Supplemental Information

Bioequivalence of long-chain omega-3 polyunsaturated fatty acids from foods enriched with a novel vegetable-based omega-3 delivery system compared to gel capsules – a randomized controlled cross-over acute trial

Welma Stonehouse¹, Bradley Klingner¹, Rachel Tso², Pey Sze Teo², Netsanet Shiferaw Terefe³, Ciarán G. Forde²-⁴†

¹Commonwealth Scientific Industrial Research Organisation (CSIRO), Health and Biosecurity, Adelaide, South Australia, Australia

²Clinical Nutrition Research Centre, A*STAR Singapore Institute of Food and Biotechnology Innovation, Singapore

³Commonwealth Scientific Industrial Research Organisation (CSIRO), Agriculture and Food, Werribee, Victoria, Australia

⁴Department of Physiology, Yong Loo Lin School of Medicine, National University of Singapore, Singapore

†Current address: Wageningen University, Sensory Science and Eating Behaviour, Division of Human Nutrition and Health, Wageningen, The Netherlands.
Supplemental Table 1. Descriptive statistics for plasma DHA, EPA and DHA + EPA iAUC₀⁻²₄h, Cmax and Tmax for the total group and stratified for ethnic groups

| Variable                                      | Total group (n=27) | Soup | Extruded rice snack | Gel capsule |
|-----------------------------------------------|--------------------|------|---------------------|-------------|
| DHA iAUC₀⁻²₄h (µg/mL·hour)                   | Mean (SD)          | 8069 | 7367                | 9864        |
|                                               | Median (25, 75 Percentile) | 8568 | 10999               | 7969        |
| DHA Cmax (µg/mL)                              | Mean (SD)          | 52.5 | 51.1                | 55.6        |
|                                               | Median (25, 75 Percentile) | 45.7 | 30.3                | 42.9        |
| DHA Tmax (hour)                               | Mean (SD)          | 7.19 | 5.56                | 7.41        |
|                                               | Median (25, 75 Percentile) | 4.00 | 2.00                | 6.00        |
| EPA iAUC₀⁻²₄h (µg/mL·hour)                   | Mean (SD)          | 1192 | 1241               | 1331        |
|                                               | Median (25, 75 Percentile) | 982  | 1446               | 976         |
| EPA Cmax (µg/mL)                              | Mean (SD)          | 18.2 | 18.7                | 18.7        |
|                                               | Median (25, 75 Percentile) | 14.6 | 32.2                | 8.16        |
| EPA Tmax (hour)                               | Mean (SD)          | 6.15 | 8.96                | 8.67        |
|                                               | Median (25, 75 Percentile) | 6.00 | 8.00                | 6.00        |
| DHA + EPA iAUC₀⁻²₄h (µg/mL·hour)              | Mean (SD)          | 8872 | 8396                | 11054       |
|                                               | Median (25, 75 Percentile) | 7627 | 2902               | 9059        |
| DHA + EPA Cmax (µg/mL)                        | Mean (SD)          | 70.2 | 69.4                | 73.9        |
|                                               | Median (25, 75 Percentile) | 59.2 | 34.1                | 50.9        |
| DHA + EPA Tmax (hour)                         | Mean (SD)          | 6.81 | 6.89                | 7.26        |
|                                               | Median (25, 75 Percentile) | 4.00 | 2.00                | 6.00        |
| Australian Europeans (n=12)                   |                    |      |                     |             |
| DHA iAUC₀⁻²₄h (µg/mL·hour)                   | Mean (SD)          | 10158| 9310                | 10590       |
|                                               | Median (25, 75 Percentile) | 10144| 9310                | 10590       |
| DHA Cmax (µg/mL)                              | Mean (SD)          | 74.0 | 74.1                | 81.0        |
|                                               | Median (25, 75 Percentile) | 74.6 | 54.8                | 81.7        |
| DHA Tmax (hour)                               | Mean (SD)          | 4.50 | 3.83                | 7.17        |
|                                               | Median (25, 75 Percentile) | 4.00 | 2.00                | 6.00        |
| EPA iAUC₀⁻²₄h (µg/mL·hour)                   | Mean (SD)          | 1642 | 2112               | 1943        |
|                                               | Median (25, 75 Percentile) | 1204 | 2949               | 1127        |
| EPA Cmax (µg/mL)                              | Mean (SD)          | 29.9 | 34.3                | 34.2        |
|                                               | Median (25, 75 Percentile) | 28.4 | 33.6                | 31.3        |
| EPA Tmax (hour)                               | Mean (SD)          | 5.00 | 9.67                | 5.83        |
|                                               | Median (25, 75 Percentile) | 6.00 | 8.00                | 6.00        |
| Singaporean Chinese (n=15)                    |                    |      |                     |             |
| DHA iAUC₀⁻²₄h (µg/mL·hour)                   | Mean (SD)          | 6397 | 4951                | 6468        |
|                                               | Median (25, 75 Percentile) | 5169 | 4987                | 7740        |
| DHA Cmax (µg/mL)                              | Mean (SD)          | 35.4 | 32.6                | 35.2        |
|                                               | Median (25, 75 Percentile) | 36.8 | 31.2                | 38.7        |
| DHA Tmax (hour)                               | Mean (SD)          | 9.33 | 6.93                | 7.60        |
|                                               | Median (25, 75 Percentile) | 4.00 | 2.00                | 6.00        |
|                                | Mean (SD) | Median (25, 75 Percentile) |
|--------------------------------|-----------|----------------------------|
| **EPA iAUC_{0-24h} (µg/mL*hour)** | 832 668 545 773 841 610 | 982 19 1339 278 37 632 976 75 1301 |
| **EPA Cmax (µg/mL)**           | 8.73 5.69 6.26 2.68 6.26 2.97 | 7.28 5.48 10.9 6.67 4.17 7.83 6.16 4.06 7.44 |
| **EPA Tmax (hour)**            | 7.07 7.48 8.40 8.42 10.93 9.82 | 6.00 2.00 8.00 6.00 2.00 8.00 6.00 2.00 24.00 |
| **DHA + EPA iAUC_{0-24h} (µg/mL*hour)** | 7006 4422 5415 3859 7271 4689 | 5667 4400 10628 4864 2063 8310 9027 3002 10021 |
| **DHA + EPA Cmax (µg/mL)**     | 44.0 14.1 38.8 9.51 41.3 9.63 | 43.0 32.9 53.0 35.0 33.0 47.0 44.1 32.5 47.9 |
| **DHA + EPA Tmax (hour)**      | 8.27 8.45 9.33 9.40 7.20 7.08 | 4.00 4.00 8.00 6.00 2.00 24.00 6.00 4.00 6.00 |

DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; iAUC_{0-24h}; incremental area under the curve over 24 hours; Cmax, maximal concentration; Tmax, time to maximal concentration

Descriptive statistics were calculated from raw data.
## Supplemental Table 2. Descriptive statistics for plasma fatty acid concentrations over 24 hours for the total group and stratified for ethnic groups

| Variable          | Time (hrs) | Total Group | Australian European | Singaporean Chinese |
|-------------------|------------|-------------|---------------------|---------------------|
|                   |            | Soup        | Extruded rice snack | Gel capsule         | Soup        | Extruded rice snack | Gel capsule | Soup        | Extruded rice snack | Gel capsule |
| DHA (ug/mL)       | 0          | 41.1        | 21.3                | 40.6                | 21.6                | 41.3        | 22.5                | 59.5        | 17.8                | 59.0        | 18.9                | 61.4        | 18.0                | 26.4        | 8.22                | 25.8        | 7.66                | 25.3        | 8.01                |
|                   | 2          | 46.5        | 21.5                | 45.6                | 23.7                | 42.9        | 21.5                | 66.2        | 15.8                | 66.8        | 19.5                | 62.6        | 16.3                | 30.6        | 7.70                | 28.6        | 7.11                | 27.2        | 7.44                |
|                   | 4          | 48.8        | 23.7                | 47.7                | 26.1                | 48.4        | 24.5                | 69.4        | 20.0                | 70.7        | 22.4                | 71.6        | 17.4                | 32.4        | 8.60                | 29.4        | 7.21                | 29.9        | 6.92                |
|                   | 6          | 47.0        | 25.4                | 47.9                | 24.8                | 53.3        | 28.4                | 68.7        | 22.8                | 69.6        | 21.9                | 79.2        | 22.8                | 29.7        | 8.07                | 30.4        | 5.74                | 32.5        | 6.81                |
|                   | 8          | 46.9        | 24.0                | 45.3                | 23.1                | 49.1        | 27.4                | 67.2        | 20.8                | 66.6        | 17.9                | 74.8        | 20.7                | 30.6        | 9.43                | 28.4        | 6.57                | 28.6        | 6.62                |
|                   | 24         | 44.9        | 21.0                | 44.7                | 22.1                | 46.6        | 24.6                | 62.7        | 18.5                | 64.3        | 17.9                | 68.1        | 21.0                | 30.7        | 7.62                | 29.0        | 7.65                | 29.5        | 8.38                |
| EPA (ug/mL)       | 0          | 16.3        | 12.4                | 16.9                | 14.1                | 16.7        | 14.7                | 27.6        | 9.01                | 31.2        | 8.00                | 31.3        | 9.23                | 7.30        | 4.89                | 5.54        | 2.63                | 5.06        | 2.57                |
|                   | 2          | 16.3        | 12.0                | 17.5                | 14.8                | 17.0        | 15.0                | 27.4        | 8.39                | 32.4        | 8.34                | 32.0        | 9.35                | 7.43        | 4.45                | 5.55        | 2.54                | 5.08        | 2.33                |
|                   | 4          | 16.6        | 11.9                | 17.4                | 14.7                | 17.5        | 15.5                | 27.7        | 8.46                | 32.1        | 9.05                | 32.9        | 9.99                | 7.70        | 4.33                | 5.67        | 2.60                | 5.22        | 2.38                |
