European Food Safety Authority

The EFSA Journal (2008) 873, 1-81

SCIENTIFIC OPINION

Consequences for the consumer of the use of vitamin A in animal nutrition[1]

Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed

(Question No EFSA-Q-2006-121)

Adopted on 19 November 2008

PANEL MEMBERS

Georges Bories, Paul Brantom, Joaquim Brufau de Barberà, Andrew Chesson, Pier Sandro Cocconcelli, Bogdan Debski, Noël Dierick, Jürgen Gropp, Ingrid Halle, Christer Hogstrand, Joop de Knecht, Lubomir Leng, Sven Lindgren, Anne-Katrine Lundebye Haldorsen, Alberto Mantovani, Miklós Mézes, Carlo Nebbia, Walter Rambeck, Guido Rychen, Atte von Wright and Pieter Wester

SUMMARY

The fat soluble vitamin A is required in humans and animals. It is essential for vision, growth differentiation and proliferation of a wide range of epithelial tissues, bone growth, reproduction and embryonic development. Vitamin A is present in the diet as preformed vitamin A (retinol and its esters) and can also be derived in humans and most animal species from dietary carotenoids, mainly ß-carotene. Vitamin A accumulates in the body, particularly in liver, and is toxic at high doses in most species studied. The use of vitamin A as a feed additive is currently authorised under Regulation (EC) No 1831/2003 as nutritional additive with maximum contents for a number of animal categories and types of feedingstuffs.

Two reports, one from the UK's Scientific Advisory Committee on Nutrition (SACN) and the other from the Agence Française de Sécurité Sanitaire des Aliments (AFSSA), both published in 2005, drew attention to the risks of high levels of vitamin A for the consumer resulting from the intake of products of animal origin.

The Commission asked the European Food Safety Authority (EFSA) to review those reports. Should the overall intake exceed the tolerable upper intake level (UL) for vitamin A, EFSA should comment on the benefit of decreasing the maximum permitted levels of addition for vitamin A. In addition, EFSA should also advise on the potential zootechnical implications of lowering the levels of vitamin A intake by food-producing animals. In that respect,

[1] For citation purposes: Scientific Opinion of the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) on a request from the European Commission on the consequences for the consumer of the use of vitamin A in animal nutrition. *The EFSA Journal* (2008) 873, 1-81

© European Food Safety Authority, 2008

consequences for the safety of target animals and the environmental impact should be assessed.

The UL set by SCF (3 000 µg RE from preformed vitamin A day^{-1}) was considered by the Panel on Additives and Products or Substances used in Animal Feed (FEEDAP) as still being appropriate, taking into account the available data. Quantitative correlations between retinol intake and bone health risk justifying the establishment of a lower UL for a specific population subgroup (elderly people) could not be established. A maximum intake of 1 500 µg RE day^{-1} would therefore — until new data indicates the necessity of a re-evaluation — serve as a guidance level (GL) for persons at a greater risk of osteoporosis and bone fracture (particularly postmenopausal women).

The FEEDAP Panel considered four national studies on the intake of vitamin A in adults (three countries) and one in children. The Panel also made a separate calculation on the vitamin A intake of adults based on the food consumption survey within the EPIC project (27 study centres, ten European countries, consumption of relevant food groups, published in 2002).

Only preformed vitamin A is to be considered of safety concern. This is only found in foods of animal origin. Whereas in the period from 1970 to 1990 an increase in liver preformed vitamin A could be observed (mainly for pigs and cattle), a reverse trend seemed to start in the early nineties. Current typical values are 50–150 µg RE g^{-1} liver, with upper values of up to 500 µg, 4–14 µg RE g^{-1} milk fat, 4–9 µg RE g^{-1} egg yolk. Other food sources (meat, kidney and fish flesh) do not contain significant amounts of preformed vitamin A. Losses of vitamin A during food processing are known but difficult to quantify for refinement of vitamin A intake estimations, and could therefore not be taken into account.

Approximately, about half of the intake of total vitamin A in European consumers comes from carotenoids in foodstuffs of plant origin, the other half from preformed vitamin A in foodstuffs of animal origin. The mean intake of preformed vitamin A in the adult population in Europe is estimated between 400 and 1 200 µg RE day^{-1} in men and between 350 and 1 000 µg RE day^{-1} in women. A small proportion of the European population shows an intake of preformed vitamin A above the UL. This proportion is about 1–2 % in Denmark, Germany, the Netherlands, Norway, Sweden and the UK, and about 3–6 % in France, Greece, Italy and Spain. The corresponding GL is exceeded by 2–3 and 8–14 %, respectively.

The main exposure to preformed vitamin A comes from consumption of liver (with about 60–80 % in some Member States) and milk, including all dairy products (with about 45–60 % in others). Despite the uncertainties associated with the assessment of preformed vitamin A intake from liver, it can be concluded that among liver eaters, the consumption of liver as such may lead to daily intakes of 2 800–7 000 µg preformed vitamin A. It is considered highly unlikely that consumers would exceed the UL from the intake of milk and dairy products alone.

It can be concluded that the risk of exceeding the UL (and GL) for preformed vitamin A is predominantly related to liver consumption, but also from the consumption of supplements containing vitamin A.

Preformed vitamin A may raise safety concerns because of its high levels in some foods of animal origin and of individual consumption patterns; therefore, feeding practice should seek to avoid any unnecessary high concentration in those foods.

The following potential maximum contents of vitamin A in feed have been derived for pigs: 16 000 IU vitamin A kg^{-1} for piglets, 6 500 IU vitamin A kg^{-1} for pigs for fattening, 12 000

IU vitamin A for gestating sows and 7 000 IU vitamin A kg^{-1} for lactating sows; for cattle: 25 000 IU vitamin A kg^{-1} for veal calves, 10 000 IU vitamin A kg^{-1} for cattle for fattening and lactating cows, and 20 000 IU vitamin A kg^{-1} for dry cows; and for poultry: 20 000 IU vitamin A kg^{-1} in the first 14 days of life for chickens reared for laying and for fattening and in the first 28 days of life for turkeys for fattening, 10 000 IU vitamin A kg^{-1} for chickens reared for laying and for fattening (after 14 days), for turkeys for fattening (after 28 days), and for laying hens and breeder turkeys. For fish and minor species (other poultry, other ruminants, rabbits and horses), there are insufficient data available to derive maximum contents with the necessary accuracy.

The derived maximum concentrations in feed for food-producing animals will probably not reduce the typical preformed vitamin A concentrations in tissues and products but result in more uniform contents, thus avoiding extreme high values.

The FEEDAP Panel recommends as a measure for the protection of consumers the introduction of revised maximum vitamin A contents for feed for most food-producing animals. The Panel further recommends (i) the limitation of vitamin A in the daily ration by regulating complementary feedingstuffs, (ii) the monitoring of preformed vitamin A in foods of concern after introduction of revised maximum contents and (iii) the extension of advice to consumers to avoid excessive intake of preformed vitamin A.

Key words: vitamin A, preformed vitamin A, retinol, RE (retinol equivalents), intake in humans, toxicity, UL (tolerable upper intake level), GL (guidance level), vitamin A requirement, vitamin A allowance, maximum content, food of animal origin, liver, milk, dairy products, eggs

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY EC

The UK's Scientific Advisory Committee on Nutrition (SACN) issued in 2005 a report entitled "Review of Dietary advice on Vitamin A". The Agence Française de Sécurité Sanitaire des Aliments (AFSSA) also issued a report in 2005 on the evaluation of the animal nutritional requirements for vitamins A, D and E and the risks for animal and consumer health linked to high amounts provided to food-producing animals. Both the UK and the French authorities have forwarded this information to the Commission services for consideration with the request that it should also be submitted to EFSA for examination. The two reports draw attention to the risks of high levels of vitamin A in products of animal origin and formulate several recommendations.

This issue has been discussed on several occasions with the Member States during 2005 and 2006 at the Standing Committee of the Food Chain and Animal Health – Section Animal Nutrition.

The addition of vitamin A is currently authorised under Regulation 1831/2003 on additives in animal nutrition with maximum limits for a number of animal categories and types of feedingstuffs.

TERMS OF REFERENCE AS PROVIDED BY EC

The Commission asks the European Food Safety Authority to review the reports from the UK and France and to take into account any other relevant information.[2] The opinion should also estimate the dietary contribution of vitamin A for European consumers from the various different sources. Should the overall intake exceed the Upper Level, the opinion should comment on the benefit of decreasing the maximum permitted levels of addition for vitamin A as a nutritional additive under Regulation 1831/2003. The fact that the levels of vitamin A addition to foodstuffs are covered by several regulatory schemes (food supplements, foods for special nutritional purposes, food additives, and others) should also be taken into account.

In addition, EFSA opinion should also advise on the potential zootechnical implications of lowering the levels of vitamin A intake by food-producing animals, taking into account all possible sources of vitamin A (added as nutritional additive but also in the form of precursors, natural presence in feedingstuffs, etc…). In the respect the safety for the animals should be assessed and also the environmental impact as is mandatory for the evaluation of all feed additives.

ACKNOWLEDGEMENTS

The European Food Safety Authority wishes to thank Prof. Andrew Renwick and Davide Arcella for their valuable contribution to this opinion. We would also like to thank Dr. Robin Ørnsrud and the following Institutions for their collaboration in the submission of the data requested: Austrian agency for health and food safety GmbH (AGES), Federal Office for food safety (Austria); Service Public Fédéral. Santé Publique, Sécurité de la Chaine Alimentaire et environnement. Direction-Générale Animaux, Végétaux et Alimentation. Service Denrées Alimentaires, Aliments pour animaux et Autres Produits de Consommation (Belgique); Department of Public Health and Nutrition, National Center of Public Health Protection (Bulgaria); Croatian National Institute of Public Health, Nutrition Unit (Croatia); Ministry of Agriculture, Natural Resources and Environment, Department of Agriculture

[2] EFSA reference: FAD-2006-0026

(Cyprus); Centre for the Hygiene of Food Chains, National Institute of Public Health and Central Institute for Supervising and Testing in Agriculture Division of Feedingstuffs (Czech Republic); Bundesministerium für Ernährung, Landwirtschaft und Verbraucherschutz (Deutschland), Danish Plane Directorate (Denmark); Finnish Food Safety Authority Evira (Finland); UCD Agriculture and Food Science Centre, School of Agriculture, Food Science and Veterinary Medicine, University College Dublin (Ireland); National Research Institute for Food and Nutrition (INRAN) (Italy); Centre for Nutrition and Health, National Institute for Public Health and the Environment (the Netherlands); National Food and Nutrition Institute (Poland); Norwegian Institute of Public Health (Norway); Ministry of Agriculture, Directorate-General for Veterinary Services (Portugal); National Food Administration (Sweden); Food Standards Agency (FSA) (UK); FEFAC; FEFANA.

ASSESSMENT

1. Introduction

The fat soluble vitamin A is required in humans and animals. It is essential for vision, growth differentiation and proliferation of a wide range of epithelial tissues, bone growth, reproduction and embryonic development.

Vitamin A is present in the diet as preformed vitamin A (retinol and its esters) and can also be derived in humans and most animal species from dietary carotenoids, mainly ß-carotene. Vitamin A accumulates in the body, particularly in liver (as retinylester), and is toxic at high doses in most species studied.

A more extended review on the functions of Vitamin A and the units used to express vitamin A activity is given in Appendix 1.

In animal nutrition (in the EU), the vitamin A content of feedingstuffs and consequently the definition of requirements is still expressed in international units (IU) and refers only to retinol and its esters.

Sources of total vitamin A in human nutrition are foodstuffs of vegetable origin providing the provitamin A carotenoids and foodstuffs of animal origin providing the preformed vitamin A (retinol, retinylesters). Intake and requirement (recommended daily allowance, RDA) of humans are expressed on the basis of retinol equivalents (RE), which take also into consideration the contribution of certain (provitamin A) carotenoids to the vitamin A supply.

The vitamin A intake which should not be exceeded because of safety concerns is called tolerable upper intake level (UL). Because provitamins A are known not to cause vitamin A toxicity (Tanumihardjo, 2002), reference values for the upper safe intake are expressed in terms of preformed vitamin A (RE) not considering the provitamin A carotenoids.

Population reference intakes (RDA) and UL for Vitamin A, expressed as retinol equivalents (RE) and as established by different scientific bodies, are given in Table 1.

Table 1. **Population reference intakes and tolerable upper intake level**

	RDA [1]		**RDA** [1]		**RDA** [2]		**UL** [3]
Body	SCF, 1993		D-A-CH. 2001 [4]		US, 2001 [5]		SCF/US
Units [6]	µg RE d^{-1} and person		µg RE d^{-1} and person		µg RAE d^{-1} and person		µg RE d^{-1}
Sex	Males	Females	Males	Females	Males	Females	Both
	700	600	1 000	800	900	700	3 000

(1) Recommended daily allowances
(2) Recommended dietary allowances
(3) Tolerable upper intake level
(4) (D-A-CH: German Nutrition Society, Austrian Nutrition Society, Swiss Society for Nutrition Research and Swiss Nutrition Association)
(5) Food and Nutrition Board of the Institute of Medicine
(6) RE (and RAE, see Appendix 1) for RDA's include provitamin A carotenoids, RE in the UL column do not (only preformed vitamin A).

2. Health consequences of human exposure to high dietary doses of vitamin A

The Scientific Committee on Food (SCF), in its opinion on the tolerable upper level intake of preformed vitamin A (retinol and retinylesters; EC, 2002), evaluated the data available at that time and noted that there was a narrow margin between the population reference intake and intakes associated with adverse effects. The derivation of an upper level for the intake of vitamin A considered the teratogenic risk (risk to the developing baby during gestation), hepatotoxicity (which was reported largely in men) and a possible increase in risk of bone fracture (which was reported largely in postmenopausal women). Setting a single upper level was complicated because the different risks relate to different life stages. The tolerable upper intake level was set at 3 000 µg RE day^{-1} of preformed vitamin A for adults, based on the risk to women of child-bearing age. Because alterations of embryogenesis may occur following a single or a small number of doses of vitamin A, for women of child-bearing age the upper level should be compared with intake estimates that reflect short-term rather than long-term exposure. The upper level was about 2.5-fold lower than the lowest daily intake associated with hepatotoxicity during chronic intake. The tolerable upper intake levels for children were based on the adult value with correction for the differences in basal metabolic rate compared to adults (body weight $kg^{0.75}$).

The SCF considered that the upper level may not provide an adequate margin of safety in relation to the possible decrease in bone density and the risk of bone fracture, and that it would be advisable that postmenopausal women, who are at greater risk of osteoporosis and bone fracture, should restrict their intake of preformed vitamin A to 1 500 µg RE day^{-1}. The SCF noted that this recommendation should be considered in the light of the fact that the 97.5th percentile intake for adults in most of Europe is greater than 3 000 µg RE day^{-1} (see Table 2), and that the only dietary source is food of animal origin (liver being the major contributor). These relations give rise to large inter-individual and temporal variations in intake.

Table 2. **Daily intake (µg day^{-1}) of preformed vitamin A (retinol and retinylesters) in EU countries (adapted from SCF, 2002)**

	Population	N	Method	Supplements	Mean	97.5 %
Austria [(a)]	men + women	2488	24h recall	Not defined	1120	4230
Germany [(b)]	men	854	Not defined	Not defined	890	4220
	women	1134		Not defined	810	3760
Italy [(c)]	household	1978	7-day record	+	759	4377
Netherlands [(d)]	household	5958	2-day record	-	891	3230
UK [(e)]	men	1087	7-day record	-	1226	6564
	women	1110		-	1058	5698
	men	1087		+	1277	6671
	women	1110		+	1133	5779

[(a)] Elmadfa et al. (1998)
[(b)] Heseker et al. (1992) - median not mean value reported as preformed vitamin A
[(c)] Turrini (INRAN, 2001) – mean as preformed vitamin A
[(d)] Hülshof and Kruizinga (1999)
[(e)] Gregory et al. (1990)

Two recent reports ('Review of Dietary Advice on Vitamin A' from the UK Scientific Advisory Committee on Nutrition (SACN, 2005) and 'Evaluation des besoins nutritionnels des animaux en vitamines A, D et E ainsi que des risques pour la santé animale et la santé du consommateur, lies à des apports élevés chez les animaux producteurs d'aliments' from the French Food Safety Authority (AFSSA, 2005)) have reconsidered the safety of vitamin A

based on further publications in those key areas and have provided more guidance on the interpretation of the tolerable upper intake level.

The two following sections (2.1. and 2.2.) summarise those reports.

2.1. SACN Review of Dietary Advice on Vitamin A

The UK Scientific Advisory Committee on Nutrition undertook a Review of Dietary Advice on Vitamin A (SACN, 2005) in the context of the guidance level (GL) of 1 500 µg RE day^{-1} established by the UK Expert Group on Vitamins and Minerals. The report included a number of sections important to the present evaluation:

1. Review of the evidence on retinol and bone health;
2. Dietary intakes of retinol and provitamin A carotenoids in Great Britain;
3. Retinol content of liver and animal feeding practices;
4. The potential impact of dietary change to reduce intakes of retinol.

Only the updated information on bone health is summarised below. The other information is introduced in the relevant parts of this opinion.

2.1.1. Review of the evidence on retinol and bone health

This issue is critical since the SCF opinion (EC, 2002) recognised that the findings on bone density and the risk of fracture were reported at lower daily intakes than other adverse effects, but that the data available at that time did not provide sufficient evidence of causality and were not appropriate for establishing a tolerable upper intake level. The SCF recommended that the possible link between bone density, the risk of fracture and vitamin A intake should be reviewed when further data would become available. The data on bone fractures considered in the SCF opinion were from Sowers and Wallace (1990), Melhus et al. (1998), Feskanich et al. (2002), while the studies on bone metabolism and/or bone mineral density were from Freudenheim et al. (1986), Sowers and Wallace (1990), Houtkooper et al. (1995), Ballew et al. (2001), Kawahara et al. (2002).

The SACN report included additional studies on fracture risk by Michaelsson et al. (2003) and Lim et al. (2004). Michaelsson et al. (2003) investigated the relationship between serum retinol, retinol intakes and the risk of fracture in 2047 men aged 49–51 years. The overall fracture rate showed a non-linear increase between quintiles of serum retinol with the greatest effect at the highest quintile. However, no relationship between retinol intake the risk of fracture was observed in individuals where data were available. This study may add to evidence supporting a general link between retinol and the risk of bone fracture, which had been reported previously based on dietary intakes (Melhus et al., 1998; Feskanich et al., 2002). Lim et al. (2004) studied the relationship between the risk of fractures and the intake of retinol and total vitamin A in 34703 postmenopausal women aged 55–69 years. A small but non-significant increase in fracture risk was reported and there was no intake-response relationship. Thus more recent studies have not convincingly confirmed or rejected the possibility of a risk of fracture at high dietary intakes of vitamin A. Out of a total of five studies, three of which were based on very large cohorts, two found a significant relationship with dietary intake and one with serum retinol.

The studies on bone mineral density that were considered by SACN but not in the SCF opinion were from Sigurdsson et al. (2001) and Promislow et al. (2002). Sigurdsson et al. (2001) reported no relationship between dietary intake of total vitamin A and bone mineral

density in 232 Icelandic women aged 70 years. Promislow et al. (2002) studied the relationship between retinol intake and bone mineral density in 570 women and 388 men aged 55–92 years. Different findings were reported for different groups, and multivariate analysis showed a negative association between bone mineral density and retinol intake in women taking supplements but a positive association for women not taking supplements.

SACN concluded that the available data since the EVM (Expert Group on Vitamins and Minerals) report (FSA, 2003), and therefore since the SCF report, does not strengthen evidence for an association between retinol intake and bone health.

2.2. AFSSA Report on Vitamin A

The Agence Française de Sécurité Sanitaire des Aliments (AFSSA) report (2005) provided information on dietary sources of vitamin A and the background on intakes of farmed animals. A portion of the report concerns the potential adverse health effects of excessive intakes by humans and summarises much of the data analysed in the SCF opinion of 2002.

An important part of the report is on the levels of vitamin A in the liver and tissues of farm animals (Appendix 11); those data have been incorporated into the relevant sections of the present opinion.

2.3. More recent reviews

A review of Ribaya-Mercado and Blumberg (2007) on the potential risk of vitamin A on osteoporosis and bone fracture was based on nine observational studies (between 1990 and 2005), of which two showed adverse relations, five little or no relation and two a certain protective relation. This study summarises: 'while some data suggest that adverse impact of vitamin A or high serum retinol status on bone health, the results in literature are inconsistent and firm conclusions cannot be drawn from these relationships. Further confounding the results are the colinearity of vitamin A intake with intake of other nutrients that influence bone health and differences between studies in skeletal sites examined, menopausal status, and variables used for adjusting estimates.'

2.4. Conclusions

The reviews undertaken by SACN and AFSSA (and those of Ribaya-Mercado and Blumberg, 2007) showed that the data available since the SCF opinion would not substantially alter the risk assessment for preformed vitamin A.

Consequently, the current opinion of the FEEDAP Panel on the impact of the use of vitamin A in animal nutrition for the consumer refers to the UL set by the SCF (3 000 µg RE from preformed vitamin A day^{-1}) and to the specific advice of SCF for persons (i.e. post-menopausal women) at greater risk of osteoporosis and bone fracture (restriction of the intake of preformed vitamin A to 1 500 µg RE day^{-1}).

3. Current findings on vitamin A intake in humans

The Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Preformed Vitamin A (retinol and retinylesters) (EC, 2002) stated that the intakes of the general population in developed countries met the population reference intakes (recommended daily allowance) of 700 µg day^{-1} for men and 600 µg day^{-1} for women. Intake

data for various European countries (Table 2) indicated that the mean intakes were well above the population reference intakes.

3.1. Estimation of vitamin A intake in Great Britain from the SACN report

Retinol means preformed vitamin A. The SACN (2005) analysis of dietary intakes of retinol and provitamin A carotenoids in Great Britain used data from the 2000/2001 National Diet and Nutrition Survey (NDNS) of 19–64-year-old adults (Henderson et al., 2003), and the 1994/1995 NDNS of those over 65 years (Finch et al., 1998) were evaluated. The mean values are summarised in Table 3.

