

SUMMARY OF ACTION TAKEN BY THE VITAMIN A SUBGROUP TO RESPONSES RECEIVED ON DRAFT REPORT ON VITAMIN A

Procedure

The Vitamin A Subgroup agreed to alert interested parties to the draft report on Vitamin A when it had been placed on the website. The Secretariat wrote to interested parties on 11 January 2005 requesting any comments on the draft report to be submitted by 8 April 2005.

Response

- 8 responses were received and are available, in full, on the SACN website.

- Responses were received from the following organisations & individuals:
 - 1 Agricultural Industries Confederation (AIC)
 - 2 Dr Susan A New representing the Nutrition Society and the National Osteoporosis Society (NS/NOS)
 - 3 French Food Safety Agency (AFSSA)
 - 4 Professor David Richardson, DPR Nutrition Ltd on behalf of the Council of Responsible Nutrition (CRN)
 - 5 Meat and Livestock Commission (MLC)
 - 6 World Community Autism Program (WCAP)
 - 7 Health Food Manufacturers Association (HFMA)
 - 8 MRC Human Nutrition Research (MRC-HNR)
 - 9 Dr Helen Macdonald representing the National Osteoporosis Society (NOS)

- An overview of the responses received is provided in Table 1.
 - 7 respondents were in general agreement with the conclusions of the report
 - 1 respondents agreed with parts of the draft report
 - 1 respondents raised specific points but did not comment on whether they agreed with overall conclusions
 - 1 respondents did not agree with conclusions

Table 1: Overview of responses received to SACN Report on vitamin A and actions agreed by the vitamin A Subgroup

General response	Comments	Actions agreed by Subgroup	Organisation
<p><i>Organisations in general agreement with report</i></p>	<p>1. An excellent report: clear, concise and well referenced. A few comments on specific points were made to improve clarity (which are contained in Table 2). It was stressed that a more forceful comment regarding cod liver oil use, given that cod liver oil does contain appreciable amounts of retinol and older women could easily be in a situation of overdosing.</p>	<p>Wording relating to retinol containing supplements amended to include fish liver oils.</p>	<p>NS/NOS</p>
	<p>2. The draft report was considered to be of good quality. Two major comments were made. The first relates to data on the content of retinol present in animal liver and the second relates to the retinol content of animal feeds.</p>	<p>Comments passed to Animal Feed Division for consideration – the main conclusions of the report are outside the remit of the Subgroup.</p>	<p>AFSSA</p>
	<p>3. The SACN paper has come to fair and reasonable conclusions.</p>	<p>No action.</p>	<p>CRN</p>
	<p>4. This summarises current knowledge well. It was written in a straight forward style that made it easy to follow</p>	<p>No action.</p>	<p>NOS</p>
	<p>5. Broadly agree with the content of this thorough review. Two specific comments re pts 116-118. It would be interesting to: cover trends at lower end of retinol intakes in this section; include whether retinol content of liver also decreased over time.</p>	<p>Trends at lower end of retinol intake not within remit of report. Info on changes in levels of retinol over time incorporated.</p>	<p>HFMA</p>
	<p>6. Agree with the recommendations that have been made by the Committee, based on the evidence to date. There are a number of areas that require further clarification. See table 2 for further detail.</p>	<p>See Table 2</p>	<p>MRC-HNR</p>
<p><i>Organisations supportive of parts of draft report</i></p>	<p>7. Overall, the recommendations in the draft report are balanced and proportionate. There are some sections of the report that give cause for concern particularly in relation to the use of data from the NDNS. See Table 2 for further information.</p>	<p>See Table 2.</p>	<p>MLC</p>

<i>Organisations that made specific comments but made no general comments about draft report</i>	8. See Table 2	See Table 2.	AIC
<i>Organisations not supportive of draft report</i>	9. See Table 2	See Table 2.	WCAP

