REVIEW OF THE STANDARD FOR FOLLOW-UP FORMULA

(CODEX STAN 156-1987)

(Chaired by New Zealand and co-chaired by Indonesia and France)

First Consultation Paper
Submitters Response Form

June 2016

Please respond by **19th July 2016**

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Please provide your responses to the first consultation paper in the response form below. Note, to fill in a check box please right click on the box and select "Properties", under the "Default Action" sub-heading, select "Checked".

Name of Member Country/Organisation:

International Council on Amino Acid Science (ICAAS), Brussels, Belgium

ESSENTIAL COMPOSITION OF FOLLOW-UP FORMULA FOR OLDER INFANTS (6-12 MONTHS)

In your responses to the following section please provide scientific justification for your response and where possible, references for the scientific rationale.

Protein

Protein

No agreement was reached on the establishment of a minimum or maximum protein value. Please provide scientific rationale to support your preferred value:

Protein

Unit	**Minimum**	**Maximum**	**GUL**
g/100 kcal	[1.8] or [1.65]	[3.5] or [3.0] or [2.5]	-
g/100 kJ	[0.43] or [0.39]	[0.84] or [0.72] or [0.60]	-

Minimum

☒ Codex Infant Formula standard 1.8 g /100 kcal 0.43 g /100 kJ	☐ 1.65 g /100 kcal 0.39 g /100 kJ

Maximum

☒ 3.5 g /100 kcal 0.84 g /100 kJ	☒ Codex IF std 3.0 g /100 kcal 0.72 g /100 kJ	☐ EFSA 2.5 g /100 kcal 0.60 g /100 kJ

ICAAS continues supporting minimum protein levels in follow-up formula at 1.8 g/100 kcal and maximum at either 3.0 or 3.5 g/100 kcal; depending on the majority support within this eWG.

We cannot provide additional scientific substantiation besides the arguments provided and already reviewed by the Chairs. It seems apparent that the minimum level should exceed the metabolic requirement (1.65 g/100 kcal) because of the differences in protein utilization, sources, health conditions and so on.

We note that the above min/max levels were supported by 70% of the eWG participants and substantiated by history of safe use. Both 3.0 and 3.5 g/100 kcal would fall below 20%/energy level.

Considering the absence of scientific consensus we do not see an option for resolving the discrepancies by science-based consensus.

Footnote 6
The majority of the eWG supported retaining elements of footnote 6.
[6]Follow-up formula based on ~~non-hydrolysed~~ **intact** milk protein containing [~~less than 2~~ 1.65 to 1.8 g protein/100 kcal] and follow-up [formula based on hydrolysed protein [containing less than 2.25 g protein/100 kcal] should be clinically evaluated

Regarding formulas based on **hydrolysed** protein, please state whether you think that all, or only those containing less than [2.25 g/100 kcal] should be clinically evaluated.

☐ All formulas based on hydrolysed protein should be clinically evaluated	☐ Formulas based on hydrolysed protein containing less than 2.25 g/100 kcal should be clinically evaluated

ICAAS does not have sufficient expertise to address this issue.

Regarding formulas based on **intact/non-hydrolysed** protein please note that your responses to these questions do not imply that you support a minimum of 1.8 g/100 kcal or 1.65 g/100 kcal. They will be used to refine the wording in square brackets if the eWG cannot come to agreement on a minimum value.

Please state whether you support the proposal to amend the reference these types of formulas to **intact milk protein**.

☒ intact milk protein	☐ non-hydrolysed milk protein

The intact milk protein is well absorbed and has more beneficial health effects

Regardless of the minimum protein level agreed to in Section 3.1, do you think that clinical evaluation would be required for any formulas based on intact/non-hydrolysed milk protein?

☒ Yes, all formulas containing 1.65-1.8 g/100 kcal require clinically evaluation	☐ Yes, all formulas containing 1.65-2.0 g/100 kcal require clinically evaluation	☐ no requirements for clinical evaluation of non-hydrolysed formulas would be required at 1.65-1.8 g/100 kcal

We do not think there are any data to support one of the above values. Considering precaution, ICAAS supports clinical evaluation of formulas containing 1.65-1.8 g/100 kcal protein.

If the eWG and Committee supported adoption of a minimum of 1.65 g/100 kcal for formula based on intact/non-hydrolysed milk protein, do you support the recommendation that the minimum protein level which requires clinical evaluation is placed in the footnote, rather than in the table? See エラー! 参照元が見つかりません。 above

☐ Yes	☒ No

ESSENTIAL COMPOSITION OF FOLLOW-UP FORMULA FOR OLDER YOUNG CHILDREN (12-36 MONTHS)

