CENTER FOR DRUG EVALUATION AND RESEARCH

Approval Package for:

APPLICATION NUMBER:

21-042 / S-001

Trade Name: Vioxx

Generic Name: Rofecoxib

Sponsor: Merck & Co

Approval Date: February 25, 2000

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-042 / S-001

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CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-042 / S-001

APPROVAL LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-042/S-001

Merck Research Laboratories
Attention: Eric A. Floyd, Ph.D.
Associate Director, Regulatory Affairs
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, Pennsylvania 19486

FEB 25 2000

Dear Dr. Floyd:

Please refer to your supplemental new drug application dated July 15,1999, received July 16, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vioxx™ (rofecoxib tablets) 12.5 mg, 25 mg and 50 mg.

We acknowledge receipt of your submissions dated August 23 and November 19, 1999; January 20, February 4, 11, 18, and 25, 2000. Your submission of November 19, 1999 constituted a complete response to our November 16, 1999 action letter.

This supplemental new drug application provides for adding an additional tablet size of 50 mg.

We have completed the review of this supplemental application and it is approved.

We remind you of your Phase 4 commitments specified in your submission dated February 25, 2000 listed below.

[ ]

In addition, we have the following recommendation. The statistical criterion o' [ ] only provides information for reproducibility of the method but not the ability of discrimination. Final selection of the dissolution method will be based on full dissolution data set to be submitted.

Protocols, data, and final reports should be submitted to your IND for this product and a copy of the cover letter sent to this NDA. If an IND is not required to meet your Phase 4 commitments, please submit protocols, data and final reports to this NDA as

correspondence. In addition, under 21 CFR 314.82(b)(2)(vii), we request that you include a status summary of each commitment in your annual report to this NDA. The status summary should include the number of patients entered in each study, expected completion and submission dates, and any changes in plans since the last annual report. For administrative purposes, all submissions, including labeling supplements, relating to these Phase 4 commitments must be clearly designated "Phase 4 Commitments."

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, call Leslie Vaccari, Acting Chief Project Management , at (301) 827-2538.

Sincerely,

Karen Midthun 2/25/00

Karen Midthun, M.D.
Director
Division of Anti-Inflammatory, Analgesic
and Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
Archival NDA 21-042/S-001
HFD-550/Div. Files
HFD-550/LVaccari
HFD-550/BHo
HFD-550/MZarifa
HFD-550/DBashaw
HFD-550/KMidthun
HFD-095/DDMS-IMT
HFD-830/DNDC Division Director
DISTRICT OFFICE

Drafted by: lav/February 25, 2000
Initialed by: BHo(Chemist)/2-25-00
MZarifa (Chemistry Team Leader)/2-25-00
DBashaw (Biopharm Team Leader)/2-25-00
KMidthun (DD)/2-25-00
final:
filename: 21042S01

APPROVAL (AP) (with Phase 4 Commitments)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-042 / S-001

APPROVABLE LETTER

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville MD 20857

NDA 21-042/S-001

NOV 16 1999

Merck Research Laboratories
Attention: Eric A. Floyd, Ph.D.
Associate Director, Regulatory Affairs
Sumneytown Pike
P.O. Box 4, BLA-20
West Point, Pennsylvania 19486

Dear Dr. Floyd:

Please refer to your supplemental new drug application dated July 15, 1999, received July 16, 1999, submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for Vioxx (rofecoxib tablets) Tablets, 12.5 mg and 25 mg.

We acknowledge receipt of your submission dated August 23, 1999.

This supplement proposes adding a 50 mg tablet.

We have completed the review of this application as amended, and it is approvable. Before this application may be approved, however, it will be necessary for you to address the following:

1. The following comment pertains to your proposed change of paddle speed from [redacted] r the dissolution testing of the 50 mg tablet:

   Based on your criteria #4, dissolution rates with paddle speed at [redacted] inutes or [redacted] utes are more sensitive to non-significant changes in the manufacturing process than the [redacted] lease provide evidence that, for the 50 mg tablet, variations in dissolution data with paddle speed at [redacted] re not significant and that the test is too sensitive to minor differences present in the manufacturing process.

