

Supplementary materials:

Table S1. Molecular weight distribution in HWP-F

| Molecular weight range, Da | HWP-F, % |
|----------------------------|----------|
| <180 | 3.69 |
| 180~500 | 5.55 |
| 500~1,000 | 3.85 |
| 1,000~2,000 | 6.49 |
| 2,000~3,000 | 4.03 |
| 3,000~5,000 | 3.84 |
| 5,000~10,000 | 5.46 |
| >10,000 | 67.09 |

HWP-F, Infant formula containing hydrolyzed whey protein.

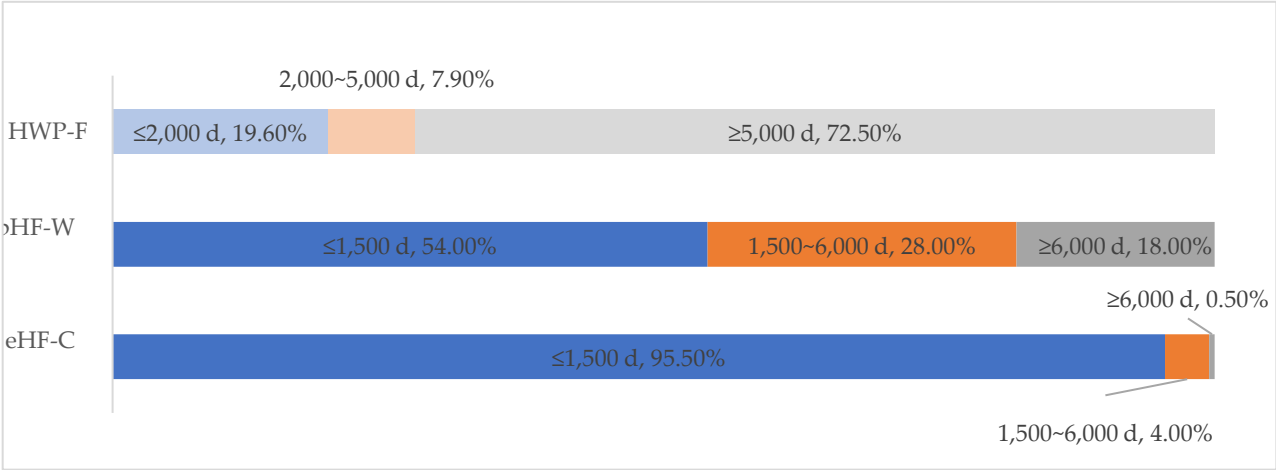


Figure S1. Comparison of Molecular weight distribution between HWP-F and commercial pHF-W and eHF-C. HWP-F, Infant formula containing hydrolyzed whey protein. pHF-W and eHF-C are well-established products [1].

Table S2. Weight, length, head circumference, and BMI and their z-scores at baseline, and 7 and 13 weeks of age of breast-, IWP-F-, and HWP-F-fed term infants (Per protocol analyzed).

| | Baseline | | | p^3 | 7wk | | | p^3 | 13wk | | | p^3 | p^4 |
|------------------------------------|------------|------------|------------|-------|-----------|------------|------------|-------|------------|------------|------------|-------|-------|
| | BF | IWP-F | HWP-F | | BF | IWP-F | HWP-F | | BF | IWP-F | HWP-F | | |
| Absolute values ¹ | | | | | | | | | | | | | |
| Weight, kg | 3.6±0.5 | 3.5±0.4 | 3.6±0.5 | 0.707 | 5.3±0.5 | 5.3±0.6 | 5.2±0.7 | 0.763 | 6.5±0.7 | 6.5±0.6 | 6.5±0.8 | 0.926 | 0.475 |
| Crown-heel Length, cm | 51.3±2.1 | 51.3±2.0 | 51.7±2.4 | 0.505 | 57.4±2.1 | 57.5±2.2 | 57.6±2.4 | 0.894 | 61.5±2.1 | 61.7±2.2 | 61.6±2.8 | 0.853 | 0.591 |
| Head circumference, cm | 34.9±1.4 | 34.8±1.2 | 35.1±1.3 | 0.604 | 38.1±1.2 | 37.7±1.1 | 38.1±1.3 | 0.096 | 39.9±1.1 | 39.8±1.1 | 39.9±1.2 | 0.914 | 0.234 |
| BMI, kg/m ² | 13.5±1.4 | 13.4±1.2 | 13.4±1.4 | 0.907 | 16.1±1.3 | 15.9±1.2 | 15.7±1.6 | 0.371 | 17.2±1.5 | 17.0±1.5 | 17.1±1.6 | 0.889 | 0.699 |
| z-scores ^{1,2} | | | | | | | | | | | | | |
| Weight-for age z-score | 0.20±0.89 | 0.20±0.76 | 0.28±0.97 | 0.836 | 0.40±0.68 | 0.42±0.81 | 0.16±1.05 | 0.205 | 0.49±0.73 | 0.48±0.74 | 0.35±0.93 | 0.547 | 0.310 |
| Length-for-age z-score | 0.31±1.11 | 0.36±1.10 | 0.52±1.25 | 0.562 | 0.42±0.98 | 0.57±1.04 | 0.45±1.07 | 0.720 | 0.46±0.96 | 0.54±1.08 | 0.34±1.23 | 0.627 | 0.246 |
| Weight-for-length z-score | -0.35±1.20 | -0.40±1.15 | -0.42±1.20 | 0.951 | 0.15±1.08 | -0.00±1.07 | -0.07±1.08 | 0.546 | 0.28±1.03 | 0.22±1.02 | 0.22±1.26 | 0.940 | 0.832 |
| Head circumference-for-age z-score | 0.07±1.13 | -0.00±1.00 | 0.15±1.06 | 0.738 | 0.00±0.98 | -0.29±0.97 | -0.13±1.13 | 0.321 | -0.08±0.88 | -0.15±0.92 | -0.27±0.98 | 0.542 | 0.276 |
| BMI-for-age z-score | 0.03±1.02 | -0.02±0.88 | -0.02±1.07 | 0.953 | 0.23±0.88 | 0.15±0.90 | 0.02±0.96 | 0.464 | 0.33±0.96 | 0.26±0.93 | 0.22±1.13 | 0.840 | 0.941 |

