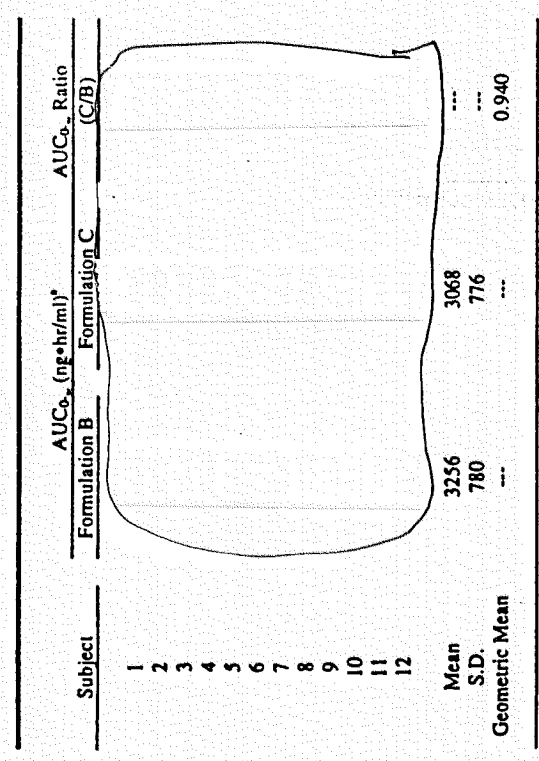
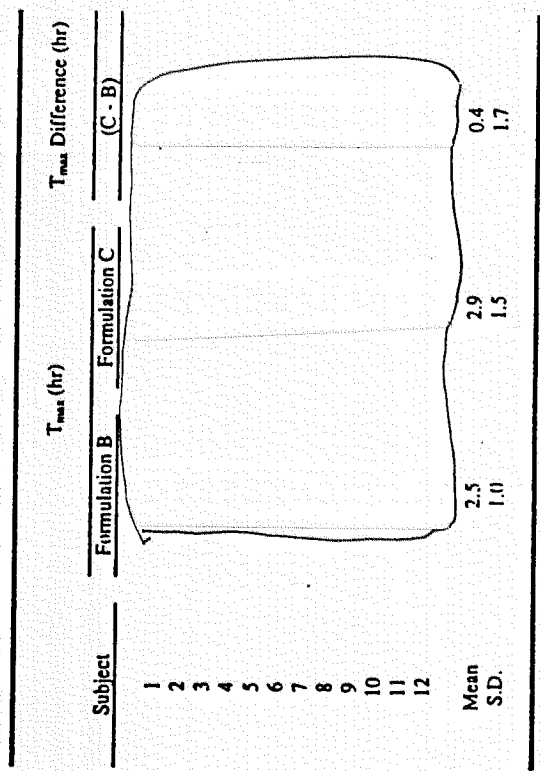


5-tu-36

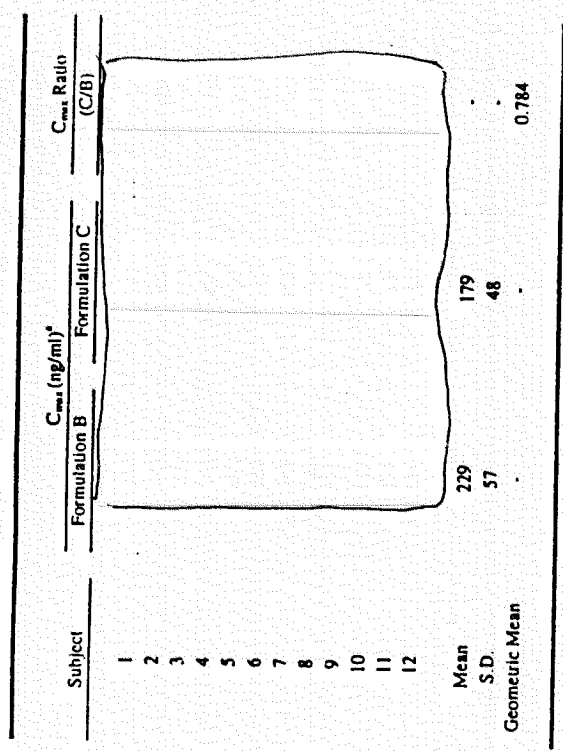
Areas Under the Plasma Concentration-Time Curves (AUC<sub>0-∞</sub>) of MK-0966 and AUC<sub>0-∞</sub> Ratios Following Administration of Single Doses of 25-mg Tablet Formulations of MK-0966



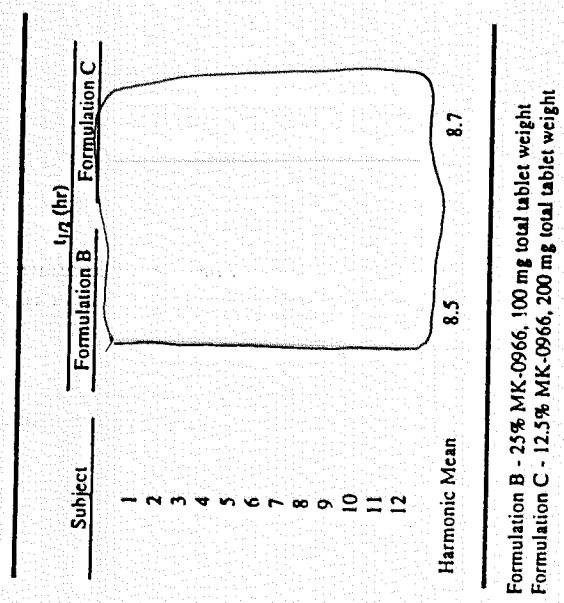
Times of Occurrence (T<sub>max</sub>) of Maximum Concentrations of MK-0966 Observed in Plasma and T<sub>max</sub> Differences Following Administration of Single Doses of 25-mg Tablet Formulations of MK-0966



Maximum Concentrations of MK-0966 Observed in Plasma (C<sub>max</sub>) and C<sub>max</sub> Ratios Following Administration of Single Doses of 25-mg Tablet Formulations of MK-0966



Apparent Terminal Half-Lives (t<sub>1/2</sub>) of MK-0966 in Plasma Following Administration of Single Doses of 25-mg Tablet Formulations of MK-0966



Clinical Pharmacology/Biopharmaceutics Study Summary Sheet

|                |  |                  |         |
|----------------|--|------------------|---------|
| NDA/IND#       | SUPL/AMEND. #  | SUBMISSION DATE: | VOLUME: |
| 21047<br>21057 |  | 23 Nov. 98       |         |
| Study Type:    | Pharmacokinetics   | Study 048        |         |
| Study Title:   | A 3-Period, Balanced, Single-Dose, Crossover Study in Healthy Subjects to Investigate the Comparative Bioavailability of Tablet and Suspension Formulations of MK-0966 |                  |         |

|                       |      |                         |                |
|-----------------------|------|-------------------------|----------------|
| CLINICAL INVESTIGATOR | SITE | ANALYTICAL INVESTIGATOR | SITE           |
|                       |      | Merck                   | West Point, PA |

|              |   |                |    |                 |         |
|--------------|---|----------------|----|-----------------|---------|
| SINGLE DOSE: | X | MULTIPLE DOSE: | NA | WASHOUT PERIOD: | 10 Days |
| CROSS-OVER   | X | PARALLEL       | NA | OTHER DESIGN:   | NA      |

|                             |               |                                 |                        |    |
|-----------------------------|---------------|---------------------------------|------------------------|----|
| FASTED                      | X             | FOOD STUDY                      | FDA HIGH FAT BREAKFAST | NA |
| If fasted, how long (hrs.)? | 8 hrs predose | Meals consistant in each period | NA                     | NA |

