Accordingly, we request that you adopt one of the following representations for use in labeling:

1. Neurontin (gabapentin capsules and gabapentin tablets)

2. Neurontin (gabapentin) Capsules and Tablets

Biopharmaceutics

1. We note that your application included a request for waiver of bioequivalence studies for the Neurontin 800mg tablets. We will notify you of our final determination on this request at such time when this application is deemed to be approvable. However, at this time, it does appear likely that we would grant such a waiver.

2. At such time when this application is deemed to be approvable, we will ask that the following dissolution methodology and specification be adopted for Neurontin Tablets, 600mg and 800mg:

Apparatus:	USP Apparatus II (paddle)
Agitation:	50 rpm
Medium:	900mL of 0.06N HCl at 37°C
Specification:	NLT

Chemistry

1. Please describe your If none are planned, please state so.

2. Please provide samples of all packaging labels.

Within 10 days after the date of this letter, you are required to amend the application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.120. In the absence of any such action FDA may proceed to withdraw the application. Any amendments should respond to all the deficiencies listed. We will not process a partial reply as a major amendment nor will the review clock be reactivated until all deficiencies have been addressed.

Under 21 CFR 314.102(d) of the new drug regulations, you may request an informal meeting or telephone conference with the Division to discuss what further steps need to be taken before the application may be approved.

If you have any questions, please contact Jacqueline H. Ware, Pharm.D., Regulatory Management Officer, at (301) 594-5793.

Sincerely yours.

/S/

7/1/98

Paul Leber, M.D.
Director
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Archival NDA 20-882
HFD-120/Div. files
HFD-002/ORM
HFD-101/Office Director
HFD-810/ONDC Division Director
DISTRICT OFFICE
HFD-92/DDM-DIAB /S/ 6/22/98 /S/ 9-JUN-98
HFD-120/J.Ware /S/ 6/18/98
HFD-120/Leber/Katz/Guzewska/Rzesotarski/Fitzgerald/Fisher /S/ 6/18/98
HFD-860/Sahajwalla/Tammara - /S/ 06/15/98 /S/ 6/15/98 /S/ /S/ 6/19/98

Drafted by: JHW/May 28, 1998/20882na.ltr
Initialed by:
final:

NOT APPROVABLE (NA)

ITEM 13.

Market Exclusivity Information and Certification for Generic Drug Enforcement Act

ITEM 13.1.

Request and Justification for 3-Year Marketing Exclusivity

PATENT INFORMATION

(1) NDA Number: 20-882

(2) Applicant: Parke-Davis Pharmaceutical Research Division
Warner-Lambert Company
P.O. Box 1047
Ann Arbor, MI 48106

(3) Active Ingredient: 1-(aminomethyl)-1-cyclohexaneacetic acid

(4) Medical Use: This supplement seeks approval for an additional 600 mg and 800 mg tablet solid oral dosage form for gabapentin.

(5) Strength: 600, 800 mg tablets

(6) Dosage Form: Tablets for oral administration

(7) Trade Name: Neurontin®

(8) Generic Name: Gabapentin

(9) Patent Statement: US Patent Number 4, 087,544 which issued May 2, 1978, and which expires January 16, 2000, claims a method of treating certain forms of epilepsy, as well as faintness attacks, hypokinesia and cranial traumas, by enteral or parenteral administration of 1-(aminomethyl)-1-cyclohexaneacetic acid.

US Patent Number 4,894,476 which issued January 16, 1990, and which expires May 2, 2008, claims a crystal form of 1-(aminomethyl)-1-cyclohexaneacetic acid.

US Patent Number 5,084,479 which issued January 28, 1992, and which expires on January 2, 2010, claims a method for treating neurodegenerative diseases with 1-(aminomethyl)-1-cyclohexaneacetic acid.

Each of US 4,087,544, US 4,894,476, and US 5,084,479 is assigned to Warner-Lambert Company.

PATENT INFORMATION
Neurontin® (Gabapentin) NDA #20-882
Page 2

(9) Patent Statement: (Continued)

The undersigned declares that Patent Numbers 4,087,544, 4,894,476 and 5,084,479, cover a crystal form and the use of Neurontin® (gabapentin) (1-(aminomethyl)-1-cyclohexaneacetic acid). Neurontin® is approved under section 505 of the Federal Food, Drug and Cosmetic Act.

June 18, 1997
Date

Elizabeth M. Anderson
Elizabeth M. Anderson
Senior Patent Agent
Registration No. 31,585

APPEARS THIS WAY
ON ORIGINAL

20-882

Exclusivity Summary for NDA

Exclusivity Summary Form

EXCLUSIVITY SUMMARY FOR NDA # **20-882** SUPPL #_____

Trade Name: **Neurontin** Generic Name: **gabapentin tablets**

Applicant Name: **Parke-Davis Pharmaceutical Research**

HFD#: **HFD-120** Approval Date If Known: October 9, 1998

PART I: IS AN EXCLUSIVITY DETERMINATION NEEDED?

1. *An exclusivity determination will be made for all original applications, but only for certain supplements. Complete PARTS II and III of this Exclusivity Summary only if you answer "yes" to one or more of the following question about the submission.*

a) Is it an original NDA? YES/_X_/ NO /___/

b) Is it an effectiveness supplement? YES /___/ NO /_X_/

c) Did it require the review of clinical data other than to support a safety claim or change in labeling related to safety? (If it required review only of bioavailability or bioequivalence data, answer "no.")
YES /__/ NO /_X_/

If your answer is "no" because you believe the study is a bioavailability study and, therefore, not eligible for exclusivity, EXPLAIN why it is a bioavailability study, including your reasons for disagreeing with any arguments made by the applicant that the study was not simply a bioavailability study.

If it is a supplement requiring the review of clinical data but it is not an effectiveness supplement, describe the change or claim that is supported by the clinical data:

---

d) Did the applicant request exclusivity? YES /_X_/ NO /__/

If the answer to (d) is "yes," how many years of exclusivity did the applicant request?
The applicant requested 3 years of marketing exclusivity.

