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## Pfizer Australia

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Food Standards Australia New Zealand  
PO Box 7186  
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Australia

By Email: [submissions@foodstandards.gov.au](mailto:submissions@foodstandards.gov.au)

Dear Standard Management Officer,

### **Re: Minimum L-histidine in Infant Formula Products (A1074)**

Pfizer Nutrition welcomes the opportunity to comment on the proposal to reduce the minimum required level of L-histidine in infant formula products within the Food Standards Code from 12mg/100kJ to 10mg/100kJ.

Pfizer Nutrition supports breastfeeding and acknowledges that breast milk is the normal and ideal method of infant feeding. When an infant is not breastfed, for a variety of medical, practical or personal reasons, the only suitable and safe alternative is an infant formula product.

Pfizer Nutrition supports the alignment of the essential compositional requirement of infant formula (0-6 months) in Standard 2.9.1 with the Codex infant formula standard (*CODEX STAN 72 – 1981, Revision 2007*) as the Codex standard represents some of the most recent science on infant formula composition. Compositional differences between Codex and Standard 2.9.1 currently exist, resulting in international trade barriers.

In addition to acting as a trade barrier, these minimum amino acid levels may restrict the provision of lower protein formulas in Australia & New Zealand, or result in unnecessary amino acid fortification when increasing evidence has linked high protein intake in infancy with potential long-term negative health consequences. A large randomised controlled trial has recently demonstrated that an infant formula containing 1.25 g / 100 mL (N x 6.25) of protein provides a more favourable effect on body weight and BMI at 2 years of age than a higher protein formula, with no detrimental consequences on anthropometric measurements (Koletzko, 2009).

Other research with a formula containing 1.28 g / 100mL protein (N x 6.25), of which the histidine quantity was 10.77mg/100kJ, demonstrated acceptable growth outcomes. Table 1 demonstrates the macronutrient composition between the study and experimental formula.

Table 1 Macronutrient composition of study formulas<sup>a</sup>

	SF	EF	Recommendations <sup>b</sup>			
			Codex alimentarius		EU commission	
			Min	Max	Min	Max
Energy, kcal/l	672	666	600	700	600	700
Protein: energy ratio, g protein per 100 kcal	2.1	1.9	1.8	3.0	1.8	3.0
Protein, g/l	14.1	12.8	See above		See above	
Histidine, mg/100 kcal	51	45	40		41	
Isoleucine	113	103	90		92	
Leucine	205	186	166		169	
Lysine	182	170	113		114	
Threonine	122	110	77		77	
Tryptophan	36	37	32		33	
Methionine + cysteine <sup>c</sup>	84	76	61		62	
Tyrosine + phenylalanine <sup>d</sup>	176	170	159		156	
$\alpha$ -Lactalbumin, g/l	2.2	2.3	No recommendations		No recommendations	
Whey:casein	60:40	66:34	No recommendations		No recommendations	
Carbohydrate, g/100 kcal	10.8	10.8	9.0	14.0	9.0	14.0
Fat, g/100 kcal	5.4	5.4	4.4	6.0	4.4	6.0

Abbreviations: EF, experimental formula; EU, European union; Min, minimum; Max, maximum; SF, standard formula.

<sup>a</sup>Nutrient composition analyzed by Covance Laboratories, Madison, WI, USA; total protein calculated as total nitrogen  $\times$  6.25.

<sup>b</sup>Codex and EU recommendations for infant formula composition are based on a compilation of published literature values on human milk composition.

<sup>c</sup>The concentration of methionine and cystine/cysteine may be added together if the ratio between methionine and cystine is not greater than 2.

<sup>d</sup>The concentration of tyrosine and phenylalanine may be added together if the ratio between tyrosine:phenylalanine is not greater than 2.

Table 2 shows as a result of this study essential amino acid levels that were generally similar and within one standard deviation of the human milk reference group (Trabulsi, 2011). This formula was already supplemented with small amounts of L-tyrosine and L-tryptophan for regulatory reasons, which would appear unnecessary from a safety perspective.

Table 2 – Mean plasma essential Amino Acids concentrations by feeding group

	SF (n = 108)	EF (n = 103)	HM (n = 110)
Cystine, $\mu$ mol/l	13.67 (7.24)	13.80 (6.27)	12.47 (5.73)
Histidine	85.36 (12.02) <sup>b</sup>	84.45 (12.89)	81.86 (9.61)
Isoleucine	60.80 (2.64) <sup>b,c</sup>	58.66 (13.86) <sup>d</sup>	53.45 (12.52)
Leucine	105.24 (19.37)	101.59 (21.77)	104.23 (20.72)
Lysine	193.74 (33.74) <sup>b,c</sup>	192.52 (39.71) <sup>d,e</sup>	169.93 (35.08)
Methionine	33.73 (7.77) <sup>b,c</sup>	33.49 (6.76) <sup>d,e</sup>	29.99 (5.86)
Phenylalanine	54.47 (8.06) <sup>b,c</sup>	52.83 (8.99) <sup>d,e</sup>	48.57 (9.65)
Threonine	182.11 (44.02) <sup>b,c</sup>	183.65 (40.84) <sup>d,e</sup>	132.50 (29.42)
Tryptophan	62.79 (13.13)	64.78 (11.78) <sup>d</sup>	60.89 (11.73)
Tyrosine	79.86 (15.87)	88.31 (21.48) <sup>d,e</sup>	77.95 (15.11)
Valine	166.17 (27.44) <sup>b,c</sup>	154.26 (29.52) <sup>d</sup>	143.75 (31.93)

Abbreviations: HM, human milk; EF, experimental formula; SF, standard formula; values presented are means (s.d.).

<sup>a</sup>Efficacy analyzable population.

<sup>b</sup>Significant difference between SF vs HM,  $P < 0.05$  ( $P$ -value based on two-sample  $t$ -test).

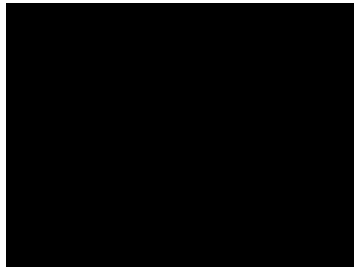
<sup>c</sup>Significant difference between SF vs HM adjusted for multiplicity,  $P < 0.0015$  ( $P$ -value based on two-sample  $t$ -test).

<sup>d</sup>Significant difference between EF vs HM,  $P < 0.05$  ( $P$ -value based on two-sample  $t$ -test).

<sup>e</sup>Significant difference between EF vs HM adjusted for multiplicity,  $P < 0.0015$  ( $P$ -value based on two-sample  $t$ -test).

In summary Pfizer Nutrition support the proposal to reduce the minimum required level of L-histidine to 10mg/100kJ in infant formula products and further a re-evaluation of amino acid requirements in the upcoming review of Standard 2.9.1.

Yours faithfully,



Scientific & Regulatory Affairs Director – Pfizer Nutrition



#### References

Koletzko B et al 2009. Lower protein in infant formula is associated with lower weight up to 2y: a randomised clinical trial. Am J Clin Nutr 2009;89:1836-45

Trabulsi J et al 2011. Effect of an alpha-lactalbumin enriched infant formula with lower protein on growth. Euronean J Clin Nutr 2011;65 (2):167-74