BF, breast-fed; IWP-F, Infant formula containing intact whey protein; HWP-F, Infant formula containing hydrolyzed whey protein; BMI, body mass index; SD, standard deviation; IQR, interquartile range. ¹ Values are means ± SDs. ² z-scores were calculated by using the World Health Organisation (WHO) growth standards. ³ The p values were derived from one-way analysis of variance (ANOVA) model tests for the difference between the three groups. ⁴ The p values represent the time × treatment interactions, derived from repeated measures ANOVAs.

Table S3. Gains in weight, length, and head circumference of study infants (Per protocol analyzed).

| | Group | | | <i>p</i> ² | <i>p</i> ³ |
|---|-----------|-----------|-----------|-----------------------|-----------------------|
| | BF | IWP-F | HWP-F | | |
| Weight, g/day ¹ | | | | | |
| Baseline – 7 wk | 40.0±10.2 | 41.6±11.8 | 37.6±14.7 | 0.215 | 0.085 |
| Baseline – 13 wk | 34.4±6.5 | 35.1±7.3 | 34.1±8.6 | 0.787 | 0.465 |
| Crown-heel Length, cm/day ¹ | | | | | |
| Baseline – 7 wk | 0.14±0.05 | 0.15±0.05 | 0.13±0.05 | 0.137 | 0.157 |
| Baseline – 13 wk | 0.12±0.02 | 0.12±0.03 | 0.12±0.03 | 0.287 | 0.337 |
| Head circumference, cm/day ¹ | | | | | |
| Baseline – 7 wk | 0.08±0.03 | 0.07±0.03 | 0.07±0.03 | 0.291 | 0.224 |
| Baseline – 13 wk | 0.06±0.01 | 0.06±0.02 | 0.06±0.02 | 0.629 | 0.576 |

BF, breast-fed; IWP-F, Infant formula containing intact whey protein; HWP-F, Infant formula containing hydrolyzed whey protein; ¹ Values are means ± SDs; ² The p values were derived from one-way analyses of variance; ³ The p values were derived from covariance analyses, adjusting for infant birth weight, gender, recruited center and growth indices at baseline.

Table S4. Feeding tolerance of study infants (Per protocol analyzed).

| | Group | | | p^2 |
|--|---------|----------------------|----------------------|-------|
| | BF | IWP-F | HWP-F | |
| Number of daily feeding ¹ | | | | |
| 2wk | 9.7±1.9 | 8.7±1.8 ³ | 8.6±1.8 ³ | 0.002 |
| 7wk | 9.4±1.8 | 8.4±1.8 ³ | 8.4±1.6 ³ | 0.002 |
| 13wk | 8.8±1.8 | 7.7±1.7 ³ | 7.8±1.7 ³ | 0.002 |
| Volume of formula intake, mL/kg/day ¹ | | | | |
| 2wk | N/A | 127.9±49.2 | 134.7±53.4 | 0.470 |
| 7wk | N/A | 126.7±39.1 | 153.9±52.6 | 0.002 |
| 13wk | N/A | 116.4±35.6 | 141.3±39.9 | 0.001 |
| Number of daily crying ¹ | | | | |
| 2wk | 1.3±2.2 | 1.2±2.1 | 1.1±1.7 | 0.950 |
| 7wk | 0.9±1.9 | 1.3±2.2 | 1.0±1.8 | 0.441 |
| 13wk | 0.4±1.2 | 0.8±1.9 | 0.7±1.5 | 0.385 |

BF, breastfeeding; IWP-F, Infant formula containing intact whey protein; HWP-F, Infant formula containing hydrolyzed whey protein; N/A, not available; ¹ Values are expressed as means ± SDs; ² *p* values were derived from ANOVAs for normally-distributed data, and chi-square tests or Fisher's exact tests for categorical data; ³ Pairwise comparison was done using the Bonferroni test, a significantly difference from the BF group was indicated by *p* < 0.05.