|                   |   |          |    |       |   |         |    |       |    |         |    |
|-------------------|---|----------|----|-------|---|---------|----|-------|----|---------|----|
| SUBJECT BREAKDOWN |   |          |    |       |   |         |    |       |    |         |    |
| Normal            | X | Patients | NA | Young | X | Elderly | NA | Renal | NA | Hepatic | NA |

|        |              |           |   |       |     |     |       |    |    |    |    |    |    |
|--------|--------------|-----------|---|-------|-----|-----|-------|----|----|----|----|----|----|
|        | SUBJECT TYPE |           |   |       |     |     | GROUP | N= | 12 | M= | 4  | F= | 8  |
| Weight | Mean         | 166.5lbs  | M | Range | 155 | 174 | Group | N= | NA | M= | 4  | F= | NA |
| Age    | Mean         | 26 Yr     | M | Range | 20  | 31  | Group | N= | NA | M= | 4  | F= | NA |
|        | SUBJECT TYPE |           |   |       |     |     | GROUP | N= | NA | M= | NA | F= | 8  |
| Weight | Mean         | 145.3 lbs | F | Range | 113 | 162 | Group | N= | NA | M= | NA | F= | 8  |
| Age    | Mean         | 31Yr      | F | Range | 22  | 44  | Group | N= | NA | M= | NA | F= | 8  |

|                 |          |                 |              |         |          |
|-----------------|----------|-----------------|--------------|---------|----------|
| TREATMENT GROUP | DOSE(mg) | DOSAGE FORM     | STRENGTH     | LOT#    | LOT SIZE |
| MK-0966 25 mg   | 25       | Tablet          | 25 mg        | MR-3359 | NA       |
| MK-0966 12.5 mg | 12.5     | Oral suspension | 12.5 mg/5 mL | FE-1551 | NA       |
| MK-0966 25 mg   | 25       | Oral suspension | 25 mg/5 mL   | FE-1552 | NA       |

|                |   |
|----------------|---|
| SAMPLING TIMES |   |
| Plasma         | Predose and 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7.5, 9, 12, 16, 18, 20, 22, 23, 24, 25, 26, 30, 33, 36, 39, 42, 46, 47, 48, 49, 50, 55, 60, 72, 96, and 120 hours postdose. |
| Urine          | NA  |
| Feces          | NA  |

|                   |  |
|-------------------|--|
| ASSAY METHOD:     |  |
| Assay Sensitivity |  |
| Assay Accuracy    |  |

|                            |                  |
|----------------------------|------------------|
| LABELING CLAIMS FROM STUDY | Pharmacokinetics |
|----------------------------|------------------|

**Clinical Pharmacology/Biopharmaceutics Study Summary Sheet**

|              |   |                  |         |
|--------------|---|------------------|---------|
| NDA/IND#     | SUPL/AMEND. #   | SUBMISSION DATE: | VOLUME: |
| 21042        |   | 23 Nov. 98       |         |
| Study Type:  | Pharmacokinetics  | Study 057        |         |
| Study Title: | An Open-Label, Randomized, 2-Period, Crossover Study to Investigate the Influence of Hepatic Insufficiency on the Pharmacokinetics of MK-0966 |                  |         |

|                       |      |                         |                |
|-----------------------|------|-------------------------|----------------|
| CLINICAL INVESTIGATOR | SITE | ANALYTICAL INVESTIGATOR | SITE           |
|                       |      | Merck                   | West Point, PA |

|              |    |                |    |                 |         |
|--------------|----|----------------|----|-----------------|---------|
| SINGLE DOSE: | X  | MULTIPLE DOSE: | X  | WASHOUT PERIOD: | 14 days |
| CROSS-OVER   | X- | PARALLEL       | NA | OTHER DESIGN:   | NA      |

|                             |       |            |  |                        |  |
|-----------------------------|-------|------------|--|------------------------|--|
| FASTED                      | X     | FOOD STUDY |  | FDA HIGH FAT BREAKFAST |  |
| If fasted, how long (hrs.)? | 8 hrs | NA         |  | NA                     |  |

|                   |    |          |   |       |   |         |    |       |    |         |   |
|-------------------|----|----------|---|-------|---|---------|----|-------|----|---------|---|
| SUBJECT BREAKDOWN |    |          |   |       |   |         |    |       |    |         |   |
| Normal            | NA | Patients | X | Young | X | Elderly | NA | Renal | NA | Hepatic | X |

|        | SUBJECT TYPE |         |   |       | GROUP |     | N= | M= | F= |
|--------|--------------|---------|---|-------|-------|-----|----|----|----|
| Weight | Mean         | 178 lbs | M | Range | 152   | 191 | 8  | 5  | 3  |
| Age    | Mean         | 49 Yr   | M | Range | 44    | 57  | NA | 5  | NA |
|        |              |         |   |       |       |     | NA | 5  | NA |
|        |              |         |   |       |       |     | NA | NA | 3  |
| Weight | Mean         | 155 lbs | F | Range | 144   | 165 | NA | NA | 3  |
| Age    | Mean         | 58 Yr   | F | Range | 47    | 67  | NA | NA | 3  |

| TREATMENT GROUP | DOSE(mg)     | DOSAGE FORM | STRENGTH | LOT#           | LOT SIZE |
|-----------------|--------------|-------------|----------|----------------|----------|
| MK-0966         | 25           | Tablet      | 25 mg    | MR-3359        | NA       |
| MK-0966         | 1<br>(200mL) | Solution    | 5 µg/mL  | 0966HSS001A007 | NA       |

| SAMPLING TIMES |  |
|----------------|--|
| Plasma         | FOLLOWING ORAL DOSE 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7.5, 9, 12, 16, 18, 21, 24, 26, 30, 33, 36, 39, 42, 48, 55, 60, 72, 96, and 120 hours postdose. Predose and FOLLOWING LV. DOSE end of infusion, and 0.5, 1.0, 1.5, 2, 3, 4, 5, 6, 7.5, 9, 12, 16, 18, 21, 24, 26, 30, 33, 36, 39, 42, 48, 55, 60, 72, 96, and 120 hours FOLLOWING END OF INFUSION. |
| Urine          | NA   |
| Feces          | NA   |

|                   |  |
|-------------------|--|
| ASSAY METHOD:     |  |
| Assay Sensitivity |  |
| Assay Accuracy    |  |

|                            |   |
|----------------------------|---|
| LABELING CLAIMS FROM STUDY | Pharmacokinetics in patients with liver disease |
|----------------------------|---|

Study 057

Baseline Patient Characteristics

| AN             | Sex | Age (yrs) | Height (in) | Weight (lb) | Race              | Child-Pugh Scores <sup>†</sup> |
|----------------|-----|-----------|-------------|-------------|-------------------|--------------------------------|
| 001            | F   |           |             |             | Hispanic American | 7                              |
| 002            | F   |           |             |             | Hispanic American | 6                              |
| 003            | F   |           |             |             | White             | 5                              |
| 004            | M   |           |             |             | Hispanic American | 9                              |
| 005            | M   |           |             |             | Native American   | 6                              |
| 006            | M   |           |             |             | Hispanic American | 5                              |
| 007            | M   |           |             |             | White             | 7                              |
| 008            | M   |           |             |             | Hispanic American | 8                              |
| Mean           |     | 53        | 66          | 169         |                   |                                |
| Range          |     | 44 to 67  | 63 to 71    | 144 to 191  |                   |                                |
| Range (Male)   |     | 44 to 57  | 64 to 71    | 152 to 191  |                   |                                |
| Range (Female) |     | 47 to 67  | 63 to 64    | 144 to 165  |                   |                                |

<sup>†</sup> 5 to 6 (mild), 7 to 9 (moderate) hepatic insufficiency.