Table 3. **Average vitamin A intake in the two cohorts of the SACN report**

Study	**NDNS 2001**		**NDNS 1994/5**	
Age	19–64 years		> 65 years	
Sex	Man	Woman	Man	Woman
Total vitamin A (µg RE day^{-1})	1 018	799	1 262	1 076
Retinol (µg RE day^{-1})	674	472	937	805

Liver was identified as a major source of preformed vitamin A in the UK and accounted for an average of 21–46 % of total retinol intake in different groups, but the consumption was unevenly distributed across the population. Another important source is the ingestion of supplements, such as fish liver oils, which accounted for 10–26 % of retinol intake in different groups. There was a wide range of retinol intakes within each group analysed and the distribution of intakes was highly skewed. In the age range of 19–64 years, 9 % of men and 4 % of women had intakes of more than 1 500 µg day^{-1}, and liver was the main source in those individuals.

All individuals with intakes > 1 500 µg day^{-1} consumed liver and/or supplements, and liver accounted for > 70 % of the total retinol intakes in those individuals. The average retinol intake by male liver consumers was 2 540 µg day^{-1} with 2 061 µg day^{-1} from liver; the average retinol intake by female liver consumers was 1 920 µg day^{-1} with 1 514 µg day^{-1} from liver. A higher percentage of elderly men (11 %) and women (10 %) had intakes > 1 500 µg day^{-1}, with almost 80 % of those who consumed liver having intakes > 1 500 µg day^{-1}.

A trend analysis showed that retinol intakes have decreased in the recent years, largely due to the reduced consumption of liver and partly to the decrease in retinol content in animal liver between 1991 and 2002. The percentage decreases in retinol contents of calf, chicken, lamb, ox and pig liver over this period were 37, 14, 13, 14 and 1 % respectively.

The SACN review concluded that the limited strength of the association between retinol intake and effects on bone did not warrant changes to the dietary advice for all consumers, but as a precaution regular consumers of liver should not increase their intake or take retinol supplements, such as fish liver oil. In addition, those at increased risk of osteoporosis should restrict their intakes to less than 1 500 µg day^{-1}, advice similar to that given by the SCF. The advice that pregnant women or those planning to become pregnant should not consume liver, liver products or supplements containing retinol was restated.

3.1.1. Potential impact of dietary changes on vitamin A intake

The SACN review analysed the potential impact of dietary changes to reduce intakes of retinol. A modelling exercise was undertaken to explore the impact of an advice not to exceed an intake of 1 500 µg retinol day^{-1} by changing the consumption behaviour or by reducing liver vitamin A content. Details on the scenarios and the modelling are described in Appendix 2.

The SACN conclusions of the modelling were that:

- A 25 % reduction in liver retinol content made little or no difference to the proportion of the population with intakes > 1 500 µg day^{-1};
- A decrease in liver consumption to 25 g day^{-1} reduced the proportion with intakes > 1 500 µg day^{-1} to approximately 3 % of the population;
- Complete removal of liver from the diet reduced the proportion with intakes > 1 500 µg day^{-1} to approximately 2 % of the population;
- Complete removal of retinol from supplements reduced the proportion with intakes > 1 500 µg day^{-1} to 2 % and 6 % in women and men aged 19–64 years and about 8 % in those aged 65 or more. This scenario increased the proportion with intakes below the LRNI (Lower Reference Nutrient Intake) by about 2 % to about 8 % in 19–64 year olds but did not influence the % in the elderly;
- Complete removal of retinol from both liver and supplements reduced the proportion in both age groups with intakes > 1 500 µg day^{-1} to 0 %. The influence on individuals with low intakes was similar to that produced by the elimination of retinol from supplements only;
- None of those scenarios influenced the intakes of the other essential nutrients investigated.

The necessity for and the levels of overages, in both animal feeds and human supplements, should be reconsidered. Consideration should be given to reducing the levels of vitamin A in animal feeds and in human supplements. Reducing the levels in animal feeds would require the evaluation of the impact on animal welfare and productivity.

3.2. Estimation of vitamin A intake in Germany

The (German) NVS II study, based on 15 371 participants aged between 14 and 80 years, was performed between November 2005 and end of December 2006; it was published in May 2008. Details on the methods are given in Appendix 3.

3.2.1. Results

The total intake of vitamin A and retinol is given in Table 4, indicating the mean values plus standard error. The 5^{th}, 10^{th}, 25^{th}, 50^{th}, 75^{th}, 90^{th} and 95^{th} percentiles and age related subgroups can be seen in Appendix 3, Tables A3.1 and A3.2.

Table 4. **Average vitamin A intake in German NVS II study report***

Sex	Man		Woman	
	Mean	SE	Mean	SE
Total vitamin A (µg RE day^{-1})	2 100	20	1 800	10
Preformed vitamin A (µg RE day^{-1})	1 000	10	600	10

* Units in the report are milligrams which were transformed into micrograms to facilitate comparisons.

The median for total vitamin A is lower than the mean, amounting to 1 800 µg for men and 1 500 µg day^{-1} for women. The mean intake of preformed vitamin A in the age groups 35–50, 51–64 and 65–80 years did not differ in men and women. The main sources for total vitamin A are carotenoids from non-animal derived food. These include vegetables and dishes based on vegetables (also soups and stews), fruits and juices (see Appendix 3, Figure A3.1.). Foods of animal origin (meat (including offal), meat dishes, sausages, milk and dairy products, and other animal fat) provide about 48 % of preformed vitamin A in men and about 33 % in women.

The 95th percentile of preformed vitamin A intake in men was near to the UL (3 000 µg day^{-1}) and in women only at about two thirds of the UL. The data allow also to conclude that more than 10 % (but less than 25 %) of men and more than 5 % (but less than 10 %) of women have a preformed vitamin A intake > 1 500 µg day^{-1} (Table A3.2).

It should be noted that the above data (see Table 4) refer to the average consumers. Data on liver (or other retinol-rich food) consumers are not available from this study.

3.3. Estimation of vitamin A intake in a British low income population

The recent Low Income Diet and Nutrition Survey (LIDNS) was carried out from November 2003 to January 2005. The sample size was 3728 individuals with complete records. Details on the methods are given in Appendix 4 as well as data of different age groups and the 97.5th percentile of the mean.

The females of all age groups consumed less total vitamin A and preformed vitamin A (Table 5) than the males in the corresponding age groups. The average vitamin A intake increased with age in both males and females, from 625 µg RE day^{-1} in males and 568 µg RE day^{-1} in females in the 11–18 years age group to around 1 200 µg RE day^{-1} in elderly men and about 1 100 µg day^{-1} in elderly women (Table A4.1.).

Table 5. **Average vitamin A intake in LIDNS study report (selected age groups)**

Sex	Man				Woman			
Age group (years)	50–64		> 65		50–64		> 65	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Total vitamin A (µg RE day^{-1})	1 342	2 089	1 114	1 475	982	1 363	1 096	1 484
Preformed vitamin A (µg RE day^{-1})	852	1 979	661	1 398	498	1 262	620	1 401

Such trend was not obvious among high intake males (97.5th percentile) of vitamin A. In contrast to males, there was a positive trend among the high intake females of increasing amounts of vitamin A consumed with increasing age (Table A4.1.).

The average intake of preformed vitamin A (Table 5, Table A4.2.) for all age classes of both males and females is considerably below the UL (18 and 13 % of the UL for males and females, respectively). Considering the high intake of preformed vitamin A, three values (males, 2–10, 11–18 and 50–64 years old) appear very different from the rest; no explanation is given in the report hence it is difficult to ascertain if those differences are real or data anomalies. The intake of preformed vitamin A in more than 97.5 % of all men and women between 19–49 years of age is below the UL. In the age group > 65, about 70 % of men and more than 80 % of women have an intake of preformed vitamin A below the UL.

Among people with average vitamin A intake of all age groups, animal products contribute to 36–47 % of the intake of total vitamin A (Appendix 4, Table A4.3). Cheese and other milk products are the main animal sources of vitamin A; combined, those contribute to 36 % (females > 65 years) to 61 % (males 2–18 years) of the intake of total vitamin A from animal products. Vitamin A from liver and other offal products in the average vitamin A consumer is only of particular importance in people over 50 years old, where consumption of such products is responsible for 10–17 % of total vitamin A intake from animal products. The LIDNS report does not present data on sources of vitamin A specifically among high consumers. The sources of vitamin A from provitamin A carotenoids can be seen in Appendix 4 (Tables 4A.3 and 4A.4).

3.4. Estimation of vitamin A intake in German children and adolescents

The EsKiMo study (Ernährungsstudie als KiGGS (Kinder- und Jugendgesundheitssurvey)-Modul) consists of 2506 participants (49.8 % boys, 50.2 % girls). Those include 1234 children between 6 and 11 years old and 1272 youths between 12 and 17 years old. Approximately 100 boys and 100 girls per age group of each year were included. The data were collected between January 2006 and the end of December 2006.

Details on the method and more extended data are given in Appendix 5.

The intake of boys and girls aged 6–11 years is 1.0 and 0.9 mg RE day^{-1} and of boys and girls aged 12–17 years 1.6 and 1.5 mg RE day^{-1}, respectively (Appendix 5, Table A5.1).

Children and youths obtain only about one third of the total vitamin A from food of animal origin (preformed vitamin A): boys between 6 to 11 years, 33 %; girls between 6 to 11 years old, 32 %; boys between 12 to 17 years, 36 %, and; girls between 12 to 17 years, 30 %). Sausages (and meat and offal) contribute approximately to the same extent as dairy products (including milk and cheese) to the intake of preformed vitamin A (Appendix 5, Figure A5.1.).

3.5. Estimation of preformed vitamin A intake in the Netherlands

Kloosterman and Ocké published in 2007 a calculation of the human intake of preformed vitamin A in the Netherlands, based on a National Food Consumption Survey from 1997-1998. Details are described in Appendix 6.

The median for preformed vitamin A intake from all sources in the adult population (2155 men and 2568 women) was estimated to be 528 and 383 µg RE day^{-1} in men and women, respectively. The 90^{th} percentile in men and women equalled 1 761 and 1 189 µg RE day^{-1}, respectively.

The percentage of liver consumers in adults amounted to 3.5 and 1.9 % of all men and women, respectively. The median consumption of preformed vitamin A from liver alone was

2 366 and 1 419 µg RE day^{-1} for men and women, respectively. Most of the liver consumed was from pork.

The percentage of consumers of 'pâté de foie de porc' was 23.7 and 18.7 % in men and women, respectively. This corresponds to the second highest source of preformed vitamin A intake; those individuals received a median of 880 and 635 µg RE day^{-1} of preformed vitamin A from 'pâté de foie de porc' alone.

The percentage of consumers of total dairy products and of cheese was 92 and 79 % for adult men and 93 and 81 % for adult women, respectively. From those products, the individuals received a median of 61 and 73 in men and 49 and 65 µg RE day^{-1} in women, respectively.

Egg consumption (about 50 % of adult consumers) resulted in an intake of 48 µg RE preformed vitamin A day^{-1} without differences between men and women.

3.6. Estimation of preformed vitamin A intake based on a probabilistic model

The FEEDAP Panel made a separate calculation based on the food consumption survey carried out within the European Prospective Investigation into Cancer and Nutrition (EPIC) project, which offers the opportunity to study the diversity of food habits in Europe since it includes 35 955 subjects (22 924 women and 13 031 men), who participated in the EPIC calibration study between 1995 and 1998 (except Norway: 1999–2000), from 27 study centres in ten European countries (France, Italy, Spain, Greece, the Netherlands, the United Kingdom, Germany, Denmark, Sweden, Norway). The age of the participants ranged from 35 to 74 years old at recruitment. Further details are described in Appendix 7. Country-specific data of the concentrations of preformed vitamin A in foodstuffs (see Section 4 and Appendix 7) were used.

The main data resulting from that probabilistic calculation are summarised in Table 6.

Table 6. **Intake estimates of preformed vitamin A (µg RE day^{-1})**

	Men			Women		
	N	Mean [1]	95th percentile [2]	N	Mean [1]	95th percentile [2]
Denmark	1 923	441	1 361	1 995	401	1 318
France	.	.	.	4 639	992	3 445
Germany	2 268	561	1 685	2 150	481	1 494
Greece	1 312	973	3 556	1 374	492	1 683
Italy	1 444	1 008	3 699	2 512	623	2 222
Norway				1 798	433	1 363
Spain	1 777	1 220	4 346	1 443	839	2 904
Sweden	2 765	390	1 147	3 285	345	1 077
The Netherlands	1 024	438	1 397	2 960	343	1 063
United Kingdom	404	520	1 675	571	395	1 257

[1] The average intake of vitamin A was estimated by summing the average intakes from all sources.
[2] The high intake of vitamin A was estimated by summing the high intakes from all sources.

With the caveat that the intake of preformed vitamin A was estimated using aggregated food consumption data, the following general conclusions may be drawn:

- Italy, Greece and Spain present an average intake for men around 1 000 µg RE day^{-1}, which is almost the double of that for the other countries considered within the EPIC study, whilst the high intake of preformed vitamin A was 19–45 % higher than the UL.
- Average intake of preformed vitamin A in women is lower than 1 000 µg RE day^{-1} for all countries, with France and Spain presenting the highest figures. For the high intake group the UL, was only exceeded in France.

The percentages of the population with an estimated intake of preformed vitamin A above the UL (3 000 µg RE day^{-1}) and the GL for persons at specific risk (1 500 µg RE day^{-1}) were estimated by means of a probabilistic model. Within this model, consumption levels for all the above-mentioned food products were simulated using a lognormal distribution with mean and standard deviation taken from the EPIC study.

In all countries, there was a certain proportion of the population with a retinol intake above the UL. Two groups of countries could be identified, one (Denmark, Germany, the Netherlands, Norway, UK and Sweden) with a population percentage of 1–2 above the UL and the other (France, Greece, Italy and Spain) with a population percentage of 3–6 above the UL.

The percentages above the GL for persons at specific risk follow a similar pattern, with the first group showing 2–3 % of the population being above and the second group with 8–14 % of the population.

The contribution of the food of animal origin groups to the intake of preformed vitamin A for average and high consumers in Germany and Italy is shown in Figure 1a and 1b, respectively. Both countries are taken because of typical differences. In Germany (Figure 1a), only about two fifth of the retinol intake comes from meat and meat products (including offal), whereas in Italy (Figure 1b) the same food group represents about three quarters of retinol intake. In Germany, more than half of the dietary retinol originates from milk and milk products (including cheese), whereas in Italy it is less than one quarter. Those relations are not essentially different for average and high consumers.

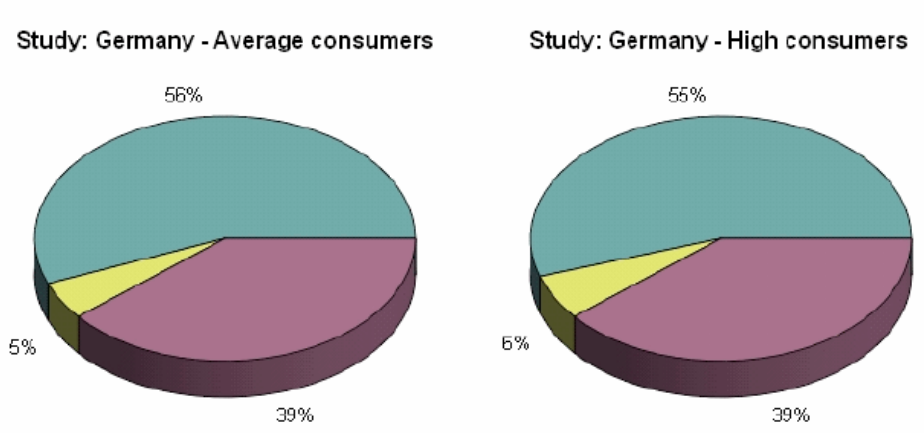


Figure 1a. **Contribution of major food sources to retinol intake in Germany**

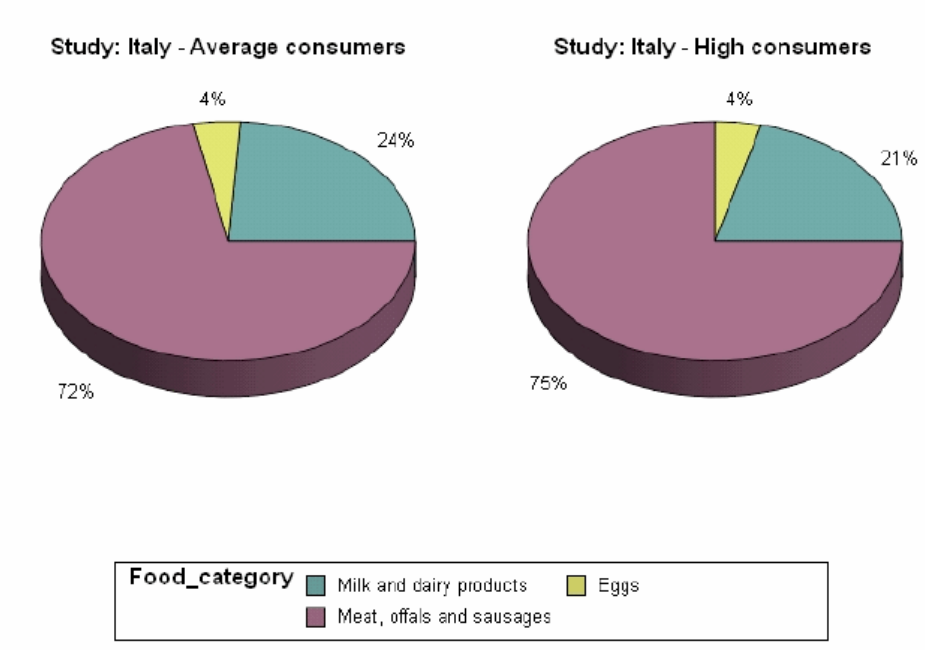


Figure 1b. **Contribution of major food sources to retinol intake in Italy**

The details showing all the data for the other countries are given in Tables A7.1 and A7.2 (Appendix 7). In France, Greece and Spain, liver (estimated as 90 % of offal) is the predominant source of preformed vitamin A (Table A7.1, Appendix 7), as in Italy, whereas in Norway, Sweden and the Netherlands milk, butter and dairy products show the highest proportion of the intake of preformed vitamin A, as in Germany. A considerable proportion of the total intake for the average consumers of preformed vitamin A from eggs is calculated for Denmark (7–11 %), Norway (10 %), Sweden (7–12 %) and the Netherlands (5–11 %). In all countries, meat and fatty fish are only minor sources of preformed vitamin A (1–3 %).

The predominant role of liver on the intake of preformed vitamin A is confirmed by the figures calculated for high consumers in some countries (France, Greece, Italy and Spain), being somewhat higher than that for the average consumer (Table A7.2., Appendix 7). This increase in the relative contribution to the total intake of preformed vitamin A is mainly at the expense of milk, butter and dairy products. The role of eggs in the supply of preformed vitamin A became more significant in high consumers in countries which showed already a significant contribution of eggs to the intake of preformed vitamin A for the average consumer.

3.7. Estimation of preformed vitamin A intake from liver consumption

Data from three studies (Italy: Turrini et al., 2001; Germany: Mensink and Beitz, 2004; and Ireland: Harrington et al., 2001) on the consumption among adults of liver of different origins (for the total population and consumers only and for average and high consumers) were used by the FEEDAP Panel to estimate the intake of preformed vitamin A. Details can be found in Appendix 8.

Table A8.1 shows typical differences of the sources of liver consumed in the three countries considered. Among the different sources of liver identified in the studies, beef liver and pork

liver from liver products are predominantly consumed in Germany, whereas calf and lamb liver are mainly consumed in Italy and Ireland, respectively.

The percentage of liver consumers in Germany ranges from 0.04 (pork and lamb liver) to 4.7 (beef liver), 51 % of the population results to consume pork liver from liver products. The corresponding figures in Italy are 0 (beef liver) to 5.2 (calf liver), in Ireland 0 (beef liver) to 2.9 (lamb liver). On average for the total population, the consumption of pork liver from liver products in Germany is estimated to result in a retinol intake of 221 µg RE day^{-1}, that of calf liver in Italy to 368 and that of lamb liver in Ireland to 81 µg RE day^{-1}.

Among consumers only, the consumption of pork liver (2 out of 4030 persons) and pork liver from liver products (2044 out of 4030 persons) in Germany results in an average retinol intake of 4 695 and 435 µg RE day^{-1}, that of calf (80 out of 1544 persons) and of pork liver (11 out of 1544 persons), in Italy to 7 015 and 3 444 µg RE day^{-1}, that of lamb liver (40 out of 1379 persons) in Ireland to 2 796 µg RE day^{-1}. With the exception of pork liver from liver products in Germany, conclusions on high consumers (95^{th} percentile) among consumers only (Table A8.1) are not possible due to the low number of subjects involved.

3.8. Estimation of vitamin A intake of persons taking supplements

Three studies (Sichert-Hellert et al., 2006 (see Appendix 9), EsKiMo study (see Section 3.4, and Appendix 5), NVS II study (see Section 3.2. and Appendix 3)) allow an estimation of the vitamin A intake of German persons taking supplements.

In German children and adolescents (2–18 years of age), the intake of vitamin A from supplements exceeded the tolerable upper intake level in most age groups and was most pronounced in the two to three years old group (32 % above the UL). The frequency of intake above the UL decreased with age (Sichert-Hellert et al., 2006).

The EsKiMo study showed that in the age group of 6 to 11 years old only 7.5 % of the boys and 8.7 % of the girls took supplements containing mainly minerals and vitamin D, E, C, folate and niacin, but no vitamin A. In the age group of 12 to 17 years, supplements were taken more frequently (19.6 % of the boys and 19.7 % of the girls). But again, vitamin A does not play a role in the supplements.

In the NVS II study, supplements were taken by 27.6 % (4261 persons, of which 1696 men and 2565 women) of adults; people above 35 years of age took supplements more frequently than younger ones. Seventeen percent of the male supplement takers and 16 % of the female supplement takers used (also) vitamin A-containing supplements. The average daily intake of those vitamin A supplement takers amounted to 900 µg in men and 1 200 µg retinol in women, which corresponds approximately to the quantity of retinol calculated for the average of all male participants and twice the one calculated for women.