Protein

Protein
Considering the eWG's varied views, are minimum and maximum requirements necessary? If so, please state your preferred approach on how to establish protein requirements?
MINIMUM REQUIREMENT: In this age group, conducting a traditional dose-response study to determine protein requirements is ethically difficult. The factorial method of calculation is how current DRI provide estimates. The minimum has been set at 0.87 and a population safe level at 1.05 g/kg/day (app. 6%/energy which is in agreement with 2015 IEG). But, academic experts involved with ICAAS do not agree with 2015 IEG and assume that the estimate is too low. In that sense, a minimum reqis decision until science catches-up (see below comment on METHODOLOGY). METHODOLOGY FOR PROTEIN REQUIREMENTS: ● PDCAAS methodology has been recently criticized (see attached report from a FAO Expert Working group (2014). DIAAS (digestible indispensable amino acid score) is a more rigorous approach. ● Please, note that a novel method has been developed to determine protein requirements, which is called "indicator of amino acid oxidation" (IAAO). This technique (Ref. 1) has been validated in adults by a comparison with the "gold standard" nitrogen balance. IAAO has documented that minimum protein requirements have been underestimated in adults by as much as 30%. It is highly possible that a comparable (or larger) underestimation is happening in young children. MAXIMUM REQUIREMENT: ICAAS would like to highlight two new studies (Ref. 2,3) which indicated that protein should be regulated at 20% of energy intake. It was not clear from the studies if it was protein as such or the corresponding caloric intake caused the observed adverse results at levels higher than 20% of energy. Considering that the current protein intake in this age group worldwide is between 15 and 20% of energy; a maximum requirement is not necessary at this moment. If it was applied, ICAAS argues for formulating maximum requirement in the form of %/energy and limiting protein intake to 20%/energy. References: 1. Pencharz PB, Elango R, Wolfe RR. Recent developments in understanding protein needs - How much and what kind should we eat? Appl Physiol Nutr Metab. 2016;41:577-80. 2. Haschke F, Grathwohl D, Detzel P, Steenhout P, Wagemans N, Erdmann P. Postnatal High Protein Intake Can Contribute to Accelerated Weight Gain of Infants and Increased Obesity Risk. Nestle Nutr Inst Workshop Ser. 2016;85:101-9.

3. Pimpin L, Jebb S, Johnson L, Wardle J, Ambrosini GL. Dietary protein intake is associated with body mass index and weight up to 5 y of age in a prospective cohort of twins. Am J Clin Nutr. 2016 Feb;103(2):389-97

Should there be requirements for protein quality? If so how this might be achieved? Please consider both the current Follow-up formula standard, and proposals within the draft standard for older infants.

ICAAS strongly argues that requirement for protein quality in terms of essential and semi-essential amino acid composition is of key importance (e.g., Ref. 1 below).
Rather than duplicating the amino acid composition of breast milk defined in Annex I of the Codex Standard for Infant Formula (0 – 6 months), ICAAS proposes to adopt values for 12 – 48 month-old children listed in the Joint WHO/FAO/UNU Expert Consultation (Ref. 2, Table 36, page 180 copied below).

References:

1. Ghosh S, Smriga M, Vuvor F, Suri D, Mohammed H, Armah SM, Scrimshaw NS. Effect of lysine supplementation on health and morbidity in subjects belonging to poor peri-urban households in Accra, Ghana. Am J Clin Nutr. 2010 Oct;92(4):928-39.
2. Protein and amino acid requirements in human nutrition. 2007 WHO Technical Report Series 935, Report of a Joint WHO/FAO/UNU Expert Consultation

Table 36

Amino acid requirements of infants, children and adolescents (males and females combined)

			His	Ile	Leu	Lys	SAA	AAA	Thr	Trp	Val
Tissue amino acid pattern[a]			27	35	75	73	35	73	42	12	49
Maintenance amino acid pattern[b]			15	30	59	45	22	38	23	6	39
Protein requirements (g/kg per day) for Amino acid requirements (mg/kg per day)[d]											
Age (years)	Maintenance	Growth[c]									
0.5	0.66	0.46	22	36	73	64	31	59	34	9.5	49
1–2	0.66	0.20	15	27	54	45	22	40	23	6.4	36
3–10	0.66	0.07	12	23	44	35	18	30	18	4.8	29
11–14	0.66	0.07	12	22	44	35	17	30	18	4.8	29
15–18	0.66	0.04	11	21	42	33	16	28	17	4.5	28
>18	0.66	0	10	20	39	30	15	25	15	4.0	26
			Scoring pattern (mg/g protein requirement)[e]								
0.5			20	32	66	57	28	52	31	8.5	43
1–2			18	31	63	52	26	46	27	7.4	42
3–10			16	31	61	48	24	41	25	6.6	40
11–14			16	30	60	48	23	41	25	6.5	40
15–18			16	30	60	47	23	40	24	6.3	40
>18			15	30	59	45	22	38	23	6.0	39

His, histidine; Ile, isoleucine; Leu, leucine; SAA, sulfur amino acids; AAA, aromatic amino acids, Thr, threonine, Trp, tryptophan; Val, valine.

[a] Amino acid composition of whole-body protein (*37*).

[b] Adult maintenance pattern (see section 8).

[c] From Tables 32 and 33, calculated as average values for the age range growth adjusted for protein utilization of 58%.

[d] Sum of amino acids contained in the dietary requirement for maintenance (maintenance protein x the adult scoring pattern) and growth (tissue deposition adjusted for a 58% dietary efficiency of utilization x the tissue pattern).

[e] Amino acid requirements/protein requirements for the selected age groups.