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Table : Pharmacokinetics Stratified by Grade of Hepatic Insufficiency and Gender in Protocol 057

| Subject                            | Child-Pugh Score | Level of Hepatic Failure | Sex | AUC <sub>(0-∞)</sub> (ng•hr/mL) | C <sub>max</sub> (ng/mL) | T <sub>max</sub> (Hour) | t <sub>1/2</sub> (Hour) | Dose-Adjusted AUC Ratio (Oral/I.V.) |                                 |                         |                    |                      |  |
|------------------------------------|------------------|--------------------------|-----|---------------------------------|--------------------------|-------------------------|-------------------------|-------------------------------------|---------------------------------|-------------------------|--------------------|----------------------|--|
| Following a Single 25-mg Oral Dose |                  |                          |     |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 3                                  | 5                | Mild                     | F   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 6                                  | 5                | Mild                     | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 2                                  | 6                | Mild                     | F   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 5                                  | 6                | Mild                     | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 1                                  | 7                | Moderate                 | F   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 7                                  | 7                | Moderate                 | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 8                                  | 8                | Moderate                 | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 4                                  | 9                | Moderate                 | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| Subject                            | Child-Pugh Score | Level of Hepatic Failure | Sex |                                 |                          |                         |                         |                                     | AUC <sub>(0-∞)</sub> (ng•hr/mL) | t <sub>1/2</sub> (Hour) | Clearance (mL/min) | V <sub>dss</sub> (L) |  |
| Following a Single 1-mg I.V. Dose  |                  |                          |     |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 3                                  | 5                | Mild                     | F   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 6                                  | 5                | Mild                     | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 2                                  | 6                | Mild                     | F   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 5                                  | 6                | Mild                     | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 1                                  | 7                | Moderate                 | F   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 7                                  | 7                | Moderate                 | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 8                                  | 8                | Moderate                 | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |
| 4                                  | 9                | Moderate                 | M   |                                 |                          |                         |                         |                                     |                                 |                         |                    |                      |  |

Data Source: [2.1]

Summary Statistics for MK-0966 AUC<sub>(0-∞)</sub> (ng·hr/mL) Following Administration of a Single Oral Dose of MK-0966 (Dose Adjusted to 50 mg)

| Population (Protocol)           | N  | Dose  | AUC <sub>(0-∞)</sub> (ng·hr/mL) |        |         | Between-Subject CV (%) <sup>†</sup> |
|---------------------------------|----|-------|---------------------------------|--------|---------|-------------------------------------|
|                                 |    |       | Mean                            | Median | Minimum |                                     |
| Hemodialysis (064) <sup>†</sup> | 6  | 50 mg | 6927                            | 7078   |         | 51.8                                |
| Hepatic insufficiency (057)     | 8  | 25 mg | 11494                           | 9900   |         | 49.8                                |
| Healthy young (037)             | 11 | 50 mg | 7751                            | 6934   |         | 34.9                                |
| Healthy young (043)             | 12 | 50 mg | 7236                            | 7696   |         | 27.7                                |
| Healthy young (048)             | 12 | 25 mg | 8460                            | 9057   |         | 25.6                                |
| Healthy elderly (052)           | 12 | 25 mg | 9625                            | 9769   |         | 30.2                                |
| Healthy young (076)             | 15 | 25 mg | 6579                            | 7280   |         | 23.9                                |

<sup>†</sup> Between-subject SD on the log scale x 100; CV = coefficient of variation.  
<sup>‡</sup> Part I—Hemodialysis initiated 48 hours postdose.  
<sup>§</sup> Back transformed from log scale.

Summary Statistics for MK-0966 T<sub>max</sub> Following Administration of a Single Dose of MK-0966

| Population (Protocol)           | N  | Dose  | Mean | Median | Minimum | Maximum |
|---------------------------------|----|-------|------|--------|---------|---------|
| Hemodialysis (064) <sup>†</sup> | 6  | 50 mg | 3.2  | 3.0    |         |         |
| Hepatic insufficiency (057)     | 8  | 25 mg | 6.5  | 4.0    |         |         |
| Healthy young (037)             | 11 | 50 mg | 4.4  | 3.0    |         |         |
| Healthy young (043)             | 12 | 50 mg | 3.2  | 2.5    |         |         |
| Healthy young (048)             | 12 | 25 mg | 3.6  | 3.0    |         |         |
| Healthy elderly (052)           | 12 | 25 mg | 4.0  | 2.0    |         |         |
| Healthy young (076)             | 15 | 25 mg | 4.2  | 2.5    |         |         |

<sup>†</sup> Part I—Hemodialysis initiated 48 hours postdose.

Summary Statistics for MK-0966 t<sub>1/2</sub> (Hour) Following Administration of a Single 25- (or 50-) mg Oral Dose of MK-0966

| Population (Protocol)       | Dose of MK-0966 | N  | Harmonic Mean | Median | Min | Max | Between-Subject SD <sup>†</sup> |
|-----------------------------|-----------------|----|---------------|--------|-----|-----|---------------------------------|
| Hepatic insufficiency (057) | 25 mg           | 8  | 15.5          | 16.1   |     |     | 5.6                             |
| Healthy young (037)         | 50 mg           | 11 | 9.4           | 9.7    |     |     | 2.7                             |
| Healthy young (043)         | 25 mg           | 12 | 10.3          | 10.4   |     |     | 2.4                             |
| Healthy young (048)         | 25 mg           | 12 | 9.6           | 9.5    |     |     | 1.7                             |
| Healthy elderly (052)       | 25 mg           | 12 | 14.0          | 13.9   |     |     | 4.4                             |

<sup>†</sup> Jackknife standard deviation.  
 Data Source: [2.1]

Summary Statistics for MK-0966 C<sub>max</sub> (ng/mL) Following Administration of a Single Oral Dose of MK-0966 (Dose Adjusted to 50 mg)

| Population (Protocol)           | N  | Dose  | Mean | Median <sup>†</sup> | Minimum | Maximum | Between-Subject CV (%) |
|---------------------------------|----|-------|------|---------------------|---------|---------|------------------------|
| Hemodialysis (064) <sup>†</sup> | 6  | 50 mg | 395  | 408                 |         |         | 33.5                   |
| Hepatic insufficiency (057)     | 8  | 25 mg | 462  | 463                 |         |         | 27.8                   |
| Healthy young (037)             | 11 | 50 mg | 412  | 381                 |         |         | 35.9                   |
| Healthy young (043)             | 12 | 50 mg | 390  | 400                 |         |         | 20.2                   |
| Healthy young (048)             | 12 | 25 mg | 477  | 459                 |         |         | 37.2                   |
| Healthy elderly (052)           | 12 | 25 mg | 547  | 536                 |         |         | 32.0                   |
| Healthy young (076)             | 15 | 25 mg | 441  | 421                 |         |         | 21.6                   |

<sup>†</sup> Between-subject SD on the log scale x 100; CV = coefficient of variation.  
<sup>‡</sup> Part I—Hemodialysis initiated 48 hours postdose.  
<sup>§</sup> Back transformed from log scale.

4.1.2: Historical Information for Comparisons of PK Results Between Studies/Populations (Cont.)