IF YOU HAVE ANSWERED "NO" TO ALL OF THE ABOVE QUESTIONS, GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4.

2. *Has a product with the same active ingredient(s), dosage form, strength, route of administration, and dosing schedule, previously been approved by FDA for the same use? (Rx to OTC switches should be answered NO - please indicate as such)* YES /_X_/ NO /__/

If yes, NDA # **20-235** Drug Name **Neurontin (gabapentin) Capsules**

IF THE ANSWER TO QUESTION 2 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4.

20-882

Exclusivity Summary for NDA

3. *Is this drug product or indication a DESI upgrade?* YES /___/ NO /_X_/

IF THE ANSWER TO QUESTION 3 IS "YES," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4 (even if a study was required for the upgrade).

PART II: FIVE-YEAR EXCLUSIVITY FOR NEW CHEMICAL ENTITIES.

(Answer either #1 or #2 as appropriate)

1. Single active ingredient product.

Has FDA previously approved under section 505 of the Act any drug product containing the same active moiety as the drug under consideration? Answer "yes" if the active moiety (including other esterified forms, salts, complexes, chelates or clathrates) has been previously approved, but this particular form of the active moiety, e.g., this particular ester or salt (including salts with hydrogen or coordination bonding) or other non-covalent derivative (such as a complex, chelate, or clathrate) has not been approved. Answer "no" if the compound requires metabolic conversion (other than deesterification of an esterified form of the drug) to produce an already approved active moiety. YES /___/ NO /__/

2. Combination product.

If the product contains more than one active moiety(as defined in Part II, #1), has FDA previously approved an application under section 505 containing any one of the active moieties in the drug product? If, for example, the combination contains one never-before-approved active moiety and one previously approved active moiety, answer "yes." (An active moiety that is marketed under an OTC monograph, but that was never approved under an NDA, is considered not previously approved.) YES /___/ NO /__/

IF THE ANSWER TO QUESTION 1 OR 2 UNDER PART II IS "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4. IF "YES" GO TO PART III.

PART III THREE-YEAR EXCLUSIVITY FOR NDA'S AND SUPPLEMENTS.

To qualify for three years of exclusivity, an application or supplement must contain "reports of new clinical investigations (other than bioavailability studies) essential to the approval of the application and conducted or sponsored by the applicant." This section should be completed only if the answer to PART II, Question 1 or 2 was "yes."

1. Does the application contain reports of clinical investigations?
(The Agency interprets "clinical investigations" to mean investigations conducted on humans other than bioavailability studies.) **If the application contains clinical investigations only by virtue of a right of reference to clinical investigations in another application, answer "yes," then skip to question 3(a).** If the answer to 3(a) is "yes" for any investigation referred to in another application, do not complete remainder of summary for that investigation. YES /__/ NO /___/

IF "NO," GO DIRECTLY TO THE SIGNATURE BLOCKS ON PAGE 4.

2. A clinical investigation is "essential to the approval" if the Agency could not have approved the application or supplement without relying on that investigation. Thus, the investigation is not essential to the approval if 1) no clinical investigation is necessary to support the supplement or application in light of previously approved applications (i.e., information other than clinical trials, such as bioavailability data, would be sufficient to provide a basis for approval as an ANDA or 505(b)(2) application because of what is already

Exclusivity Summary for NDA

known about a previously approved product), or 2) there are published reports of studies (other than those conducted or sponsored by the applicant) or other publicly available data that independently would have been sufficient to support approval of the application, without reference to the clinical investigation submitted in the application.

(a) In light of previously approved applications, is a clinical investigation (either conducted by the applicant or available from some other source, including the published literature) necessary to support approval of the application or supplement? YES /__/ NO /___/

If "no," state the basis for your conclusion that a clinical trial is not necessary for approval **AND GO DIRECTLY TO SIGNATURE BLOCK ON PAGE 4:**

(b) Did the applicant submit a list of published studies relevant to the safety and effectiveness of this drug product and a statement that the publicly available data would not independently support approval of the application? YES /___/ NO /__/

(1) If the answer to 2(b) is "yes," do you personally know of any reason to disagree with the applicant's conclusion? If not applicable, answer NO. YES /___/ NO /___/

(2) If the answer to 2(b) is "no," are you aware of published studies not conducted or sponsored by the applicant or other publicly available data that could independently demonstrate the safety and effectiveness of this drug product? YES /___/ NO /__/

(c) If the answers to (b)(1) and (b)(2) were both "no," identify the clinical investigations submitted in the application that are essential to the approval:

Studies comparing two products with the same ingredient(s) are considered to be bioavailability studies for the purpose of this section.

3. In addition to being essential, investigations must be "new" to support exclusivity. The agency interprets "new clinical investigation" to mean an investigation that 1) has not been relied on by the agency to demonstrate the effectiveness of a previously approved drug for any indication and 2) does not duplicate the results of another investigation that was relied on by the agency to demonstrate the effectiveness of a previously approved drug product, i.e., does not redemonstrate something the agency considers to have been demonstrated in an already approved application.

a) For each investigation identified as "essential to the approval," has the investigation been relied on by the agency to demonstrate the effectiveness of a previously approved drug product? (If the investigation was relied on only to support the safety of a previously approved drug, answer "no.")

Investigation #1 YES /__/ NO /__/ Investigation #2 YES /__/ NO /__/

b) For each investigation identified as "essential to the approval", does the investigation duplicate the results of another investigation that was relied on by the agency to support the effectiveness of a previously approved drug product?