2. The stability testing of the drug product packaged in blisters [redacted] nd physician samples a [redacted] oes not include 3 and 9 month time points. The testing for these packaging systems at [redacted] iled to include a 3 month time point.

   Please provide justification for exclusion of these time points from the stability testing.

3. We remind you that the stability testing of the drug product packaged in [redacted] hould be performed using samples from the same bottle (that used at t=0) at each time point. This is to assure in-use stability of the drug product.

4. In reviewing the dissolution rates for the three batches submitted (nos. MR-3428, 837-40 and 837-45) it appeared that the dissolution rates for batch 837-45 were slightly higher than those for batches 837-40 and MR-3428, regardless of the container/closure system in which they were stored. Please clarify.

In addition, it will be necessary for you to submit final printed labeling (FPL) for the drug. The labeling should be identical in content to the submitted draft labeling (package insert submitted July 15, 1999).

In addition, all previous revisions as reflected in the most recently approved labeling must be included. To facilitate review of your submission, please provide a highlighted or marked-up copy that shows the changes that are being made.

Please submit 20 copies of the final printed labeling, ten of which are individually mounted on heavy weight paper or similar material.

If additional information relating to the safety or effectiveness of this drug becomes available, revision of the labeling may be required.

Within 10 days after the date of this letter, you are required to amend the supplemental application, notify us of your intent to file an amendment, or follow one of your other options under 21 CFR 314.110. In the absence of any such action FDA may proceed to withdraw the application. Any amendment 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.

This product may be considered to be misbranded under the Federal Food, Drug, and Cosmetic Act if it is marketed with this change prior to approval of this supplemental application.

If you have any questions, contact Sandra N. Cook, Project Manager, at (301) 827-2090.

Sincerely,

Karen Midthun 11/16/99

Karen Midthun, M.D.
Acting Director
Division of Anti-Inflammatory, Analgesic and
Ophthalmic Drug Products
Office of Drug Evaluation V
Center for Drug Evaluation and Research

cc:
Archival NDA 21-042
HFD-550/Div. Files
HFD-550/S.Cook Orig & 2 sc 11/16/99
HFD-550/Mitra/Ho Orig for AM 11/16/99
HFD-550/Villalba/Hyde
HFD-880/Wang/Bashaw cc 11/16/99
DISTRICT OFFICE

Drafted by: SNC/November 12, 1999

APPROVABLE (AE)

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-042 / S-001

MEDICAL REVIEW(S)

MEDICAL OFFICER REVIEW

ANTI-INFLAMMATORY, ANALGESIC AND OPHTHALMIC DRUG PRODUCTS DIVISION -- HFD-550

sNDA 21-042

Submission date (letter):	July 15, 1999
Submission type:	NDA supplement
Review date:	September 29, 1999
Drug name:	VIOXX
Applicant	Merck Research Laboratories phone (610) 397 7788
Pharmacologic category:	COX-2 inhibitor
Proposed indications:	Management of acute pain.
Dosage form and route:	50 mg oral tablet

Orig NDA # 21042
HFD-550/Div File
HFD-550/PM/Cook
HFD-880/Biopharm/
HFD-550/MO/JHyde
HFD-550/MO/MLVillalba

Villalba 11/12/99
Maria Lourdes Villalba, M.D, M.O.

JEH 11-12-99
John Hyde, M.D, PhD, Acting
Deputy Director DAAODP

Background and overview

Rofecoxib (VIOXX®), a non-steroidal anti-inflammatory drug with COX-2 selective inhibition activity was approved in May 20, 1999 for the management of acute pain, treatment of the signs and symptoms of osteoarthritis and for the treatment of dysmenorrhea. Approved formulations: VIOXX 12.5 mg and 25 mg tablets and VIOXX 12.5 and 25 mg/5 ml oral formulation. The aim of this supplemental NDA is to provide evidence that two 25 mg tablets are bioequivalent to one 50 mg tablet.