Table 5

Summary for Demographic Variables Within Each Study

| Study (MK-0966) | N  | Sex  |        | Race  |          |       |
|-----------------|----|------|--------|-------|----------|-------|
|                 |    | Male | Female | White | Hispanic | Black |
| Prot. #037      | 11 | 8    | 3      | 2     | 7        | 2     |
| Prot. #043      | 12 | 12   | 0      | 7     | 3        | 2     |
| Prot. #048      | 12 | 4    | 8      | 1     | 0        | 11    |
| Prot. #052      | 12 | 8    | 4      | 8     | 3        | 1     |

| Study (MK-0966) | N  | Age (yrs) |     | Weight (lbs) |      |     | Height (in) |      |     |
|-----------------|----|-----------|-----|--------------|------|-----|-------------|------|-----|
|                 |    | Mean      | Min | Max          | Mean | Min | Max         | Mean | Min |
| Prot. #037      | 11 | 36        | 20  | 46           | 139  | 202 | 68          | 57   | 72  |
| Prot. #043      | 12 | 36        | 20  | 45           | 188  | 230 | 70          | 64   | 74  |
| Prot. #048      | 12 | 29        | 20  | 44           | 152  | 174 | 67          | 62   | 71  |
| Prot. #052      | 12 | 72        | 66  | 81           | 159  | 228 | 67          | 62   | 73  |

|              |   |                  |         |
|--------------|---|------------------|---------|
| NDA/IND#     | SUPPL/AMEND. #  | SUBMISSION DATE: | VOLUME: |
| 21042        |   | 23 Nov. 98       |         |
| Study Type:  | Pharmacokinetics  | Study 064        |         |
| Study Title: | An Open-Label, Three-Part, Oral Study to Investigate the Pharmacokinetics, Safety, and Tolerability of MK-0966 in Patients With Renal Insufficiency |                  |         |

|                       |      |                         |                |
|-----------------------|------|-------------------------|----------------|
| CLINICAL INVESTIGATOR | SITE | ANALYTICAL INVESTIGATOR | SITE           |
|                       |      | Merck                   | West Point, PA |
|                       |      |                         |                |

|              |    |                |    |                 |                  |
|--------------|----|----------------|----|-----------------|------------------|
| SINGLE DOSE: | X  | MULTIPLE DOSE: | NA | WASHOUT PERIOD: | At least 1 month |
| CROSS-OVER   | NA | PARALLEL       | NA | OTHER DESIGN:   | NA               |

|                             |       |            |  |                        |  |
|-----------------------------|-------|------------|--|------------------------|--|
| FASTED                      | X     | FOOD STUDY |  | FDA HIGH FAT BREAKFAST |  |
| If fasted, how long (hrs.)? | 8 hrs | NA         |  | NA                     |  |

|                   |    |          |   |       |   |         |    |       |   |         |    |
|-------------------|----|----------|---|-------|---|---------|----|-------|---|---------|----|
| SUBJECT BREAKDOWN |    |          |   |       |   |         |    |       |   |         |    |
| Normal            | NA | Patients | X | Young | X | Elderly | NA | Renal | X | Hepatic | NA |


|        |              |          |   |       |     |     |       |  |    |    |    |    |    |    |
|--------|--------------|----------|---|-------|-----|-----|-------|--|----|----|----|----|----|----|
|        | SUBJECT TYPE |          |   |       |     |     | GROUP |  | N= | 6  | M= | 4  | F= | 2  |
| Weight | Mean         | 175.5lbs | M | Range | 139 | 227 | Group |  | N= | NA | M= | 4  | F= | NA |
| Age    | Mean         | 46.5Yr   | M | Range | 41  | 60  | Group |  | N= | NA | M= | 4  | F= | NA |
|        | SUBJECT TYPE |          |   |       |     |     | GROUP |  | N= | NA | M= | NA | F= | 2  |
| Weight | Mean         | 159lbs   | F | Range | 156 | 162 | Group |  | N= | NA | M= | NA | F= | 2  |
| Age    | Mean         | 53Yr     | F | Range | 49  | 57  | Group |  | N= | NA | M= | NA | F= | 2  |

|                 |          |             |          |         |          |
|-----------------|----------|-------------|----------|---------|----------|
| TREATMENT GROUP | DOSE(mg) | DOSAGE FORM | STRENGTH | LOT#    | LOT SIZE |
| MK-0966         | 50       | Tablet      | 50 mg    | MR-3370 | NA       |

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A<sub>11</sub> -7

| SAMPLING TIMES |  |
|----------------|--|
| Plasma         | <p><b>Part 1</b><br/> Plasma for protein-binding predose or within 24 hours predose and samples drawn at 4, 8, and 48 hours postdose for in vivo protein binding. Hemodialysis was completed prior to dosing on Day 1, except in the case where there were 3 days between hemodialyses (e.g., Friday to Monday). In this case the patient took study drug 48 hours before their next scheduled hemodialysis (e.g., on the Saturday before the Monday hemodialysis). Day 3 hemodialysis started immediately following the 48-hour blood draw. If hemodialysis was initiated before 48 hours postdose, a sample for MK-0966 was collected just prior to hemodialysis. Plasma for MK-0966 levels were drawn every half hour during hemodialysis on Day 3.</p> <p>Sample dialysate for MK-0966: Predose and 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7.5, 9, 12, 16, 18, 20, 24, 30, 33, 36, 39, 42, 48, 60, 72, 96, and 120 hours postdose. In addition, blood was collected every half hour during Day 3 hemodialysis (e.g., 48.5, 49, 49.5, 50, 50.5, and 51 hours postdose).</p> <p>Blood collection for MK-0966: Dialysate samples were obtained every half hour during dialysis until dialysis was complete (48.5, 49, 49.5, 50, 50.5, and 51 hours postdose).</p> <p><b>Part 2</b><br/> Day 1 hemodialysis start 4 hours postdose on Day 1. Plasma for MK-0966 levels were drawn every half hour during hemodialysis on Day 1. Or as normally scheduled.</p> <p>Dialysate samples for MK-0966 assay were obtained every half hour during dialysis until dialysis was complete. It was anticipated that these samples would be collected at the same time as the plasma samples (4.5, 5, 5.5, 6, 6.5, and 7 hours postdose).</p> <p>Sample dialysate for MK-0966: Predose and 0.5, 1, 1.5, 2, 3, 4, 4.5, 5, 5.5, 6, 6.5, 7, 8, 9, 12, 16, 18, 20, 24, 30, 33, 36, 39, 42, 48, 52, 60, 72, 96, and 120 hours postdose. Blood was collected every half hour during Day 1 hemodialysis.</p> <p>Part 3 was nor carried out.</p> |
| Urine          | NA   |
| Feces          | NA   |

|                   |   |
|-------------------|---|
| ASSAY METHOD:     |  |
| Assay Sensitivity |   |
| Assay Accuracy    |   |

|                            |                                    |
|----------------------------|------------------------------------|
| LABELING CLAIMS FROM STUDY | Pharmacokinetics in Renal patients |
|----------------------------|------------------------------------|

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Study 06

Baseline Subject Characteristics

| AN  | Sex | Age (yrs)          | Height (in)        | Weight (lb)           | Plasma Creatinine Concentration† (mg/dL) | Race     |
|---|-----|--------------------|--------------------|-----------------------|--|----------|
| 001   | M   | 48.7<br>(41 to 60) | 67.5<br>(62 to 74) | 170.0<br>(139 to 227) | ---                                      | Hispanic |
| 002   | M   |                    |                    |                       |  | White    |
| 003   | M   |                    |                    |                       |  | Black    |
| 004   | F   |                    |                    |                       |  | Black    |
| 005   | M   |                    |                    |                       |  | White    |
| 006   | F   |                    |                    |                       |  | White    |
| Mean (Range)  |     | 48.7<br>(41 to 60) | 67.5<br>(62 to 74) | 170.0<br>(139 to 227) | ---                                      |          |
| † Mean of 5 values obtained during prestudy, Part I, Part 2 screening, Part 2, and poststudy. |     |                    |                    |                       |  |          |