Investigation #1 YES /___/ NO /__/ Investigation #2 YES /___/ NO /__/

c) If the answers to 3(a) and 3(b) are no, identify each "new" investigation in the application or supplement that is essential to the approval (i.e., the investigations listed in #2(c), less any that are not "new"):

Exclusivity Summary for NDA ~~20-782~~ 20-852 LVC

4. To be eligible for exclusivity, a new investigation that is essential to approval must also have been conducted or sponsored by the applicant. An investigation was "conducted or sponsored by" the applicant if, before or during the conduct of the investigation, 1) the applicant was the sponsor of the IND named in the form FDA 1571 filed with the Agency, or 2) the applicant (or its predecessor in interest) provided substantial support for the study. Ordinarily, substantial support will mean providing 50 percent or more of the cost of the study.

a) For each investigation identified in response to question 3(c): if the investigation was carried out under an IND, was the applicant identified on the FDA 1571 as the sponsor?

Investigation #1 YES /__/ NO /___/

Investigation #2 YES /__/ NO /___/

(b) For each investigation not carried out under an IND or for which the applicant was not identified as the sponsor, did the applicant certify that it or the applicant's predecessor in interest provided substantial support for the study?

(c) Notwithstanding an answer of "yes" to (a) or (b), are there other reasons to believe that the applicant should not be credited with having "conducted or sponsored" the study? (Purchased studies may not be used as the basis for exclusivity. However, if all rights to the drug are purchased (not just studies on the drug), the applicant may be considered to have sponsored or conducted the studies sponsored or conducted by its predecessor in interest.)

YES /___/ NO /__/

Signature: /S/ ***Date:*** 6/12/98

Title: Project Manager

Signature of Office/Division Director

Signature: /S/ ***Date:*** 6/30/98

Form OGD-011347 Revised 8/27/97
cc: Original NDA Division File HFD-93 Mary Ann Holovac

PEDIATRIC PAGE

(Complete for all original applications and all efficacy supplements)

NOTE: A new Pediatric Page must be completed at the time of each action even though one was prepared at the time of the last action.

/BLA # ***NDA 20-882*** Supplement Circle one: SE1 SE2 SE3 SE4 SE5 SEE

nrD-120 Trade and generic name/dosage form: ***Neurontin (gabapentin) Tablets*** ction: AP AE **NA**

Applicant: ***Parke-Davis Pharmaceutical Research*** Therapeutic Class: ***Anticonvulsant***

Indication(s) previously approved: ***None.***

Pediatric information in labeling of approved indication(s) is adequate __X__ inadequate ____

Proposed indication in this application: ***As adjunctive therapy in the treatment of partial seizures with and without secondary generalization in adults with epilepsy.***

ANSWER THE FOLLOWING QUESTIONS IN RELATION TO THE PROPOSED INDICATION.

IS THE DRUG NEEDED IN ANY PEDIATRIC AGE GROUPS? __X__Yes (Continue with questions) ____No (Sign and return the form)

WHAT PEDIATRIC AGE GROUPS IS THE DRUG NEEDED? (Check all that apply)

____Neonates(Birth-1month) _X_ Infants (1month-2yrs) _X_ Children (2-12yrs) _X_ Adolescents (12-16yrs)

____1. **PEDIATRIC LABELING IS ADEQUATE FOR ALL PEDIATRIC AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling far all pediatric age groups. Further information is not required.

___ 2. **PEDIATRIC LABELING IS ADEQUATE FOR CERTAIN AGE GROUPS.** Appropriate information has been submitted in this or previous applications and has been adequately summarized in the labeling to permit satisfactory labeling for certain pediatric age groups (e.g., infants, children, and adolescents but not neonates). Further information is not required.

__X_3. **PEDIATRIC STUDIES ARE NEEDED.** There is potential for use in children, and further information is required to permit adequate labeling for this use.

____a. A new dosing formulation is needed, and applicant has agreed to provide the appropriate formulation.

____b. A new dosing formulation is needed, however the sponsor is either not willing to provide it or is in negotiations with FDA.

__X_c. The applicant has committed to doing such studies as will be required.

__X_ (1) Studies are ongoing,

____ (2) Protocols were submitted and approved.

____ (3) Protocols were submitted and are under review.

____ (4) If no protocol has been submitted, attach memo describing status of discussions.

____d. If the sponsor is not willing to do pediatric studies, attach copies of FDA's written request that such studies be done and of the sponsor's written response to that request.

____4. **PEDIATRIC STUDIES ARE NOT NEEDED.** The drug/biologic product has little potential for use in pediatric patients. Attach memo explaining why pediatric studies are not needed.

__ __5. If none of the above apply, attach an explanation, as necessary.

ARE THERE ANY PEDIATRIC PHASE IV COMMITMENTS IN THE ACTION LETTER? ____Yes _X_No

ATTACH AN EXPLANATION FOR ANY OF THE FOREGOING ITEMS, AS NECESSARY.

This page was completed based on information from general knowledge (e.g., medical review, medical officer, team leader)

/S/ 7/1/98

Signature of Preparer and Title Date

Orig NDA/BLA# **20-882**
HFD-120 Div File
NDA/BLA Action Package
HFD-006/KRoberts

(revised 10120197)

FOR QUESTIONS ON COMPLETING THIS FORM CONTACT, KHYATI ROBERTS, HFD-6 (ROBERTSK)

ITEM 13.2.
Certification for Generic Drug Enforcement Act of 1992

Warner-Lambert hereby certifies that it did not and will not use in any capacity the services of any person debarred under Section 306 of the Act, in connection with this application.

MEMORANDUM

Date: June 3, 1998

From: Deputy Director
Division of Neuropharmacological Drug Products

To: File, NDA 20-882

Subject: Supervisory Review of NDA 20-882, for the introduction of new dosage forms for Neurontin (600 and 800 mg tablets)

Parke-Davis Pharmaceutical Research submitted NDA 20-882 on July 1, 1997 for the addition of 600 and 800 mg film coated tablets of Neurontin. Neurontin is already approved as 100, 200, 300, and 400 hard gelatin capsules for Neurontin.

