**Supplementary Table 3: Effect of fasting and food on the Day 8 PK parameters in Part 2.**

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| --- | --- | --- | --- |
| **Amino acid** | **PK parameter** | **AXA1665 14.7 g TID** | **AXA1665 4.9 g TID** |
| **Fasted** | **Fed** | **Fed/fasted** | **Fasted** | **Fed** | **Fed/fasted** |
| **n** | **GM** | **n** | **GM** | **GM ratio(90% CI)** | **n** | **GM** | **n** | **GM** | **GM ratio(90% CI)** |
| Leucine | AUC (μM\*h) | 9 | 1210 | 9 | 1210 | 1.00 (0.95, 1.05) | 7 | 683 | 7 | 784 | 1.15 (0.94, 1.40) |
| AUCcontrol corrected (μM\*h) | 9 | 667 | 9 | 497 | 0.75 (0.65, 0.85) | 7 | 49.2 | 7 | 29.2 | 0.59 (0.03, 11.08) |
| Cmax (μM) | 9 | 609 | 9 | 421 | 0.69 (0.61, 0.78) | 7 | 252 | 7 | 242 | 0.96 (0.79, 1.17) |
| Isoleucine | AUC (μM\*h) | 9 | 539 | 9 | 573 | 1.06 (1.01, 1.13) | 7 | 340 | 7 | 424 | 1.25 (0.96, 1.62) |
| AUCcontrol corrected (μM\*h) | 9 | 243 | 9 | 129 | 0.53 (0.34, 0.84) | 6 | 43.0 | 7 | 26.6 | 0.70 (0.07, 6.80) |
| Cmax (μM) | 9 | 269 | 9 | 205 | 0.76 (0.64, 0.90) | 7 | 133 | 7 | 135 | 1.01 (0.80, 1.27) |
| Valine | AUC (μM\*h) | 9 | 2530 | 9 | 2640 | 1.05 (1.00, 1.09) | 7 | 1460 | 7 | 1580 | 1.08 (0.95, 1.23) |
| AUCcontrol corrected (μM\*h) | 9 | 1570 | 9 | 1480 | 0.95 (0.88, 1.02) | 7 | 450 | 7 | 451 | 1.00 (0.72, 1.40) |
| Cmax (μM) | 9 | 931 | 9 | 863 | 0.93 (0.83, 1.03) | 7 | 489 | 7 | 481 | 0.98 (0.89, 1.08) |
| Histidine | AUC (μM\*h) | 9 | 418 | 9 | 430 | 1.03 (1.00, 1.06) | 7 | 311 | 7 | 347 | 1.12 (1.01, 1.24) |
| AUCcontrol corrected (μM\*h) | 9 | 62.0 | 9 | 37.6 | 0.61 (0.35, 1.05) | 4 | 18.7 | 4 | 42.5 | 1.14 (0.78, 1.66) |
| Cmax (μM) | 9 | 150 | 9 | 142 | 0.95 (0.85, 1.06) | 7 | 96.1 | 7 | 104 | 1.08 (0.93, 1.26) |
| Lysine | AUC (μM\*h) | 9 | 1040 | 9 | 1100 | 1.05 (1.03, 1.08) | 7 | 907 | 7 | 1030 | 1.14 (0.96, 1.35) |
| AUCcontrol corrected (μM\*h) | 9 | 252 | 6 | 148 | 0.54 (0.28, 1.04) | 5 | 97.0 | 5 | 60.1 | 0.69 (0.07, 6.55) |
| Cmax (μM) | 9 | 362 | 9 | 343 | 0.95 (0.84, 1.07) | 7 | 286 | 7 | 305 | 1.07 (0.90, 1.27) |
| Threonine | AUC (μM\*h) | 9 | 565 | 9 | 543 | 0.96 (0.92, 1.00) | 7 | 564 | 7 | 587 | 1.04 (0.90, 1.20) |
| AUCcontrol corrected (μM\*h) | 8 | 118 | 5 | 121 | 0.71 (0.48, 1.05) | 7 | 94.9 | 6 | 125 | 1.14 (0.59, 2.20) |
| Cmax (μM) | 9 | 186 | 9 | 168 | 0.90 (0.84, 0.97) | 7 | 171 | 7 | 172 | 1.00 (0.89, 1.13) |
| Ornithine | AUC (μM\*h) | 9 | 655 | 9 | 629 | 0.96 (0.91, 1.01) | 7 | 432 | 7 | 430 | 1.00 (0.90, 1.11) |
| AUCcontrol corrected (μM\*h) | 9 | 398 | 9 | 329 | 0.83 (0.73, 0.93) | 7 | 133 | 7 | 98.4 | 0.74 (0.59, 0.92) |
| Cmax (μM) | 9 | 319 | 9 | 252 | 0.79 (0.69, 0.90) | 7 | 163 | 7 | 132 | 0.81 (0.65, 1.00) |
| Aspartate | AUC (μM\*h) | 9 | 22.2 | 9 | 19.6 | 0.88 (0.76, 1.03) | 7 | 13.5 | 7 | 16.2 | 1.20 (0.96, 1.52) |
| AUCcontrol corrected (μM\*h) | 9 | 5.26 | 4 | 2.47 | 0.25 (0.21, 0.29) | 4 | 3.42 | 5 | 2.75 | 0.75 (0.42, 1.33) |
| Cmax (μM) | 9 | 12.0 | 9 | 7.56 | 0.63 (0.43, 0.91) | 7 | 4.89 | 7 | 5.23 | 1.07 (0.77, 1.49) |
| Note: Only subjects with both fasted and fed data were included in the calculation of GM ratio and 90% CI.AUCcontrol corrected (fasted)=AUC0–4 h (AXA1665) – AUC0–4 h (control).AUCcontrol corrected (fed)=AUC5–9 h (AXA1665) – AUC5–9 h (control).AUC, area under the plasma concentration-time curve; AUCcontrol corrected, AUC corrected for control; Cmax, peak plasma concentration; CI, confidence interval; GM, geometric mean; TID, 3 times a day.  |