Meeting

Item 6 - Reserved Minutes

Item 6: R Safety of Nitrates and Nitrites as Food Additives- Presentation from RSM UK Consulting LLP (reserved) (TOX/2025/20)

1. Professor Thorhallur Ingi Halldórsson declared an interest due to chairing a working group for the Danish Environmental Protection Agency regarding revising the parametric value of nitrate in drinking water. This did not preclude him from taking part in the discussion. No other interests were declared.

2. Sodium and potassium nitrates, and sodium and potassium nitrites are salts commonly used as food additives for their antimicrobial properties, as well as their ability to maintain properties such as colour, texture and flavour. The safety of nitrates and nitrites as food additives was last evaluated by the European Food Safety Authority (EFSA) in 2017. In 2023, over concerns due to the additives' contribution to the formation of nitrosamines following an assessment on the safety of nitrosamines, the EU announced a decision to change the maximum permitted levels of nitrites and nitrates used as food additives to levels lower than those allowed in GB. This prompted a review of the current understanding of the safety of these additives in food sources in the context of GB legislation.

3. The report had already been peer reviewed by several COT Members and therefore was presented as a paper largely for information. However, Members were invited to comment or ask questions following the presentation. The report was still pending FSA's final review and therefore it was not the final version, however, only minor edits were expected at that stage.

4. The RSM UK Consulting team delivered a presentation on their FSA-funded literature review of the safety of nitrates and nitrites as food additives. The presentation covered topics such as the research questions explored, the methodology used and the scope applied, as well as the findings resulting from the literature review and a brief discussion around these findings. RSM highlighted the uncertainties of the project, advised on ideas for future research

and summarised the main conclusions of the literature review.

5. Members questioned why animal studies were excluded from the scope. RSM clarified that, since enough human epidemiological and in vitro data were available, animal models were excluded due to time and resource constraints: this decision had been discussed and agreed with the FSA. The exclusion was acknowledged as a limitation of the project, since key studies might have been missed, and was suggested as a topic for future research. Members highlighted that animal *in vivo* studies should be considered in future research concerning the safety of nitrates and nitrites. This would avoid restriction of the data to in vitro and epidemiological studies, which may not provide the extent of the potential harmful effects.

6. The Committee questioned whether nitrates and nitrites having an impact on the gut microbiome structure had been considered. RSM noted that the impact of nitrates and nitrites intake on the microbiome and vice versa had been explored.

7. Members requested clarification on the meaning of ‘plant-based food’. RSM clarified that nitrates and nitrites found in plant-based food are those naturally occurring, mostly in green leafy vegetables such as chard, celery, broccoli, etc.

8. The Committee also requested clarification on the meaning of ‘organic’. RSM clarified that, in the context of the literature review, ‘organic’ meant sourced from plant-based foods, rather than referring to the method of production.

9. Members raised the limitation of using the impact factor of a journal to rank studies. RSM acknowledged that ranking papers based on the impact factor of their journal was a key weakness of the literature review and was already mentioned in the report. However, given the large volume of data available and the time and resource constraints, this ranking method was selected in consultation with the FSA as the most efficient shortlisting method. RSM noted that they had ensured enough cover for each research question but recognized that key literature might have been missed. Members highlighted that toxicology journals tend to have a lower impact factor than journals covering other areas, and therefore ranking papers by the impact factor of their journal might not be the best shortlisting method for toxicology studies. The Committee considered that more specialist journals with a lower impact factor might have published more detailed data. The Members that reviewed the draft report commented that

this limitation had been appropriately reflected in the final document, as well as the holistic approach used to evaluate the quality of the papers.

10. The Committee questioned whether the FSA would retrieve the excluded literature to evaluate its relevance to the research questions. Members suggested that the report should specify how future work would address the missed references.

11. The Committee questioned whether a comparison of findings with a different ranking system had been considered. RSM clarified that this exercise had not been carried out due to time and resource constraints.

12. Members noted that drinking water had not been considered as a source, despite the large amount of data available (particularly on exposure during pregnancy). RSM reminded Members that the focus of this study was on the additive use of the chemicals and thus naturally occurring nitrates and nitrites in vegetables or present in drinking water were not included.

13. The Committee asked whether exposure during pregnancy had been considered. RSM explained that some studies exploring the link between nitrates and nitrites intake and birth and heart defects, as well as preterm birth had been identified and included in the report.

14. Members highlighted that the International Agency for Research on Cancer (IARC) classified ingested nitrates and nitrites under conditions that result in endogenous nitrosation as probably carcinogenic to humans (Group 2A) in 2010. This was based on mechanistic data and rodent studies, where excreted nitrosamines were found following ingestion. However, when evaluating human studies, literature has shown that nitrosamine formation depends on the type of food ingested.

15. To complement the information presented on potential health risks, the Committee referred to an exposure assessment conducted across Europe that indicated a risk of methaemoglobinaemia for young infants and high consumers of green leafy vegetable smoothies.

16. Members discussed that adding figures in future reports with the chemical structures and reactions described would be beneficial for the reader’s understanding.

17. The Committee questioned whether the benefits of plant polyphenols and ascorbic acid as alternatives to nitrates and nitrites had been evaluated. RSM

explained that the literature explored used simulated conditions to elucidate whether these compounds would reduce nitrosamines levels, but did not investigate the potential benefits of these alternatives. This topic has been suggested as an idea for future research in the report.

18. Members questioned whether the literature reviewed overlaps with the IARC monographs on the evaluation of carcinogenic risks to humans from consumption of nitrates and nitrites (2010), and red meat and processed meat (2018). RSM explained that the timeframe used for this research project was 2016 to present, i.e. the period following EFSA’s re-evaluation of the additives. However, the IARC 2018 monograph was not identified during the search. The Committee requested these monographs to be summarised in the report.

19. RSM clarified that the literature originally searched had been provided to the FSA for reference.

20. The Committee thanked RSM for their hard work on this project and for delivering an insightful presentation.