As support for approval of this application, the sponsor has submitted the results of 2 bioequivalence studies. The first compares the kinetics of a single 600 mg dose given as tablet (from batches manufactured at Morris Plains, NJ, to a single 600 mg dose given as two 300 mg marketed capsules. The second study compares a single 800 mg dose given as the tablet (manufactured in Morris Plains) to a single 800 mg dose, given as two 400 mg marketed capsules. The sponsor requests a waiver of the requirement for a bioequivalence study for the 800 mg tablet manufactured in based on several considerations. The sponsor proposes that the product to be marketed be manufactured at the

In addition to the bioequivalence data, the sponsor has submitted CMC information, which includes manufacturing data, stability data, and proposed specifications. A recent submission (4/14/98) presents stability data for the 800 mg tablet manufactured in

The bioequivalence studies have been reviewed by Dr. Tammara (review dated 3/12/98), the CMC data by Dr. Rzeszotarski (reviews dated 3/18/98 and 5/28/98) and pharmacology issues by Dr. Fisher (review dated 4/30/98).

BIOPHARMACEUTICS

Dr. Tammara has concluded that the bioequivalence data are acceptable, and that a waiver for such demonstration for the 800 mg tablet produced in can be granted. He recommends the adoption of a specific dissolution methodology and specifications as described in his review.

CMC

Two lots of the 600 mg tablet manufactured in Morris Plains, NJ were subjected to stability studies. Twenty four (24) month testing of the lot used in the bioequivalence studies under standard

Stability testing was performed on a single lot of the 800 mg tablet manufactured in Morris Plains.

. Under accelerated conditions at 6 months,
Three month stability testing at standard conditions of the 800 mg tablet manufactured in

As Dr. Fisher notes, the is considerably more toxic than the parent, as judged by LD50 (200-500 mg/kg vs. greater than 8000 mg/kg in mice and rats).

Beyond acute toxicity studies, the sponsor has performed a 4 week tox study in rats, and an Ames test with the . In the tox study, the high dose was 80 mg/kg, and the only finding of note was hyaline droplet accumulation in the proximal tubular epithelium of the kidney in males at all doses (a finding similar to that seen at 6 months at doses of 300 mg/kg and greater in a study of gabapentin). The Ames test was negative.

The sponsor calculated a safety margin of the maximum daily human dose (they used 4800 mg/day, which they proposed for use in monotherapy; since their application for monotherapy was turned down, the maximum daily dose in labeling currently is 3600 mg). Based on the currently approved 3600 mg/day, the safety margin (compared to the 80 mg/kg/day) would be about 160 on a mg/kg basis, and greater than 20 on a mg/m2 basis.

As. Dr. Fisher notes, these studies would ordinarily not be sufficient to qualify this level of the impurity under current ICH guidelines. The study was too short, the doses too low, and there are no reproductive or developmental toxicity studies.

COMMENTS

The sponsor has presented evidence of acceptable biopharmaceutic performance of their proposed 600 and 800 mg tablets. However, they are proposing that the specification for the lactam impurity be increased from As noted above appears to be considerably more toxic than parent gabapentin, at least as assessed by acute toxicity studies in rodents. The sponsor has performed a one month study which yielded a safety margin of greater than 20 on a mg/m2 basis, compared to which humans would be exposed at the highest approved dose. As Dr. Fisher notes, however, this study would ordinarily not be sufficient under current ICH guidelines. A calculation based on reasonable assumptions reveals that, in chronic animal studies of gabapentin, animals at the highest gabapentin doses were exposed essentially equal (on a mg/kg basis) to levels to which humans would be exposed at the highest labeled dose.

In addition, 2 year stability data at standard conditions for the 600 mg tablet manufactured at Morris Plains yielded levels One year stability data at standard conditions for the 800 mg tablet manufactured at Morris Plains yielded While the to be marketed product will be manufactured in the 600 tablet under standard conditions yielded for the 800 mg tablet under standard indeed, 3 month stability testing of the 800 mg tablet manufactured in under accelerated

conditions , all indications from the data at present suggest that the increased levels of lactam that the sponsor suggests necessitate the adoption of the proposed specifications occur only under accelerated conditions (40o C/75% RH). Indeed, based on the sponsor's submission of 4/15/98, Dr. Rzeszotarski recommends that the product be granted 18 month stability for the 600 mg tablet (although this data is not explicitly described in his review of 5/28/98, he notes that the sponsor has submitted 12 month stability data for the 600 mg tablet manufactured in Vega Baja) and 6 month stability for the 800 mg tablet.

The sponsor has submitted no clinical data addressing the issue of how much people have actually been exposed to.

While the sponsor has performed a short study in rodents examining the effects of the lactam, this study, by itself, is insufficient to qualify this compound, as discussed by Dr. Fisher. Beyond this, however, my view is that animal studies, alone, can never be relied upon to establish the safety of a compound in humans. It is impossible, in the absence of evidence gathered in patients, to draw conclusions about the safety of these in people. Although we may have permitted the original specification without examination of the levels to which patients had been exposed, I see no reason at this time to permit an increase in these levels without evidence that these levels can be given safely to patients (indeed, if we had inadequate data about the safety at the time of the NDA approval, permitting even more of it at this time, in the absence of empirical evidence that that level is tolerated, seems particularly ill advised).

The sponsor has demonstrated that they can manufacture product in that, under standard stability conditions, contains that are within the current for up to 18 months for the 600 mg tablet and 6 months for the 800 mg tablet (based on 12 month and 3 month stability testing, respectively, as per Dr. Rzeszotarski).

I also note that the Establishment Evaluation Report (EER) for the site found this site to be unacceptable as a Finished Dosage Manufacturer on 3/16/98. The nature of the problem has not yet been described to us (see page 18 of Dr. Rzeszotarski's review of 5/28/98).

Finally, the nomenclature committee has found the sponsor's proposal to label this product "gabapentin capsules and tablets" unacceptable, and prefers "gabapentin tablets" and "gabapentin capsules" (see Dr. Rzeszotarski's review, page 21).

