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## Appendix I

### Cumulative permeation amount of NFP from NFP transdermal patch

Cumulative permeation amount of NFP from NFP transdermal patch containing no surfactant (control formulation, F1)

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 4.55   | 3.07   | 1.46   | 3.03    |
| 2            | 9.56   | 5.06   | 4.45   | 6.36    |
| 4            | 16.50  | 5.74   | 6.51   | 9.58    |
| 7            | 19.63  | 5.49   | 6.48   | 10.53   |
| 10           | 31.86  | 5.33   | 10.49  | 15.89   |
| 13           | 66.28  | 15.92  | 23.15  | 35.12   |
| 16           | 117.14   | 38.86  | 46.16  | 67.39   |
| 20           | 134.07   | 67.09  | 78.03  | 93.06   |
| 24           | 220.49   | 110.79 | 96.05  | 142.44  |

Cumulative permeation amount of NFP from NFP transdermal patch containing 0.5% sodium lauryl sulfate (F2)

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 2.98   | 1.80   | 3.13   | 2.64    |
| 2            | 4.67   | 4.08   | 3.18   | 3.98    |
| 4            | 11.62  | 9.55   | 7.28   | 9.48    |
| 7            | 19.89  | 23.78  | 19.06  | 20.91   |
| 10           | 31.26  | 41.49  | 32.48  | 35.08   |
| 13           | 45.36  | 66.47  | 154.36 | 88.73   |
| 16           | 62.92  | 94.28  | 284.98 | 147.39  |
| 20           | 83.10  | 132.43 | 299.00 | 171.51  |
| 24           | 122.57   | 170.20 | 313.47 | 202.08  |
| 28           | 153.91   | 198.35 | 347.88 | 233.38  |

**Cumulative permeation amount of NFP from NFP transdermal patch containing 1.0% sodium lauryl sulfate (F3)**

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 0.00   | 0.00   | 3.15   | 1.05    |
| 2            | 0.00   | 0.00   | 6.89   | 2.30    |
| 4            | 0.11   | 0.54   | 13.23  | 4.63    |
| 7            | 0.46   | 0.02   | 18.25  | 6.24    |
| 10           | 4.22   | 1.85   | 25.81  | 10.63   |
| 13           | 12.64  | 10.34  | 44.34  | 22.44   |
| 16           | 42.83  | 52.23  | 66.05  | 53.70   |
| 20           | 75.68  | 108.81 | 108.28 | 97.59   |
| 24           | 141.54   | 232.34 | 170.15 | 181.34  |

**Cumulative permeation amount of NFP from NFP transdermal patch containing 2.0% sodium lauryl sulfate (F4)**

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 1.15   | 0.80   | 0.99   | 0.98    |
| 2            | 1.28   | 0.70   | 1.40   | 1.13    |
| 4            | 1.21   | 0.80   | 1.82   | 1.28    |
| 7            | 1.41   | 0.85   | 2.19   | 1.48    |
| 10           | 3.47   | 6.37   | 7.52   | 5.79    |
| 13           | 6.42   | 80.12  | 26.95  | 37.83   |
| 16           | 16.50  | 190.21 | 85.48  | 97.40   |
| 20           | 30.49  | 233.08 | 181.41 | 148.33  |
| 24           | 40.48  | 353.70 | 341.40 | 245.19  |

**Cumulative permeation amount of NFP from NFP transdermal patch containing 1.0% cetyltrimethylammonium bromide (F5)**

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 3.45   | 0.00   | 1.84   | 1.76    |
| 2            | 8.56   | 3.89   | 4.33   | 5.59    |
| 4            | 2.63   | 5.48   | 5.85   | 4.65    |
| 7            | 3.47   | 9.35   | 9.54   | 7.45    |
| 10           | 5.21   | 10.57  | 11.59  | 9.12    |
| 13           | 8.10   | 21.74  | 16.92  | 15.59   |
| 16           | 13.25  | 38.09  | 38.47  | 29.94   |
| 20           | 29.07  | 67.37  | 79.38  | 58.61   |
| 24           | 46.40  | 129.31 | 102.51 | 92.74   |

**Cumulative permeation amount of NFP from NFP transdermal patch containing 2.0% cetyltrimethylammonium bromide (F6)**

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |         |
|--------------|--|--------|---------|
|              | Cell A   | Cell B | Average |
| 0            | 0.00   | 0.00   | 0.00    |
| 1            | 3.93   | 5.34   | 4.64    |
| 2            | 3.49   | 9.13   | 6.31    |
| 4            | 6.59   | 16.13  | 11.36   |
| 7            | 8.65   | 29.29  | 18.97   |
| 10           | 21.00  | 65.24  | 43.12   |
| 13           | 45.59  | 106.88 | 76.24   |
| 16           | 94.37  | 171.15 | 132.76  |
| 20           | 177.11   | 264.80 | 220.96  |
| 24           | 324.88   | 355.77 | 340.33  |
| 28           | 394.23   | 342.26 | 368.25  |

**Cumulative permeation amount of NFP from NFP transdermal patch  
containing 1.0% Cetylpyridinium chloride (F7)**

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 2.43   | 3.05   | 2.17   | 2.55    |
| 2            | 4.65   | 3.98   | 3.15   | 3.93    |
| 4            | 7.09   | 6.09   | 4.44   | 5.87    |
| 7            | 11.56  | 8.94   | 7.57   | 9.36    |
| 10           | 10.75  | 21.34  | 15.62  | 15.90   |
| 13           | 46.70  | 38.67  | 30.78  | 38.72   |
| 16           | 48.84  | 72.79  | 58.11  | 59.91   |
| 20           | 102.27   | 80.13  | 55.97  | 79.46   |
| 24           | 126.40   | 186.64 | 128.96 | 147.33  |
| 28           | 237.64   | 216.07 | 190.36 | 214.69  |