In the supplement takers of the LIDNS (11 % of men and 17 % of women), supplements contributed to 55 and 52 % of the preformed vitamin A intake, respectively (see Table A9.1, Appendix 9). The total retinol intake in those groups was at least twice as high as for the non-supplement takers.

3.9. Conclusions

Limited data is available on the intake of total and preformed vitamin A by European consumers. There are considerable differences among the studies that exist. Those

differences are due to variable consumption patterns in the countries and methods used for the collection and analysis of data.

3.9.1. Total Vitamin A intake

The mean total vitamin A intake in the adult population in Europe is estimated between 1000 and 2100 µg RE day^{-1} in men and between 800 and 2000 µg RE day^{-1} in women. The median is lower than the mean indicating a skewed distribution of intakes, which arises from the non-uniform distribution of retinol equivalents in the food supply, and very high retinol intakes of consumers of foods such as liver.

Children and adolescents (only German population) show a mean intake of total vitamin A expectedly lower (about half to three quarters, respectively) than adults.

Differences between genders are consistent in all studies (countries) showing a 5 to 20 % lower total vitamin A intake for females.

The higher vitamin A intake of elderly compared to adults observed in one study was not confirmed by other studies. Where such differences are observed, they are likely to be the result of typical (traditional, social, geographical) food habits.

High consumers (about 5 % of the population) have a total vitamin A intake which is about twice as high as the mean.

The data on total vitamin A intake are without concern with regards to the UL for both adults and children.

3.9.2. Preformed Vitamin A intake

Children and adolescents consume about two thirds of their total vitamin A intake as provitamin A carotenoids, which are not of toxicological relevance. Therefore, this population subgroup will not be further considered.

Preformed vitamin A contributes for adult men and women in Germany to about 48 and 33 % of total vitamin A, respectively, and to about 60 % in the UK. Data for elderly people are in the same range (about 45 % in Germany and 55–75 % in the UK).

The mean intake of preformed vitamin A in the adult population in Europe is estimated between 400 and 1200 µg RE day^{-1} in men and between 350 and 1000 µg RE day^{-1} in women. Greece, Italy and Spain (and Germany in one study) present an average preformed vitamin A intake for men of around 1000 µg RE day^{-1}, which is almost double of that for the other countries considered in the FEEDAP Panel calculation. In those three countries, the UL was exceeded in the high consumer group (5 % of the population) by 19–45 %. For women, France and Spain present the highest figures (800–1000 µg RE day^{-1}); the UL was only exceeded in the French high intake group.

A certain proportion of the population with a retinol intake above the UL can be assumed for all countries. Two groups of countries could be identified, one (Denmark, Germany, the Netherlands, Norway, Sweden and the UK) with 1–2 % of the population above the UL and the other (France, Greece, Italy and Spain) with 3–6 %. The percentages above the GL for persons at specific risk follow a similar pattern, with the first group showing 2–3 % and the second group 8–14 % of the population above the GL.

Main retinol sources are liver and milk (including all dairy products). Liver is the predominant source of preformed vitamin A (about 60–80 %) in France, Greece, Italy and

Spain. Milk, butter and other dairy products represent the highest proportion (45–60 %) of preformed vitamin A in Germany, the Netherlands, Norway and Sweden. A lower contribution comes from eggs (about 10 % in Denmark, the Netherlands, Norway and Sweden). In all countries, meat and fatty fish are insignificant sources of preformed vitamin A. This picture is not essentially different in high consumers.

3.9.3. Preformed vitamin A intake from liver

The role of liver in the preformed vitamin A supply to the individual consumer is difficult to estimate. Average figures may be of limited value since liver as such is only consumed by a low proportion of the population (0.1–5 % for liver from different animal categories in Germany, Italy, Ireland and the Netherlands). Information on liver products is incomplete; the few available figures (only from the Netherlands and Germany) indicate a range of 22 to 50 % of the population consuming liver products. Those factors result in additional uncertainties of the estimates.

Considering those caveats, it can be concluded that among liver eaters, the consumption of liver as such may lead to daily intakes of 2 800–7 000 µg preformed vitamin A.

3.9.4. Preformed vitamin A intake from supplements

Persons taking vitamin A containing supplements (5 and 14 % of two cohorts) may add to the dietary supply of preformed vitamin A another 700–1 200 µg day^{-1}.

4. Preformed Vitamin A in foodstuffs of animal origin

Vitamin A is mainly expected to be found in liver, and to a lesser extent in the animal products milk and eggs. Due to the role of the kidney in retinol recycling and the widespread occurrence of retinol in extrahepatic cells (see Appendix 1), it can also be expected in meat and kidney.

4.1. Vitamin A concentration in liver

Retinylesters are unevenly distributed in the liver (of pigs and cattle). Biopsies from different localisations of pig liver showed differences in retinylester concentrations up to 10 % (Schöne, 1981; Flachowsky et al., 1993). Different localisations of liver samples are therefore a source of variation.

4.1.1. Pig liver

Between 1960 and 1993, the vitamin A content of pig liver increased markedly, from about 30 to more than 150 µg RE g^{-1} liver, as shown in studies of Scotter et al. (1992) for the UK and Schmidt (1973) and Schindler et al. (1987) for Germany. Danish data for the time period from 1990 to 1997 showed a decrease from 150 µg vitamin A g^{-1} liver to 121 µg in 1993 and to 109 µg g^{-1} liver in 1995, without further change to 1997 (112 µg RE g^{-1} liver, range 62–213 µg RE).

Howells and Livesey (1998) analysed 133 pig liver samples (fresh, frozen, imported, home-produced) collected between 1992 and 1993 in the UK for vitamin A. The mean value was 174 ± 118 µg RE g^{-1} liver.

Recent data show close average values between France with 104 ± 56 µg RE g^{-1} liver (range 31– 279, n = 24) and Austria with 115 µg vitamin A g^{-1} liver (range 65–189, n = 18) (French monitoring plan 2002, see AFSSA 2005; Majchrzak et al., 2006). Recent food composition tables show 113 µg vitamin A g^{-1} for the Netherlands, 141 µg vitamin A g^{-1} (range 30–520) for Denmark, 236 µg vitamin A g^{-1} for Norway and 360 µg vitamin A g^{-1} for Germany (NEVO, 2006; Danish Food Composition Databank, 2005; Norwegian Food Composition Table, 2006; Souci et al., 2000).

4.1.2. Calf liver

The average vitamin A content of calf liver samples varied in some European countries between 50 and 530 µg RE g^{-1} (published between 1974 and 2002 in Belgium, Denmark, France, Germany, Italy, the Netherlands, Spain, Switzerland and the UK by McCance and Widdowson, 1991 and 2002; Howells and Livesey, 1998; Souci et al., 2000; Schindler et al., 1987, and; data provided by FEFANA collected in 1989).

Howells and Livesey (1998) analysed vitamin A contents in 42 liver samples (fresh, frozen, imported and home-produced) collected between 1992 and 1993 in the UK and found a mean value of 188 ± 125 µg RE g^{-1} liver.

In France, 58 veal liver samples showed a mean value of 363 µg RE g^{-1} with a range of 14 to 1 136 µg RE g^{-1} liver (1991, see AFSSA 2005). More recent data indicate a sharp decline; showing mean values of 98 ± 84 µg vitamin A g^{-1} liver of suckling calves (n = 21) and 135 ± 60 µg vitamin A g^{-1} liver of veal calves (n = 17; French monitoring plan, 2002, see AFSSA, 2005). Danish surveys found in 1990, 1995 and 1999 mean vitamin A concentrations in calf liver (calf liver from cattle < two years old) of 103, 76 and 48 µg vitamin A g^{-1}, respectively. Vitamin A in calf liver from the Austrian dataset was 20 ± 5.5 µg RE g^{-1} liver (six farms, three samples per farm, age of the animals 2.5 to five months; Majchrzak et al., 2006). Thus there is some evidence that the vitamin A content of calf liver has decreased in the last decades.

4.1.3. Beef liver

For bovine liver, the mean vitamin A content in European countries showed a range between 60 and 370 µg RE g^{-1} (published between 1974 and 2002 in Belgium, Denmark, Finland, France, Germany, Italy, the Netherlands, Norway, Portugal, Switzerland and the UK by McCance and Widdowson, 1991 and 2002; Howells and Livesey, 1998; Souci et al., 2000; Schindler et al., 1987; Norwegian Food Composition Table, 2006, and; provided by FEFANA collected in 1989).

An increase in liver vitamin A of cattle from 85 to 200 µg vitamin A g^{-1} was observed between 1960 and 1990 in the UK (Scotter et al., 1992). Howells and Livesey (1998) analysed 121 samples (fresh, frozen, imported and home-produced) collected between 1992 and 1993 in the UK and found a mean value of 142 ± 110 µg RE g^{-1} liver. A more complex pattern was reported from Denmark. The mean value in 1990 was 223 µg vitamin A g^{-1} ox liver and 155 µg vitamin A g^{-1} in 1992, whereas in 1995 the average was 320 µg vitamin A g^{-1} ox liver (range 190–545 µg vitamin A g^{-1}). Most recent Danish data show 156 µg RE g^{-1} ox liver.

Recent French data for bovine liver (heifers, n = 18) show an average of 64 ± 65 µg vitamin A g^{-1} (French monitoring plan, 2002, see AFSSA, 2005). The large variation may reflect different RE sources (β-carotene vs. synthetic vitamin A). Austrian data from six small

structured farms give the average vitamin A content of cattle liver with 41 ± 17 µg RE g^{-1}. Two out of six farms did reportedly not use supplemental vitamin A (Majchrzak et al., 2006).

The intake of ß-carotene leads to an increase of liver vitamin A. Cattle fed on pasture only can show vitamin A concentrations in the liver exceeding 150 µg RE g^{-1} (Landes, 1994). Daily doses of less than 40 µg ß-carotene kg^{-1} bw do not influence liver vitamin A. Dosages of about 100 µg kg^{-1} bw would result in an increase of liver vitamin A by 6 µg g^{-1} (Landes, 1994). The author concludes from the data that 1 mg ß-carotene would be equivalent to 500–600 IU vitamin A.

4.1.4. Liver of other (minor) ruminant species

Only few European data are available for lamb liver. Mean vitamin A values for liver typically vary from 64 to 190 µg RE g^{-1}, whereas higher concentrations (328 and 490 µg RE g^{-1}) are shown by Norwegian and Swedish data. (AFSSA, 2005; INRAN, 2000; Souci et al., 2000; Howells and Livesey, 1998; McCance and Widdowson, 2002; Norwegian Food Composition Table, 2006; Swedish Livsmedelsverket, 2008). The large range of mean values may reflect differences in feeding regimes, lower values coming from grazing lambs, and higher ones from lambs intensively fed.

4.1.5. Poultry liver

Data for chicken liver originating from some European countries (Austria, Denmark, Finland, France, Germany, Ireland, Italy, the Netherlands, Norway and the UK) appear highly variable as reflected by a range of 56 to 381 µg RE g^{-1}. The lowest value (56 µg RE g^{-1}) results from samples of small Austrian farms that are not representative of large scale broiler production (Majchrzak et al., 2006). The highest values have been found in the Netherlands (381 µg RE g^{-1}; FEFANA, 1988) followed by Finland (370 µg RE g^{-1}, Heinonen et al., 1990). All other values are in the range of 92 to 130 µg RE g^{-1} (Denmark, France, Ireland, Italy, Norway and the UK; Germany (Souci et al., 2000), and; publications by McCance and Widdowson, 2002; Howells and Livesey, 1998; Schindler et al., 1987; INRAN 2000; AFSSA, 2005).

4.2. Vitamin A concentration in other edible tissues

Only a limited data set is available for kidney and meat of the relevant animal species.

4.2.1. Pig tissues

Mean values for pig kidney vary from 0.6–1.5 µg RE g^{-1} (NEVO, 2006; Danish Food Composition Databank, 2005; Souci et al., 2000; AFSSA, 2005)

Pork meat is in the range of 0.02 to 0.1 µg RE g^{-1} (Danish Food Composition Databank, 2005; Norwegian Food Composition Table, 2006; NEVO, 2006; Souci et al., 2000).

4.2.2. Bovine tissues

Mean values for kidney vary from 0.8 to 2.6 µg RE g^{-1} in calves and from 0.9 to 3.5 µg RE g^{-1} in beef (Danish Food Composition Databank, 2005; AFSSA, 2005; NEVO, 2006; Norwegian Food Composition Table, 2006; Souci et al., 2000; INRAN, 2000).

Data on the mean vitamin A content of meat show a range of < 0.1 to 0.2 µg RE g^{-1} for veal and of 0.02 to 0.4 µg RE g^{-1} for beef (NEVO, 2006; Souci et al., 2000; Danish Food

Composition Databank, 2005; Norwegian Food Composition Table, 2006; Souci et al., 2000; AFSSA, 2005).

4.2.3. Tissues from other (minor) ruminant species

Vitamin A in lamb kidney varies from 1.3–3.3 µg RE g^{-1} and in lamb meat from. 0.1–0.7 µg RE g^{-1} (AFSSA, 2005; Souci et al., 2000; NEVO, 2006; Norwegian Food Composition Table, 2006).

The mean value for goat meat is given as 0.4 µg RE g^{-1} (Souci et al., 2000).

4.2.4. Poultry tissues

Mean vitamin A in chicken meat varies from 0.04–0.4 µg RE g^{-1} (AFSSA, 2005; Souci et al., 2000; Norwegian Food Composition Table, 2006; NEVO, 2006; Danish Food Composition Databank, 2005).

Vitamin A in turkey meat (0.09 to 0.2 µg RE g^{-1}) shows the same magnitude as in chicken meat (Swedish Livsmedelsverket, 2008; Danish Food Composition Databank, 2005; Souci et al., 2000).

4.2.5. Fish tissue (flesh, liver)

Fish is not a uniform food item since the vast range of species available for human consumption shows considerable variation in terms of nutritional composition, including vitamin A content. A simple categorisation as lean or oily fish does not accurately reflect the vitamin A status since this is dependent on the different feeding strategies of herbivorous, omnivorous and carnivorous fish. Some species, e.g. gadoid fish such as cod, saithe, haddock and pollack, are lean fish that contain little vitamin A in the fillet whereas the liver and roe (which are scarcely consumed) may contain considerable quantities of vitamin A (Table 7). Data on the vitamin A content in farmed fish are scarce and differ among species and tissues.

Table 7. **Vitamin A levels in fillet and liver of some finfish species**

Species	Tissue	Concentration (µg g^{-1})	Samples
Atlantic salmon farmed (*Salmo salar*)	Muscle	0.3 ± 0.02	n = 10
Herring (*Clupea harengus*)	Muscle	0.13 ± 0.01	n = 10
Mackerel (*Scomber scombrus*)	Muscle	0.12 ± 0.02	n = 10
Saithe (*Pollachius virens*)	Muscle	0.18 ± 0.02	n = 30
Seabass (*Dicentrarchus labrax*)*	Liver	33 ± 4	n = 2
Seabream (*Sparus aurata*)*	Liver	107 ± 17	n = 2
Tuna (genus not identified)*	Liver	651 ± 60	n = 2
Saithe (*Pollachius virens*)	Liver	99 ± 8	n = 30
Atlantic cod (*Gadus morhua*)*	Liver	113 ± 49	n = 4
Atlantic cod (*Gadus morhua*)	Liver	47 ± 5	n = 37

* AFSSA 2005, French monitoring plan, 2002

Note: Data are reported as sum of all-trans, 9-cis, 13-cis and 11-cis retinol and all-trans 3, 4 didehydroretinol, mean ±SEM. Data from 2005 and 2006, National Institute of Nutrition and Seafood Research (NIFES), Norway

4.3. Vitamin A concentration in milk and dairy products

Vitamin A in milk is associated with the lipid fraction. Milk and dairy products of varying fat content show therefore different vitamin A values. The retinol content of raw milk (4.2 % fat), pasteurised milk (about 3.5 %), semi-skimmed milk (1.5 %) and butter (about 80 % fat) varied following the fat content. The retinol content per unit fat was rather constant in the different products (Hulshof et al., 2006). A comparison between products can only be done at fat normalised levels.

Data on the correlation between dietary vitamin A and milk retinol could not be found.

Data for some European countries showed a range of averages between 220 and 620 µg RE kg^{-1} milk (3.5 % fat) from cows fed vitamin A-supplemented diets (Denmark, France, Germany, Ireland, Italy, the Netherlands, Norway, Portugal, Spain and the UK; publications by Fox and Sweeney, 1998; Hulshof et al., 2006, Souci et al., 2000, Calderón et al., 2007a; Calderón et al., 2007b, and; provided by National Food Authorities).

Milk with 1.5 % fat showed expectedly about half vitamin A content of 3.5 % fat milk; skimmed milk contained only traces of vitamin A. (Souci et al., 2000; Danish Food Composition Databank, 2005; Norwegian Food Composition Table, 2006).

Differences in retinol content of summer and winter milk are shown by Hulshof et al. (2006), summer milk and butter containing about 10 % more retinol. But a more striking difference was seen in β-carotene being 20 % higher in summer milk. This reflects the differences in the provitamin A carotenoids between fresh green forage and dried forage. Those relations are in principle confirmed by Nozière et al. (2006). In contrast, Agabriel et al. (2007) found only seasonal differences for carotenoids in milk but not for retinol.

Butter from some European countries showed mean vitamin A concentrations in the range of 5.9–11.7 µg RE g^{-1} (Denmark, France, Germany, Italy, the Netherlands, Norway and Sweden; publications by AFSSA, 2005; Souci *et al*., 2000; NEVO, 2006, and; provided by National Food Authorities).

Cheese revealed mean vitamin A concentrations in the range of 0.3 µg RE g^{-1} to 5 µg RE g^{-1}, with fat contents between 10 and 60 % (Denmark, France, Germany, Italy, the Netherlands, Norway and Sweden; publications by AFSSA, 2005; Souci et al., 2000; INRAN, 2000; NEVO, 2006, and; provided by National Food Authorities)**.**

Yoghurt from some European countries showed mean vitamin A concentrations between 0.3 and 0.4 µg RE g^{-1} for high fat yoghurt, 0.2 µg RE g^{-1} for medium fat and a range of 0.02 to 0.2 µg RE g^{-1} for low fat yoghurt (France, Germany, Italy, the Netherlands, Norway and Denmark; publications by AFSSA, 2005; Souci et al.; 2000; INRAN, 2000; NEVO, 2006, and; provided by National Food Authorities).

When comparing data for milk and dairy products (butter, cheese and yoghurt), the vitamin A concentration calculated per gram fat is in the same range, 4–14 µg RE g^{-1}.

Very scarce European data are available for goat milk. Mean values varying between 300 and 900 µg RE kg^{-1} could be found (AFSSA, 2005; Souci et al., 2000; INRAN, 2000; Danish Food Composition Databank, 2005; Norwegian Food Composition table, 2006).

4.4. Vitamin A concentration in eggs

European data for the whole egg is in a range between 1.9 and 2.3 µg g^{-1}, corresponding to 7.0–8.5 µg g^{-1} egg yolk (Souci et al., 2000; Danish Food Composition Databank, 2005; INRAN, 2000; NEVO, 2006; Norwegian Food Composition Table, 2006; McCance and Widdowson, 2002).

A Brasilian study could not demonstrate any difference between eggs from free-range and caged hens, both containing 5 µg retinol g^{-1} egg yolk (Ramalho et al., 2006).

4.5. Retinol losses in food due to processing

Food preparation processes may reduce the amount of certain nutrients in food. Processes that expose food to high temperatures, light or oxygen will create the greatest losses. However, nutrient data are frequently lacking for cooked foods. Vitamin A is generally considered heat stable during cooking over a wide range of temperatures. However, losses of 0–30 % in food of animal origin are reported (USDA Table of Nutrient Retention Factors, Release 5, 2003). Sungpuag et al. (1999) could show that boiling intact chicken liver resulted in 5 % loss of retinol; boiling with cutting into small pieces and grilling resulted in losses of 8 and 16 %, respectively. Greater losses (43 %) were observed in that study for egg omelette compared to hard-boiled egg (11 %). The cooking loss of retinol in eggs shown by Ramalho et al. (2006) was 17–20 %.

4.6. Conclusions

Whereas in the period from 1970 to 1990 an increase in liver vitamin A could be observed mainly for pigs and cattle, a reverse trend seemed to start in the early nineties.

Liver is the main body's store for preformed vitamin A and therefore the retinol richest food of animal origin. Recent data indicate the typical retinol content of:

- pork liver with 100–140 µg RE and high values of about 400 µg RE g^{-1}
- calf liver with 100–140 µg RE and high values of about 500 µg RE g^{-1}
- beef liver with 50–150 µg RE and high values of about 400 µg RE g^{-1}

- poultry liver with 60–130 µg RE and high values of about 400 µg RE g^{-1}

Typical data for liver of small ruminants cannot be given because of limited data.

Kidney (0.6–3 µg RE g^{-1}) and meat (0.02–0.4 µg RE g^{-1}) of pigs and ruminants contain much less vitamin A and are considered as insignificant sources of human vitamin A supply. Also fish flesh (from farmed salmon, herring, mackerels and saithe) contains insignificant amounts of vitamin A (0.12–0.35 µg RE g^{-1}).

Vitamin A in milk is associated with the lipid fraction. A comparison between products can only be done at fat normalised levels. The vitamin A concentration calculated per gram fat of milk and dairy products (butter, cheese and yoghurt) is comparable, showing a range of 4–14 µg RE g^{-1}. A range of 220–620 µg RE vitamin A kg^{-1} is typical for 3.5 % fat milk and 6–12 µg RE vitamin A g^{-1} butter.

Eggs contain between 4–9 µg retinol g^{-1} egg yolk (corresponding to a mean of 120 µg RE vitamin A for a standardised 60 g egg).

The large standard deviation of preformed vitamin A concentrations found in the different surveys, particularly for liver, (not comparable with the range of averages given in food composition tables) makes the prediction of the actual retinol intake of the consumer difficult. Only long-term predictions could use the averages, assuming that in a longer consumption period high concentrations of preformed vitamin A would be compensated by lower food contents.

