

Author's response to reviews

Title: Does the evidence about health risks associated with nitrate ingestion warrant an increase of the nitrate standard for drinking water?

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point-by-point response to review comments to

Title : Does the evidence about health risks associated with nitrate ingestion warrant an increase of the nitrate standard for drinking water?

Authors: Hans JJM van Grinsven, Mary MH Ward, Nigel N Benjamin and Theo TM de Kok

Dear Dr Philippe Grandjean and Dr David Ozonoff,

First of all we thank you and Dr Dieter for your positive and constructive review.

We have revised the manuscript and responded to the reviewers comments as follows.

[Comment 1]

In addition, part of the commentary is phrased as excerpts from conference discussions or email exchanges, which may be how this Commentary came into being. However, we would prefer if the manuscript could focus on the key issues, rather than how the authors communicated about them. The section on Authors' Contributions already contains relevant information in regard to the latter issue, and some further detail could be added here, if so desired.

Response

We have moved all information on the authors, and their role in both conferences to the authors section

[Comment 2]

Also, a reference to Lomborg's concerns hardly serves as proper justification for this very timely commentary, since Lomborg did not review the nitrate question in any detail. Instead, the issues raised in the discussion deserve to be clearly identified and justified in the Introduction.

Response

Your are correct. Still we prefer to maintain this reference as it is used in this context by Addiscott and Benjamin: in fact they conclude that Lomborg's general conclusion also applies to the nitrate issue. We have modified the text clarify this.

[Comment 3]

The Table and the Figure do not seem essential and could be left out.

Response

We would suggest to maintain both Table and Figure for two reasons. First, the demonstration of potential large scale exposure to drinking water exceeding 50 mg/l is an essential argument against raising the nitrate standard. The other two arguments are addressed in our paper and include some evidence for chronic health effects and expected net benefits from keeping the standard. The second reason for maintaining Table and Figure is that we could not find a recent paper that estimates exposure to drinking water exceeding 50 mg/l nitrate. Therefore, we believe it is important to present the data here.

[Comment 4]

Finally, please correct the spelling of heme (not 'heam')

Response

Done, except in the original reference [14],

[Comment 5]

and make sure that there is only one space between words and sentences.

Done.

Response to Hermann H. Dieter:

Major concerns:

1. Citation 18 (Weyer et al., 2001) should refer not only on the increased cancer rates in urinary bladder and ovaries but also on decreased rates in uterus and colon as it was observed in that study. Since NOC formation/suppression at relatively low pH is the biochemical background for the carcinogenic potential of nitrite/nitrate, only promotion/initiation or suppression of cancer by nitrate/nitrite in urinary bladder and stomach seems plausible. In total, the study by Weyer et al. is - if ever - a very questionable argument in favour of a carcinogenic potential of nitrite/nitrate in drinking water at such low (here 11 mg/l) concentrations. The results could easily have been generated by chance.

Response: The paper of Weyer et al indeed reports an increased bladder and ovary cancer risk associated with drinking water nitrate and inverse relationships with uterine and rectal cancer. Therefore, we modified the text to acknowledge this observation.

2. In their (semi-)quantitative risk/benefit assessment, the authors should also take into account the documented possibility that the resorption rate from pure drinking water of small ions in the gastric tract often is distinctly higher than from food. This is the more important as many persons drink water not only during a meal but also (or only) between meals. Under such a condition, not only the resorption might be higher but also the first pass antioxidant concentration be lower than if food is taken up simultaneously with drinking water

Response: Although we appreciate the argument that small ions may possibly be less readily absorbed from a food matrix as compared to absorption from pure drinking water, we are not aware of any study that clearly demonstrates this for drinking water nitrate. Therefore, we feel that this argument would be too speculative without a good reference indicating this phenomenon.

3. On page 6, third line from second last paragraph, the statement "this trend is not related to concerns about nitrate" seems questionable. At least in Germany, parents living in supply areas with more than 10 - 20 mg/l in their drinking water nitrate use very often bottled water to prepare formula food although concentrations of at least up to 50 mg/l nitrate are safe for babies.

Response: It is correct that in some regions use of bottled water is related to nitrate concerns, however the overall trend in use is market related. Bartram states that " purchased of bottled water is largely a market phenomenon". We have modified the text to address this comment.

4. A strong argument in favour of keeping the 50 mg/l-value to protect babies from acute toxicity of nitrate/nitrite is the published observation that additional risk factors (digestive tract diseases, contamination of standing food or water with nitrate reducing bacteria) might strongly enhance the nitrate/nitrite body burden. Such factors can only be individually controlled, whereas a limit value (here 50 mg/l nitrate) must be applicable and safe under any condition of possible acute intoxication.

Response: We fully agree with the comment that additional risk factors form an additional argument in favour of keeping the present drinking water limit value. In the revised manuscript we now emphasize the importance of such individual risk factors, and the fact that a limit value must be applicable and safe under any condition.

Minor concerns:

1. The 1st line of the first paragraph on p.4 should be complemented by an information against what Nigel Benjamin is skeptic. The present text explains this only in the following paragraph of that page.

Response: this clarified, in the section: Authors contributions"

2. in the 3rd line of the 4th paragraph, "(McKnight et al. 1997)" must be replaced by "[9]"

Response: this is corrected

3. 2nd line of page 6: write "no" instead of "not".

Response: this is corrected

4. The authors should consider also the indirect effects of environmental nitrate/nitrite on human health as they were outlined e.g. in detail in a very recent review by Camargo JA and Alonso A [Environ Int June 15 (2006)], although indirect effects do not seem to have been subject of discussion in November 2005 in Salt Lake City.

Response: we found this interesting reference and added the statement about human hazard due to algal toxins

The environmental and indirect health effects should be complemented by the fact or problem that nitrate is a transport form of oxygen into oxygen poor groundwater. If microbiologically denitrified, the groundwater redox state might be changed with the consequence that toxic metals are oxidized and mobilized from insoluble sulfides to easily soluble sulfates (as has been published for Nickel).

Response: this is correct, we included this addition, together with a reference

5. It would be worthwhile to mention that a maximal value for nitrate in drinking water as based on chronic toxicity (babies and adults) could be set lege artis at 13 mg/l nitrate. Such a value would correspond to a 10%-allocation of the TDI = 260 mg/kg per body mass and day on two liters of Drinking water per day and person. The present allocation (40% , corresponding with 50 mg/l, resp.) is extremely high for an environmental contaminant. A reasonable compromise between all stakeholders (toxicologists, agriculture, analytics, environmental hygiene) could be an upper quality goal between 20 and 30 mg/l nitrate in waters which are influenced by agriculture.

Response: Both points are interesting.

We are aware that the origin of the 50 mg/l standard by WHO considering chronic exposure and cancer risks is different from that for other toxic substances. The WHO mentions provisional guideline values as low as 0.2 mg/L for nitrate. In view of apparent uncertainties and the fact that nitrate itself is not a carcinogen, the WHO maintains the standard at 50 mg/l.

What is a "reasonable compromise" in part is a political discussion. The suggested compromise in fact applies to untreated groundwater instead of drinking water itself. (regional) Differentiation of nitrate standards for groundwater and surface waters based on assessments of ecological and human health risks indeed could be feasible.

We think both points are relevant but somewhat beyond the scope of this commentary paper, but they may be relevant in a follow up.