Maximum Concentrations of MK-0966 Observed in Plasma ( $C_{max}$ , ng/mL) and  $C_{max}$  Ratios Following Administration of 50-mg Single Oral Doses of MK-0966 to Six Hemodialysis Patients

| Subject        | $C_{max}$ |         | $C_{max}$ Ratio<br>Part II / Part I |
|----------------|-----------|---------|-------------------------------------|
|                | Part I    | Part II |                                     |
| 1              | 411       | 337     | ---                                 |
| 2              | 150       | 124     | ---                                 |
| 3              | ---       | ---     | ---                                 |
| 4              | ---       | ---     | ---                                 |
| 5              | ---       | ---     | ---                                 |
| 6              | ---       | ---     | ---                                 |
| Mean           | ---       | ---     | ---                                 |
| SD             | ---       | ---     | ---                                 |
| Geometric Mean | ---       | ---     | 0.823                               |

Areas Under the Plasma Concentration-Time Curves (AUC, ng·hr/mL) of MK-0966 and AUC<sub>0-3hr}</sub> Ratios Following Administration of 50-mg Single Oral Doses of MK-0966 to Six Hemodialysis Patients

| Subject        | AUC <sub>0-3hr}</sub> |         | AUC    |         | AUC <sub>0-3hr}</sub> Ratio<br>Part II / Part I |
|----------------|-----------------------|---------|--------|---------|---|
|                | Part I                | Part II | Part I | Part II |   |
| 1              | 6721                  | 7309    | 6808   | ---     | ---   |
| 2              | 2796                  | 3336    | 3103   | ---     | ---   |
| 3              | ---                   | ---     | ---    | ---     | ---   |
| 4              | ---                   | ---     | ---    | ---     | ---   |
| 5              | ---                   | ---     | ---    | ---     | ---   |
| 6              | ---                   | ---     | ---    | ---     | ---   |
| Mean           | ---                   | ---     | ---    | ---     | ---   |
| SD             | ---                   | ---     | ---    | ---     | ---   |
| Geometric Mean | ---                   | ---     | ---    | ---     | 0.913   |

Part I - Three hours of hemodialysis initiated 48 hours postdose  
Part II - Three hours of hemodialysis initiated four hours postdose

Times of Occurrence ( $T_{max}$ , hr) of Maximum Concentrations of MK-0966 Observed in Plasma Following Administration of 50-mg Single Oral Doses of MK-0966 to Six Hemodialysis Patients

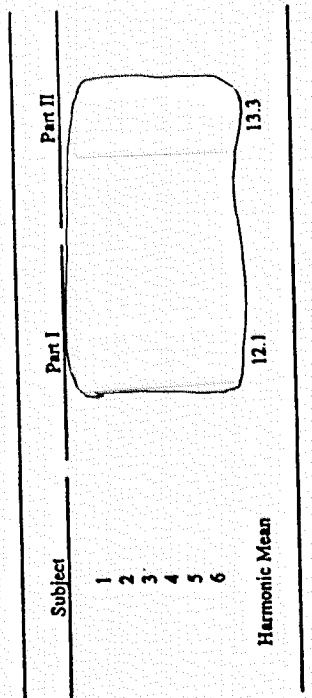
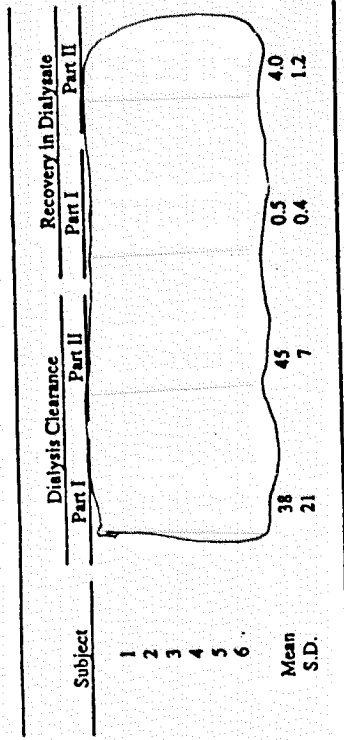
| Subject | $T_{max}$ |         |
|---------|-----------|---------|
|         | Part I    | Part II |
| 1       | 1.3       | 4.6     |
| 2       | ---       | ---     |
| 3       | ---       | ---     |
| 4       | ---       | ---     |
| 5       | ---       | ---     |
| 6       | ---       | ---     |
| Mean    | ---       | ---     |
| SD      | ---       | ---     |



Study

Dialysis Clearances (mL/min) and Recoveries of MK-0966 in Dialysate (% of Dose) Following Administration of 50-mg Single Oral Doses of MK-0966 to Six Hemodialysis Patients

Apparent Terminal Half-lives (hr) of MK-0966 in Plasma Following Administration of 50-mg Single Oral Doses of MK-0966 to Six Hemodialysis Patients



Part I - Three hours of hemodialysis initiated 48 hours postdose  
 Part II - Three hours of hemodialysis initiated four hours postdose

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In vitro protein binding of <sup>14</sup>C-MK-0966 in plasma from patients with renal insufficiency.

Summary Statistics for In Vitro Protein Binding of <sup>14</sup>C-MK-0966 in Plasma From Patients on Hemodialysis

| Concentration (ng/mL) | Percent <sup>14</sup> C-MK-0966 Bound <sup>a</sup> |       |       |       |       | Mean  |
|-----------------------|--|-------|-------|-------|-------|-------|
|                       | #001   | #002  | #003  | #004  | #005  |       |
| 50                    |  |       |       |       |       |       |
| 100                   |  |       |       |       |       |       |
| 500                   |  |       |       |       |       |       |
| Mean                  | 90.6   | 88.2  | 82.4  | 82.6  | 80.1  | 85.9  |
| S.D. <sup>b</sup>     | 0.7  | 0.2   | 0.8   | 0.5   | 1.4   | 4.8   |
| Mean f. <sup>c</sup>  | 0.094  | 0.118 | 0.176 | 0.174 | 0.199 | 0.141 |

| Concentration   | N | Mean | Median | Min | Max | Between-Subject SD |
|---|---|------|--------|-----|-----|--------------------|
| Percent In Vitro Protein Binding of <sup>14</sup> C-MK-0966 |   |      |        |     |     |                    |
| 50 ng/mL  | 6 | 85.9 | 85.7   |     |     | 5.2                |
| 100 ng/mL   | 6 | 86.5 | 85.9   |     |     | 4.5                |
| 500 ng/mL   | 6 | 85.4 | 85.0   |     |     | 4.8                |
| Overall <sup>d</sup>  | 6 | 85.9 | 85.4   |     |     | 4.8                |

<sup>d</sup> Averaged over the 3 concentration levels per patient.

<sup>a</sup> Values at each concentration represent the mean of duplicate determinations.  
<sup>b</sup> Value represents one sample.  
<sup>c</sup> Represents the fraction unbound.

Summary Statistics for MK-0966  $AUC_{(0-\infty)}$  (ng·hr/mL) Following Administration of a Single Oral Dose of MK-0966 (Dose Adjusted to 50 mg)

| Population (Protocol)           | N  | Dose  | $AUC_{(0-\infty)}$ (ng·hr/mL) |        |         | Between-Subject CV (%) <sup>†</sup> |
|---------------------------------|----|-------|-------------------------------|--------|---------|-------------------------------------|
|                                 |    |       | Mean                          | Median | Minimum |                                     |
| Hemodialysis (064) <sup>‡</sup> | 6  | 50 mg | 6927                          | 7078   |         | 51.8                                |
| Hepatic insufficiency (057)     | 8  | 25 mg | 11491                         | 9900   |         | 49.8                                |
| Healthy young (037)             | 11 | 50 mg | 7351                          | 6934   |         | 34.9                                |
| Healthy young (043)             | 12 | 50 mg | 7236                          | 7696   |         | 27.7                                |
| Healthy young (048)             | 12 | 25 mg | 8460                          | 9057   |         | 25.6                                |
| Healthy elderly (052)           | 12 | 25 mg | 9625                          | 9769   |         | 30.2                                |
| Healthy young (076)             | 15 | 25 mg | 6579                          | 7280   |         | 23.9                                |

† Between-subject SD on the log scale x 100; CV = coefficient of variation.  
‡ Part I—Hemodialysis initiated 48 hours postdose.  
‡ Back transformed from log scale.