Retinol losses due to food processing amount to 0–43 %. Thus retinol intake data from food consumption surveys may be somewhat overestimated.

5. Correlation between dietary vitamin A in animals and liver content

The relation of dietary supply and liver storage has been often examined and is therefore well documented, albeit the majority of studies were performed before 1992. Because of the affinity of vitamin A to lipids, the retinol concentration in liver, milk fat and eggs can ideally be expected to reflect the vitamin A supply of the animal. However, some uncertainties (liver content of vitamin A at start of the study, duration of experiment, dosage(s), bioavailability of the preparation, intake of provitamins with the feed material, degradation of vitamin A in the intestinal tract, homoeostatic mechanisms and release from liver for specific requirements) can prevent the establishment of reliable quantitative correlations which would allow to predict the tissue vitamin A content from a given dietary concentration.

5.1. Pork liver

The data on the correlation between vitamin A intake and liver store are extracted from a comprehensive review published in 1994 by Landes.

For piglets (based on a total of 33 trials with vitamin A concentrations between 125 and 20 000 IU kg^{-1} feed), Landes (1994) calculated a significant linear regression between dietary vitamin A and liver vitamin A (Y (IU g^{-1} liver) = 15.5 + 0.025x (IU kg^{-1} feed), r = 0.82).

For pigs for fattening, a total of 18 trials (17 published between 1986 and 1993, one in 1969) was available for statistical analysis (covering a range of 125 to 40 000 IU vitamin A kg^{-1} feed). As in piglets, the linear correlation (Y (IU g^{-1} liver) = -63.1 + 0.075x (IU kg^{-1} feed)) was highly significant (r = 0.99). If data (4 x 12 pigs) from one of the most recent studies (Hoppe et al., 1992) was considered separately, the regression line (Y (IU g^{-1} liver) = -88.9 +

0.077x (IU kg^{-1} feed)) is quite similar to that derived from the totality of 18 trials. Table 8 allows concluding on liver vitamin A for selected dietary concentrations and vice versa.

Table 8. **Vitamin A in feed and in the liver of pigs for fattening**

Vitamin A (IU kg^{-1} feed)	Expected vitamin A in liver (µg RE g^{-1})	
	Regression Landes (1994)*	Regression Hoppe *et al.* (1992)**
5 000	95	90
7 500	151	148
10 000	208	206
13 500	288	288
15 000	322	323

* Y (IU g^{-1} liver) = -63.1 + 0.075x (IU kg^{-1} feed), r = 0.99, N = 18 trials
** Y (IU g^{-1} liver) = -88.9 + 0.077x (IU kg^{-1} feed), r = 0.94, n = 4 x 12 pigs

The regression can be validated for practical use by comparing average liver concentrations with reported dietary levels. The mean value reported by Howells and Livesey (1998) would correspond to 8 500 IU vitamin A kg^{-1} feed.

The ranges for vitamin A, which are given as supplementation rate to grower and finisher feed (see Appendix 10), vary in Europe from 4 500 to 15 000 and 4 000 to 13 500 IU kg^{-1}, respectively. A mean supplementation, estimated from the ranges, of about 9 500 and 8 500 IU vitamin A kg^{-1} grower and finisher feed, respectively, would result in liver concentrations of < 200 µg RE retinol g^{-1} liver.

Danish recommendations for pig feed fortification were in the range of 5 000–6 000 IU vitamin A kg^{-1} feed. The liver concentration found in Danish surveys would — according to the above equation — correspond to 5 800 IU vitamin A kg^{-1} feed. The correspondence of all comparisons validates the regression for pigs for fattening.

5.2. Products from ruminants

5.2.1. Beef liver

Landes (1994) calculated for ruminating calves (a total of 29 trials, 95–190 kg bw, vitamin A dosages between 25 and 860 IU kg^{-1} bw) a significant linear regression between dietary vitamin A and liver vitamin A (Y (IU g^{-1} liver) = 16.7 + 0.158x (IU kg^{-1} bw), r = 0.76). Factors influencing variation are study duration and liver vitamin A concentration at study start.

One hundred IU vitamin A kg^{-1} bw would add about 5 µg vitamin A to the existing liver store on a per g basis. Assuming that the feeding rate is about 2 % of the body weight, as much as 65 000 IU vitamin A kg^{-1} complete feed would be required for an increase of only 67 µg vitamin A g^{-1} liver. Landes (1994) comments further that the large discrepancy between calculated values and realistic dietary vitamin A concentrations in practice supports the assumption of an additional (oral or parenteral) supply. However, the above regressions are based on short-term studies (mean 90 days) and longer administration would lead to higher vitamin A liver stores.

For cattle for fattening (27 trials, 344–1025 kg bw, vitamin A dosages between 3 and 1 000 IU kg^{-1} bw), a significant linear regression between dietary vitamin A and liver vitamin A (Y

(IU g^{-1} liver) = 10.6 + 0.43x (IU kg^{-1} bw), r = 0.92)) was also calculated by Landes (1994). An increase in the daily vitamin A intake by 100 IU kg^{-1} bw would then result in an increase of liver vitamin A by about 12 µg RE g^{-1} liver. Based on the same assumptions as for calves, a cattle liver vitamin A concentration of about 150 µg g^{-1} would require a concentration of 62 500 IU kg^{-1} complete feed. This seems equally unrealistic as the value derived for calves. In case of cattle for fattening, study duration (in most cases about 200 days or more) cannot help to explain the discrepancies at the same extent as for calves.

The limited applicability of the regression equations for calves and cattle for fattening may result from different reasons. Feeding time is in all cases considerably longer than in the feeding studies. When supplementing calf or cattle diets with vitamin A, the intake of ß-carotene is usually not considered in practice; the additional supply with the vitamin A precursor may increase the liver vitamin A. As a third factor invalidating the regression equations, the FEEDAP Panel considers the feeding regimes in cattle. Complete diets are rarely formulated by feed compounders. The vitamin A allowance is covered by different complementary feedingstuffs (e.g. concentrates, mineral mixtures), each may be formulated to cover the allowance. This may lead, in a worst case simulation, to a supply of approximately double the allowance. Milk replacer with vitamin A content up to 75 000 IU vitamin A kg^{-1} and concentrates for calves and cattle with vitamin A levels up to 40 000 and 30 000 IU kg^{-1}, respectively, are currently in use (Appendix 10). Considering also differences in the bioavailability of vitamin A preparations (Alosilla et al., 2007), those four uncertainty factors may indicate why the regression equations derived from studies under controlled feeding conditions contribute poorly to explain the liver vitamin A contents observed in the field. Other sources for the liver vitamin A than oral supply with vitamin A and its precursors are almost excluded.

Data which would allow establishing a ratio between vitamin A intake and vitamin A content of food from minor ruminants are not available.

5.2.2. Milk

Quantitative relations between vitamin A in feed and milk retinol could not be found in literature.

5.3. Poultry products

5.3.1. Poultry liver

In an experiment with chickens for fattening, that lasted for 33–37 days, hepatic vitamin A concentrations were linearly and strongly correlated with the dietary vitamin A level ($r^{2:}$ 0.98, $P < 0.001$). Because only a graph and no regression equation was given in the publication (Sklan et al., 1994), it can only be roughly estimated that 10 000 IU kg^{-1} feed would result in a liver concentration of about 135 µg vitamin A g^{-1} liver, and 20 000 IU kg^{-1} feed in 290 µg vitamin A g^{-1} liver. Poultry liver retinol, as indicated by food composition tables and national surveys, correspond more or less to a maximum feed concentration of 10 000 IU kg^{-1} complete feed for chickens for fattening if the two sets of highest values are omitted.

In an experiment with turkeys for fattening, that lasted for 41 days, Sklan et al. (1995) found a significant linear relationship between vitamin A in feed (0, 825, 1 650, 6 600, 19 800 and 43 560 IU kg^{-1} feed) and liver vitamin A. From the published graph, a liver concentration of 300 µg RE g^{-1} can roughly be derived at a feed concentration of 19 800 IU vitamin A kg^{-1}.

This value is not essentially different from the chicken liver concentration (286 µg RE g^{-1}) estimated at the same feed concentration.

5.3.2. Eggs

Laying hens were fed diets supplemented with 0; 4 000; 8 000 and 16 000 IU vitamin A kg^{-1} feed (one, two and four times the requirement; NRC, 1984) for 27 weeks (Squires and Naber, 1993). After 25 weeks of feeding, the vitamin A content of egg yolk was closely related to the dietary level. The three dietary dose levels resulted in significant differences in vitamin A content of the egg yolk (Table 9).

Table 9. **Egg yolk vitamin A content (µg RE g^{-1}) from hens fed different vitamin A levels**

	Dietary vitamin A (IU kg^{-1})			
Time (weeks)	**0**	**4 000**	**8 000**	**16 000**
13 to 18	2.8 ± 0.5 $^{(b)}$	3.2 ± 0.5 $^{(b)}$	3.6 ± 0.5 $^{(a, b)}$	4.8 ± 0.6 $^{(a)}$
19 to 24	1.7 ± 0.6 $^{(c)}$	3.7 ± 0.5 $^{(b)}$	5.1 ± 0.5 $^{(b)}$	7.2 ± 0.6 $^{(a)}$
25 to 27	0.7 ± 0.7 $^{(d)}$	3.1 ± 0.7 $^{(c)}$	5.1 ± 0.7 $^{(b)}$	7.3 ± 0.7 $^{(a)}$

$^{(a, b, c, d)}$ Means within rows with no common superscript differ significantly ($P < 0.05$)
Note: Data reported as mean ± SE (n = 4 to 8 observations of four eggs each treatment time).

From the data presented in Table 9, it could be roughly estimated that the mean concentration of vitamin A in the egg yolk derived from food composition tables (4–9 µg g^{-1}) would be obtained with feed levels between 6 000 and 20 000 IU vitamin A kg^{-1}, which corresponds to concentrations used by feed compounders (8 000–17 000 IU vitamin A kg^{-1}; see Appendix 10).

Surai et al. (1998) studied the effect of high dietary vitamin A levels (10 000, 100 000 and 400 000 IU kg^{-1} feed) on vitamin A in liver and egg yolk after three months of feeding. Ten thousand IU kg^{-1} feed resulted in 627 µg RE g^{-1} liver and 7 µg RE g^{-1} egg yolk.

In addition to vitamin A and its main precursor β-carotene, there are other carotenoids with vitamin A activity, either naturally occurring in feed materials or added to the feed as feed additives, such as citranaxanthin, capsanthin and β-cryptoxanthin. They all contribute to the vitamin A status, and the content of total preformed vitamin A in eggs (EFSA, 2006). Although this contribution will be marginal, it adds under practical conditions to the uncertainty of the relationship between dietary vitamin A level and the retinol concentration of eggs.

5.4. Fish

Retinol (vitamin A_1), but also didehydroretinol (vitamin A_2), are present in fish tissues.

A significant linear regression (Y (IU g^{-1} liver) = 189 + 0.0035x (IU kg^{-1}), r = 0.99) was found between dietary vitamin A and liver vitamin A in six different feeding trials, with 0 to 8 104 000 IU vitamin A kg^{-1} feed for Sunshine bass (*Morone chrysops* ♀, *M. saxatilis* ♂; Hemre et al., 2004), Japanese flounder (*Paralichthys olivaceus*; Hernandez et al., 2005), Carp (*Cyprinus carpio*; Aoe et al., 1968), Sea bream (*Chrysophrys major*; Hernandez et al. 2004), Rainbow trout (*Oncorhynchus mykiss*; Hilton et al., 1983) and Atlantic salmon (*Salmo salar*;

Ørnsrud et al., 2002). Factors influencing variation were species difference, supra-physiological vitamin A concentrations, feed preference (e.g. herbivore vs. carnivore), study duration and liver vitamin A at the study start. However, the correlation between vitamin A in fish feed and liver was considerably poorer at realistic feed vitamin A concentrations, presumably due to species differences.

The equation cannot be used to predict liver retinol content from the vitamin A concentration in feed under practical conditions.

5.5. Conclusions

The regression equation available to predict liver retinol from dietary vitamin A in pigs for fattening shows useful practical applicability.

The regression equations for the relationship between vitamin A in feed and liver vitamin A of calves and cattle for fattening cannot be applied to explain liver vitamin A content in field samples. Moreover, liver of cattle not given vitamin A via feed (but the precursor ß-carotene on pasture) may show vitamin A levels comparable to those obtained after vitamin A supplementation to feed. The FEEDAP Panel concludes that it is not possible in practice to calculate preformed vitamin A contents in liver from vitamin A levels in feed. Quantitative relations between vitamin A in feed and milk retinol could not be found in literature.

For poultry, close relations between the concentrations in feed, liver and eggs could be observed. However, most results are published in form of graphs, others in tables, not giving access to the individual data which are necessary to establish regression equations. For a given feed concentration (in a limited range), only rough estimates of the retinol content of liver and eggs are therefore possible.

A database to predict the retinol concentration in edible fish tissues from dietary vitamin A at levels of practical significance does not exist.

6. Vitamin A in food-producing animals

Current EU regulations consider vitamin A as a feed additive. Vitamin A is routinely added to feed at industrial or farm level. Directive 91/249 established maximum concentrations of 13 500 IU kg^{-1} complete feed for pigs for fattening, chickens for fattening, turkeys for fattening, ducks for fattening, for bovines for fattening and lambs for fattening. For calves, a maximum of 25 000 IU kg^{-1} milk replacer is set. The vitamin A content for other pig, poultry and ruminant categories is not specifically regulated and neither is the vitamin A content of fish feed. Directive 94/39/EC allows for a feedingstuff with the particular nutritional purpose 'compensation for malabsorption' in poultry, excluding goose and pigeons, in the first two weeks after hatching, 'high levels of fat soluble vitamins'. This indicates that the 'maximum' of 13 500 IU kg^{-1} complete feed could legally be exceeded (to an unknown level) for a certain but limited time span.

Vitamin concentrates containing also vitamin A are often applied in animal husbandry to stabilise health under special circumstances (e.g. infections, poor feed quality). This administration of vitamin concentrates ('supplementary feed') is not specifically controlled by current legislation.

According to AFSSA (2005), the practice of feed manufacturers of overdosing, to ensure that products contain at least the amount of vitamin stated throughout shelf life (up to three years) and to compensate losses from pelleting and other procedures, is no longer applied.

The demand for a specific essential nutrient is expressed in the literature as requirement or allowance. The FEEDAP Panel follows the definitions formulated by SCAN in its opinion on the use of zinc in feedingstuffs (EC, 2003). A nutrient requirement is defined as 'the individual demand of a specific nutrient under defined conditions; whilst allowance is defined as the 'estimate of the necessary nutrient supply to meet the average gross demand of the population under common conditions plus safety factor considering the individual variability and bioavailability due to the specific chemical compound and interactions between nutrients.' Both requirements and allowances are set by scientific bodies; additional recommendations are often formulated by agricultural advice centres or the industry.

To verify the vitamin A supply of food-producing animals in field, EFSA requested information on the current practices of vitamin A supplementation (minimum and maximum levels of vitamin A in feedingstuffs, mainly supplemental synthetic retinylesters due to the restriction in use of animal by-products) in all categories of livestock in Europe. Questionnaires were also sent to industry associations (FEFAC, FEFANA). Responses (from Austria, the Czech Republic, Denmark, Croatia, Finland, Germany, Cyprus, Belgium and Portugal) are summarised in Appendix 10.

The following species-specific subchapters provide (i) an overview of typical vitamin A deficiency symptoms, requirements and allowances, (ii) a description of the current practice of feed compounders in supplementing vitamin A and, finally, (iii) options for and consequences of lowering the current vitamin A supply to food-producing animals, with special emphasis on welfare.

6.1. Pigs

6.1.1. Deficiency, requirements, supply in field and hypervitaminosis

In pigs, the deficiency of vitamin A results mainly in neurological symptoms such as unsteady gait, spasms, trembling legs and paralysis. There is no strong effect on appetite or weight gain (Cunha, 1977). However, in sows for reproduction, vitamin A deficiency causes failure of oestrus, increased incidence of embryonic resorption and stillborn piglets.

Table 10 summarises briefly current vitamin A requirements and allowances. Recent allowances for growing pigs (GfE, 2006) are about double of the requirements, whereas for gestating and lactating sows very little difference exists. Minimum dietary vitamin A concentrations in practice exceed the allowances roughly by a factor 1–2, whereas the maximum observed feed levels are considerably above allowances (by factors of 5 in piglets, 6 in pigs for fattening, 7 for gestating and 13 for lactating sows). Moreover, differences between the Member States are also considerable. The AFSSA report noted that very occasionally 'light' piglets (runts) and sows at the end of lactation may be given an injection of the combination of vitamin A, D and E.

Table 10. **Pigs: vitamin A requirements, allowances and in feed use (IU vitamin A kg^{-1} complete feed)**

Pig categories	Requirements*	Allowances**	In feed use (minimum –maximum)***
Piglet (< 20 kg bw)	2 200	4 000	7 000–22 000
Pig for fattening	1 300	2 200	4 000–15 000
Gestating sow	4 000	4 000	4 000–31 000
Lactating sow	2 000	2 300	5 000–31 000
Boar	4 000		

* NRC (National Research Council), 1998
** GfE (Gesellschaft für Ernährungsphysiologie), 2006
*** Appendix 10

The conversion of ß-carotene to vitamin A decreases with increasing carotene intake (from 1 200 IU mg^{-1} carotene at 2 mg carotene kg^{-1} piglet feed to 260 IU mg^{-1} carotene at 100 mg carotene kg^{-1} feed (Schöne et al., 1988)).

Gross toxicity signs of hypervitaminosis include skin lesions with bleedings, blood in urine and feaces, loss of control of the legs and periodic tremors (Anderson et al., 1966). Bone structure is also affected (Wolke et al., 1968). About 436 000 IU vitamin A kg^{-1} (from retinyl palmitate) caused toxicity symptoms after 43 days in young pigs, whereas 218 000 IU kg^{-1} complete diet for eight weeks appeared safe (Anderson et al., 1966). However, when very high doses of vitamin A (multiples of the NRC 1988 requirement: 11 000; 22 000; 110 000; 220 000 IU kg^{-1}) were fed to piglets of 8 kg initial body weight up to 90 kg, no clinical signs of toxicity were recorded, and no effect on bone was seen, though plasma and liver levels were increased (Blair et al., 1992). French field observations confirmed the high tolerance of pigs to vitamin A; hypervitaminosis has practically not been diagnosed in any occasion (AFSSA, 2005). However, hypervitaminosis A may occur under extreme circumstances as a result of feeding high amounts (40–50 %) of fish silage. The vitamin A content of those fish silages varied considerably from 152 000 (without pathological findings) up to 750 000 IU kg^{-1} (Coates et al., 1998).

6.1.2. Synopsis and options

With regard to potential maximum contents for vitamin A in complete pig feeds, the FEEDAP Panel considers the most recent allowance data as a sound basis to recalculate maximum contents. Such a calculation should regard a compensation for manufacturing and storage losses and differences in the health status of animals. The last argument gives reasons for a wider ratio maximum content to allowances in piglets than in pigs, also considering extreme individual variations in feed intake after weaning. Genetic improvements, which have increased yields per unit of feed intake, may demand for a higher dietary nutrient density, including vitamin A.

The maximum vitamin A content in feedingstuffs for piglets is currently not restricted by legislation. When introducing a factor of 2 to the allowance for compensation of manufacture and storage losses and a further factor of 2 for variation in feed intake and maintenance of health, a maximum content of 16 000 IU vitamin A kg^{-1} feed could be derived for complete feed for piglets. This concentration would allow piglets to build up a liver vitamin A reserve

(ca. 125 µg vitamin A g^{-1} liver), which can be (partially) mobilised in case of a sudden demand.

Four out of nine European countries reported maximum contents of 20 000–22 000 IU vitamin A kg^{-1} feed; in the remaining countries, the reported maximum values do not exceed the proposed value. Therefore, the impact of the derived maximum content on supplementation practice in Europe would be low.

Applying the same procedure (deriving potential maximum contents from allowances) for pigs for fattening, a factor of 2 should also be used to compensate for manufacture and storage losses, but only 1.5 for maintenance of health. This would lead to a maximum concentration of 6 600 IU vitamin A kg^{-1} feed.

The derived maximum level is in line with Danish field practice (4 000–5 000 IU vitamin A kg^{-1} grower and finisher diet) and with finisher diets in two other countries.

Both derived maximum contents for piglet and pig complete feed would result in liver retinol of about 130 µg RE g^{-1} liver. This value is 35 % lower than that used by SACN for calculations of human retinol intake. Although it is in line with recent average data on liver retinol, the proposed maxima in feed are expected to cut the high variability of liver retinol.

The FEEDAP Panel favours setting both derived maximum values as maximum contents, 16 000 IU vitamin A kg^{-1} complete feedingstuffs for piglets and 6 500 IU vitamin A kg^{-1} complete feed for pigs for fattening (grower and finisher diets). No negative consequences of implementing the proposed maximum content on animal health, welfare and performance are expected.

Under the aspect of consumer safety, sows and boars deserve less attention than pigs for slaughtering. Reduction of dietary vitamin A for sows and boars will not substantially decrease consumer exposure because livers of sows and boars are not widely consumed. If for reasons of consistency a maximum vitamin A content is considered in feed for sows, the same additional safety factors as those applied for pigs for fattening could be used. An upper limit of 12 000 IU for gestating sows (with lower feed intake) and of 7 000 IU vitamin A kg^{-1} feed for lactating sows would then be derived.

6.2. Ruminants

6.2.1. Symptoms of deficiency, requirement, supply in field, hypervitaminosis

In ruminants, vitamin A deficiency signs (NRC, 1981, 2000 and 2001) observed relate mostly to problems in epithelial tissues and in vision and to abnormal bone development. The classic sign of vitamin A deficiency is night blindness. Numerous studies have also shown an increased and more severe infection rate, since a lack of vitamin A results in decreased antibody production. The immune response is decreased in lambs (Bruns and Webb, 1990). Vitamin A deficiency lowers reproductive efficiency in both males and females. In goats, insufficient vitamin A supply causes reduced fertility of the female and the male, with poor semen quality and conception rate (Guss, 1977). The most susceptible to vitamin A deficiency are newborn calves deprived of colostrum and cattle unable to establish or maintain liver stores. The symptoms include reduced feed intake, rough hair coat, oedema of the joints and higher susceptibility to respiratory infections (NRC update, 2000).