**Cumulative permeation amount of NFP from NFP transdermal patch  
containing 2.0% Cetylpyridinium chloride (F8)**

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 0.35   | 1.46   | 0.39   | 0.73    |
| 2            | 1.94   | 2.73   | 1.00   | 1.89    |
| 4            | 4.48   | 7.24   | 5.20   | 5.64    |
| 7            | 10.30  | 13.78  | 12.72  | 12.27   |
| 10           | 17.84  | 20.27  | 23.26  | 20.46   |
| 13           | 32.07  | 28.43  | 38.17  | 32.89   |
| 16           | 48.26  | 54.18  | 59.58  | 54.01   |
| 20           | 81.50  | 88.94  | 96.66  | 89.03   |
| 24           | 114.16   | 113.19 | 128.98 | 118.78  |
| 28           | 147.95   | 166.89 | 170.49 | 161.78  |

**Cumulative permeation amount of NFP from NFP transdermal patch  
containing 1.0% Cremophor A25 (F9)**

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 0.48   | 0.00   | 0.82   | 0.43    |
| 2            | 0.98   | 1.38   | 1.01   | 1.12    |
| 4            | 1.29   | 5.16   | 3.00   | 3.15    |
| 7            | 5.95   | 11.93  | 9.81   | 9.23    |
| 10           | 17.44  | 20.74  | 17.79  | 18.66   |
| 13           | 30.66  | 29.76  | 27.74  | 29.39   |
| 16           | 34.79  | 44.14  | 29.25  | 36.06   |
| 20           | 127.54   | 70.88  | 100.46 | 99.63   |
| 24           | 153.63   | 87.30  | 130.40 | 123.78  |
| 28           | 216.35   | 213.59 | 194.93 | 208.29  |

**Cumulative permeation amount of NFP from NFP transdermal patch  
containing 2.0% Cremophor A25 (F10)**

| Time<br>(hr) | Permeation amount/surface area ( $\mu\text{g}/\text{cm}^2$ ) |        |        |         |
|--------------|--|--------|--------|---------|
|              | Cell A   | Cell B | Cell C | Average |
| 0            | 0.00   | 0.00   | 0.00   | 0.00    |
| 1            | 1.37   | 1.16   | 0.90   | 1.14    |
| 2            | 0.49   | 0.81   | 0.64   | 0.65    |
| 4            | 1.58   | 1.24   | 0.97   | 1.26    |
| 7            | 3.76   | 1.62   | 2.38   | 2.59    |
| 10           | 12.80  | 3.20   | 4.07   | 6.69    |
| 13           | 17.19  | 15.33  | 12.52  | 15.01   |
| 16           | 19.42  | 33.73  | 36.99  | 30.05   |
| 20           | 35.42  | 163.40 | 66.59  | 88.47   |
| 24           | 45.01  | 163.82 | 98.05  | 102.29  |
| 28           | 67.22  | 193.79 | 193.63 | 151.55  |

## Appendix II

### NFP concentration in rabbit plasma

**From single oral administration Adalat® 10 mg**

| Time<br>(hr) | NFP concentration in rabbit plasma (ng/ml) |        |         |        |        |
|--------------|--|--------|---------|--------|--------|
|              | No.1                                       | No.2   | No.3    | No.4   | No.5   |
| 0.5          | 11081.2                                    | 321.1  | 975.3   | 1290.5 | 347.4  |
| 1            | 10652.0                                    | 314.3  | 8030.2  | 6794.1 | 394.4  |
| 2            | 5416.2                                     | 502.7  | 10038.8 | 7721.1 | 667.2  |
| 4            | 2095.8                                     | 267.6  | 4844.2  | 9637.0 | 627.2  |
| 8            | 959.0                                      | 420.7  | 524.2   | 9111.7 | 1361.6 |
| 12           | 57.4                                       | 6599.1 | 187.3   | 842.4  | 4515.1 |
| 24           | 123.5                                      | 52.4   | 14.3    | 91.5   | 97.7   |

**From NFP transdermal patch administration**

| Time<br>(hr) | Plasma concentration/Dose (ng/ml) |       |       |        |        |
|--------------|-----------------------------------|-------|-------|--------|--------|
|              | No.1                              | No.2  | No.3  | No.4   | No.5   |
| 0            | 0.00                              | 0.00  | 0.00  | 0.00   | 0.00   |
| 1            | 5.41                              | 0.90  | 1.75  | 1.09   | 1.02   |
| 2            | 3.35                              | 1.87  | 1.44  | 1.61   | 1.80   |
| 4            | 1.65                              | 3.37  | 1.53  | 3.81   | 1.31   |
| 8            | 95.45                             | 47.16 | 85.46 | 212.60 | 218.32 |
| 12           | 79.78                             | 5.73  | 1.10  | 110.95 | 30.20  |
| 18           | 55.64                             | 11.20 | 1.76  | 47.51  | 13.16  |
| 24           | 9.06                              | 7.88  | 1.93  | 13.72  | 8.75   |

## VITAE

Miss Monthip Adunyanon was born on September 3, 1967.  
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