Table 2: Issues for discussion arising from responses received to report and actions agreed by vitamin A Subgroup

Subject	Comments	Actions agreed by Subgroup	Organisation
<i>General drafting and terminology</i>	1. It would be useful to qualify the term ‘some’ re individuals being above 1500µg RE of vitamin A (para 4). This point is also relevant to the conclusions section.	Text amended.	NS/NOS
	2. There needs to be a mention of osteocytes with regard to skeletal turnover (para 30).	Bone text amended to include osteocytes.	NS/NOS
	3. Change the order of nutrients listed in order of importance to bone health, bringing vitamin D higher up the list; quantify further the protein effect; include potassium in the list; consider a mention regarding sodium. (Para 31).	Text amended as suggested.	NS/NOS
	4. Additional nutrients that have been positively associated with bone health and should be added include vitamin C, potassium and silicon (Para 31)	Text amended to include vit C & potassium which are mentioned COMA bone report, but not silicon.	MRC-HNR
	5. Helpful to include quantification at para 32 – e.g. 1SD change in BMD will result in a 50% reduction in fracture risk.	Text amended to include increased risk of fracture with 1SD decrease	NS/NOS

	<p>6. That bone mineral density predicts fracture should be mentioned. (para 34)</p> <p>7. At para 163, cod liver oil use needs to be emphasised.</p> <p>8. Para 164 should discuss cod liver oil</p> <p>9. The varying uses of the terms vitamin A, preformed retinol, preformed vitamin A, total vitamin A and retinol equivalents are confusing, especially in section 1, section 2 and section 4. Since retinyl esters are present in food and supplements, it would be helpful to define preformed vitamin A as retinol and retinyl esters.</p> <p>10. The report does not give appropriate acknowledgement to the teratogenic effects of vitamin A and therefore it may be useful to state in para 8 that the evidence for teratogenicity has been previously reported in the EVM report.</p>	<p>BMD.</p> <p>This is already stated but text expanded.</p> <p>Wording amended to include liver oils.</p> <p>Wording amended to include fish liver oils.</p> <p>All references to preformed vitamin A, amended to retinol.</p> <p>Teratogenicity covered in para 6-13. Text amended to state that teratogenicity previously reported by EVM.</p>	<p>NOS</p> <p>NS/NOS</p> <p>NOS</p> <p>MRC-HNR</p> <p>MRC-HNR</p>
<i>Evidence base</i>	<p>11. The human studies included are detailed in exemplary fashion but all the studies listed are either from the USA or Sweden. The study by the Sheffield group, funded by the Agency has been presented in abstract form at the Sept 2004 ASBMR conference so it would be useful to include here.</p> <p>12. It would be helpful to clarify the term total vitamin A in the bone studies by mentioning which form of vitamin A was measured in the studies.</p> <p>13. No paragraph on study limitations has been given for the first three bone mineral density studies. Some limitations of these studies include:</p>	<p>Sheffield study not included as it is only available as an abstract.</p> <p>Text referring to vitamin A in studies reviewed and clarified.</p>	<p>NS/NOS</p> <p>MRC-HNR</p> <p>MRC-HNR</p>