Swanson et al. (2000) measured different clinical signs in preruminating calves after feeding 2 300, 6 200; 9 000; 18 300 or 44 000 IU vitamin A kg^{-1} feed for 28 days. A strong negative

correlation between incidence of hyperthermic temperature and vitamin A intake was found. A comparable negative correlation existed also between faecal score and vitamin A intake. Arnett et al. (2007) fed diets with no or with high supplementation of vitamin A (6 600 IU kg^{-1}) for 112 days to lambs. Vitamin A supplementation increased significantly total intramuscular lipids.

In cattle in general, considerable amounts of supplemented vitamin A is destroyed by ruminal microbes (Rode et al., 1990). This may account, depending on the type of diet, for 20 % (high forage diet) up to 80 % (acidotic high grain diet). In sheep, the type of diet influences ruminal degradation of β-carotene to a lesser extent, if at all, than in cattle (Potanski et al., 1974). Also, differences in the bioavailability of vitamin A from commercially available preparations in cattle have been described (Alosilla et al., 2007).

Swanson et al. (2000) proposed 11 000 IU vitamin A kg^{-1} milk replacer as requirement for veal calves. The suggestion of Flachowsky et al. (1990) for preruminant calves (12 500 IU kg^{-1} milk replacer) is in the same order. About 25 000 IU vitamin A per 100 kg bw day^{-1} (equivalent to 12 000 IU kg^{-1} feed) was required to maintain the initial level of vitamin A concentration in the liver. Below that content, the vitamin A in liver decreased to 51 % of the initial level.

Weiss (1998) proposed at least 100 IU vitamin A kg^{-1} bw as requirement for dairy cows. Supplementing the dam's diet increases the vitamin A content in the liver of the new born. It is assumed that liver vitamin A of the newborn will support survival and resistance to infectious diseases.

Table 11 summarises briefly current vitamin A requirements and allowances. The allowance, which is by definition higher than the requirement, is lower in cattle for fattening and at approximately the same level in dairy cows.

Table 11. **Cattle: vitamin A requirements, allowances and in feed use (IU vitamin A kg^{-1} dry matter of complete diets)**

Ruminant categories	Requirements*	Allowances**	In feed use (minimum - maximum)***
Growing cattle	3 200	2 500	5 000–30 000
Lactating cows	2 700–3 700	5 000	8 000–30 000
Dry cows	5 600–8 200	10 000	
Calf (milk replacer)		12 500 (1)	10 000–75 000

* NRC (National Research Council), 2001. Direct comparison to European data is limited because of different body weight and feed intake. The scientific data are 110 IU kg bw^{-1} of dry and lactating cows and 80 IU kg^{-1} bw for growing cattle
** GfE (Gesellschaft für Ernährungsphysiologie), 2001
*** Appendix 10
(1) Flachowsky et al., 1990.

Data from the European feed industry (Appendix 10) indicate a lowest vitamin A concentration of 10 000 IU kg^{-1} milk replacer, with a maximum content of 40 000 and above in three countries. Data for growing cattle and dairy cows are difficult to compare because of variable feeding regimes (proportion of complementary feed in the daily ration).

Requirements for minor ruminant species are given by the NRC (1981) for goats (1 500 IU vitamin A kg^{-1} dry matter), ewes (1 800–3 300 IU vitamin A kg^{-1} dry matter) and lambs (940–2 000 IU vitamin A kg^{-1} dry matter).

Beef cattle are reported to be tolerant to vitamin A overdoses (NRC, 2000). The presumed upper safe level for vitamin A is 66 000 IU vitamin A kg^{-1} dry matter for both lactating and non-lactating cattle (NRC, 2001).

6.2.2. Contribution of ß-carotene in forages to vitamin A in ruminants

In feeding practice, β-carotene as a vitamin A precursor in food-producing animals plays only a significant role in ruminants (and in horses). Main sources are green forages and dried alfalfa.

As can be seen from Table 12, the average carotene content between the different plants varies less than between different samples of the same plant. This is presumably due to different harvesting times and conditions during harvesting (Steinhöfel und Schönherr, 2008). Between an early cut of clover and a late cut, there is a decrease of 20 % in carotene content. In general the β-carotene content of green forage is between 100 and 400 mg kg^{-1} dry matter (LFL, 2007).

Table 12. **ß-Carotene content in green forage (mg kg^{-1} dry matter)***

		ß-Carotene content
Cocksfoot (Orchard grass)	Dactylis glomerata	318 (63–870)
Timothy grass	Phleum pratense	224 (75–473)
Meadow fescue	Festuca pratense	337 (80–689)
Kentucky blue grass	Poa pratensis	200 (41–489)
Red clover	Trifolium pratense	184 (85–270)
Alfalfa (Lucerne)	Medicago sativa	198 (73–391)

* Data from Kirchgessner (2004) and DLG Futterwerttabelle (1962)

Conservation of green forage strongly lowers the carotene content due to oxidation. The decline of β-carotene in different conservation products of red clover compared to the initial content can be seen in table 13. In silage and in hay, less than one third of the original carotene is left (Steinhöfel, 2007).

Table 13. **ß-Carotene content in red clover and in its conservation products (mg kg^{-1} dry matter)**

	Early cut	Late cut
Fresh material	217.1 ± 13.6	172.9±16.9
Silage material before ensiling	97.0 ± 12.0	52.5 ± 13.0
Silage	62.2 ± 14.4	42.6 ± 9.8
Hay	67.7 ± 9.2	29.0 ± 9.5

(Steinhöfel, 2007)

Since β-carotene is not only a precursor of vitamin A but also plays a discrete role concerning fertility (Schweigert et al., 1988), cows deficient or marginal in β-carotene status are often recommended to be supplemented.

In ruminants, the conversion rate from β-carotene to vitamin A is assumed to be 1 mg to 400 IU (NRC, 1981). Applying this conversion rate, 100 mg β-carotene kg^{-1} would correspond to 40 000 IU vitamin A kg^{-1} DM. The consumption of 10 kg green forage DM with this β-carotene concentration would provide 400 000 IU vitamin A per animal. Taking the same model for forage containing 400 mg β-carotene kg^{-1}, the daily supply to cattle would amount to 1.6 million IU vitamin A; this is about 2.5 times above the presumed upper safe level. In terms of hypervitaminosis A, β-carotene is considered non-toxic.

There is strong evidence that the conversion rate of β-carotene decreases not only with the increasing supply of β-carotene but also of preformed vitamin A. The FEEDAP Panel concludes that it is under practical conditions not possible to quantify the contribution of β-carotene to total vitamin A supply in ruminants.

6.2.3. Synopsis and options

The reduction or introduction of maximum vitamin A contents in feeds for cattle for fattening and dairy cattle, respectively, would regulate the vitamin A supplementation to complete feed which is not routinely produced at feed industry level. However, it may not alter supplementation practices for complementary feed, considering the different feeding regimes and feed bases used in field.

Reducing the maximum content of vitamin A in complete feed for ruminating calves and cattle for fattening to a three- or fourfold of the allowances (7 500–10 000 IU vitamin A kg^{-1} DM), as proposed for piglets and pigs for fattening, is not expected to substantially reduce liver vitamin A because feeding regimes for calves and cattle are based on complementary feed, the use of which varies with the feeding regime and composition of the complementary feed. Complementary feeds with vitamin A concentrations as high as 30 000 IU kg^{-1} are currently in use.

If in spite of the above, a maximum vitamin A content of complete feed for cattle for fattening and lactating cows were to be reduced and/or introduced, the theoretical maximum content could be 10 000 IU vitamin A kg^{-1} complete feed. The same level is not considered sufficient for dry cows because of the lower feed intake and the embryo's requirement to build up its liver reserves. Therefore, a higher level of about 20 000 IU vitamin A kg^{-1} complete feed should be applied.

Concerning the maximum content of vitamin A in milk replacer for calves, the FEEDAP Panel recommends not to alter the existing limit (25 000 IU kg^{-1}), considering that the allowance (12 500 IU kg^{-1} milk replacer) is already half of the maximum set.

The potential derived maximum contents in feed for dairy cows and cattle for fattening do not allow any prediction of vitamin A in liver and milk. However, it can be concluded that those levels are safe for the target animals; a negative impact on animal health, welfare and performance is not expected.

The available data for small ruminant species appears too limited to make recommendations.

6.3. Poultry

6.3.1. Symptoms of deficiency, requirement, supply in field, hypervitaminosis

The characteristic symptoms of vitamin A deficiency are also found in poultry. Keratinisation of secretory epithelia is the most prominent symptom: corneal, conjunctival, esophageal and tracheal secretory membranes were affected (Aydelotte, 1963). Mucus formation has been shown to depend on vitamin A (De Luca et al., 1971). The appearance of keratinised secretory surfaces resulted in a characteristic ataxia. A loss in mobility followed alterations in bone growth due to the creation of several areas of compression (Howell and Thompson, 1967). The loss of membrane integrity altered water retention (Lopen et al., 1973) and impaired the ability to withstand infections (Singh and Donovan, 1973; Sijtsma et al., 1989). A pre-existing marginal vitamin A status increased the severity of the Newcastle disease virus (NDV) infection in chickens and, conversely, an NDV infection reduced marginal plasma vitamin A levels to deficient levels (Sijtsma et al., 1989). Insufficient vitamin A also reduced the immune system's response to challenge and further contributed to disease susceptibility (Davis and Sell, 1989; Sklan et al., 1989). Vitamin A deficiency also adversely affected the pituitary-gonadal axis (Fletcher, 1971). Hypothyroidism was an early indication of vitamin A deficiency in chicks (Nockels et al., 1984). Further signs of vitamin A deficiencies were reductions in testes size, circulating testosterone, fertility and hatchability (Padedes and Garcia, 1959; Hall et al., 1980; Squires and Naber, 1993).

Beta-carotene, the most important vitamin A precursor, is largely converted to vitamin A during intestinal absorption in chickens (Sklan, 1983). Optimal conversion ratios can only be obtained in poultry under experimental vitamin A deficiency conditions, where 1 mg ß-carotene could be equal to 0.5 mg vitamin A (1 665 IU). The ratio becomes wider with increasing amounts of ß-carotene in the diet (Brubacher et al., 1985).

Requirements, allowances and feed concentrations in use in some Member States for the main chicken categories and for turkeys are given in Table 14. Vitamin A requirements are 2 500 and 4 000 IU kg^{-1} for growing and reproductive ducks, 1 500 and 4 000 IU for growing and reproductive geese, and 1 650 and 3 300 IU kg^{-1} for growing and breeding quails, respectively (NRC, 1994).

Table 14. **Vitamin A requirements, allowances and in feed use in poultry (IU Vitamin A kg^{-1} complete feed)**

Poultry category	Requirements*	Allowances**	In feed use (minimum-maximum)***
Chicken	1 500	chicken starter 2 500 for replacement 1 000 for fattening 2 500	10 000–20 000 8 000–15 000 8 000–17 000 (1)
Laying hen	2 500–3 750	4 500	8 000–17 000
Growing turkey	5 000	5 000	6 000–17 000 (2)
Reproductive turkey	5 000		6 000–15 000
Growing duck	2 500	–	8 000–15 000

* NRC (National Research Council), 1994
** GfE (Gesellschaft für Ernährungsphysiologie), 1999 and 2004
*** Appendix 10
(1) 13 500 IU Vitamin A kg^{-1} for finisher diets
(2) 15 000 IU Vitamin A kg^{-1} for finisher diets

Sklan et al. (1994 and 1995) studied the effect of increasing doses of vitamin A (0, 2 750, 5 000, 11 000, 22 000 and 43 500 IU kg^{-1}) on growth, antibody production (against β-casein) and T-cell proliferation (response to β-casein or *Mycobacterium tuberculosis*) in chickens. As it can be seen from figure 2, the vitamin A concentration required for optimal growth (about 5 000 IU kg^{-1}) is considerably less than that required for optimal immune response (about 20 000 IU kg^{-1}). Comparable results were obtained by the same research group with turkeys (Sklan et al., 1995).

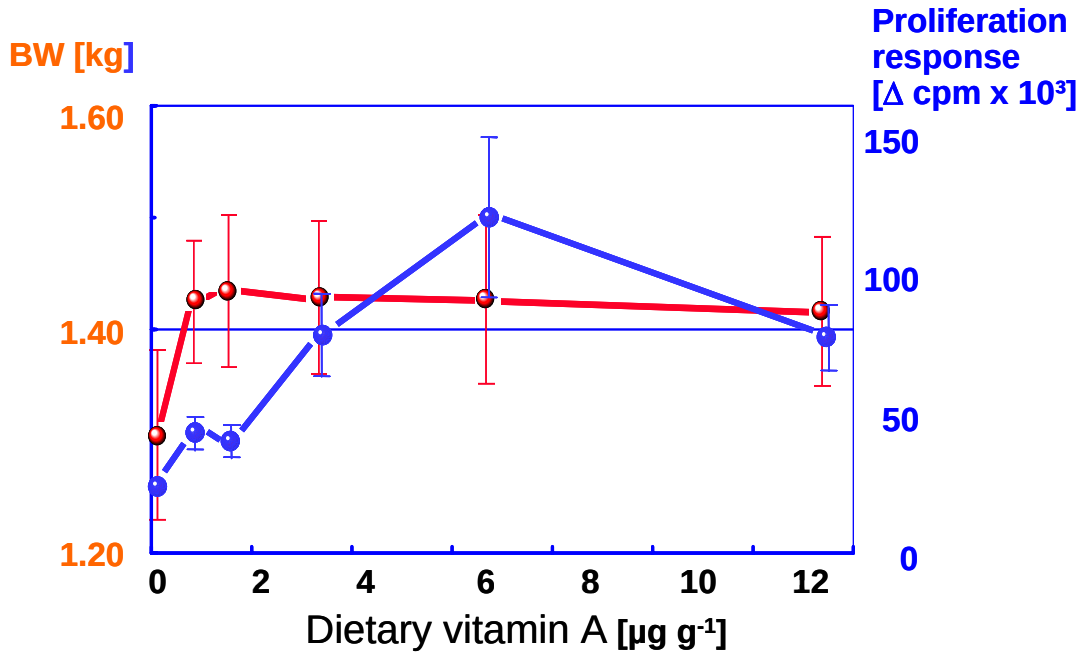


Figure 2. **Influence of dietary vitamin A on body weight and immune response of chickens for fattening** (Sklan et al., 1994)

Hypervitaminosis A in poultry is rare, the presumed upper safe level (NRC, 1987) is four to ten times the nutritional requirement (15 000 IU kg^{-1} feed for growing chickens, 40 000 IU for laying hens and for ducks, and 15 000 and 24 000 for growing and breeding turkeys, respectively). However, the presumed upper safe levels for orally administered vitamin A are only estimates because experiments with appropriate design have not been conducted to determine the maximum amount of vitamin A that can be administered without adverse effects.

6.3.2. Synopsis and options

The average vitamin A supplementation to poultry feed exceeds in practice considerably the allowances, as does minimum vitamin A supplementation in some European countries.

Considering the allowances for chickens (starter, for replacement and for fattening; see Table 14) and applying the same factors for compensation of manufacture and storage losses and for variation in feed intake and maintenance of health, 10 000 IU seem safe as maximum content.

Ten thousand IU kg^{-1} feed for chickens for fattening is estimated to result in a liver concentration of about 135 µg vitamin A g^{-1} liver, and 20 000 IU kg^{-1} feed in 290 µg vitamin A g^{-1} liver (derived from Sklan et al., 1994). Poultry liver retinol as indicated by food

composition tables and national surveys correspond more or less to a maximum feed concentration of 10 000 IU kg^{-1} complete feed for chickens for fattening if the two sets of highest values are omitted.

However, it is unclear whether and to what extent the allowances consider also the more recent findings on vitamin A and optimum immune response. Consequently, a chicken starter feed (for the first 14 days) should be allowed to contain up to 20 000 IU vitamin A kg^{-1}. For later production stages (chickens reared for laying and for fattening as well as laying hens), 10 000 vitamin A kg^{-1} complete feed appear appropriate. The FEEDAP Panel does not expect any negative impact on animal health, welfare and performance from those adjustments.

No reduction of the mean liver retinol of chickens is expected as the consequence of setting the proposed maximum contents for chickens, but a reduction of the variability (by cutting the highest values) is likely.

The recognised requirement and allowance data for growing and reproductive turkeys does not allow comparably low maximum contents for vitamin A as for chickens. Applying a safety factor of 2 for compensation of manufacture and storage losses and another 2 for variation in feed intake and maintenance of health, 20 000 IU vitamin A kg^{-1}complete feed appears an appropriate maximum content for turkeys. However, this value is close to the upper safe level identified by the NRC; so the FEEDAP Panel recommends that the 20 000 IU should be restricted to the starter phase and thereafter a maximum value of 10 000 IU should be applied.

There are not enough scientific data available to derive maximum contents for other poultry with the necessary accuracy.

6.4. Minor species

Dietary vitamin A contribution of food derived from minor species (e.g. rabbits, horses) is mainly of local significance. Data on vitamin A content in such foods are scarce and therefore not highly reliable.

6.4.1. Horses: deficiency, requirements, supply in field, hypervitaminosis

In horses, the classical vitamin A deficiency symptoms (night blindness, etc.) are not so pronounced, and extremely low vitamin A intake is necessary to induce them. The results suggest that horses are somewhat resilient to vitamin A deficiency, at least when those common parameters are used as indicator. Parameters associated with growth and hematopoiesis appear to be more sensitive. Immunity and reproduction are two other parameters influenced by vitamin A status, but this requires further studies.

Requirements for horses are not well defined for the different physiological states. For maintenance, growth and work, 2000 IU kg^{-1} feed is set as requirement, and for gestation and lactation, 3 000 IU kg^{-1} feed (NRC, 1989). The most recent NRC publication (2007) establishes a daily requirement for horses of 15 000 IU. Recommendations for maintenance and work as given by Meyer (1995) are: 75 IU kg^{-1} bw, 150–200 IU kg^{-1} bw for foals and 100–250 IU kg^{-1} bw for pregnant (late stage) and lactating mares. Recent data of a German feed compounder show 10 000–25 000 IU kg^{-1} complementary feed.

Bone fragility, hyperostosis, exfoliated epithelium and teratogenicity have been reported as signs of vitamin A hypervitaminosis in horses (NRC, 1987). In addition, orthopaedic diseases have been observed in growing horses as a result of an excess of vitamin A (Donoghue et al.,

1981; Kronfeld et al., 1990). The formerly established presumed upper safe level of vitamin A in the diet (16 000 IU kg^{-1} diet; NRC, 1987) has more recently been considered erroneous (NRC, 2007), because toxicity was absent at this amount.

For horses, one mg β-carotene is considered equivalent to 400 IU vitamin A, but no vitamin A toxicosis may occur even after high intake of β-carotene. The effect of beta-carotene on reproduction of mares is still uncertain, as results are inconsistent.

6.4.2. Rabbits: deficiency, requirements, supply in field, hypervitaminosis

Only few and weak data are available for rabbits. Signs of vitamin A deficiency in rabbits are similar to those described for other animals, including retarded growth and impaired reproduction (NRC, 1977).

Reproductive abnormalities, abortions and poor survivability of kits are reported to be associated with vitamin A toxicosis (St. Claire et al., 2004). The requirement of growing rabbits is given as 580 IU vitamin A kg^{-1} feed (NRC, 1977), that of reproductive rabbits as > 1 160 IU. In feed use, the data showed a supplementation range of 8 000–16 000 IU kg^{-1} feed (Appendix 10). More recent data of a German feed compounder show a range of 12 000–22 000 IU kg^{-1}.

6.4.3. Synopsis

Due to the limited data available for minor species, a scientifically reasonable deduction of maximum contents in feeds is not possible. Also, no reduction of consumer supply with preformed retinol could be expected from limiting vitamin A for rabbits and horses because liver of those species plays an insignificant role in the eating habits in Europe.

6.5. Fish

6.5.1. Symptoms of deficiency, requirements, supply in field, hypervitaminosis

Signs of vitamin A deficiency in fish are comparable among species such as salmonids, catfish, carp and yellowtail; they include increased mortality, reduced growth, skin malpigmentation, eye disorders (e.g. exopthalmia), bone malformations (e.g. malformed opercula), oedema and haemorrhages of fins and skin (NRC, 1993). Table 14 summarises vitamin A requirements for some species. A recent article on zebrafish stresses the fundamental role of vitamin A in reproduction (Alsop et al., 2007).

Table 15. **Vitamin A requirements in fish**

Species	Vitamin A (IU kg^{-1} complete diet)
Rainbow trout (*Oncorhynchus mykiss*) [(1)]	2 500*
Channel Catfish (*Ictalurus punctatus*) [(2)]	1 000–2 000
Common carp (*Cyprinus carpio*) [(3)]	1 000–2 000
Yellowtail (*Seriola quinqueradiata*) [(4)]	19 000
Hybrid tilapia (*Oreochromis niloticus* x *O. aureus*) [(5)]	~ 6 000
Atlantic salmon (*Salmo salar*) [(3)]	2 500

(1) Kitamura et al., 1967
(2) Dupree, 1970
(3) Halver, 2002
(4) Shimeno, 1991
(5) Hu et al., 2006
* Thompson et al. (1995) proposed 60 000 IU vitamin A kg^{-1} for immunocompetence.