This submission consist of a single study (study # 087) and a revised label.

Study 087

Design: Open-label, 2-period, single-dose, crossover study to establish the bioequivalence of 2 tablet strengths of rofecoxib.

Subjects: 25 healthy subjects

Treatment: Two 25 mg tablets or one 50 mg tablet, single dose, with a minimum of 7 days washout between doses. Total duration of the study: 4 weeks.

Endpoints: PK parameters: AUC, C_{max} and apparent half life (t ½). Safety parameters.

Statistical analyses: ANOVA model.

Results:

The rofecoxib AUC geometric mean of the 50 mg tablet and the 2 x 25 mg tablets was 9903 ng.hr/mL and 10416 ng.hr/mL, respectively. Rofecoxib GMR of the 50 mg tablet to the 2 x 25 mg tablets was 0.95 with 90% bounds of (0.92, 0.98).

Similarly, the rofecoxib C_{max} GM of the 50 mg tablet and the 2 x 25 mg tablets was 411 and 462 ng/mL respectively. The GMR of the 50 mg tablet to the 2 x 25 mg tablets was 0.89 with 90% bounds of (0.81, 0.97).

Since both CI for the AUC and C_{max} fell within the pre-specified bounds of 0.80 to 1.25, no difference in bioavailability between the 50 mg and the 2 x 25 mg tablets was concluded.

Safety: Only one patient discontinued the protocol due to and adverse event: AN 23 was a 65 year old man who presented acute abdominal pain/appendicitis approximately 7 hours after the first dose of rofecoxib 50 mg. He underwent uncomplicated appendectomy and fully recovered. There were two additional adverse events not requiring withdrawal: AN 16 presented mild/transient headache and AN 17 presented mild/transient epigastric discomfort. There were no laboratory adverse experiences. Physical examination, ECG and vital signs were within normal limits.

Conclusions:

Rofecoxib 2 x 25 mg tablets and one 50 mg tablet were bioequivalent. There was no clinically meaningful difference in the apparent t ½ of both treatments. The treatment was well tolerated.

The revised label contains minimal editorial changes and adds information about the 50 mg dose. The proposed changes are acceptable.

Appenidx I

NDA: 21-042 Volume 1.1

Study Type: Bioequivalence *Study #: 087*

Study Title: An Open-Label, 2-Period, Balanced, Single-Dose, Crossover Study in Healthy Subjects to Establish the Bioequivalence of 2 Tablet Strengths of MK-0966

Study Site	
Clinical Site	*Analytical Site*

Study Design								
Single Dose	*Multiple Dose*	*Washout Period*	*Cross-over*	*Parallel*	*Other Design*	*Fasted/ Fed*	*FDA Diet*	*No. of fasted hrs.*
X		*7 days*	*X*			*Fast*		*From midnignt*

Subject Category					
Normal	*Patients*	*Young*	*Elderly*	*Renal*	*Hepatic*
X		*X*	*X*		

Subject Type			
Males		***Females***	
Age	*Weight*	*Age*	*Weight*
42.7 (28-63) yrs	*81.1 (66.23 – 104.78) kg*	*49.86 (35-63) yrs*	*70.85 (46.27 – 88.45) kg*

Subject Treatment Group			
Group No.	*Total No.*	*Males*	*Females*
1	*12*	*5*	*7*
2	*12*	*4*	*8*

Treatment Group	*Dose*	*Dosage Form*	*Strength*	*Lot #*
1	*2 x 25 mg*	*MK-0966 25 mg biobatch tablet*	*25 mg*	*MR-3426*
2	*1 x 50 mg*	*MK-0966 50 mg biobatch tablet*	*50 mg*	*MR-3428*

Sampling Times

Plasma: predsoe and 1, 2, 3, 4, 6, 8, 10, 13, 16, 22, 24, 27, 30, 36, 48, 60, 72, 96, 120 hrs posedose.