	<ul style="list-style-type: none"> • Sowers and Wallace 1990 - Measurement of only one bone site, the radius, as bone mineral status at one site may not reflect status at other sites. • Mehus et al 1998 - Retinol intake was not significantly associated with BMD in the univariate analysis but was significantly associated in the multivariate analysis and diet records were used rather than FFQ to measure retinol intake. • Ballew et al 2001 - Measurement of serum retinyl esters rather than serum retinol. • Houtkooper (1995) - Small sample size and all subjects were taking calcium supplements, as a result of the study being part of a randomised trial. <p>14. Most studies reviewed measured BMD, Freudenheim et al (1986) analysed Bone Mineral Content and Sowers and Wallace (1990) measured Bone Mass. It would be helpful if these differences were emphasised in Section 4 and Annex 5.</p> <p>15. The evidence suggests that BMD and BMC measurements are limitations of cross-sectional studies and that BMD measurements may be more useful for prospective studies. It may be helpful to</p>	<p>Limitations of study included in the previous section on bone fractures. Text amended to indicate this.</p> <p>Point about univariate analysis not included as limitation after seeking advice from FSA statistics division. Diet records not included as a limitation as the dietary assessment (from 4 sets of 1-week records) was more thorough than other studies.</p> <p>Text amended to include that serum retinyl esters have not been found to correlate with intakes of total vitamin A.</p> <p>Small sample size added as limitation. The fact that all subjects were taking calcium supplements was not added as limitation as the purpose of calcium supplements was to ensure that calcium was not a limiting nutrient and also no association was found between calcium intake and BMD.</p> <p>Text amended to indicate differences.</p> <p>Text amended.</p>	<p>MRC-HNR</p> <p>MRC-HNR</p>
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	state which bone measurements are more useful for cross-sectional studies, ie size adjusted BMC.		
	16. There is a need for more scientific research in specialised aspects such as the effects of vitamin A on bone and interactions with other nutrients.	No action taken – research recommendations remain as outlined in para 166.	MRC-HNR
	17. Para 48 does not give the conversion factor for total vitamin A since the US recommend 1/12 ratio as opposed to 1/6. It is worth mentioning the US ratios, perhaps at para 18	Text amended to include 1/12 conversion factor.	NOS
	18. Para 49 should mention whether this was with or without supplements, it was done with both but it is not clear which the figures in this section refer to.	Text clarified.	NOS
	19. Para 54 does not mention that retinol extremes can also be a marker of dietary patterns rich in protein and fat which correlate well with retinol – this should be a design concern particular to this study.	No action taken as no clear evidence for this.	NOS
	20. Para 56 – it should be mentioned that many +45 year supplement users take cod liver oil which contains vitamin D as well as n-3 polyunsaturated fats.	No action taken – para 56 reports results of study and would not be appropriate to add this information.	NOS
	21. Para 68 does not mention that the method used to measure BMD was not DXA and therefore not as accurate a determinant.	Methods of bone measurement are detailed in Table 2, Annex 5. Merits of different bone assessment techniques were not considered in detail.	NOS
	22. Para 74 – No mention is made that supplement users tend to be lighter than non supplement users, lighter people are more at risk of low BMD.	No action taken. Insufficient evidence to suggest that supplement users are lighter than non supplement users.	NOS
	23. Para 95 – explain how the dose used relates to humans.	No action taken. Unable to	NOS

		extrapolate to human levels of exposure.	
<i>Retinol content of liver</i>	<p>24. Lower retinol intakes in 2001 NDNS vs. 1986 NDNS are explained by a lower percentage of liver consumers of liver in 2001 vs. 1986 NDNS, but has the content of vitamin A in liver also decreased over this time period?</p> <p>25. Data on retinol content of liver in calf, pig, lamb and chicken are given without standard deviation and number of data used in the calculation of the means.</p> <p>26. No data is given on retinol content of fish liver when it has been highlighted that large quantities of retinol is present in fish livers.</p>	<p>Report amended to include this information.</p> <p>No action taken. Figures used are referenced.</p> <p>As fish livers are not usually consumed as a food in the UK this information was not added to report. Information regarding retinol content of fish liver oils added.</p>	<p>HFMA</p> <p>AFSSA</p> <p>AFSSA</p>
<i>Retinol intakes</i>	<p>27. It would be interesting to also cover trends at the lower end of retinol/vitamin A intakes (para 116-118)</p> <p>28. Para 102 notes that NDNS, may over or under-estimate the habitual intake of rarely consumed foods at an individual level. The contrast between liver consumers and non liver consumers in the diary week is, in reality, not nearly as stark as presented in the report. No reliable estimate can be made of the percentage consumers with retinol intakes above the defined threshold based on these data. Scenario planning as set out in the report should also consider the effect of different possible distributions of liver consumption around the mean. It is noted that the way the recommendations related to liver consumption have been framed takes account of this uncertainty by addressing people on the basis of their individual behaviour in terms of liver consumption.</p> <p>29. High intakes of retinol may be a concern for the elderly as liver consumption and bone fracture are higher in this group. However, it is also important to include reference to the importance of vitamin A</p>	<p>No action taken as this is not within the scope of the report.</p> <p>No action taken. Caveats and limitations of the NDNS data are fully covered in the report in para 102. Para 145 and Appendix 7 explain how adjustments to lessen these limitations were made.</p> <p>Recommendations amended to include importance of not reducing consumption to levels below RNI.</p>	<p>HFMA</p> <p>MLC</p> <p>MRC-HNR</p>