RECOMMENDATIONS

I recommend that the sponsor be sent a Not Approvable letter, describing the reasons for our view that the new specification for the The letter should also let the sponsor know that we would be willing to accept 18 month and 6 month expiration dating for the 600 and 800 mg tablets, respectively, with the current specification of

/S/

Russell Katz, M.D.

cc:
NDA 20-882
HFD-120
HFD-120/Katz/Leber/Ware
HFD-120/Fisher/Fitzgerald/Rzeszotarski/Guzewska

APPEARS THIS WAY
ON ORIGINAL

(868)
OUTGOING

REQUEST FOR PROPRIETARY/ESTABLISHED NAME REVIEW

SEP 11 1997

To: CDER Labeling and Nomenclature Committee
Attention: Dan Boring, R.Ph., Ph.D., Chair
HFD-530
9201 Corporate Blvd, Room N461

From: HFD-120 - Division of Neuropharmacological Drug Products

Paul Leber, M.D., Director /S/

Date: September 11, 1997

RECEIVED JAN 3 0 1998

Application Status (IND/NDA/ANDA): NDA 20-882

Proposed Proprietary Name: Neurontin

Trademark registration status/Countries registered(if known): Registered but country unknown
Company tradename: **Parke-Davis**

Other proprietary names by same firm for companion products: Neurontin Capsules

United States Adopted Name, dosage form, strength and dosing schedule:
Gabapentin Tablets, 600 mg and 800 mg, 900-1800 mg/day given in divided doses (3 times daily)

Indication for use: Adjunct therapy for the treatment of partial seizures with and without secondary generalization in adults.

Comments from submitter (concerns, observations, etc.):
Note: The chemist has requested a review of the USAN name as listed in the proposed labeling (see highlighted area). Specifically, the appropriateness of the firm using the USAN name "Gabapentin Tablets and Capsules" versus using two separate phrases, ie. "Gabapentin Tablets" and "Gabapentin Capsules".

Meetings of the Committee are scheduled for the 4th Tuesday of each month. Please submit this form at least one week before the meeting. Responses will be as timely as possible.
Rev. 2/97

cc
NDA 20-789
HFD-120/Division File
HFD-120/CSO/JWare

Pharmaceutical Research
2800 Plymouth Road
Ann Arbor, MI
48105
Phone: 313-996-7596
Facsimile: 313-996-7890

PARKE-DAVIS
People Who Care

Sean Brennan, Ph.D.
Senior Director
Worldwide Regulatory Affairs

July 1, 1997

NDA 20-882
Ref. No. 001
Neurontin® (gabapentin tablets)

Re: New Drug Application

Paul Leber M.D.
Director
Division of Neuropharmacological
Drug Products (HFD-120)
Document Control Room 4037
Center for Drug Evaluation and Research
Food and Drug Administration
Woodmont Office Center 2
1451 Rockville Pike
Rockville, Maryland 20852

Dear Dr. Leber:

Pursuant to 21 CFR 314.50, enclosed is a New Drug Application for Neurontin (gabapentin tablets). This NDA seeks approval of an additional new solid-oral dosage form of gabapentin in strengths of 600- and 800-mg film-coated tablets for the indications identified in approved NDA 20-235 for Neurontin (gabapentin capsules). The NDA number 20-882 was preassigned by the Central Document Control Room on June 17, 1997.

As required under the Prescription Drug and User Fee Act of 1992, 1997 has been sent to the Food and Drug Administration in care of the . A User Fee Cover Sheet, Form FDA 3397, precedes this letter

The proposed contents of this NDA were provided to FDA in our correspondence to IND On May 6, 1997, we were informed by FDA that a pre-submission meeting was not necessary for this NDA.

Patent and exclusivity information and the Generics Drug Enforcement Act Certification are provided in Item 13, contained in Volume 1 of this NDA. Please refer to the attached Form FDA 356H and the NDA Index which detail the complete contents of this NDA.

Pursuant to 21 CFR 314.440, a copy of the Chemistry, Manufacturing and Controls section of this NDA has been sent to the FDA District Office in North Brunswick, New Jersey.

If you need additional information or have any questions regarding this submission, please contact me at 313/996-7596 or FAX 313/996-7890, or Mr. Alexander Brankiewicz at 313/996-1399.
734-622-1399

Sincerely,

Sean Brennan

Sean Brennan

SB\ab\rm
t:\nda\20-882\063097-001

Attachments

APPEARS THIS WAY
ON ORIGINAL

cc: Ms. Regina Brown, North Brunswick, New Jersey District Office
(Forms 3397, 356h, cover letter, and Sections 1, 2, and 3 only)

APPEARS THIS WAY
ON ORIGINAL

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Ware

Food and Drug Administration
Rockville MD 20857

NDA 20-882

Parke-Davis Pharmaceutical Research
Division of Warner-Lambert Company
Attention: Sean Brennan
2800 Plymouth Road, P.O. Box 1047
Ann Arbor, MI 48106-1047

JUL 24 1997

Dear Mr. Brennan:

We have received your new drug application (NDA) submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for the following:

Name of Drug Product: Neurontin® (gabapentin) Tablets, 600mg and 800mg

Therapeutic Classification: Standard

Date of Application: July 1, 1997

Date of Receipt: July 2, 1997

Our Reference Number: 20-882

Unless we notify you within 60 days of our receipt date that the application is not sufficiently complete to permit a substantive review, this application will be filed under section 505(b) of the Act on August 30, 1997 in accordance with 21 CFR 314.101(a).

If you have any questions, please contact Jacqueline H. Ware, Pharm.D., Regulatory Management Officer, at (301) 594-5793.

Please cite the NDA number listed above at the top of the first page of any communications concerning this application.