Assay Method:

Assay Sensitivity: LOQ =

Assay Accuracy: *Precision*

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

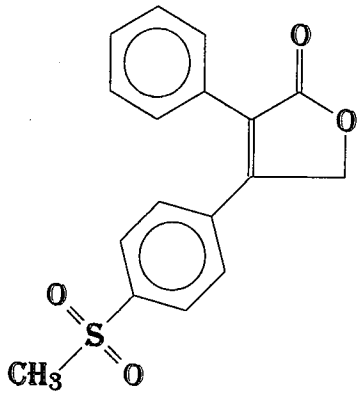
21-042 / S-001

CHEMISTRY REVIEW(S)

NOV 12 1999

Chemistry Review #1	1. Division, HFD-550	2. NDA Number: 21-042
3. Name and Address of Applicant Merck & Co. Inc., Sumneytown Pike, P O. Box 4, BLA-20, West Point PA 19486	4. Supplement Number: SE2-001	
	Letter Date 7-15-99	Stamp Date 7-16-99
		Due Date 11-16-99
5. Name of Drug:: Vioxx	6. Nonproprietary Name: Rofecoxib	
7. Supplement Provides for: A new dosage form, 50 mg per tablet		8. Amendment(s): NA
9. Pharmacological Category NSAID	10. How Dispensed Rx	11. Related Documents NA
12. Dosage Form: Tablets	13. Potency(ies), 12.5, 25 & 50 mg	

14. Chemical Name and Structure:



FORMULA: $C_{17}H_{14}O_4S$

M. W.: 314.36

15. Supporting Document: Provided on the following page

16. Comments:

Drug Substance: There are no changes in the drug substance. See NDA 21-042 for details.

Drug Product:

The manufacture and control of the 50 mg tablet have been described in NDA 21-042. Clinical studies were also conducted for the 50 mg tablet. Formulations for 12.5 mg, 25 mg, and 50 mg are proportionally the same except the variations in the amount of the coloring agent [redacted] Clinical studies demonstrated bioequivalence of the three formulations containing different amount of [redacted]

Packaging systems for commercial distributions of the 50 mg tablet are basically the same as the [redacted] systems for the 12.5 mg and 25 mg tablets. Satisfactory twenty-four months stability data on 3 batches of the drug product stored in proposed market [redacted] stems are provided.

The supplement, from the chemistry point of view, is approvable. Deficiencies in this review should be forwarded to the applicant for response::

17. Conclusions and Recommendations: Approvable

18. Name:	Signature:	Date
Review Chemist	Bart Ho	November 12, 1999
Acting Team Leader:	Amit Mitra	11-12-99

15. Supporting Document:

Type/No.	Subject	Holder	Status	Review Date	Letter Date
			Adequate	4/5/99	8-18-98
			Adequate	Acceptable*	8-18-98
			Adequate	Acceptable*	8-14-98
			Adequate	4-9-99	8-14-98
			Adequate	Acceptable*	8-18-98
			Adequate	4-1-97	8-11-98
			Adequate	Acceptable*	3-17-98
			Adequate	2-24-99	6-5-98
			Adequate	11-13-97	6-13-97
			dequate	4-3-97	8-11-98
			dequate	10-23-97	8-14-98
			dequate	2-17-99	8-14-98
			dequate	7-31-98	8-11-98
			dequate	Acceptable*	8-19-98

Information above is from the Chemistry Review #1, NDA 21-042.

cc:

NDA 21-042
HFD-550/Division File
HFD-550/B. Ho
HFD-550/Mitra
HFD-550/Cook
HFD-830/Chen

