Reviewer’s report

Title: There is (still) too much aluminium in infant formulas

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Reviewer: Mary S Fewtrell

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2/7/10
Title: There is (still) too much aluminium in infant formulas (resubmitted version)
Authors: Shelley-Ann M Burrell, Christopher Exley

Thank you for asking me to review the resubmitted version of the above manuscript. This is indeed an interesting topic, concerning the potential health effects of a contaminant in products fed, as the authors state ‘to literally millions of infants’. I think it is precisely because of the widespread use of infant formulas that it is important to be extremely careful how these findings and concerns are reported. The authors make a valid point – that my recent publication on the long-term follow-up of our aluminium trial is my only experience of aluminium and human exposure to aluminium. I do, however, have a large amount of experience in issues surrounding the composition and health effects of infant formulas. In the light of this previous experience, I am concerned that if the manuscript is published in its current form, it has the potential to cause considerable anxiety amongst parents who do not currently have an available ‘low aluminium’ alternative (other than of course breastfeeding!).

I should emphasise that I am not suggesting that the findings and concerns are ‘suppressed’ in any way – rather that their reporting and discussion should be very carefully handled.

My thoughts are as follows:

1. I do not dispute the fact that infant formulas contain considerable quantities of aluminium. Given that aluminium has no useful biological purpose, in an ideal world we should remove it from the food-chain. However, we all know that this is impossible; and that attempts to lower exposure from foods such as infant formulas and parenteral nutrition will be costly.

2. The important question then, which the authors have addressed to a greater degree in the revised manuscript, is whether the aluminium present in infant formulas poses a health risk to the infant and therefore, by implication, should be subject to regulatory controls to force change. The potential for harm must depend on the extent to which aluminium is absorbed/excreted, and/or laid down in tissues such as brain and bone. The authors have, as they point out, cited some papers that have attempted to address this issue. In the revised discussion they have added the statement that ‘previous research ….has highlighted the
potential toxicity of aluminium in infants fed such formulas. However, the papers cited do not, to my mind, provide convincing evidence for toxicity or harm;

- reference 10 reports toxicity in two infants with severe renal problems and uraemia – of uncertain relevance to healthy infants with normal renal function;
- reference 11 reports plasma aluminium in infants (GA 36 weeks, mean age 10 days) receiving antacid medication and does seem to demonstrate absorption, with potentially toxic blood levels, in these slightly preterm infants, albeit with higher acute exposure than would be likely from infant formula;
- reference 12 also reports high aluminium concentrations in formulas compared to human milk (especially LBW and hydrolysed formulas) but, interestingly, did not find significant differences in the plasma levels of aluminium between breast-fed and formula-fed infants apart from those fed the hydrolysed formulas – and these infants had underlying gut abnormalities;
- reference 13 reports an association between plasma aluminium concentration and bone mineralisation – but only in low birth weight infants. This association could easily reflect confounding by the many other factors relating to illness severity that would typically be associated with both bone development and aluminium exposure in this patient group.

Thus, overall, I am not very convinced by the published evidence that a high exposure to aluminium via infant formulas – at least in healthy term infants – shows adverse health effects. Perhaps there are some other studies that provide more convincing evidence of absorption/health effects?

3. Having said all this, I agree with the authors’ comment, in response to Dr Greer, that absence of proof of harm does not equate to absence of harm: it is plausible, certainly in low birth weight or sick infants, that aluminium exposure via infant formulas may have adverse health effects. In my opinion, this question could only be answered definitively by performing a randomised trial using a standard versus an aluminium-depleted formula, measuring exposure, plasma levels and health effects – in the same way that we did for parenteral exposure. Such a study would, in the current research climate, be expensive and time-consuming – and would almost certainly need industry support in preparing an experimental formula. However, I believe that this is what would probably be needed to initiate any form of regulatory process to require manufacturers to alter their products.

In summary, I think this manuscript should be published, and that it is entirely reasonable to highlight the potential for adverse effects of aluminium exposure from infant formulas and the desirability of minimising aluminium exposure. However, I think speculation about potential harm needs to be carefully balanced by a discussion that includes the fact that we do not currently have convincing data supporting adverse effects, at least in healthy term infants; and the need for an experimental study to address this issue.

Mary Fewtrell
**Level of interest:** An article of importance in its field

**Quality of written English:** Acceptable

**Statistical review:** No, the manuscript does not need to be seen by a statistician.

**Declaration of competing interests:**

'I declare that I have no competing interests'