Summary Statistics for MK-0966  $T_{max}$  Following Administration of a Single Dose of MK-0966

| Population (Protocol)           | N  | Dose  | Mean | Median | Minimum | Maximum |
|---------------------------------|----|-------|------|--------|---------|---------|
| Hemodialysis (064) <sup>‡</sup> | 6  | 50 mg | 3.2  | 3.0    |         |         |
| Hepatic insufficiency (057)     | 8  | 25 mg | 6.5  | 4.0    |         |         |
| Healthy young (037)             | 11 | 50 mg | 4.4  | 3.0    |         |         |
| Healthy young (043)             | 12 | 50 mg | 3.2  | 2.5    |         |         |
| Healthy young (048)             | 12 | 25 mg | 3.6  | 3.0    |         |         |
| Healthy elderly (052)           | 12 | 25 mg | 4.0  | 2.0    |         |         |
| Healthy young (076)             | 15 | 25 mg | 4.2  | 2.5    |         |         |

† Part I—Hemodialysis initiated 48 hours postdose.

Summary Statistics for MK-0966  $t_{1/2}$  (Hour) Following Administration of a Single 25- (or 50-) mg Oral Dose of MK-0966

| Population (Protocol)       | Dose of MK-0966 | N  | Harmonic |        | Minimum | Maximum | Between-Subject SD <sup>†</sup> |
|-----------------------------|-----------------|----|----------|--------|---------|---------|---------------------------------|
|                             |                 |    | Mean     | Median |         |         |                                 |
| Hepatic insufficiency (057) | 25 mg           | 8  | 15.5     | 16.1   |         |         | 5.6                             |
| Healthy young (037)         | 50 mg           | 11 | 9.4      | 9.7    |         |         | 2.7                             |
| Healthy young (043)         | 25 mg           | 12 | 10.3     | 10.4   |         |         | 2.4                             |
| Healthy young (048)         | 25 mg           | 12 | 9.6      | 9.5    |         |         | 1.7                             |
| Healthy elderly (052)       | 25 mg           | 12 | 14.0     | 13.9   |         |         | 4.4                             |

† Jackknife standard deviation.

Data Source: (2.1)

Summary Statistics for MK-0966  $C_{max}$  (ng/mL) Following Administration of a Single Oral Dose of MK-0966 (Dose Adjusted to 50 mg)

| Population (Protocol)           | N  | Dose  | Mean | Median <sup>†</sup> | Minimum | Maximum | Between-Subject CV (%) <sup>†</sup> |
|---------------------------------|----|-------|------|---------------------|---------|---------|-------------------------------------|
| Hemodialysis (064) <sup>‡</sup> | 6  | 50 mg | 395  | 408                 |         |         | 33.5                                |
| Hepatic insufficiency (057)     | 8  | 25 mg | 462  | 463                 |         |         | 27.8                                |
| Healthy young (037)             | 11 | 50 mg | 412  | 381                 |         |         | 35.9                                |
| Healthy young (043)             | 12 | 50 mg | 390  | 400                 |         |         | 20.2                                |
| Healthy young (048)             | 12 | 25 mg | 477  | 459                 |         |         | 37.2                                |
| Healthy elderly (052)           | 12 | 25 mg | 547  | 536                 |         |         | 32.0                                |
| Healthy young (076)             | 15 | 25 mg | 441  | 421                 |         |         | 21.6                                |

† Between-subject SD on the log scale x 100; CV = coefficient of variation.  
‡ Part I—Hemodialysis initiated 48 hours postdose.  
‡ Back transformed from log scale.

4.1.2. Historical Information for Comparisons of PK Results Between Studies/Populations (Cont.)

Table 5

Summary for Demographic Variables Within Each Study

| Study (MK-0966) | N  | Sex  |        | Race  |       |
|-----------------|----|------|--------|-------|-------|
|                 |    | Male | Female | White | Black |
| Prot. #037      | 11 | 8    | 3      | 2     | 2     |
| Prot. #043      | 12 | 12   | 0      | 7     | 3     |
| Prot. #048      | 12 | 4    | 8      | 1     | 0     |
| Prot. #052      | 12 | 8    | 4      | 8     | 3     |

| Study (MK-0966) | N  | Age (yrs) |     | Weight (lbs) |      | Height (in) |     |
|-----------------|----|-----------|-----|--------------|------|-------------|-----|
|                 |    | Mean      | Min | Max          | Mean | Min         | Max |
| Prot. #037      | 11 | 36        | 20  | 46           | 164  | 139         | 202 |
| Prot. #043      | 12 | 36        | 20  | 45           | 188  | 142         | 230 |
| Prot. #048      | 12 | 29        | 20  | 44           | 152  | 113         | 174 |
| Prot. #052      | 12 | 72        | 66  | 81           | 159  | 123         | 228 |

|              |   |                  |         |
|--------------|---|------------------|---------|
| NDA/IND#     | SUPPL/AMEND. #  | SUBMISSION DATE: | VOLUME: |
| 21042        |   | 23 Nov. 98       |         |
| Study Type:  | Pharmacokinetics  | Study 070        |         |
| Study Title: | A 2-Part, Open, Balanced, Crossover Study in Healthy Subjects to Establish the Bioequivalence of MK-0966 Tablet and Suspension Formulations |                  |         |

|                       |      |                         |                |
|-----------------------|------|-------------------------|----------------|
| CLINICAL INVESTIGATOR | SITE | ANALYTICAL INVESTIGATOR | SITE           |
|                       |      | Merck                   | West Point, PA |

|              |   |                |    |                 |        |
|--------------|---|----------------|----|-----------------|--------|
| SINGLE DOSE: | X | MULTIPLE DOSE: | NA | WASHOUT PERIOD: | 7 Days |
| CROSS-OVER   | X | PARALLEL       | NA | OTHER DESIGN:   | NA     |

|                             |                     |                               |                        |
|-----------------------------|---------------------|-------------------------------|------------------------|
| FASTED                      | X                   | FOOD STUDY                    | FDA HIGH FAT BREAKFAST |
| If fasted, how long (hrs.)? | 8 hrs prior to Labs | Part I fasting<br>Part II fed | NA                     |

|                   |   |          |    |       |   |         |    |       |    |         |    |
|-------------------|---|----------|----|-------|---|---------|----|-------|----|---------|----|
| SUBJECT BREAKDOWN |   |          |    |       |   |         |    |       |    |         |    |
| Normal            | X | Patients | NA | Young | X | Elderly | NA | Renal | NA | Hepatic | NA |

Part I

|        | SUBJECT TYPE |          |   | GROUP |     |     | N= | M= | F= |
|--------|--------------|----------|---|-------|-----|-----|----|----|----|
| Weight | Mean         | 172.3lbs | M | Range | 129 | 228 | 24 | 12 | 12 |
| Age    | Mean         | 36.5Yr   | M | Range | 18  | 62  | NA | 12 | NA |
|        |              |          |   |       |     |     | NA | 12 | NA |
|        | SUBJECT TYPE |          |   | GROUP |     |     | N= | M= | F= |
| Weight | Mean         | 159.4lbs | F | Range | 123 | 191 | NA | NA | 12 |
| Age    | Mean         | 48.6Yr   | F | Range | 20  | 64  | NA | NA | 12 |