Doc ID: 21042S01R1.DOC

22 Page(s) Withheld

✓ Trade Secret / Confidential

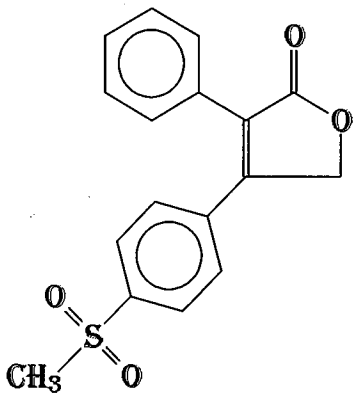
_____ Draft Labeling

_____ Deliberative Process

Withheld Track Number: Chemistry- 1a

Chemistry Review #2	1. Division, HFD-550		2. NDA Number: 21-042
3. Name and Address of Applicant Merck & Co. Inc., Sumneytown Pike, P O. Box 4, BLA-20, West Point PA 19486	4. Supplement Number: SE2-001		
	Letter Date 11-19-99	Stamp Date 11-23-99	Due Date 3-23-00
5. Name of Drug:: Vioxx	6. Nonproprietary Name: Rofecoxib		
7. Supplement Provides for: A new strength of 50 mg/tablet			8. Amendment(s): 11-19-99
9. Pharmacological Category NSAID	10. How Dispensed Rx		11. Related Documents NA
12. Dosage Form: Tablets	13. Potency(ies), 12.5, 25 & 50 mg		

14. Chemical Name and Structure:



FORMULA: $C_{17}H_{14}O_4S$

M. W.: 314.36

15. Supporting Document: NA

16. Comments:

Firm has provided all responses to FDA review chemist's comments.

17. Conclusions and Recommendations: The submission is approvable with comment (See page 6 of review notes)

18. Name:	Signature:	Date
Review Chemist	Bart Ho	January 31, 2000
Acting Team Leader:	Mona Zarifa	

15. Supporting Document: NA

cc:

NDA 21-042
HFD-550/Division File
HFD-550/Wang
HFD-550/B. Ho
HFD-550/Zarifa
HFD-550/Cook
HFD-830/Chen

Doc ID: 21042S01R2.DOC

4 Page(s) Withheld

✓ Trade Secret / Confidential

_____ Draft Labeling

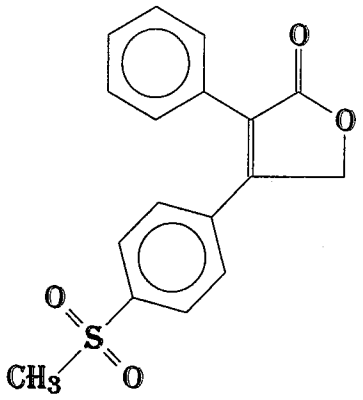
_____ Deliberative Process

Withheld Track Number: Chemistry- 2a

FEB 29 2000

Chemistry Review #3	1. Division, HFD-550	2. NDA Number: 21-042
3. Name and Address of Applicant Merck & Co. Inc., Sumneytown Pike, P O. Box 4, BLA-20, West Point PA 19486	4. Supplement Number: SCS-001 Letter Date 7-15-99 / Stamp Date 7-16-99 / Due Date 11-16-99	
5. Name of Drug:: Vioxx	6. Nonproprietary Name: Rofecoxib	
7. Supplement Provides for: A new dosage regimen of 50 mg and a new dissolution specification, Q — in 15 minutes. — or 50 mg tablet.		8. Amendment(s): 2/3/00, 2/11/00 and 2/18/00 4
9. Pharmacological Category, NSAID	10. How Dispensed, Rx	11. Related Documents, NA
12. Dosage Form: Tablets	13. Potency(ies), 12.5, 25 & 50 mg	

14. Chemical Name and Structure:



FORMULA: $C_{17}H_{14}O_4S$

M. W.: 314.36

15. Supporting Document: NA

16. Comments:

Merck requests to revise the dissolution specifications as follows:

12.5 mg and 25 mg tablets: Q — 20 minutes to Q — n 20 minutes, — supplement 4).

50 mg tablet — 1 15 minutes, paddle speed at —

We request that Merck — , 12.5 mg, 25 mg, and 50 mg tablets as follows:

Q = — 20 minutes, r —

Merck responded to the AE letter with a phase IV commitment on 2/11/00 that Merck would perform appropriate validation of the 50 mg methodology and commits to provide to the Agency within four weeks.

