Reviewer’s report

Title: Maternal iron metabolism gene variants modify umbilical cord blood lead levels by gene-environment interaction: a birth cohort study

Version: 2 Date: 10 July 2014

Reviewer: Claudia Gundacker

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Minor Essential Revisions:
My first conclusion from the very interesting findings of Karwowski and co-workers would be that research is needed to clarify the mechanisms behind the complex iron and lead story, in general and specifically for the placenta. Genotype/phenotype association studies can provide very valuable hints on gene-environment interactions but per se are weak instruments in detecting causal functional relationships, particularly when a phenotype is the result of several, if not numerous genetic influences. I would not propose genetic markers to be integrated into risk assessment as long as their downstream effects are so poorly understood.

I recommend to omit paragraph 7 of the Discussion because it is based on tenuous premises. There is no need to speculate about a „lead-sink in which lead moves freely into placental tissues via up-regulation of metal transport mechanisms...“ or about saturation of the eventually involved metal transporters „specifically by zinc or manganese“ through „higher maternal levels of micronutrients“.

Level of interest: An article of importance in its field

Quality of written English: Acceptable

Statistical review: Yes, and I have assessed the statistics in my report.

Declaration of competing interests:
I declare to have no competing interests.