Part II

|        | SUBJECT TYPE |          |   | GROUP |     |     | N= | M= | F= |
|--------|--------------|----------|---|-------|-----|-----|----|----|----|
| Weight | Mean         | 173.2lbs | M | Range | 146 | 198 | 25 | 12 | 13 |
| Age    | Mean         | 44.5Yr   | M | Range | 28  | 57  | NA | 12 | NA |
|        |              |          |   |       |     |     | NA | 12 | NA |
|        | SUBJECT TYPE |          |   | GROUP |     |     | N= | M= | F= |
| Weight | Mean         | 141.8lbs | F | Range | 104 | 176 | 13 | NA | 13 |
| Age    | Mean         | 43.0Yr   | F | Range | 24  | 61  | NA | NA | 13 |

| TREATMENT GROUP      | DOSE(mg) | DOSAGE FORM     | STRENGTH   | LOT#    | LOT SIZE |
|----------------------|----------|-----------------|------------|---------|----------|
| MK-0966 25 mg        | 25       | Tablet          | 25 mg      | MR-2426 | NA       |
| MK-0966 25 mg/5 mL   | 25       | Oral suspension | 25 mg/5 mL | FE-1582 | NA       |
| MK-0966 12.5 mg      | 12.5     | Tablet          | 12.5 mg    | MR-3427 | NA       |
| MK-0966 12.5 mg/5 mL | 12.5     | Oral suspension | 12.5 mg    | FE-1581 | NA       |

| SAMPLING TIMES |  |
|----------------|--|
| Plasma         | Predose and 0.5, 1, 1.5, 2, 3, 4, 5, 6, 7.5, 9, 12, 15, 18, 21, 24, 27, 30, 33, 36, 39, 42, 48, 52, 60, 72, 96, and 120 hours postdose |
| Urine          | NA   |
| Feces          | NA   |

|                                   |   |
|-----------------------------------|---|
| <b>ASSAY METHOD:</b>              |   |
| Assay Sensitivity                 |   |
| Assay Accuracy                    |   |
| <b>LABELING CLAIMS FROM STUDY</b> | Bioequivalence of tablet and suspension |

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Study 070, Part I

Areas Under the Plasma Concentration-Time Curves (AUC<sub>0-∞</sub>) of MK-0966 and AUC<sub>0-∞</sub> Ratios Following Administration of 12.5-mg Single Oral Doses of Tablet and Suspension Formulations of MK-0966 to Twenty-Four Healthy Subjects

| Subject        | AUC <sub>0-∞</sub> (ng·hr/mL) |            | AUC <sub>0-∞</sub> Ratio<br>Suspension/<br>Tablet |
|----------------|-------------------------------|------------|---|
|                | Tablet                        | Suspension |   |
| 1              |                               |            |   |
| 2              |                               |            |   |
| 3              |                               |            |   |
| 4              |                               |            |   |
| 5              |                               |            |   |
| 6              |                               |            |   |
| 7              |                               |            |   |
| 8              |                               |            |   |
| 9              |                               |            |   |
| 10             |                               |            |   |
| 11             |                               |            |   |
| 12             |                               |            |   |
| 13             |                               |            |   |
| 14             |                               |            |   |
| 15             |                               |            |   |
| 16             |                               |            |   |
| 17             |                               |            |   |
| 18             |                               |            |   |
| 19             |                               |            |   |
| 20             |                               |            |   |
| 21             |                               |            |   |
| 22             |                               |            |   |
| 23             |                               |            |   |
| 24             |                               |            |   |
| Mean           | 2061                          | 1958       | ---   |
| SD             | 903                           | 897        | ---   |
| Geometric Mean | ---                           | ---        | 0.932   |

Maximum Concentrations of MK-0966 Observed in Plasma (C<sub>max</sub>) and C<sub>max</sub> Ratios Following Administration of 12.5-mg Single Oral Doses of Tablet and Suspension Formulations of MK-0966 to Twenty-Four Healthy Subjects

| Subject        | C <sub>max</sub> (ng/mL) |            | C <sub>max</sub> Ratio<br>Suspension/<br>Tablet |
|----------------|--------------------------|------------|---|
|                | Tablet                   | Suspension |   |
| 1              |                          |            |   |
| 2              |                          |            |   |
| 3              |                          |            |   |
| 4              |                          |            |   |
| 5              |                          |            |   |
| 6              |                          |            |   |
| 7              |                          |            |   |
| 8              |                          |            |   |
| 9              |                          |            |   |
| 10             |                          |            |   |
| 11             |                          |            |   |
| 12             |                          |            |   |
| 13             |                          |            |   |
| 14             |                          |            |   |
| 15             |                          |            |   |
| 16             |                          |            |   |
| 17             |                          |            |   |
| 18             |                          |            |   |
| 19             |                          |            |   |
| 20             |                          |            |   |
| 21             |                          |            |   |
| 22             |                          |            |   |
| 23             |                          |            |   |
| 24             |                          |            |   |
| Mean           | 127                      | 118        | ---   |
| SD             | 35                       | 35         | ---   |
| Geometric Mean | ---                      | ---        | 0.921   |

Times of Occurrence (T<sub>max</sub>) of Maximum Concentrations of MK-0966 Observed in Plasma and T<sub>max</sub> Differences Following Administration of 12.5-mg Single Oral Doses of Tablet and Suspension Formulations of MK-0966 to Twenty-Four Healthy Subjects

| Subject | T <sub>max</sub> (hr) |            | T <sub>max</sub> Difference (hr)<br>Suspension<br>- Tablet |
|---------|-----------------------|------------|--|
|         | Tablet                | Suspension |  |
| 1       |                       |            |  |
| 2       |                       |            |  |
| 3       |                       |            |  |
| 4       |                       |            |  |
| 5       |                       |            |  |
| 6       |                       |            |  |
| 7       |                       |            |  |
| 8       |                       |            |  |
| 9       |                       |            |  |
| 10      |                       |            |  |
| 11      |                       |            |  |
| 12      |                       |            |  |
| 13      |                       |            |  |
| 14      |                       |            |  |
| 15      |                       |            |  |
| 16      |                       |            |  |
| 17      |                       |            |  |
| 18      |                       |            |  |
| 19      |                       |            |  |
| 20      |                       |            |  |
| 21      |                       |            |  |
| 22      |                       |            |  |
| 23      |                       |            |  |
| 24      |                       |            |  |
| Mean    | 2.4                   | 2.5        | 0.1  |
| SD      | 1.1                   | 1.8        | 2.0  |

study 070; Part II

Areas Under the Plasma Concentration-Time Curves (AUC<sub>0-∞</sub>) of MK-0966 and AUC<sub>0-24</sub> Ratios Following Administration of 25-mg Single Oral Doses of Tablet and Suspension Formulations of MK-0966 to Twenty-Four Healthy Subjects