Division of BioPharm reviewed Merck's response and found the proposal is adequate. A copy of the review from BioPharm is attached.

Chemistry reviewer concurs with BioPharm's decision.

17. Conclusions and Recommendations: Recommend Approve.

18. Name:	Signature:	Date
Review Chemist	Bart Ho	February 25, 2000
Acting Team Leader:	Mona Zarifa	2/29/00

cc: NDA 21-042
HFD-550/Division File / BASHAW/8800 Ellr 3/3/00
HFD-550/B. Ho
HFD-550/DangW
HFD-550/Zarifa
HFD-550/Cook
HFD-830/Chen

Doc ID: 21042S01R3.DOC

CENTER FOR DRUG EVALUATION AND RESEARCH

APPLICATION NUMBER:

21-042 / S-001

CLINICAL PHARMACOLOGY AND BIOPHARMACEUTICS REVIEW(S)

CLINICAL PHARMACOLOGY / BIOPHARMACEUTICS REVIEW

NDA 21-042
PRODUCT: Rofecoxib tablets
BRAND NAME: VIOXX™
SPONSOR: Merck & Co., Inc.
P.O. Box 4
West Point, PA 19486

SUBMISSION DATE: 7/15/99, 11/5/99

REVIEWER: Dan Wang, Ph.D.

TYPE OF SUBMISSION:
Supplement

In this supplemental NDA, the sponsor submitted clinical (bioequivalent study) and chemistry (dissolution study) data supporting a labeling change adding 50 mg dose tablet. The bioequivalence trial compared the MK-0966 plasma concentration profiles of the biobatch preparation of two tablet strengths (25 and 50 mg). Although these doses as the 25-mg tablet formulation have been included in Phase III efficacy trials, a direct efficacy comparison of 2 x 25-mg and a single 50-mg tablet had not been made. Demonstration of bioequivalence of these two tablet strengths and adequate dissolution specification for 50 mg tablets would warrant the approval of 50 mg tablets. The dissolution data were submitted to Chemistry and reviewed by Dr. Bartholomew Ho. Dr. Ho and the PK reviewer have had discussions about the proposed dissolution specification. The PK reviewer agrees with Dr. Ho that the proposed dissolution specification is not discriminating enough for quality control purpose. A tighter dissolution specification should be used. The bioequivalent study was reviewed by the PK reviewer and summarized below.

Bioequivalence Study

Study 087. An Open-Label, 2-Period, Balanced, Single-Dose, Crossover Study in Healthy Subjects to Establish the Bioequivalence of 2 Tablet Strengths of MK-0966

Study Design: An open-label, 2-period, balanced, crossover study in 24 healthy subjects. A single dose of 2 x 25-mg tablets or a 50-mg tablet was administered in each of 2 periods. Subjects were randomized to treatment groups according to the allocation schedule. In both periods, blood samples for plasma MK-0966 concentrations were collected at intervals over 120 hours following each dose. There were 7 days between doses of MK-0966. See Appendix I for more information.

Data Analysis: The MK-0966 pharmacokinetic parameters (e.g., AUC(0-∞), Cmax, Tmax, and apparent $t_{1/2}$) were analyzed using an analysis of variance (ANOVA) model. The ANOVA model contained terms for sequence, subject within sequence, treatment and period effects. The log transformation was applied to AUC(0-∞) and Cmax. Similarly, the rank and inverse transformations were applied to Tmax and apparent t½, respectively. Ninety percent CIs, based upon the t-distribution, were generated for the GMR comparison for AUC(0-∞) and Cmax.

Results: The mean plasma concentration-time profiles following 25 and 50 mg MK-0966 tablets are shown in Figure 1. The mean plasma concentration profiles after first 6 hours of dosing are plotted in Figure 2. Summary statistics of AUC and Cmax are listed in Table 1, Tmax and $T_{1/2}$ are listed in Tables 2 and 3, respectively.