|                   | 6          | 16.6        | 12.7                | 17.4                | 14.5                | 17.9        | 15.5                | 28.4        | 9.19                | 31.9        | 8.76                | 33.2        | 10.0                | 7.16        | 4.00                | 5.74        | 2.39                | 5.69        | 2.40                |
|                   | 8          | 17.0        | 12.5                | 17.9                | 14.9                | 17.9        | 15.7                | 28.3        | 8.98                | 33.1        | 8.19                | 33.3        | 10.2                | 8.04        | 5.73                | 5.80        | 2.67                | 5.47        | 2.35                |
|                   | 24         | 15.9        | 11.8                | 17.3                | 14.3                | 17.0        | 14.4                | 26.9        | 8.88                | 31.7        | 8.14                | 31.2        | 9.03                | 7.15        | 3.49                | 5.73        | 2.72                | 5.58        | 3.02                |
| DHA + EPA (ug/mL) | 0          | 57.4        | 32.3                | 57.5                | 34.2                | 58.1        | 36.0                | 87.1        | 23.2                | 90.2        | 23.4                | 92.7        | 24.3                | 33.7        | 12.3                | 31.4        | 9.86                | 30.4        | 9.96                |
|                   | 2          | 62.8        | 32.0                | 63.1                | 37.2                | 60.0        | 35.4                | 93.7        | 19.8                | 99.2        | 24.6                | 94.6        | 22.3                | 38.1        | 11.0                | 34.2        | 9.07                | 32.3        | 9.15                |
|                   | 4          | 65.4        | 34.3                | 65.2                | 39.7                | 65.9        | 39.1                | 97.1        | 25.3                | 103.2       | 28.7                | 104.5       | 24.4                | 40.1        | 11.6                | 35.0        | 9.33                | 35.1        | 8.48                |
|                   | 6          | 63.6        | 36.8                | 65.2                | 38.3                | 71.2        | 42.9                | 97.1        | 29.1                | 101.8       | 28.5                | 112.4       | 30.3                | 36.8        | 11.0                | 36.2        | 7.46                | 38.2        | 8.23                |
|                   | 8          | 63.9        | 35.1                | 63.3                | 36.8                | 67.0        | 42.2                | 95.5        | 26.2                | 99.7        | 22.4                | 108.1       | 28.4                | 38.6        | 14.5                | 34.2        | 8.85                | 34.1        | 8.42                |
|                   | 24         | 60.9        | 31.7                | 62.0                | 35.2                | 63.6        | 37.9                | 89.6        | 24.6                | 96.0        | 23.0                | 99.3        | 27.2                | 37.8        | 10.5                | 34.8        | 10.0                | 35.0        | 10.9                |
Supplemental Figure 1. Box plots of DHA + EPA iAUC<sub>0-24h</sub> by treatment.
DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; iAUC<sub>0-24h</sub>; incremental area under the curve over 24 hours.
#Outlier (1.5-3 box lengths); *Extreme outlier (>3 box lengths); A4, A7, Australian European participants number 4 and 7.

Supplemental Figure 2. Individual participant’s incremental area under the curve (iAUC<sub>0-24hr</sub>) for plasma DHA + EPA (C) by treatment.
DHA, docosahexaenoic acid; EPA, eicosapentaenoic acid; iAUC<sub>0-24h</sub>; incremental area under the curve over 24 hours.
Participants numbered A1-12 = Australian European; S1=17 = Singaporean Chinese