Vitamin A deficiency is unlikely to occur, even if commercial feeds based on fish meal and oil are not supplemented with vitamin A, due to the high background levels of vitamin A in raw materials used in fish feeds. For example, the feed composition of commercial salmonid feed generally contains high lipid (30–40 %) and protein (35–55 %) contents and low carbohydrate content (10 %) (Einen, 2001). Fish oil and fish meal are commonly used as the main lipid and protein sources in commercial salmonid feeds. The vitamin A concentration in fish meal varies according to the species used: fish meal from a vitamin A poor species such as capelin (*Mallotus villosus*) is generally around 1 mg RE kg^{-1} (~ 3 300 IU vitamin A kg^{-1}) whereas the vitamin A concentration in a vitamin A-rich species, such as blue whiting (*Micromesistius poutassou*), may reach levels above 70 mg RE kg^{-1} (~ 233 000 IU vitamin A kg^{-1}). Marine fish oils (Opstvedt et al., 1997) also contain varying levels of vitamin A, from 6 (20 000 IU kg^{-1}) to 690 mg RE kg^{-1} lipid (2 300 000 IU vitamin A kg^{-1}). Consequently, the vitamin A level in fish feed is dependent on the species used to produce the fish oil and fish meal.

Table 15 gives the concentration of retinol in a random selection of commercial feed samples. The minimum concentration of vitamin A analysed was 10 000 IU vitamin A kg^{-1}, suggesting that vitamin A deficiency is unlikely considering that the requirement is approximately 2 500 IU vitamin A kg^{-1}, and the maximum level analysed was about 400 000 IU vitamin A kg^{-1} feed.

Table 16. **Concentration of vitamin A (IU kg^{-1} and mg kg^{-1}) in commercial salmonid feed samples selected at random (n = 20 per year, n = 21 in 2004)**

Year	Average (kg^{-1})		S.D (kg^{-1})		Minimum (kg^{-1})		Maximum (kg^{-1})	
	IU	mg	IU	mg	IU	mg	IU	mg
2002	60 000	18	3 000	9	26 667	8	146 667	44
2003	53 333	16	40 000	12	23 333	7	190 000	57
2004	103 333	31	93 333	28	33 333	10	403 333	121
2005	63 333	19	50 000	15	16 667	5	230 000	69
2006	60 000	18	53 333	16	10 000	3	240 000	72

Note: Data are the sum of all-trans A_1, 9-cis A_1, 13-cis A_1 and all-trans A_2 from the national surveillance programme at NIFES for the Norwegian Food Safety Authority.

In recent years, the vitamin A-rich species, blue whiting (*M. poutassou*), has constituted a major part of the total catch delivered to the Norwegian fish feed industry. However, there is an increasing trend to include alternative ingredients of vegetable origin such as rapeseed oil, soybean oil, maize and corn in commercial fish feeds, which will result in reduced vitamin A levels in the feed.

Several toxicity studies have been conducted on the effects of elevated vitamin A in feed on fish, indicating considerable differences in tolerance among species. Ørnsrud et al. (2002) showed that about 400 000 IU vitamin A kg^{-1} feed induced symptoms of stress and reduced growth in juvenile Atlantic salmon (*Salmo salar*) after 14 weeks of feeding. Hilton (1983) suggested a maximum tolerable level of about 900 000 IU vitamin A as retinyl palmitate kg^{-1} feed in rainbow trout juveniles (*O. mykiss*) after 16 weeks of feeding. This conclusion was based on abnormal and eroded fins, scoliosis and lordosis and pale fragile livers, although increased activity of plasma alkaline phosphatase and reduced iron stores in liver and kidney were already found in fish exposed to about 100 000 IU vitamin A kg^{-1} feed. Grisdale-Helland et al. (1991) fed Atlantic salmon fry for 30 weeks and found a slight increase in mortality at 123 000 IU vitamin A kg^{-1} feed. In Japanese flounder (*Paralichthys olivaceus*) larvae fed for six weeks, the safe level of vitamin A in the larval stage was estimated to be less than 50 000 IU vitamin A kg^{-1} while vitamin A inclusion above this level gave lower body weight and length and increased occurrence of vertebral deformities (Dedi et al., 1995). In tilapia (*Oreochromis niloticus*) fingerlings fed for 18 weeks, 10 000 IU vitamin A kg^{-1} induced slightly reduced weight gain while 40 000 IU vitamin A kg^{-1} induced growth depression, increased mortality, abnormal bone formation, fin necrosis and enlarged liver and spleen (Saleh et al.,1995). Thus, in fish the sensitivity to hypervitaminosis A is species-dependent, as shown also for mammals.

6.5.2. Synopsis and options

Under farming conditions, vitamin A in edible salmonid tissues does not primarily result from supplemental dietary vitamin A. Instead, the vitamin A supply to salmonids originates chiefly from raw materials (fish meal, fish oil) used in fish feed formulation. The resulting dietary vitamin A concentrations considerably exceed the requirements in most cases. A similar nutritional situation can be assumed for other farmed piscivorous fish, like seabass and seabream. Data for fish other than salmonids are scarce and therefore of limited reliability.

A predictability of fish flesh (and fish oil) retinol content from a given dietary vitamin A concentration could not be found, particularly under commercial conditions.

In view of the above, introducing a maximum vitamin A content for salmonids feed in the EU legislation could limit the use of fish meal and fish oil in feeding and consequently influence the economics of fish production.

The vitamin A content of edible fish tissues can therefore in practice not be controlled by manipulating the vitamin A supplementation of feed.

6.6. Conclusions

The practice of vitamin A supplementation of feedingstuffs exceeds the current requirements/allowances of food-producing animals. The permitted maximum contents for vitamin A in feed for growing animals are also considerably above allowances. Thus, there is a certain scope to reduce levels of vitamin A, at least in some cases. However, any proposal

for a revision/introduction of maximum contents of vitamin A in feedingstuffs for food-producing animals must exclude negative effects on animal health and on the economics of food production. Considering this imperative, potential maximum contents of vitamin A in complete diets are derived:

For pigs: 16 000 IU vitamin A kg^{-1} for piglets, 6 500 IU vitamin A kg^{-1} for pigs for fattening, 12 000 IU vitamin A for gestating sows and of 7 000 IU vitamin A kg^{-1} for lactating sows. Boars were not considered further.

For cattle: 25 000 IU vitamin A kg^{-1} (unchanged) for veal calves, 10 000 IU vitamin A kg^{-1} for cattle for fattening and for lactating cows, 20 000 IU vitamin A kg^{-1} for dry cows.

For poultry: 20 000 IU vitamin A kg^{-1} in the first 14 days of life for chickens reared for laying and for fattening, and in the first 28 days of life for turkeys for fattening, 10 000 IU vitamin A kg^{-1} for chickens reared for laying and for fattening (after 14 days), for turkeys for fattening (after 28 days), and for laying hens and breeder turkeys.

For minor species (other poultry, other ruminants, rabbits and horses), there are insufficient data available to derive maximum contents with the necessary accuracy.

The proposed maximum concentrations for pigs and chickens for fattening will not reduce the current typical liver preformed vitamin A levels but are expected to cut the upper bound of the observed range. In general the introduction of maximum contents would result in a more uniform vitamin A content of tissues and products.

When considering the total vitamin A content of fish feed, supplemental vitamin A plays a minor role. Fish meal and oil are the main contributors of vitamin A in fish feed. Because of the above, introducing a maximum vitamin A content for salmonids feed in the EU legislation could limit the use of fish meal and fish oil in feeding and, consequently, influence the economics of fish production. Therefore, the FEEDAP Panel did not derive maximum contents for fish feed.

7. Environmental consequences of vitamin A supplementation to feed

The FEEDAP Panel is not aware of any evidence suggesting that vitamin A from use in farm animals at its current level presents a risk to the environment. There is, however, very limited published information on toxicity of vitamin A to environmentally relevant species, except for fish used in aquaculture. As discussed in Section 6.9 above, fish are not particularly sensitive to dietary vitamin A. However, considerable species differences in tolerance do appear to exist, with 10 000 IU vitamin A kg^{-1} feed decreasing growth rate in tilapia (*O. niloticus*; Saleh et al., 1995) and 100 000 IU vitamin A kg^{-1} reducing survival in Atlantic salmon fry (*S. salar*; Grisdale-Helland et al., 1991). Data on a few ecotoxicity studies, carried out with suspensions of retinol, are available from information leaflets that accompany retinol products. However, given the strong lipophilic nature of retinol, waterborne exposure can be considered irrelevant in terms of environmental risk.

Vitamin A and its precursors are sensitive to oxidation and are rapidly degraded in the environment. There is no reason to suspect that feed supplementation at current levels elevates the concentrations of vitamin A in the environment above those naturally present, for example during the decay of dead organisms. No further environmental risk assessment is therefore deemed to be required.

CONCLUSIONS AND RECOMMENDATIONS

CONCLUSIONS

Risk assessment for consumers

Only preformed vitamin A, not total vitamin A equivalents, is to be considered of safety concern. The UL set by SCF (3 000 µg RE from preformed vitamin A day^{-1}) was considered by the FEEDAP Panel as still being appropriate, taking into account the available data. Quantitative correlations between retinol intake and bone health risk justifying the establishment of a lower UL for a specific population subgroup (elderly people) could not be established. A maximum intake of 1 500 µg RE from preformed vitamin A day^{-1} would therefore — until new data indicates the necessity of a re-evaluation — serve as a guidance level (GL) for individuals at a greater risk of osteoporosis and bone fracture (particularly post-menopausal women).

Approximately about half of the intake of total vitamin A in European consumers comes from carotenoids in foodstuffs of plant origin, the other half from preformed vitamin A in foodstuffs of animal origin. The mean intake of preformed vitamin A in the adult population in Europe is estimated between 400 and 1 200 µg RE day^{-1} in men and between 350 and 1 000 µg RE day^{-1} in women.

A small proportion of the European population shows an intake of preformed vitamin A above the UL. This proportion is about 1–2 % in Denmark, Germany, the Netherlands, Norway, Sweden and the UK, and about 3–6 % in France, Greece, Italy and Spain. The corresponding GL is exceeded by 2–3 and 8–14 %, respectively.

The main exposure to preformed vitamin A comes from consumption of liver (with about 60–80 % of average preformed vitamin A intake in France, Greece, Italy and Spain) and of milk, including all dairy products (with about 45–60 % of average preformed vitamin A intake in Germany, the Netherlands, Norway and Sweden).

Despite the uncertainties associated with the assessment of preformed vitamin A intake from liver, it can be concluded that among liver eaters, the consumption of liver as such may lead to daily intakes of 2 800–7 000 µg preformed vitamin A. As it is considered highly unlikely that consumers would exceed the UL from the intake of milk and dairy products alone, the risk of exceeding the UL (and GL) for preformed vitamin A is predominantly related to liver consumption. Taking a maximum retinol concentration of 150 µg RE g^{-1} liver and assuming a consumption of 100 g $week^{-1}$, there would result a daily intake of about 2 140 µg RE. Persons taking supplements containing vitamin A may add to the dietary supply of preformed vitamin A another 700–1 200 µg day^{-1}. Thus, regular liver consumption in combination with supplements containing vitamin A can be considered a particular risky behaviour.

Preformed vitamin A may raise safety concerns because of its high levels in some food of animal origin and of individual consumption patterns; therefore, feeding practice should seek to avoid any unnecessary high concentration in those foods.

Adjusting the vitamin A supply to animals and its implications

In general, there is a correlation between dietary vitamin A and preformed vitamin A in animal tissues and products. However, any proposal for a reduction in the feed content of vitamin A for food-producing animals must consider the allowances and ensure a satisfactory supply under worst case conditions.

The preformed vitamin A concentration in liver can only be predicted from vitamin A concentrations in feed in pigs. Concentrations of 16 000 IU vitamin A kg^{-1} for piglets and 6 500 IU vitamin A kg^{-1} for pigs for fattening could be derived as appropriate maximum contents. The proposed maximum concentrations for pigs will not reduce the current typical liver preformed vitamin A levels but are expected to cut the upper bound of the observed range.

Any acceptable modification of the vitamin A content in feed for other food-producing animals does not lead to a predictable reduction of preformed vitamin A in foodstuffs of animal origin. However, a reduction would in general result in a more uniform content of preformed vitamin A in tissues and products.

The main vitamin A source for salmonids is not supplemental vitamin A but feed materials, like fish meal and fish oil.

Uncertainties inherent to the risk assessment

It should be noted that there are several limitations in the information available to deliver precise conclusions. The FEEDAP Panel had access to consumption surveys from a limited number of Member States and in those there was a low representation of liver consumers. Moreover, the surveys were not designed to assess vitamin A from the relevant groups of foodstuffs containing preformed vitamin A. There were also methodological differences in collecting and reporting data in various consumption surveys, which could have influenced the results.

The conclusions reached by the FEEDAP Panel take into consideration those caveats. In spite of all limitations and restrictions, there was remarkable consistency in the conclusions that could be drawn from different surveys, strengthening the confidence of the overall opinion.

RECOMMENDATIONS

The FEEDAP panel favours as a consumer protection measure a general introduction of maximum contents for vitamin A in complete feed for most food-producing animals.

Introduction of maximum contents of vitamin A in feed for food-producing animals

The FEEDAP Panel recommends the introduction of the following maximum contents:

> For pigs: 16 000 IU vitamin A kg^{-1} for piglets, 6 500 IU vitamin A kg^{-1} for pigs for fattening, 12 000 IU vitamin A for gestating sows and of 7 000 IU vitamin A kg^{-1} for lactating sows. Boars were not considered further.
>
> For cattle: 25 000 IU vitamin A kg^{-1} for veal calves, 10 000 IU vitamin A kg^{-1} for cattle for fattening and for lactating cows, 20 000 IU vitamin A kg^{-1} for dry cows.
>
> For poultry: 20 000 IU vitamin A kg^{-1} in the first 14 days of life for chickens reared for laying and for fattening, and in the first 28 days of life for turkeys for fattening, 10 000 IU vitamin A kg^{-1} for chickens reared for laying and for fattening (after 14 days), for turkeys for fattening (after 28 days), and for laying hens and breeder turkeys.

Maximum contents for complete feed for salmonids should not be introduced.

EU-wide updated information on vitamin A content of foods of concern

It is presently not possible to fully predict the quantitative consequences of the recommended introduction of maximum contents of vitamin A in feed for food-producing animals on the preformed vitamin A content in relevant tissues and products. The FEEDAP Panel recommends therefore the commissioning of comprehensive and representative surveys on the preformed vitamin A in foods of concern (liver, milk and eggs) in the EU.

Complementary measures to the introduction of maximum contents

The FEEDAP Panel recommends extended nutritional advice to consumers:

Liver remains as a food associated with a particular hazard of vitamin A intake exceeding the UL, and this would not change even if measures to limit the vitamin A supply to food-producing animals are introduced. Specific advice should consider relevant subgroups of the population with different sensitivities.

The FEEDAP Panel endorses the SACN recommendations to restrict the simultaneous intake of liver and retinol containing supplements.

Compliance with the GL for persons at specific risk could probably only be reached by individual advice. Bone health is affected by a multitude of nutritional factors, including vitamin D, Ca and Zn, which should also be considered in an individual advice for nutrition behaviour.

Specific issues of complementary feed, in particular for ruminants

The vitamin A content of complementary feed is normally derived from the amount of vitamin A which can be calculated as a result of the maximum content in complete feed, and from the percentage to which the complementary feed contributes to the daily ration. If two or more types of complementary feeds are used simultaneously, and if the vitamin A content of each complementary feed is calculated to supply the animal at a level derived from the maximum content, this could lead to an excessive vitamin A intake by the animal.

Therefore, the FEEDAP Panel recommends the introduction of rules should be set for the vitamin A content of complementary feeds to prevent the amount of vitamin A delivered to the animals through the daily ration from exceeding the maximum authorised level of vitamin A.

DOCUMENTATION PROVIDED TO EFSA

1. Review of Dietary Advice on Vitamin A. 2005. Scientific Advisory Committee on Nutrition.
2. Evaluation des besoins nutritionnels des animaux en vitamines A, D et E ainsi que des risques pour la santé animale et la santè du consommateur, lies à des apports élevés chez les animaux producteurs d'aliments. 2005. Agence Francaise de Sécurité Sanitaire des Aliments.
3. Information submitted on consumption data of Vitamin A by the Database Managers of the EU Network on Food Consumption.
4. Information submitted by the Member States on consumption data/Current practices of Vitamin A supplementation in all the categories of livestock in the EU.
5. Information submitted by FEFAC on the current practices of Vitamin A supplementation in all the categories of livestock in the EU.

REFERENCES

Agabriel C, Cornu A, Journal C, Sibra C, Grolier P, Martin B (2007). Tanker milk variability according to farm feeding practices: vitamins A and E, carotenoids, color, and Terpenoids. J. Diary Sci. 90, 4884-4896

Agence Française de sécurité sanitaire des aliments (AFSSA), 2005. Evaluation des besoins nutritionnels des animaux en vitamins A, D et E ainsi que des risques pour la santé animale et la santé du consommateur, lies à des apports élèves chez les animaux producteurs d'aliments. <www.afssa.fr>

Alosilla CE Jr., McDowell LR, Wilkinson NS, Staples CR, Thatcher WW, Martin FG, Blair M (2007). Bioavailability of vitamin A sources for cattle. Journal of Animal Science 85, 1235-1238.

Alsop D, Matsumoto J, Brown S, Van Der Kraak G (2007). Retinoid requirements in the reproduction of zebrafish. General and comparative endocrinology 156(1), 51-62.

Anderson LE, Myer SrRO, Brendemuhl JH, McDowell LR (1995). The effects of excessive dietary vitamin A on performance and vitamin E status in swine fed diets varying in dietary vitamin E. J. Anim. Sci., 73:1093.

Anderson MD, Speer VC, McCall JT, Hays VW (1966): Hypervitaminosis A in the young pig. J. Anim. Sci 25, 1123-1127.

Aoe H, Masuda I, Mimura T, Saito T (1968). Requirement of young carp for vitamin A. Bulletin of the Japanese Society of Scientific Fisheries, 34, 959-964.

Arnett AM, Dikeman ME, Spaeth CW, Johnson BJ, Hildabrand B. Effects of vitamin A supplementation in young lambs on performance, serum lipid, and longissimus muscle lipid composition. J Anim Sci. 2007 Nov;85(11), 3062-71.

Aydelotte MB (1963). The effects of vitamin A and citral on epithelial differentiation in vitro 1. The chick tracheal epithelium. J. Embryol. exp. Morph. 11, part 1: 279-291.

Ballew C, Galuska D, Gillepsie C (2001). High Serum retinyl esters are not associated with reduced bone mineral density in the Third National Health And Nutrition Examination Survey, 1988-1994. Journal of Bone and Mineral Research; 16(12):2306-12.

Bauerfeind JC (1980). The safe user of vitamin A. A report of the International vitamin A Consultative Group, (IVACG). The Nutrition Foundation, Washington D.C., pp. 1- 44.

Bell S, Braun G, Brombach C, Eisinger-Watzi M, Götz A, Hartmann B, Heuer T, Heyer A, Hilbig A, Huth R, Krems C, Möseneder J, Oltersdorf U, Pfau C, Pust S, Richter A, Siewe-Reinke A, Straβburg A, Tschida A, Wagner, U, Vásquez-Caicedo AL. Nationale Verzehrs Studie II (NVS II). Max Rubner Institut, Bundesforschungsinstitut für Ernährung und Lebensmittel, Germany, 2008.

Blair R, Aherne FX, Doige CE (1992). Tolerance of growing pigs for dietary vitamin A, with special reference to bone integrity. Int. J. Vitamin Res. 1992; 62(2):130-3.

Blomhoff et al.: Vitamin A metabolism: new perspectives on absorption, transport, and storage. Physiol. Rev. 1991; 71: 951-990.

Brubacher GB, Weiser H (1985): The vitamin A activity of betecarotene. Int. J. Vitam. Nutr. Res. 1985; 55(1), 5-15.

Bruns NJ and Webb KE (1990). Vitamin A deficiency: serum crotiso and humoral immunity in lambs. Journal of Animal Science 68, 454-459.

Calderón F, Chaveau-Duriot B, Martin B, Graulet B, Doreau M, Nozière P (2007a). Variation in carotenoids, vitamins A and E, and color in cow's plasma and milk during late pregnancy and the first three months of lactation. J. Diary Sci. 90, 2335-2346.

Calderón F, Chaveau-Duriot B, Pradel P, Martin B, Graulet B, Doreau M, Nozière P (2007b). Variations in carotenoids, vitamins A and E, and color in cow's plasma and milk following a shift from hay diet to diets containing increasing levels of carotenoids and vitamin E. Journal of. Dairy Science. 90, 5651-5664.

Carnovale E & Marletta L (2000). Tabelle di composizione degli alimenti. INRAN, Roma <http://www.int.inran.it/servizi_cittadino/per_saperne_di_piu/tabelle_composizione_alimenti>

Coates JW, Holbek NE, Beames RM, Puls R, O'Brien P (1998). Gastric ulceration and suspected vitamin A toxicosis in grower pigs fed fish silage. Canadian Veterinary Journal 39(3), 167–170.

Cunha TH (1977). Swine Feeding and Nutrition. Academic Press, New York.

D-A-CH Referenzwerte für die Nährstoffzufuhr, 2001. Editor: Deutsche Gesellschaft für Ernährung e.V., 1. Auflage 2. Korrigierter Nachdruck Umschau/Braus.

Davis CY, Sell JL. Immunoglobulin concentrations in serum and tissues of vitamin A-deficient broiler chicks after Newcastle disease virus vaccination. Poult-Sci. 1989 Jan; 68(1), 136-44.

Dedi J, Takeuchi T, Seikai T, Watanabe T, 1995. Hypervitaminosis and safe levels of vitamin A for larval flounder (Paralichthys olivaceus) fed Artemia nauplii. Aquaculture 133, 135-146.

DeLuca L, Schumacher M, and Nelson DP. 1971. Localization of the retinol-dependent fucose-glycopeptide in the goblet cell of the rat small intestine. J. Biol. Chem. 246:5762.

DLG Futterwerttabellen Band 85 (1962). DLG Verlag GBMH Frankfurt.

Donoghue S, Kronfeld DS, Berkowitz SJ, Copp RL (1981). Vitamin A nutrition of the equine: growth, serum biochemistry and hematology. J. Nutr. 111, 365-374.

Dupree HK (1970). Dietary requirement of vitamin A acetate and beta carotene pp 148-150 In Progress in Sport Fishery Research 1969. Resource Publication No. 88. Washington, D.C., Bureau of Sport Fisheries and Wildlife.