Figure 1

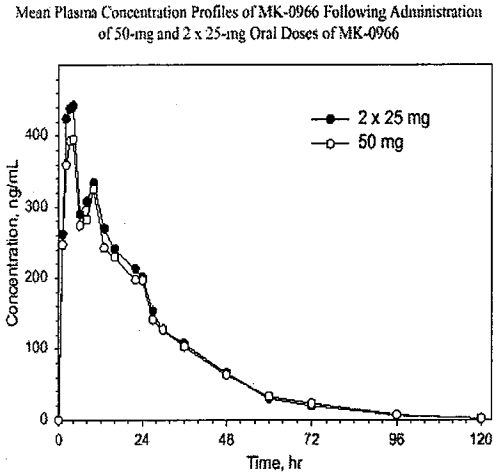


Figure 2.

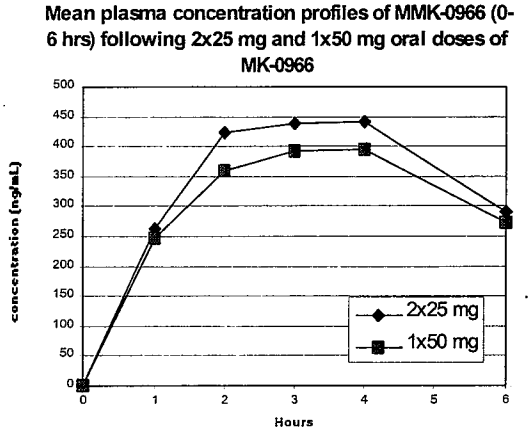


Table 1.

Summary Statistics for $AUC_{(0-\infty)}$ (ng•hr/mL) and C_{max} (ng/mL) of MK-0966 Following Single-Dose 2 x 25-mg Tablets and Single-Dose 50-mg Tablet

Parameter	Treatment	N	Geometric Mean†	Median†	Min, Max†	Between-Treatment p-Value	Approximate Within-Subject CV (%)‡	GMR†	90% CI† for GMR
$AUC_{(0-\infty)}$	50-mg tablet	24	9903	9856		0.018	6.86	0.95	(0.92, 0.98)
	2x25-mg tablets	24	10416	10526					
C_{max}	50-mg tablet	24	411	426		0.034	18.09	0.89	(0.81, 0.97)
	2x25-mg tablets	24	462	480					

† Data is back-transformed from the log scale.
‡ RMSE on the log scale •100.

Data Source: [2.1]

Table 2.

Summary Statistics for T_{max} (hr) of MK-0966

Treatment	N	Median	Arithmetic Mean	Min, Max	Between-Subject SE	Between-Treatment p-Value
50-mg tablet	24	4.0	4.25		0.28	0.681
2 x 25-mg tablets	24	3.5	3.75		0.29	

Data Source: [2.1]

Table 3.

Summary Statistics for Apparent $t_{½}$ (hr) of MK-0966

MK-0966 Treatment	N	Harmonic Mean	Median	Min, Max	Jackknife SD	Between-Treatment p-Value
50-mg tablet	24	13.2	13.0	/ /	3.1	0.077
2 x 25-mg tablets	24	12.1	12.8		3.6	

Data Source: [2.1]

The results indicated that 2 x 25 mg and 1 x 50 mg tablets of MK-0966 are bioequivalent. There is no statistical significant difference in Tmax and $T_{1/2}$ between 2 x 25 mg and 1 x 50 mg treatments.

RECOMMENDATION

The applicant has adequately conducted the bioequivalent study. The result demonstrated that that 2 x 25 mg and 1 x 50 mg tablets of MK-0966 are bioequivalent.

11/15/99

Dan Wang
Division of Pharmaceutical Evaluation III

FT initialed by D. Bashaw, Pharm.D. 11/17/99

cc:
IND 44,258(Original)
HFD-550(Cook)
HFD-880(Division file)
HFD-880(Bashaw)
HFD-880(Wang)
HFD-850(Mira Millison, Drug, Chron Files)
HFD-205(FOI)
HFD-344(Viswanathan)
CDR: Attn: Barbara Murphy