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## Response to Forsyth

Advance online publication 11 March 2015. doi:10.1038/pr.2015.36

**To the Editor:** We are in complete agreement with Stewart Forsyth's point that, "policies need to be evidence based to ensure that the target population will experience benefit and not be at risk of iatrogenic harm." It is also correct that the commentary originated from our underlying thinking and discussions during the preparation of the recent European Food Safety Authority opinion (1). Where we disagree is on the issue of whether evidence is required in order to add arachidonic acid (AA) (or any other ingredient) to an infant formula, or whether evidence is required in order to demonstrate that AA (or any other ingredient which is present in breast milk) does not have to be added to infant formula. The former has been the norm so far. Arguing that infant formula should be similar in composition to breast milk would require the addition not only of docosahexaenoic acid (DHA) and AA, but also various immune components, as well as prebiotics and nucleotides. It would furthermore require various structural changes such as addition of the lipids as fat globules with their associated membranes as well as restructuring of the lipid molecules with palmitic acid in the sn-2 position. The European Food Safety Authority opinion does not recommend any of these things as essential either, based on the lack of evidence of their functional importance—although many of these have been suggested to have beneficial effects and a few of them may even seem promising. The conclusion of the European Food Safety Authority paper was essentially that there was not convincing evidence that adding AA to infant formulas is necessary and hence no obligatory minimum level was suggested; however, importantly, it does not suggest that the addition of AA to infant formula should be prevented (and this also applies to several other ingredients).

The basis for our conclusion in the commentary that dietary AA is likely to be less important than dietary DHA is not only the lack of clinical evidence but also, as we point out in the first part of our paper, the fact that the AA level in the brain and other tissues is little affected by intake—whereas DHA levels are highly responsive to dietary intake of preformed DHA (2). If intake does

2. Lauritzen L, Fewtrell M, Agostoni C. Dietary arachidonic acid in perinatal nutrition: a commentary. *Pediatr Res* 2015;77:263–9.
3. Brenna JT, Varamini B, Jensen RG, Diersen-Schade DA, Boettcher JA, Arterburn LM. Docosahexaenoic and arachidonic acid concentrations in human breast milk worldwide. *Am J Clin Nutr* 2007;85:1457–64.
4. Prentice AM, Paul AA. Fat and energy needs of children in developing countries. *Am J Clin Nutr* 2000;72(5 Suppl):1253S–65S.
5. European Food Safety Authority. Scientific opinion on the essential composition of infant and follow-on formulae. *EFSA J* 2014;2:3760.

not affect status (which to some extent must be expected to serve as a pool for the generation of eicosanoids and other biologically active AA-derived molecules) and there is no evidence that addition of AA has any functional effects, then it is difficult to conclude that the addition of AA to infant formula is essential. As pointed out in our commentary, the main concern about possible adverse effects on growth of adding DHA to infant formulas without AA originated from a small trial in preterm infants (3), but none of the subsequent trials in term infants have replicated these findings. Thus, we do not consider that there is evidence to suggest that adding DHA without adding an equivalent amount of AA to formula results in adverse effects for infants.

Finally, we should also to some extent consider cost. If our aim was to produce infant formulas as similar in composition to breast milk as possible this would complicate production and thus increase the price of the product, without necessarily improving functional outcomes. We all agree that breast milk is the optimum form of nutrition in early infancy and that infant formula will always be a substitute no matter how complex; but the minimum required composition of a formula should be based on the available evidence relating to outcome rather than on the composition of breast milk per se.

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