Sincerely yours,

/S/

(For) John S. Purvis
Chief, Project Management Staff
Division of Neuropharmacological Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

cc:
Original NDA 20-882
HFD-120/Div. Files
HFD-120/CSO/J.Ware
HFD-120/Leber/Katz//Fitzgerald/Fisher/Blum/Rzeszotarski
HFD-860/Baweja
DISTRICT OFFICE

Drafted by: JHW/July 22, 1997/20882ack.ll
Final: July 22, 1997

ACKNOWLEDGEMENT (AC)

Pharmaceutical Research
2800 Plymouth Road Phone 313 996 7596
Ann Arbor MI Facsimile 313 996 7890
48105

PARKE-DAVIS
People Who Care

Sean Brennan, Ph.D.
Senior Director
Worldwide Regulatory Affairs

January 9, 1998

DUPLICATE

NDA 20-882
Ref. No. 2
Neurontin® (gabapentin tablets)

Re: Amendment - Chemistry, Manufacturing and Controls - Claim for Categorical Exclusion for Preparation of an Environmental Assessment

ORIG AMENDMENT
N(30)

Paul Leber, M.D.
Director,
Division of Neuropharmacological
Drug Products (HFD-120)
Document Control Room 4037
Center for Drugs Evaluation and Research
Food and Drug Administration
Woodmont Office Center 2
1451 Rockville Pike
Rockville, Maryland 20852

Dear Dr. Leber:

Reference is made to our pending NDA 20-882 for Neurontin® (gabapentin tablets) submitted on July 1, 1997, and to a telephone conversation on January 7, 1998, between Ms. Nancy Sager of FDA with Mr. Alexander Brankiewicz of Parke-Davis.

In the telephone conversation of January 7, Ms. Sager noted that this NDA was submitted prior to the final rule published in the Federal Register notice of July 29, 1997, concerning the Revision of Policies and Procedures with respect to the National Environmental Policy Act. Ms. Sager also noted that this application appears to qualify for a Categorical Exclusion for Preparation of an Environmental Assessment under 21 CFR 25.31(a) in that the application seeks approval for a more convenient dosage form of a previously approved product for which an Environmental Assessment has been provided. After further discussion, Parke-Davis concluded that a Categorical Exclusion for Preparation of Environmental Assessment was appropriate for this submission.

Parke-Davis hereby requests withdrawal of the Confidential Environmental Assessment and Freedom of Information Environmental Assessment submitted in Items 3.4. and 3.5. in Volume 8 of the original NDA submission of July 1, 1997. Provided in the attachment is a revised Item 3.4. - Claim for a Categorical Exclusion for Preparation of an Environmental Assessment.

If you need additional information or have any questions regarding this submission, please contact me at 313/996-7596 or FAX 313/996-7890, or Mr. Alexander Brankiewicz at 313/996-1399.

Sincerely,

Sean Brennan

SB\ab\rm
t:\nda\20-882\010898-2

Attachment

cc: Ms. Regina Brown, North Brunswick, New Jersey District Office
Ms. Nancy Sager (Desk Copy)

3.4. Claim for a Categorical Exclusion for Preparation of an Environmental Assessment

NDA 20-882 provides for the manufacture, distribution and use of the drug substance gabapentin in a new convenient 600- and 800-mg tablet dosage form. This is a substitute product for the current Neurontin® 100-, 300- and 400-mg (gabapentin capsule) products approved under NDA 20-235 for which a complete environmental assessment has been provided. This application will not increase the dose, duration of treatment nor patient population currently approved in NDA 20-235. In addition, the manufacturing sites for the drug substance and 600- and 800-mg tablet products remain unchanged from the drug substance and capsule products manufacturing sites identified in NDA 20-235. This application claims an exclusion for preparation of an environmental assessment under 21 CFR 25.31(a) in that the amount of drug substance reasonably expected to be introduced into the environment will not increase with approval of this application.

Pharmaceutical Research
2800 Plymouth Road
Ann Arbor, Mi
48105
Phone 313-996-7596
Facsimile 313-996-7890

RKE-DAVIS
Who Care

Brennan, Ph.D.
Director
Regulatory Affairs

February 10, 1998

NDA 20-882
Ref. No. 3
Neurontin® (gabapentin tablets)

Re: Response to Request for Information
Division of Biopharmaceutics

Paul Leber, M.D.
Director
Division of Neuropharmacological
Drug Products (HFD-120)
Document Control Room 4037
Center for Drug Evaluation and Research
Food and Drug Administration
Woodmont Office Center II
1451 Rockville Pike
Rockville, Maryland 20852

Dear Dr. Leber:

Reference is made to NDA 20-882 for Neurontin® (gabapentin tablets) submitted on July 1, 1997 and to the telephone request of February 9, 1998 from Dr. Vijaya Tammara of the Office of Clinical Pharmacology and Biopharmaceutics.

On February 9, 1998, Dr. Tammara requested the dissolution profile for the 800-mg gabapentin tablet lot manufactured in our Morris Plains, New Jersey facility and the dissolution profiles for the three lots of gabapentin tablets manufactured at the proposed commercial manufacturing facility in . Dr. Tammara also requested data on dissolution studies for the 800-mg tablets .

Provided in the attachment are the dissolution profiles using the proposed analytical method for the gabapentin 800-mg tablet lot manufactured at the facility in Morris Plains, New Jersey (Lot CM-1731095) and the three lots manufactured at the proposed commercial facility in (Lots 80757V, 80857V and 80957V).

Studies have not been performed on the dissolution profiles in alternative media for the 800-mg tablets.

If you have any questions or require additional information, please contact me at 313/996-7596 or FAX 313/996-7890 or Mr. Alexander Brankiewicz at 313/996-1399.