	<p>in the elderly, for example in vision (para 131).</p> <p>30. Para 148 should consider the health outcome of adults falling below the LRNI.</p>	No action taken – not within scope of the report.	NOS
<i>Interaction between retinol and vitamin D</i>	31. More consideration should be given regarding the interaction between retinol and vitamin D as this is important for cod liver oil users.	No action taken. Further consideration difficult due to the current evidence base, which is explained in text.	NOS
	32. Pages 16-19 examine the interaction between retinol and vitamin D and indicate an antagonistic effect. The vitamin D content of liver should be taken into account when considering recommendations on liver consumption with respect to vitamin A.	As above.	MLC
<i>Animal Feed Issues</i>	33. Extremely disappointed about the scientific quality of the “Local Authority Sampling and Analysis Programme for Animal Feeds – Vitamin A” for a number of reasons e.g. failing to quantify the uncertainties associated with sampling and analytical errors, inaccuracies in the descriptions of samples, no data is presented on the average levels found no distribution tables showing number of samples analysed.	Comments passed on to Animal Feeds Division for their consideration. They do not affect conclusions of report.	AIC
	34. Little confidence can be drawn from the conclusions of the “Local Authority Sampling and Analysis Programme for Animal Feeds – Vitamin A”. It is hoped that these views are taken into consideration if this report is used in connection with the SACN report on vitamin A.	As above.	AIC
<i>Risk Management</i>	<p>35. Propose two advisory statements on labels of retinol-containing supplements (in addition to the existing DoH warning):</p> <ul style="list-style-type: none"> All retinol containing products should state “Supplements containing vitamin A as retinol are best avoided by those who regularly eat liver.” Supplements containing > 1150µg should also bear the statement 	No action taken in terms of report. The proposals are risk management issues and will be considered by the Food Standards Agency at a future stage.	HFMA

	<p>“Long term intakes [of this amount] of vitamin A [(as retinol)] are best avoided by postmenopausal women and older people who are at increased risk of osteoporosis.”</p> <p>36. Certain groups in the population are more at risk of having retinol intakes below the LRNI. Concern that public health announcement that retinol is harmful will result in the public to over-react in response resulting in an avoidance of retinol containing foods and increasing the number of people in the population with low intakes of vitamin A.</p> <p>37. There is evidence that some groups benefit from supplements that contain natural retinol e.g. fish oils. These include people who suffer from autism and ADHD. These groups may also have problems converting carotenoids to retinol.</p> <p>38. It would be helpful if there was a more forceful comment regarding cod liver oil use, given that cod liver oil does contain appreciable amounts of retinol and older women could easily be in a situation of overdosing.</p>	<p>This issue has been addressed in amended report. In communicating risk the Agency will take this into consideration.</p> <p>No action taken. Too specific and out of the scope of the Subgroup.</p> <p>Report amended to include fish liver oils when retinol supplements mentioned.</p>	<p>WCAP</p> <p>WCAP</p> <p>NS/NOS</p>
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