Maximum Concentrations of MK-0966 Observed in Plasma (C<sub>max</sub>) and C<sub>max</sub> Ratios Following Administration of 25-mg Single Oral Doses of Tablet and Suspension Formulations of MK-0966 to Twenty-Four Healthy Subjects

| Subject        | AUC <sub>0-∞</sub> (ng•hr/mL) |            | AUC <sub>0-24</sub> Ratio |                    |                          |
|----------------|-------------------------------|------------|---------------------------|--------------------|--------------------------|
|                | Tablet                        | Suspension | Tablet With Food          | Suspension/ Tablet | Tablet With Food/ Tablet |
| 25             |                               |            |                           |                    |                          |
| 26             |                               |            |                           |                    |                          |
| 27             |                               |            |                           |                    |                          |
| 28             |                               |            |                           |                    |                          |
| 29             |                               |            |                           |                    |                          |
| 30             |                               |            |                           |                    |                          |
| 31             |                               |            |                           |                    |                          |
| 32             |                               |            |                           |                    |                          |
| 33             |                               |            |                           |                    |                          |
| 34             |                               |            |                           |                    |                          |
| 35             |                               |            |                           |                    |                          |
| 36             |                               |            |                           |                    |                          |
| 37             |                               |            |                           |                    |                          |
| 38             |                               |            |                           |                    |                          |
| 39             |                               |            |                           |                    |                          |
| 40             |                               |            |                           |                    |                          |
| 41             |                               |            |                           |                    |                          |
| 42             |                               |            |                           |                    |                          |
| 44             |                               |            |                           |                    |                          |
| 45             |                               |            |                           |                    |                          |
| 46             |                               |            |                           |                    |                          |
| 47             |                               |            |                           |                    |                          |
| 48             |                               |            |                           |                    |                          |
| 143            |                               |            |                           |                    |                          |
| Mean           | 3999                          | 3782       | 4122                      | —                  | ---                      |
| SD             | 1313                          | 1068       | 1288                      | —                  | ---                      |
| Geometric Mean | —                             | —          | —                         | 0.957              | 1.039                    |

| Subject        | C <sub>max</sub> (ng/mL) |            |                  | C <sub>max</sub> Ratio |                          |
|----------------|--------------------------|------------|------------------|------------------------|--------------------------|
|                | Tablet                   | Suspension | Tablet With Food | Suspension/ Tablet     | Tablet With Food/ Tablet |
| 25             |                          |            |                  |                        |                          |
| 26             |                          |            |                  |                        |                          |
| 27             |                          |            |                  |                        |                          |
| 28             |                          |            |                  |                        |                          |
| 29             |                          |            |                  |                        |                          |
| 30             |                          |            |                  |                        |                          |
| 31             |                          |            |                  |                        |                          |
| 32             |                          |            |                  |                        |                          |
| 33             |                          |            |                  |                        |                          |
| 34             |                          |            |                  |                        |                          |
| 35             |                          |            |                  |                        |                          |
| 36             |                          |            |                  |                        |                          |
| 37             |                          |            |                  |                        |                          |
| 38             |                          |            |                  |                        |                          |
| 39             |                          |            |                  |                        |                          |
| 40             |                          |            |                  |                        |                          |
| 41             |                          |            |                  |                        |                          |
| 42             |                          |            |                  |                        |                          |
| 44             |                          |            |                  |                        |                          |
| 45             |                          |            |                  |                        |                          |
| 46             |                          |            |                  |                        |                          |
| 47             |                          |            |                  |                        |                          |
| 48             |                          |            |                  |                        |                          |
| 143            |                          |            |                  |                        |                          |
| Mean           | 228                      | 228        | 252              | —                      | ---                      |
| SD             | 76                       | 85         | 73               | —                      | ---                      |
| Geometric Mean | —                        | —          | —                | 0.983                  | 1.125                    |

Times of Occurrence (T<sub>max</sub>) of Maximum Concentrations of MK-0966 Observed in Plasma and T<sub>max</sub> Differences Following Administration of 25-mg Single Oral Doses of Tablet and Suspension Formulations of MK-0966 to Twenty-Four Healthy Subjects

| Subject | T <sub>max</sub> (hr) |            |                  | T <sub>max</sub> Difference (hr) |                           |
|---------|-----------------------|------------|------------------|----------------------------------|---------------------------|
|         | Tablet                | Suspension | Tablet With Food | Suspension - Tablet              | Tablet With Food - Tablet |
| 25      |                       |            |                  |                                  |                           |
| 26      |                       |            |                  |                                  |                           |
| 27      |                       |            |                  |                                  |                           |
| 28      |                       |            |                  |                                  |                           |
| 29      |                       |            |                  |                                  |                           |
| 30      |                       |            |                  |                                  |                           |
| 31      |                       |            |                  |                                  |                           |
| 32      |                       |            |                  |                                  |                           |
| 33      |                       |            |                  |                                  |                           |
| 34      |                       |            |                  |                                  |                           |
| 35      |                       |            |                  |                                  |                           |
| 36      |                       |            |                  |                                  |                           |
| 37      |                       |            |                  |                                  |                           |
| 38      |                       |            |                  |                                  |                           |
| 39      |                       |            |                  |                                  |                           |
| 40      |                       |            |                  |                                  |                           |
| 41      |                       |            |                  |                                  |                           |
| 42      |                       |            |                  |                                  |                           |
| 44      |                       |            |                  |                                  |                           |
| 45      |                       |            |                  |                                  |                           |
| 46      |                       |            |                  |                                  |                           |
| 47      |                       |            |                  |                                  |                           |
| 48      |                       |            |                  |                                  |                           |
| 143     |                       |            |                  |                                  |                           |
| Mean    | 3.9                   | 2.5        | 5.3              | -1.4                             | 1.4                       |
| SD      | 2.7                   | 1.0        | 1.6              | 3.0                              | 3.1                       |

**Table 1**

**Summary Statistics for Demographic Variables (Gender and Race Distribution)  
Within Each Study**

| Study<br>(MK-0966) | Dose   | N  | Sex  |                  | Race  |          |       |
|--------------------|--------|----|------|------------------|-------|----------|-------|
|                    |        |    | Male | Male Percent (%) | White | Hispanic | Black |
| PROT. #037         | 50mg   | 11 | 8    | 73               | 2     | 7        | 2     |
| PROT. #043         | 50mg   | 12 | 12   | 100              | 7     | 3        | 2     |
| PROT. #048         | 25mg   | 12 | 4    | 33               | 1     | 0        | 11    |
| PROT. #052         | 25mg   | 12 | 8    | 67               | 8     | 3        | 1     |
| PROT. #070         | 12.5mg | 24 | 12   | 50               | 7     | 11       | 6     |
| PROT. #070         | 25mg   | 24 | 12   | 50               | 9     | 10       | 5     |
| PROT. #076         | 25mg   | 16 | 9    | 56               | 13    | 1        | 2     |

**Table 2**

**Summary Statistics for Demographic Variables (Age, Height and Weight)  
Within Each Study**

| Study<br>(MK-0966) | Dose   | N  | Age (yrs) |     |     | Weight (lbs) |     |     | Height (in) |     |     |
|--------------------|--------|----|-----------|-----|-----|--------------|-----|-----|-------------|-----|-----|
|                    |        |    | Mean      | Min | Max | Mean         | Min | Max | Mean        | Min | Max |
| PROT. #037         | 50mg   | 11 | 36        | 20  | 46  | 164          | 139 | 202 | 68          | 57  | 72  |
| PROT. #043         | 50mg   | 12 | 36        | 20  | 45  | 188          | 142 | 230 | 70          | 64  | 74  |
| PROT. #048         | 25mg   | 12 | 29        | 20  | 44  | 152          | 113 | 174 | 67          | 62  | 71  |
| PROT. #052         | 25mg   | 12 | 72        | 66  | 81  | 159          | 123 | 228 | 67          | 62  | 73  |
| PROT. #070         | 12.5mg | 24 | 43        | 18  | 64  | 166          | 123 | 228 | 66          | 59  | 75  |
| PROT. #070         | 25mg   | 24 | 44        | 24  | 61  | 158          | 104 | 198 | 67          | 59  | 75  |
| PROT. #076         | 25mg   | 16 | 33        | 24  | 45  | 153          | 125 | 178 | 67          | 61  | 74  |