EC (European Commission), 2002. Scientific Committee on Food. Opinion of the Scientific Committee on Food on the Tolerable Upper Intake Level of Preformed Vitamin A (retinol and retinyl ester). <http://ec.europa.eu/food/fs/sc/scf/out145_en.pdf>

EC (European Commission), 2003. Scientific Committee for Animal Nutrition. Opinion of the Scientific Committee for Animal Nutrition on the use of zinc in feedingstuffs. <http://ec.europa.eu/food/fs/sc/scan/out120_en.pdf>

EFSA, 2006. Opinion of the Scientific Panel on Additives and Products or Substances used in Animal Feed on the request from the Commission on the safety of use of colouring agents in animal nutrition. PART II. Capsanthin, Citranaxanthin, and Cryptoxanthin. EFSA Journal (2006) 386, 1-40. <http://www.efsa.europa.eu/EFSA/efsa_locale-1178620753812_1178620782619.htm>

Einen O (2001). Vekst og fôrutnyttelse (In Norwegian). In: Waagbø, R., Espe, M., Hamre, K., Lie, Ø. (Eds.), Fiskeernæring. Kystnæringen Forlag & Bokklubb AS, Bergen, pp. 205-217

Elmadfa I, Burger P, Dernorfer E, Kiefer I, Kunze M, König J, Leimüller G, Manafi M, Mecl M, Papathanasiou V, Rust P, Vojir F, Wagner K-H, Zarfl B (1998). Austrian Study on Nutritional Status (ASNS). Österreichischer Ernährugngsbericht. Bundesministerium für Gesundheit, Arbeit und Soziales. Wien.

Expert Group on Vitamin and Minerals (EVM). Safe Upper Levels for Vitamins and Minerals. FSA : London, 2003.

Feskanich D, Singh V, Willet WC, Colditz GA (2002). Vitamin A intake and hip fractures among postmenopausal women. JAMA; 287(1):47-54.

Finch S, Doyle W, Lowe C, Bates CJ, Prentice A, Smithers G and Clarke PC (1998). National Diet and Nutrition Survey: people aged 65 years and over. Volume 1: report of the diet nutrition survey. TSO: London, 1998.

Flachowsky et al. (1990). Untersuchungen zum Vitamin-A-Bedarf und zum Vitamin-A-Status wachsender Rinder. 1. Mitteilung Untersuchung an Kälbern. Arch. Anim. Nutr. 40, 85-100 line 1137.

Fletcher RA 1971. Effects of vitamin A deficiency on the pituitary-gonad axis of the California quail (*Lophortyx californicus*). J. Exp. Zool. 176:25.

Fox PF and McSweeney PLH. Vitamins in Milk and Dairy Products, 1998. In Dairy Chemistry and Biochemistry. 265-291. Thomson Science.

Freudenheim JL, Johnson NE, Smith EL (1986). Relationships between usual nutrient intake and bone-mineral content of women 35-65 years of age: longitudinal and cross-sectional analysis. American Journal of Clinical Nutrition; 44(6):863-76.

GfE (Gesellschaft für Ernährungsphysiologie), 1994. Energie- und Nährstoffbedarf landwirtschaftlicher Nuztiere, Nr. 2. Empfehlungen zur Energie- und Nährstoffversorgung der Pferde, DLG-Verlag Frankfurt (Main), 67 p.

GfE (Gesellschaft für Ernährungsphysiologie), 1999. Empfehlungen zur Energie- und Nährstoffversorgung der Legehennen und Masthühner (Broiler). Nr. 7, DLG-Verlag, Frankfurt, 185 pp.

GfE (Gesellschaft für Ernährungsphysiologie), 2001. Empfehlungen zur Energie- und Nährstoffversorgung der Milchkühe und Aufzuchtrinder. Nr. 8, DLG-Verlag, Frankfurt, 136 pp.

GfE (Gesellschaft für Ernährungsphysiologie), 2004. Empfehlungen zur Energie- und Nährstoffversorgung von Mastputen. Proc. Soc. Nutr. Physiol. Nr. 13, 199-234.

GfE (Gesellschaft für Ernährungsphysiologie), 2006. Empfehlungen zu Energie- und Nährstoffversorgung von Schweinen, Nr. 10. DLG-Verlag, Frankfurt.

Gregory J, Foster K, Tyler HA, Wiseman M (1990). The dietary and nutritional survey of British adults. ISBN 0 11 691300 2. London: HMSO.

Grisdale-Helland B, Helland SJ, Åsgård T, 1991. Problems associated with the present use of menadione sodium bisulfite and vitamin A in diets for Atlantic salmon. Aquaculture 92, 351-358.

Gropp JM, Strahberger S, Merhinger U (1991): p. 18-23 in :Vitamine und weitere Zusatzstoffe bei Mensch und Tier. Wissenschaftlicher Fachverlag, Niederkleen.

Guss SB (1977). Management and diseases of dairy goats. Dairy Goat Journal Publ. Corp. Scottdale, Arizona.

Hall WC, Damjanou I, Nielsen SW, van der Heide L, and Eaton HD. 1980. Testicular changes of acute vitamin A deficiency of cockerels. Am. J. Vet. Res. 41:586.

Halver JE (2002). The vitamins. In: Halver JE and Hardy RW, Editors, 2002. Fish Nutrition, Academic Press, San Diego, CA, pp. 61–141.

Harrington KE, Robson PJ, Kiely M, Livingstone MBE, Lambe J and Gibney MJ (2001). The North/South Ireland Food Consumption Survey: survey design methodology. Public Health Nutrtion: 4(5A), 1037-1042.

Hayes KC and Hegsted DM. Toxicity of vitamins. In: Foster EM, ed. Toxicants occurring natutrally in foods. 2nd ed. Washington, DC: National Academy Press, 1973.

Heinonen M. (1990). Carotenoids and retinoids in Finnish foods and the average diet. Doctoral thesis, Department of Food Chemistry & Technology, University of Helsinki, Helsinki, Finland.

Hemre GI, Deng DF, Wilson RP, Berntssen MHG (2004). Vitamin A metabolism and early biological responses in juvenile sunshine bass (Morone chrysops x M. saxatilis) fed graded levels of vitamin A. Aquaculture 235, 645-658.

Henderson L, Grefgory J, Irving K and Swan G. The National Diet and Nutrition Survey; adults aged 19 to 64 years. Volume 2: Energy, protein, carbohydrate, fat and alcohol intake. TSO: London, 2003.

Hernandez LHH, Teshima SI, Ishikawa M, Alam S, Koshio S, Tanaka Y (2005). Dietary vitamin A requirements of juvenile Japanese flounder *Paralichthys olivaceus*. Aquaculture Nutrition 11, 3-9.

Hernandez LHH, Teshima SI, Ishikawa M, Koshio S (2004). Effects of dietary vitamin A on juvenile Red Sea Bream *Chrysophrys major*. Journal of the World Aquaculture Society 35, 436-444.

Heseker H, Adolf T, Eberhardt W, Hartmann S, Herwig A, Kübler W, Matiaske B, Moch KJ, Nitsche A, Schneider R, Zipp A (1992). Lebensmittel- und Nährstoffaufnahme Erwachsener in der Bundesrepublik Deutschland. VERA- Schriftenreihe Band III, Wiss. Fachverlag Dr. Fleck, Niederkleen.

Hilton JW, 1983. Hypervitaminosis A in rainbow trout (*Salmo gairdneri*): Toxicity signs and maximum tolerable level. Journal of Nutrition 113, 1737-1745.

Hjartåker A, Lagiou A, Slimani N, Lund E, Chirlaque MD, Vasilopoulou E, Zavitsanos X, Berrino F, Sacerdote C, Ocké MC, Peeters PH, Engeset D, Skeie G, Aller A, Amiano P, Berglund G, Nilsson S, McTaggart A, Spencer EA, Overvad K, Tjønneland A, Clavel-Chapelon F, Linseisen J, Schulz M, Hemon B, Riboli E (2002) Consumption of dairy products in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohort: data from 35 955 24-hour dietary recalls in 10 European countries. Public Health Nutr. 5(6B), 1259-71.

Houtkooper LB, Ritenbaugh C, Aickin M, Lohman TG, Going SB, Weber JL, Greaves KA, Boyden TW, Pamenter RW, Hall MC (1995). Nutrients, body composition and exercise

are related to change in bone mineral density in premenopausal women. Journal of Nutrition; 125(5):1229-37.

Howell MC and Thompson JN. Lesions associated with the developing of ataxia in vitamin A-deficient chicks. Br J Nutr. 1967 Aug; 21(3), 741-50.

Howells LC and Livesey CT (1998). A survey of vitamin A concentrations in the liver of food-producing animals. Food Additives and Contaminants, 1998, Vol. 15, No 1, 10-18. <http://www.nal.usda.gov/fnic/foodcomp/Data/index.html#retention>

Hu CJ, Chen SM, Pan CH and Huang CH (2006) Effects of dietary vitamin A or beta-carotene concentrations on growth of juvenile hybrid tilapia, Oreochromis niloticus x O-aureus. Aquaculture 253, 602-607.

Hülshof KFAM and Fruizinga AG (1999). Third Dutch National Food Consumption Survey (DNFCS-3) 1997-1998. TNO Zeist, The Netherlands.

Hulshof PJM, van Roekel-Jansen T, van de Bovenkamp P and West CE. Variation in retinol and carotenoid content of milk and milk products in the Netherlands. (2006). Journal of Food Composition and Analysis 19 2006, 67-75.

Institute of Medicine, Food and Nutrition Board (2001) Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc. National Academy Press, Washington, D.C., pp. 1-28.

Julshamn, K., Lundebye Haldorsen, A.-K., Berntssen, M.H.G., Hemre, G.-I., Ørnsrud, R., Waagbø, R., Lunestad, B.T. & Måge, M. (2004). Årsrapport 2003. Overvåkningsprogram for fôrvarer til fisk og akvatiske dyr.

Julshamn, K., Lunestad, B.T., Lundebye Haldorsen, A.-K., Berentssen, M. & Waagbø, R. (2003). Årsrapport 2002. Overvåkningsprogram for fiskefôr.

Kawahara TN, Krueger DC, Engelke JA, Harke JM, Binkley NC (2002). Short-term vitamin A supplementation does not affect bone turnover in men. Journal of Nutrition; 132(6):1169-72.

Kirchgessner M (2004). Tierernährung. DLG Verlag, Frankfurt, Germany.

Kitamura S, Suwa T, Ohara S and Nakagawa K (1967) Studies on vitamin requirements of rainbow trout. III. Requirements for vitamin A and deficiency symptoms. Bulletin of the Japanese Society of Scientific Fisheries 33, 1126-1131.

Kloosterman and Ocké (2007). Human intake data of vitamin A in the Netherlands RIVM, The Netherlands – March 2007.

Kronfeld DS, Meacham TN, Donogue S (1990). Dietary aspects of developmental orthopedic disease in young horses. P. 451 in Vet. Clinics NA: Equine Pract., Hintz H.F., ed. Philadelphia: Saunders W.B.

Landes. E. (1994). Die konzentration von vitamin A in der leber von rindern und schweinen. Ubers.Tierernahrg. 1994; 22**:** 281-320.

LFL, 2007. Bayerische Landesanstalt für Landwirtschaft, Gruber Tabelle 28. Auflage.

Lim LS, Harnack LJ, Lazovich D, Folsom AR (2004). Vitamin A intake and the risk of hip fracture in postmenopausal women: the Iowa Women's Health Study. Osteoporos International. 2004;15:552-559.

Linseisen J, Kesse E, Slimani N, Bueno-De-Mesquita HB, Ocké MC, Skeie G, Kumle M, Dorronsoro Iraeta M, Morote Gómez P, Janzon L, Stattin P, Welch AA, Spencer EA, Overvad K, Tjønneland A, Clavel-Chapelon F, Miller AB, Klipstein-Grobusch K, Lagiou P, Kalapothaki V, Masala G, Giurdanella MC, Norat T, Riboli E (2002) Meat consumption in the European Prospective Investigation into Cancer and Nutrition (EPIC) cohorts: results from 24-hour dietary recalls. Public Health Nutr. 2002 Dec.; 5(6B), 1243-58.

Lopen, G. A., R. W. Phillips, and C. F. Nockels. 1973. Body water kinetics in vitamin A-deficient chickens. Proc. Soc. Exp. Biol. Med. 144:54.

Måge, A. Julshamn, K., Hemre, G.-I. & Lunestad, B.T. (2005). Årsrapport 2004. Overvåkningsprogram for fôrvarer til fisk og akvatiske dyr.

Måge, A. Julshamn, K., Hemre, G.-I. & Lunestad, B.T. (2006). Årsrapport 2005. Overvåkningsprogram for fôrvarer til fisk og akvatiske dyr.

Måge, A. Julshamn, K., Hemre, G.-I. & Lunestad, B.T. (2007). Årsrapport 2006. Overvåkningsprogram for fôrvarer til fisk og akvatiske dyr.

Majchrzak D, Fabian E, Elmadfa I (2006). Vitamin A content (retinol and retinyl esters) in livers of different animals. Food Chemistry Vol. 98, 704-710.

McCance & Widdowson's (1991). The Composition of Foods.

McCance & Widdowson's (2002). The Composition of Foods. Compiled by UK Food Standards Agency and Institute of Food Research.

Melhus H, Michaelsson K, Kindmark A, Bergstrom R, Holmberg L, Mallmin H, Wolk A, Ljunghall S. (1998). Excessive dietary intake of vitamin A is associated with reduced bone mineral density and increased risk for hip fracture. Annal of Internal Medicine, 129(10):770-8.

Mensink GBM and Beitz R (2004). Food and nutrient intake in East and West Germany, 8 years after the reunification The German Nutrition Survey 1998. European Journal of Clinical Nutrition 58, 1000-1010.

Mensink GBM, 2002. Was essen wir heute? Ernährungsverhalten in Deutschland. Robert-Koch-Institut, Berlin. Beiträge zur Gesundheitsberichterstattung des Bundes (2002).

Mensink GBM, Heseker H, Richter A, Stahl A, Vohmann, Fischer J, Kohler S, Six J. Ernährungsstudie als KIGGS-Modul (EsKiMo). Robert Koch-Institut and Univertität Paderborn, Germany, 2007.

Meyer H. (1995) Pferdefütterung. 1995 Blackwell Wissenschafts-Verlag Berlin/Vienna.

Michaelsson K, Lithell H, Vessby B, Melhus H (2003). Serum retinol levels and the risk of fracture. New England Journal of Medicine. 2003 Jan 23; 348(4):287-94.

Møller A., Saxholt E, Christensen AT, Hartkopp HB, Hess Ygil K. Danish Food Composition Databank, revision 6.0. Food Informatics, Department of Nutrition, Danish Institute for Food and Veterinary Research. June 2005. <http://www.foodcomp.dk>

Moore T (1957). Vitamin A. Amsterdam Elsevier.

National Institute of Nutrition and Seafood Research (NIFES), Norway. <www.nifes.no>, and <www.mattilsynet.no>

National Research Council: Nutrient requirement of Rabbits, Second edition 1977, National Academy of Sciences Washington.

National Research Council: Nutrient Requirements of Beef Cattle. Seventh Revised. Edition, Update 2000, National Academic Press, Washington DC.

National Research Council: Nutrient Requirements of Dairy Cattle. Seventh Revised. Edition, 2001. National Academic Press, Washington DC.

National Research Council: Nutrient requirements of fish, 1993. National Academy Press, Washington D.C.

National Research Council: Nutrient Requirements of Goats: Angora, Dairy, and Meat Goats in Temperate and Tropical Countries, 1981. National Academic Press, Washington DC.

National Research Council: Nutrient Requirements of Horses. Fifth Revised Edition, 1989, National Academic Press, Washington DC.

National Research Council: Nutrient Requirements of Horses. Sixth Revised Edition, 2007, National Academic Press, Washington DC.

National Research Council: Nutrient Requirements of Poultry. Eighth Revised Edition, 1984, National Academic Press, Washington DC.

National Research Council: Nutrient Requirements of Poultry. Ninth Revised Edition, 1994, National Academic Press, Washington DC.

National Research Council: Nutrient Requirements of Swine. Ninth Revised Edition, 1988, National Academic Press, Washington DC.

National Research Council: Nutrient Requirements of Swine. Tenth Revised Edition, 1998, National Academic Press, Washington DC.

Nelson M, Erens B, Bates B, Church S, Boshier T. Low Income Diet and Nutrition Survey (LIDNS). London: The Stationery Office, 2007.

NEVO-tabel 2006: Nederlands Voedingsstoffenbestand 2006. Publisher Stichting NEVO/ Voedingscentrum, Den Haag 2006.

Nieman C, and Obbink HJK (1954). The biochemistry and pathology of hypervitaminosis A. Vitamin Horm 12:69-99.

Nockels CF, Ewing DL, Phetteplace H, Ritacco KA and Mero KW. 1984. Hypotheyrodism: An early sign of vitamin A deficiency in chickens. J. Nutr. 114:1733.

Nozière P, Grolier P, Durand D, Ferlay A, Pradel P and Martin B (2006). Variations in Carotenoids, Fat-soluble micronutrients, and color in cows' plasma and milk following changes in forage and feeding level. Journal of Dairy Science 89, 2634-2648.

Olson JA (1984). Serum level of Vitamin A and carotenoids as relectors of nutritional status. Journal National Cancer Institute, 73(6): 1439-44.

Ong DE and Chytil F. (1983). Vitamin A and cancer. *Vitamins and Hormones.* 40, 105-44.

Opstvedt J, Knudsen G, Asbjørnsen B (1997). Innhold av fettløselige vitaminer i fiskemel og fiskeolje produsert fra sild, lodde, tobis, kolmule og brisling (In Norwegian). Sildeolje- og sildemelindustriens forskningsinstitutt C-295, 10.

Ørnsrud R, Graff LE, Høie S, Totland GK, Hemre GI (2002). Hypervitaminosis A in first-feeding fry of the Atlantic salmon (Salmo salar L.). Aquaculture Nutrition 8, 7-13.

Padedes JR, and Garcia TP. (1959). Vitamin A as a factor affecting fertility in cockerels. Poult. Sci. 38:3.

Penniston KL and Tanumihardjo SA. (2006). The acute and chronic toxic effects of vitamin A. Am-J-Clin-Nutr. 2006 Feb; 83(2): 191-201.

Penniston KL, Tanumihardjo S (2006). The acute and chronic toxic effects of vitamin A[1,2,3,4]. American Journal of Clinical Nutrition, Vol. 83, 191–201.

Potkanski AA, Tucker RE, Mitchell GE Jr. and Schelling GT. (1974). Pre-intestinal losses of carotene in sheep fed high-starch or high-cellulose diets. Int J Vitam Nutr Res. 1974;44(2):147-50.

Promislow JH, Goodman-Gruen D, Slymen DJ, Barrett-Connor E (2002). Retinol intake and bone mineral density in the elderly: the Rancho Bernardo Study. Journal of Bone and Mineral Research. 2002 Aug; 17(8):1349-58.

Ramalho HM, Santos VV, Medeiros VP, Silva KH, Demenstein R (2006) Effect of thermal processing on retinol levels of free-range and caged hen eggs. International Journal of Food Sciences and Nutrition; 57(3-4), 244-248.

Ribaya-Mercado JD, Blumberg JB (2007). Vitamin A: Is it a Risk Factor for Osteoporosis and Bone Fracture? Nutrition Reviews Vol. 65, 425 – 438.

Rode LM, McAllister TA, Cheng KJ (1990). Microbial degradation of vitamin A in rumen fluid of steers fed concentrate, hay or straw diets. Can J. of Anim Sci. 70:227-233.

Saleh G, Eleraky W, Gropp JM, 1995. A short note on the effects of vitamin A hypervitaminosis and hypovitaminosis on health and growth of Tilapia nilotica (Oreochromis niloticus). Journal of Applied Ichtyology 11, 382-385.

Schelling GT, Roeder RA, Garber MJ and Pumfrey WM. Bioavailability and Interaction of Vitamin A and Vitamin E in Ruminants. Journal of Nutrition Vol. 125 No. 6_Suppl June 1995, pp. 1799-1803.

Schindler M, Scholz M, Feldheim W. Quantitative Bestimmung von Vitamin A in Leber und Leberwurst unter Anwendung von Hochdruck-Flüssigchromatographie (HPLC). Z Lebensm Unters Forsch (1987) 185, 208-212.

Schmidt R. (1973). Vitamin A Bestimmung bei Schweinen, Hannover, Tierärztliche Hochschule, Dissertation.

Schöne et al. (1988). The vitamin A activity of β-carotene in growing pigs. Arch. Anim. Nutr., Berlin, 3, 193-205 line 1058

Schweigert FJ, Wierich M, Rambeck WA, Zucker H (1988). Carotene cleavage activity in bovine ovarian follicles. Theriogenology 30, 923 – 930.

Schweigert FJ, Steinhagen, B, Raila J, Siemann A, Peet D, Buscher U (2003). Concentrations of carotenoids, retinol and α-tocopherol in plasma and follicular fluid of women undergoing IVF. European Society of Human Reproduction and Embryology, Vol. 18, No 6, 1259–1264.

Scientific Advisory Committee on Nutrition (SACN), 2005. Review of Dietary Advice on Vitamin A. <http://www.sacn.gov.uk>

Scotter et al. (1992). Survey of animal livers for vitamin A content. Food additives and contaminants, 1992, vol. 9, No. 3, 237-242.

Shimeno S (1991). Yellowtail, Seriola quinqueradiata. Pp. 181-191 In Handbook of Nutrient Requirements of Finfish, R. P. Wilson, ed. Boca Raton, Fla.: CRC Press.

Sichert-Hellert W, Wenz G and Kersting M (2006). Vitamin Intakes from Supplements and Fortified Food in German Children and Adolescents: Results from the DONALD Study. American Society for Nutrition J Nutr 136, 1329 – 1333, May 2006.

Sigurdsson G, Franzson L, Thorgeirsdottir H, Steingrimsdottir L (2001). A lack of association between excessive dietary intake of vitamin A and bone mineral density in seventy-year-old Icelandic women. In Buckhardt P, Dawson-Hughes B, Heaney RP, eds. Nutritional Aspects of Osteoporosis. San Diego, California: Academic Press; 2001:295-302.