Sincerely,

Alexander J Brankiewicz

for Sean Brennan

SB\ab\rm
t:\nda\20-882\021098-3

Attachment

Desk Copy: Dr. Vijaya Tammara, Office of Clinical Pharmacology and Biopharmaceutics

Pharmaceutical Research
2800 Plymouth Road Phone: (734) 622-7000
Ann Arbor, MI
48105

PARKE-DAVIS

March 12, 1998

DESK COPY

NDA 20-882
Ref. No.: 4
Neurontin® (gabapentin) Tablets

Re: General Correspondence

Paul Leber, M.D.
Director
Division of Neuropharmacological
Drug Products (HFD-120)
Document Control Room 4037
Center for Drugs Evaluation and Research
Food and Drug Administration
Woodmont Office Center 2
1451 Rockville Pike
Rockville, Maryland 20852

Dear Dr. Leber:

Reference is made to our pending NDA 20-882 for Neurontin® (gabapentin tablets) submitted on July 1, 1997 and to a telephone conversation on March 10, 1998 between review chemist Dr. J. Rzeszotarski of your Division with Mr. Alexander Brankiewicz of Parke-Davis.

In the telephone conversation of March 10, 1998, Dr. Rzeszotarski noted that his review copy of Volume 2 of NDA 20-882 was missing pages 50-75. These pages were FAXED to Dr. Rzeszotarski on March 10, 1998. In telephone conversations with Project Manager Ms. Jackie Ware of your Division on March 10, 1998 and March 11, 1998, she noted that the archival copy of the NDA submission of July 1, 1997 contained pages 50-75 in Volume 2 and that the missing pages should be submitted as general correspondence.

In response to the above request, attached are copies of pages 50-75 of Volume 2 of the NDA submission on July 1, 1997.

If you have any questions regarding this submission, please contact me at 734/622-1399 or FAX 734/622-7890.

Sincerely,

Alexander J. Brankiewicz
Manager
Worldwide Regulatory Affairs

AB\rm t:\nda\20-882\031298-4
Attachment
Desk Copy: Ms. Jackie Ware (Project Manager)
Dr. W. J. Rzeszotarski (Review Chemist)

Pharmaceutical Research
2800 Plymouth Road
Ann Arbor, MI
48105
Phone: 313-996-7596
Facsimile: 313-996 7890

PARKE-DAVIS
People Who Care

Sean Brennan, Ph.D.
Senior Director
Worldwide Regulatory Affairs

April 2, 1998

NDA 20-882
Ref. No. 5
Neurontin® (gabapentin) Tablets

Re: Amendment - Chemistry, Manufacturing and Controls, Neurontin® 600- and 800-mg Tablets

DESK COPY

Paul Leber, M.D.
Director
Division of Neuropharmacological
Drug Products (HFD-120)
Document Control Room 4037
Center for Drug Evaluation and Research
Food and Drug Administration
Woodmont Office Center 2
1451 Rockville Pike
Rockville Maryland 20852

Dear Dr. Leber:

Reference is made to our pending NDA 20-882 for Neurontin® (gabapentin) Tablets submitted on July 1, 1997 and to a telephone conversation between Project Manager, Ms. Jackie Ware of your Division and Mr. Alexander Brankiewicz of Parke-Davis on March 24, 1998. In the telephone conversation of March 24, 1998, Ms. Ware requested two additional copies of Volume 9 (Item 4), Samples, Methods Validation and Labeling for FDA. In addition, Ms. Ware requested that the specific lot identification numbers for the method validation samples and the person and address to contact for receipt of samples be provided.

In response to this request, we have revised page 5 of Volume 9 (Item 4) of the NDA submission of July 1, 1997 to identify the lots of Neurontin Tablets and analytical reference standards to be provided for methods validation. The revised page 5 is provided in Attachment 1. The requested copies of the methods validation package are provided in Attachment 2 with this revised page 5.

Pursuant to 21 CFR 314.440, a field copy of this submission has been sent to the FDA District Office in North Brunswick, New Jersey. Parke-Davis certifies that this field copy is a true copy of the technical information contained in this amendment.

If you have any questions or require additional information, please contact me at 734/622-7596 or FAX 734/622-7890 or Mr. Alexander Brankiewicz at 734/622-1399.

Sincerely,

Alexander J Brankiewicz

for Sean Brennan

SB\ab\rm
t:\nda\20-882\040298-5

Attachments

cc: Ms. Jackie Ware, Project Manager (letter only)
Dr. Janus Rzeszotarski, Reviewing Chemist (Desk Copy)
Ms Regina Brown, Preapproval Coordinator
Dept. of Health and Human Services
Public Health Service
Food and Drug Administration
120 N. Center Drive
North Brunswick, NJ 08902 (Field Copy)

APPEARS THIS WAY
ON ORIGINAL

Pharmaceutical Research
2800 Plymouth Road
Ann Arbor, MI
48105
Phone: (734) 622-7596
Facsimile: (734) 622-7890

PARKE-DAVIS

April 14, 1998

NDA 20-882
Ref. No. 6
Neurontin® (gabapentin) Tablets

Sean Brennan, Ph.D.
Senior Director
Worldwide Regulatory Affairs

DESK COPY

Re: Amendment - Chemistry,
Manufacturing and Controls,
Neurontin® 600- and 800-mg Tablets

Paul Leber, M.D.
Director
Division of Neuropharmacological
Drug Products (HFD-120)
Document Control Room 4037
Center for Drug Evaluation and Research
Food and Drug Administration
Woodmont Office Center 2
1451 Rockville Pike
Rockville Maryland 20852

Dear Dr. Leber:

Reference is made to our pending NDA 20-882 for Neurontin® (gabapentin) Tablets submitted on July 1, 1997 and to a telephone conversation between Project Manager, Ms. Jackie Ware of your Division and Mr. Alexander Brankiewicz of Parke-Davis on March 24, 1998. In the telephone discussion of March 24, Ms. Ware inquired when the stability data for the 800-mg tablet dosage form would be available. Ms. Ware was informed that the data would be available and submitted to NDA 20-882 by April 15, 1998. This submission consisting of 2 volumes, is in response to this request.