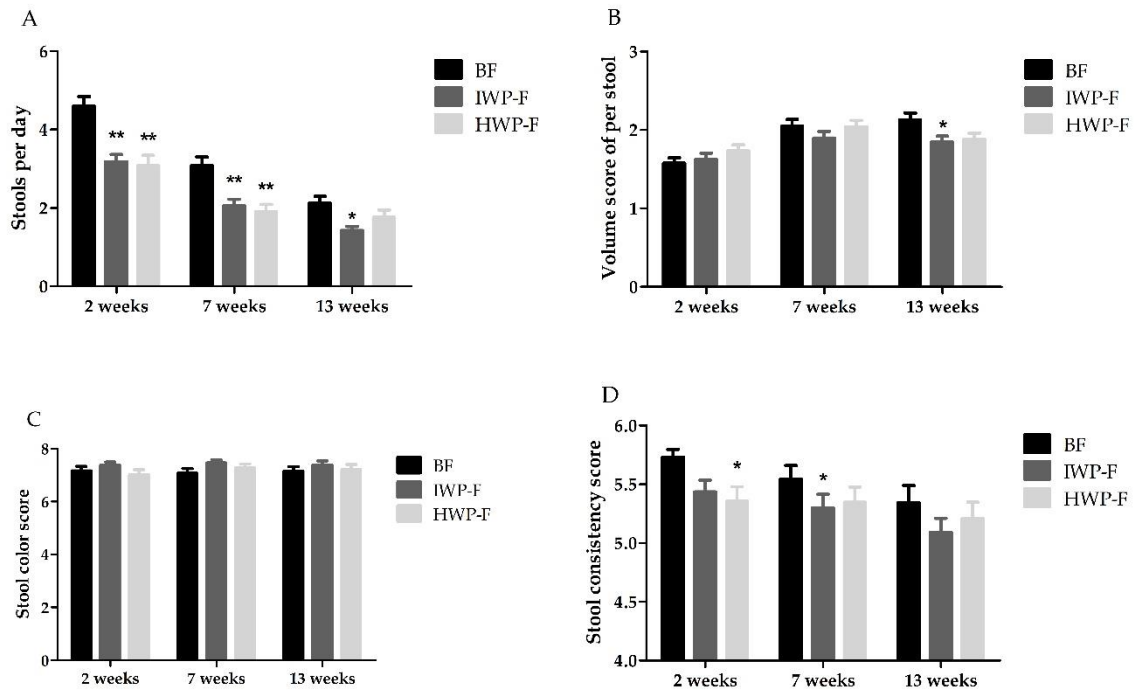


Figure S2. Stool characteristics (shown as mean and standard error) at 2, 7 and 13 weeks of age in breast-, IWP-F-, and HWP-F-fed term infants. (A) Stool frequency, indicated as stools per day. (B) Volume score per stool, expressed as stool diameter: 1 ≤ 7.5 cm; 2 > 7.5 cm and < 13.0 cm; 3 ≥ 13.0 cm. (C) Stool color score, calculated using the Infants Stool Color Chart, 1 indicates the most abnormal stool score, and 9 is the most normal. (D) Stool consistency score, rated based on the simplified Bristol Stool Form Chart, 1 = hard lumps, 2 = sausage-shaped but lumpy, 3 = formed but with cracks, 4 = smooth and soft, 5 = soft blobs with clear-cut edges, 6 = mushy. Thus, the range of possible scores is 0–6; a higher score is closer to a softer stool. Significant differences compared with the BF group are indicated as follows: **: $p < 0.001$; *: $p < 0.05$. HWP-F, Infant formula containing hydrolyzed whey protein; IWP-F, Infant formula containing intact whey protein; BF, breast-fed.

References:

1. Von Berg A.; Koletzko S.; Grubl A.; Filipiak-Pittroff B.; Wichmann H.E.; Bauer C.P.; Reinhardt D.; Berdel D. The effect of hydrolyzed cow's milk formula for allergy prevention in the first year of life: the German Infant Nutritional Intervention Study, a randomized double-blind trial. *J. Allergy Clin. Immunol.* **2003**, *111*, 533-540. [\[CrossRef\]](#) [\[PubMed\]](#)