On Page 54 in Volume 2 of the NDA submission of July 1, 1997, Parke-Davis committed to amend the NDA with stability data for the 800-mg tablet as it became available. Provided in Attachment 1 is updated 3 month normal and accelerated stability data (designated as Appendix 16) for Neurontin 800-mg tablet Lots 80757V (CV-0920997), 80857V (CV-0930997) and 80957V (CV-0940997) manufactured at the) manufacturing site and packaged in bottles of 100 and 500 and in unit dose blisters. These lots were manufactured in accordance with the information and processes outlined in Section 3.3.5. (Volume 2) of the NDA submission and tested in accordance with the methods and specifications described in Section 3.3.6. Both the 600- and 800-mg tablets are

The color of the imprinting inks are the sole difference to provide an additional distinguishing characteristic between the 600- and 800-mg tablets.

We are also providing in Attachment 1 updated stability data through 12 months (Appendix 15) for the 600-mg tablet Lots 80186V, 80286V and 80386V manufactured at the facility and through 18 months for the supportive 600- and 800-mg tablets manufactured in Morris Plains, New Jersey (Appendices 13 and 14 respectively).

Provided in Attachment 2 are the executed batch records for Neurontin 800-mg tablet lots 80757V, 80857V and 80957V. Provided in Attachment 3 are the proposed Master Batch Records for the manufacture of Neurontin 800-mg

The proposed Master Batch Records for the manufacture of Neurontin 800-mg Tablets
were previously provided in Appendices 2.1 and 2.3 of the July 1, 1997 NDA submission. Provided in Attachment 4 are the dissolution profiles for the 800-mg tablet lots manufactured in

We are also amending the NDA with revised material specifications

Provided in Attachment 5.1.
is a summary of the changes to the material specifications to those submitted in Appendix 1 of the July 1, 1997 NDA submission.

Pursuant to 21 CFR 314.440, a field copy of this submission has been sent to the FDA District Office in North Brunswick, New Jersey. Parke-Davis certifies that this field copy is a true copy of the technical information contained in this amendment.

If you have any questions or require additional information, please contact me at 734/622-7596 or FAX 734/622-7890 or Mr. Alexander Brankiewicz at 734/622-1399.

Sincerely,

Alexander J. Brankiewicz

for Sean Brennan

SB\ab\rm t:\nda\20-882\041498-6
Attachments
cc: Ms. Jackie Ware, Project Manager (letter only)
Dr. Janus Rzeszotarski, Reviewing Chemist (Desk Copy)
Ms Regina Brown, Preapproval Coordinator (Field Copy)

Pharmaceutical Research
2800 Plymouth Road Phone: (734) 622-7000
Ann Arbor, MI
48105

ARKE-DAVIS

ORIGINAL

June 2, 1998

NDA 20-882
Ref. No. 7
Neurontin® (gabapentin tablets)

DRUG AMENDMENT
N(BC)

Re: Amendment - Chemistry, Manufacturing and Controls

Paul Leber, M.D.
Director
Division of Neuropharmacological
Drug Products (HFD-120)
Document Control Room 4037
Center for Drugs Evaluation and Research
Food and Drug Administration
Woodmont Office Center 2
1451 Rockville Pike
Rockville, Maryland 20852

CENTER FOR DRUG EVALUATION AND RESEARCH

JUN 03 1998

RECEIVED HFD-120

Dear Dr. Leber:

Reference is made to our pending NDA 20-882 for Neurontin® (gabapentin tablets) submitted on July 1, 1997, the amendment of April 14, 1998 (Ref. No 6) providing additional data for the 800-mg tablet and the telephone request of May 28, 1998 from reviewing chemist Dr. J. Rzeszotarski of your Division. Dr. Rzeszotarski requested the manufacturer's Certificates of Analysis (C of As) for the gabapentin drug substance lots used in manufacture of the Neurontin 800-mg NDA stability lots.

Provided in the Attachment are the C of As for the gabapentin drug substance lots requested. The drug substance lots and the 800-mg tablet lot manufactured from each drug substance lot is identified below:

Drug Substance Lot	800-mg Tablet Lot
776255 (V25879)	CV-0940997
776256 (V25803)	CV-0930997, CV-0940997
119 (V25814)	CV-0920997

The Certificates of Analysis were FAXED to Dr. Rzeszotarski on May 29, 1998.

Pursuant to 21 CFR 314.440, a field copy of this submission has been sent to the FDA District Office in North Brunswick, New Jersey. Parke-Davis certifies that this field copy is a true copy of the technical information contained in this amendment.

If you have any questions, please contact me at 734/622-1399 or FAX 734/622-7890.

Sincerely,

Alexander J. Brankiewicz
Manager
Worldwide Regulatory Affairs

AB\rm
t:\nda\20-882\060298-7

Attachment

cc: Pre-Approval Coordinator - Field Copy
Dr. W. J. Rzeszotarski (Review Chemist) - Desk Copy

MEMORANDUM OF TELECON

NDA/IND:	N 20-882
DATE:	19-FEB-98; 26-FEB-98
PRODUCT NAME:	Neurontin (Gabapentin tablets)
FIRM's NAME:	Parke-Davis
Conversation with:	Mr Alexander J. Brankiewicz
Telephone #:	(734) 622-1399

(BACKGROUND): Parke-Davis described new 600 & 800 mg tablets as: "a white, film-coated elliptical tablet imprinted with product logo in black(for 600 mg and orange for 800 mg) ink."

****

I have called Mr Brankiewicz on 19-FEB-98 and told him I would like to see the samples of tablets since their description in text is unsatisfactory. I received them on 26-FEB-98 and called Mr Brankiewicz to inform him that the identification of tablets was unsatisfactory, since they have only inscription: "NEURONTIN" and number 600 or 800 and no company logo. I also asked him to describe the new tablets fully in the application since future reviewers may not see the samples. Mr Brankiewicz promised to introduce the logo to the commercial batches using the same inks and to provide the full description and new samples as soon as possible.

****

/S/

W. Janusz Rzeszotarski, Ph.D

Init: MEG
cc: MGuzewska
JWare

filename: D:\wpfiles\N20882t.c01