Sijtsma SR, West CE, Rombout JHWM, van Der Zijpp AJ (1989). Journal of Nutrition, Vol. 119, 932-939.

Singh SP and Donovan GA. (1973). A relationship between coccidiosis and dietary vitamin A levels in chickens. Poult. Sci. 52:1295.

Sklan D, Melamed D, and Friedman A (1994). The effect of varying levels of dietary vitamin A on immune response in the chick. Poultry Science 73:843-847.

Sklan D, Melamed D and Friedman A (1995). The effect of varying levels of vitamin A on immune response of the turkey. Br. Poult. Sci. 36:385-392.

Sklan D, Yosefov T and Friedman A. (1989). The effects of vitamin A, ß-carotene and canthaxanthin on vitamin A metabolism and immune responses in the chick. Int. J. Vitam. Nutr. Res. 59:245.

Sklan D. (1983). Carotene-cleavage activity in chick intestinal mucosa cytosol: Association with a high-molecular-weight lipid-protein aggregate fraction and partial characterization of the activity. Br. J. Nutr. 50:417.

Slimani N, Fahey M, Welch AA, Wirfält E, Stripp C, Bergström E, Linseisen J, Schulze MB, Bamia C, Chloptsios Y, Veglia F, Panico S, Bueno-de-Mesquita HB, Ocké MC, Brustad M, Lund E, González CA, Barcos A, Berglund G, Winkvist A, Mulligan A, Appleby P, Overvad K, Tjønneland A, Clavel-Chapelon F, Kesse E, Ferrari P, Van Staveren WA, Riboli E (2002). Diversity of dietary patterns observed in the European Prospective Investigation into Cancer and Nutrition (EPIC) project.Public Health Nutr. 2002 Dec., 5(6B), 1311-28.

Souci SW, Fachmann W, Kraut H (2000). Food Composition and Nutrition Tables 2000. Medpharm GmbH Scientific Publishers, Stuttgart.

Sowers MF, Wallace RB. (1990). Retinol, supplemental vitamin A and bone status. Journal of Clinical Epidemiology, 43(7):693-9.

Squires MW and Naber EC (1993). Vitamin Profiles of Eggs as Indicators of Nutritional Status in the Laying Hen: Vitamin A study. Poultry Science 72, 154 – 164.

St Claire MB, Kennett MJ, Besch-Williford CL (2004): Vitamin A toxicity and vitamin E deficiency in a rabbit colony. Contemp Top Lab Anim Sci. 2004 Jul; 43(4), 26-30.

Steinhöfel O (2007). Veränderung des Carotingehalts in unterschiedlich konserviertem Kleegras. Fachinformation zu Futter und Fütterung. Sächsische Landesanstalt für Landwirtschaft.

Steinhöfel O and Schönherr J (2008). Anwelken kostet ß-Carotin. Z.dlz-Agrarmagazin 3, 107–109.

Sungpuag P, Tangchitpianvit S, Chittchang U, Wasantwisut E (1999). Retinol and beta carotene content of indigenous raw and home-prepared foods in Northeast Thailand. Food chemistry, 64 (no 2), 163-167.

Surai PF, Ionov IA, Kuklenko TV, Kostjuk IA, Acpherson AM, Speake BK, Noble RC, Sparks NHC (1998). Effect of supplementing the hen's diet with vitamin A on the accumulation of vitamins A and E, ascorbic acid and carotenoids in the egg yolk and in the embryonic liver. British Poultry Science 39, 257–263(7).

Swanson KS, Merchen NR, Erdman JW, Drackley JK, Orias F, Morin DE, Haddad MF (2000). Influence of dietary vitamin A content on serum liver and vitamin A concentrations and health in preruminant calves fed milk replacer. J. Dairy Sci. 83: 2027-2036.

Swedish Livsmedelsverket. National Food Administration. <http://www.slv.se>

Tanumihardjo SA (2002). Factors influencing the conversion of carotenoids to retinol: bioavailability to bioconversion to bioefficacy. International Journal for vitamin and nutrition research 72, 40 – 45.

The Norwegian Food Safety Authority, Directorate for Health and Social Affairs and the University of Oslo. The Norwegian Food Composition Table 2006. <http://matportalen.no/>

The Norwegian Food Safety Authority, The Norwegian Directorate of Health and the University of Oslo. The Norwegian Food Composition Table, 2006. <http://matportalen.no/matvaretabellen>

Thompson I, Choubert G, Houlihan DF and Secombes CJ (1995). The effect of dietary vitamin A and astaxanthin on the immunocompetence of rainbow trout. Aquaculture 133, 91-102.

Turrini A, Saba A, Perrone D, Cialfa E and D'Amicis A (2001). Food consumption patterns in Italy: the INN-CA Study 1994-1996. European Journal of Clinical Nutrition (2001) 55, 571-588.

U.S. Department of Agriculture, Agricultural Research Service. 2005. USDA National Nutrient Database for Standard Reference, Release No. 18. Nutrient Data Laboratory Home Page. <http://www.ars.usda.gov/main/site_main.htm?modecode=12354500>

USDA, 2003. Table of nutrient retention factors, Release 5.

Weiser H, Probst HP and Bachmann H. Vitamin E prevents side effects of high doses of vitamin A in chicks. Ann NY Acad Sci 1992, 30 396-398.

Weiss WP. (1998). Requirement of fat soluble vitamins for dairy cows. J. Dairy Sci. 81, pp. 2493–2501.

Welch AA, Lund E, Amiano P, Dorronsoro M, Brustad M, Kumle M, Rodriguez M, Lasheras C, Janzon L, Jansson J, Luben R, Spencer EA, Overvad K, Tjonneland A, Clavel-Chapelon F, Linseisen J, Klipstein-Grobusch K, Benetou V, Zavitsanos X, Tumino R, Galasso R, Bueno-De-Mesquita HB, Ocke MC, Charrondiere UR, Slimani N (2002). Variability of fish consumption within the 10 European countries participating in the

European Investigation into Cancer and Nutrition (EPIC) study. Public Health Nutr. 5(6B), 1273-85.

Wirfält E, McTaggart A, Pala V, Gullberg B, Frasca G, Panico S, Bueno-de-Mesquita HB, Peeters PH, Engeset D, Skeie G, Chirlaque MD, Amiano P, Lundin E, Mulligan A, Spencer EA, Overvad K, Tjønneland A, Clavel-Chapelon F, Linseisen J, Nöthlings U, Polychronopoulos E, Georga K, Charrondière UR, Slimani N. (2002) Food sources of carbohydrates in a European cohort of adults. Public Health Nutr. 2002 Dec.; 5(6B), 1197-215.

Wolke RE, Nielsen SW, Rousseau JE (1968). Bone lesions of hypervitaminosis A in the pig. Am. J. Vet. Res. 29, 1009-1024.

Yamamoto K, Kobayashi S, Yoshikawav M, Onizuka N, Mikami O, Yamada M, Nakamura K, Nakajima Y (2003). Hyena Disease (Premature Physeal Closure) in Calves Due to Overdose of Vitamins A, D3, E. Veterinary and Human Toxicology 45(2), 85–87.

APPENDICES

APPENDIX 1

Vitamin A

A1. Physiological role [3]

Extensive studies in man and animals have shown that vitamin A is required for normal growth and development. Vitamin A (in physiological concentrations) stabilises the cell membrane, stimulates the synthesis of certain proteins by acting on transcription and possesses an electron transfer capacity. Vitamin A is essential for vision, growth differentiation and proliferation of a wide range of epithelial tissues, bone growth, reproduction and embryonic development. Literature clearly indicates that vitamin A accumulates particularly in liver and is a toxicant at high doses in most species studied. (Nieman and Obbink, 1954; Moore, 1957; Hayes and Hegsted, 1973; Bauerfeind, 1980; Ong and Chytil, 1983; Olson, 1984). Some adverse effects seen at high doses of vitamin A may be related to the well-known interactions with the other fat soluble vitamins D, E and K, as it could be shown for chickens, for instance, (Weiser et al., 1992, Gropp et al., 1991) and dairy cows (Schelling et al., 1995), but apparently not for vitamin E in piglets (Anderson et al., 1995).

Vitamin A is present in the diet as preformed vitamin A (retinol (see Figure A1.1.) and its esters) and can also be derived from dietary carotenoids, mainly ß-carotene.

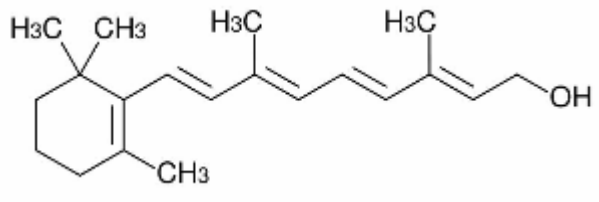


Figure A1.1. **Retinol (synonyms: Vitamin A, Axerophthol)**
IUPAC:(2E,4E,6E,8E)-3,7-Dimethyl-9-(2,6,6-trimethylcyclohex-1-enyl)nona-2,4,6,8-tetraen-1-ol

Dietary retinyl esters are hydrolysed in the intestinal lumen by a pancreatic carboxylic ester hydrolase. The resulting retinol is absorbed in the enterocytes, either by facilitated diffusion (i.e. by a protein carrier mediated process) when retinol is present at physiological concentration (up to 150 nM), or by passive diffusion when present in pharmaceutical amounts (450 to 2700 nM). A wide range of absorption values has been established in the rat and human, with a typical value of 50 %. Newly absorbed vitamin A is transported mainly (80 % in the rat and human) esterified with long-chain saturated fatty acids from enterocytes via the lymphatics to the systemic circulation as component of chylomicrons (chylomicron remnants). Most of the absorbed dietary vitamin A is delivered to hepatic parenchymal cells (hepatocytes) when chylomicron remnants are metabolised by the liver. The incoming retinyl esters are processed for hepatic storage.

The liver is the main but not the exclusive storage site for vitamin A in vitamin A-sufficient mammals. Most of the hepatic vitamin A is present as retinyl esters in perisinusoidal stellate

[3] Most data is taken from the extensive review of Blomhoff et al. (1991), based on rat and human data.

cells. A fraction of retinol undergoes metabolic transformation in the liver and extrahepatic tissues, namely oxidation to retinal (essential for vision), then retinoic acid, a key regulatory retinoid in the functional role of vitamin A. Glucuronidation of retinol occurs also in the liver.

Retinol recycles among plasma, liver and extrahepatic tissues to an extent of 50–70 %, the kidneys playing a major role. Twenty per cent of the total plasma turnover of retinol goes to the liver (vs. nonhepatic tissues) and about 20 % of plasma retinol input is from liver (vs. nonhepatic tissues). About one-half of the retinol recycling from plasma to liver is taken up by hepatocytes and about one half by parenchymal cells.

Liver retinyl will be released as retinol if required (controlled by plasma retinol) to provide the organism (target cells) with vitamin A. Except in the postprandial state, essentially all of the retinol in plasma is bound to the retinol-binding protein (RBP) in a 1:1 molecular ratio. The plasma retinol level is maintained within a normal range of concentrations (i.e. its usual set point for a given animal species) by numerous homeostatic mechanisms as long as there is some physiological level of vitamin A in liver (20–300 μg g^{-1} liver) and extrahepatic tissues. In contrast, in the face of large fluctuations of vitamin A intake: (i) the controlled secretion of retinol by the liver represents a key regulatory element for maintaining plasma retinol concentration (e.g. plasma retinol level of humans — 1.7 to 2 μg mL^{-1} — remains nearly constant when dietary vitamin A varies more than 15 fold); (ii) the liver oxidation to polar metabolites of retinoic acid produced in extrahepatic tissues (regulatory retinoid role) through a retinoic acid–inducible cytochrome P450 - CYP26 - up-regulated dose dependently ensures a protection of the organism against an 'overshoot' of retinoic acid. The serum retinol level indicates the status of vitamin A storage in the liver only if there is an extreme depletion or overconsumption of vitamin A (Flachowsky et al., 1990; Penniston and Tanumihardjo, 2006).

Retinol in the extrahepatic target cells is bound to cellular retinol-binding protein (CRBP-I). A CRBP-II binds the retinol in enterocytes. Retinol is released intracellularely converted to retinoic acid and binds to a nuclear retinoic acid receptor which induces cell differentiation (gene transcription).

The cleavage of carotenoids to retinol (by 15-15'-dioxygenase) is highly regulated and vitamin A toxicity from provitamin A is almost impossible (Tanumihardjo, 2002).

A1.1 Units

The historical and still used means to express vitamin A activity are international units (IU), which were later better defined by weight units. Later, and particularly from human nutrition, there was a requirement for a uniform assessment of the vitamin A activity intake including all provitamin A carotenoids. Vitamin A intake by human beings and animals can be as:

- preformed vitamin A (retinol and retinyl esters such as retinol palmitate from animal products);
- provitamin A carotenoids (α- and β-carotene, β-cryptoxanthin, β-apo-8'-carotenal, β-apo-8'-carotenoic acid and citranaxanthin from plant and animal products).

Such a formula must be based on constant conversion factors of the carotenoids to retinol. But the conversion factors depend on the quantitative supply and on a variety of other nutritional factors. Such a dietary concept is a simplification for use in practice because combinations of food or methods of preparation may involve greater or lesser utilisation of

provitamins. Only when a fully balanced and nutritious diet is given, the conversion factors may reflect accurately the contribution of provitamins to the total vitamin A intake.

Different formulas based on weight units are used by different authorities, which makes comparisons difficult. In the EU, the retinol equivalent (RE; 1 RE = 1 µg retinol) is used, whilst in the United States retinol activity equivalent (RAE).

The relationship between the different sources of vitamin A activity and retinol as used in the EU are given in Table A1.1.

Table A1.1. **Vitamin activity of the various vitamin A compounds in Europe***

Molecule	Activity in retinol equivalents (RE)	International units	References
Retinol (1 mg)	1 000	3 330	SCF 2002
Retinyl acetate (1 mg)	870	2 900	SCF 2002
Retinyl palmitate	550	1 830	SCF 2002
β-Carotene	167	555	SCF 1992
α-Carotene	83	277	SCF 1992
β -Cryptoxanthin	83	277	SCF 1992

* Vitamin A can be expressed on a weight basis as retinol equivalents (1 RE = 1 µg retinol) or in International Unit (IU) and the currently accepted conversion factor is 1 IU = 0.3 RE.

Details on the respective formula as used in the US are given in Table A.1.2, the RAE values are by definition somewhat lower than the RE.

Table A1.2. **Vitamin activity of the various vitamin A compounds in the US**

Retinol activity equivalents (RAE) ratios for beta-carotene and other provitamin A carotenoids		
Quantity consumed	**Quantity bioconverted to Retinol**	**RAE ratio**
1 µg of dietary or supplemental vitamin A	1 µg of retinol*	1:1
2 µg of supplemental β-carotene	1 µg of retinol	2:1
12 µg of dietary δ-carotene	1 µg of retinol	12:1
24 µg of dietary α-carotene	1 µg of retinol	24:1
24 µg of dietary β-cryptoxanthin	1 µg of retinol	24:1
1 µg of dietary or supplemental vitamin A	1 µg of retinol*	1:1

* One IU is equivalent to 0.3 microgram (µg) of retinol, and one µg of retinol is equivalent to 3.33 IU of retinol.

Recommendations for vitamin A intake for humans based on the requirement are given in the EU as recommended daily allowance (RDA), by D-A-CH (D-A-CH: German Nutrition Society, Austrian Nutrition Society, Swiss Society for Nutrition Research and Swiss Nutrition Association) as recommended intake and in the US as recommended dietary allowance (RDA). Sometimes, a Lower Recommended Nutrient Intake (LRNI) is used to define the minimum supply of vitamin A that must be provided (about 40 % of the RDA).

The vitamin A intake which should not be exceeded because of safety concerns is called tolerable upper intake level (UL). The tolerable upper intake levels for children were based on the adult value with correction for differences in basal metabolic rate compared to adults (body weight $kg^{0.75}$).

Table A1.3. **Tolerable Upper Intake Levels for the different age groups**

Age (years)	Tolerable Upper Intake Level (UL) for preformed vitamin A (retinol and retinyl esters) (µg RE day^{-1})
1–3	800
4–6	1100
7–10	1500
11–14	2000
15–17	2600
Adults*	3000

* Women of child-bearing age and men
(EC, 2002)

Because provitamins A are known not to cause vitamin A toxicity (Tanumihardjo, 2002), reference values for the upper safe intake are predominantly expressed in terms of preformed vitamin A (but also in RE), which summarises in the EU only retinol and retinyl esters (+ retinal in the US and + retinoic acid in the D-A-CH formula), both at a very low level of tissue concentration. It should be noted that the REs used in expressing the RDA and establishing the UL are different!

In animal nutrition (EU), the vitamin A content of feedingstuffs and consequently the definition of the requirements is still expressed in international units (1 IU = 0.3 RE) and refers only to retinol and its esters.

APPENDIX 2

Methods used in the SACN review to analyse the potential impact of dietary changes on the vitamin A intake

The SACN review analysed the potential impact of dietary changes to reduce intakes of retinol. A modelling exercise was undertaken to explore the impact of an advice not to exceed an intake of 1500 µg retinol day^{-1} by changes in the consumption behaviour or by reducing liver vitamin A. Such an advice would affect both ends of the intake distribution.

In addition, the consequences of reduced liver intake on the intakes of iron, zinc, folate and B_{12} were assessed. A number of scenarios were investigated, including a 25 % reduction in liver retinol content by altered animal feeding practices, the establishment of an upper limit on liver consumption of 25 g/week or 0 g/week, the elimination of retinol from all supplements and, the most draconian of all, the assumption of a zero retinol intake from either supplements or liver.

The modelling used the quantitative intakes recorded by the NDNS surveys, which were adjusted for frequency of liver consumption using a food-frequency questionnaire (the Oxford EPIC study). The NDNS data were derived from seven-day weighed records for the 2000/2001 NDNS of 19–64-year-old adults and four-day weighed records for the 1994/1995 NDNS of those over 65 years. Because only 20 % of liver consumers do so once or more per week, the NDNS study data would have captured only about one half of all liver consumers but overestimated the average intake in those identified as liver consumers. The EPIC data were used to adjust the NDNS data to provide an assessment of the average long-term eating behaviour. An important variable in such a modelling exercise is the concentration in liver, which was assumed to be 200 µg g^{-1} in the basic modelling and 150 µg g^{-1} for the 25 % reduction in liver retinol content. The output of the model provides a useful analysis of the consequences of alterations to the liver retinol content or the consumption of liver and/or supplements, but a more definitive answer would have been given if the liver retinol content had been included as a distribution rather than a single value. This would have required a complex probabilistic model but would have given more realistic data.

APPENDIX 3

German NVS II study

The (German) NVS II study was performed by the the Max Rubner Institute in the Bundesforschungsinstitut für Ernährung und Lebensmittel in Karlsruhe between November 2005 and end of December 2006. The data of this national nutrition survey of Germany were published in May 2008. 15 371 participants aged between 14 and 80 years, living in private households, were questioned by the Diet History Method (DISHES). Additional methods like CAPI (Computer Assisted Personal Interview) and food weighing were also used. The validity of the random test was guaranteed by the comparison with the 2006 microcensus. 53.9 % of the participants were women (mean age 46.1 years), 46.2 % were men (mean age 46.3 years).

The total daily vitamin A and retinol intakes are given in Tables A3.1. and A3.2, indicating the mean values plus standard error and the percentiles 5, 10, 25, 50, 75, 90 and 95 %. These values are given for men and women between 14 and 80 years of age, distributed into six subgroups. Furthermore, in Table A3.1 the RDA values from D-A-CH are also included.

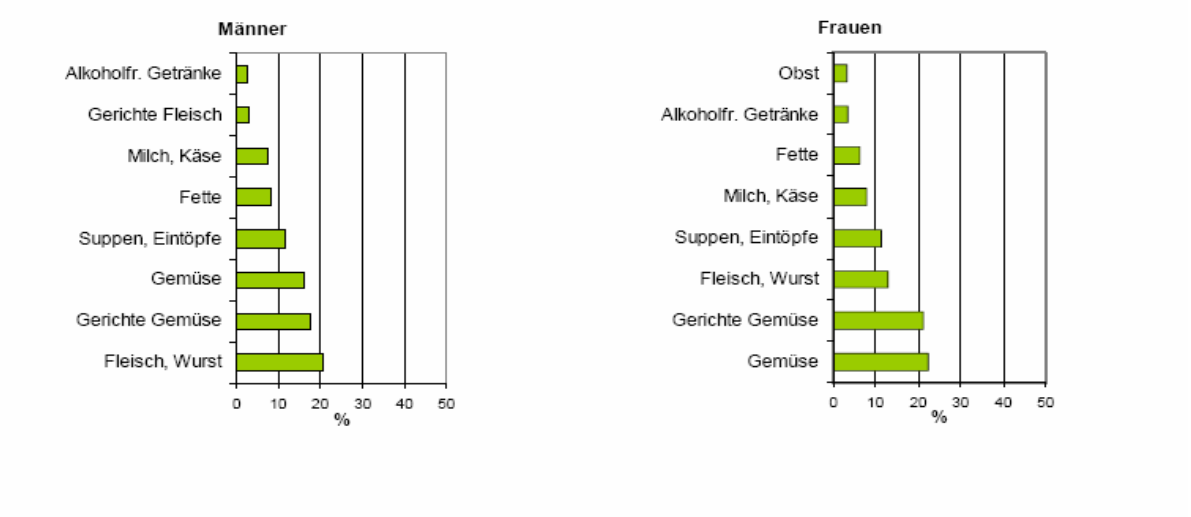
Table A3.1. **Daily intake of total vitamin A (mg RE day^{-1})**

Age groups	n	Mean	SE	P5	P10	P25	P50	P75	P90	P95	D-A-CH
Men	7093	2.1	0.02	0.7	0.9	1.2	1.8	2.6	3.5	4.4	
14–18	712	1.8	0.05	0.6	0.7	1.0	1.5	2.2	3.3	4.1	1.1
19–24	510	1.9	0.06	0.6	0.8	1.1	1.5	2.4	3.5	4.7	1.0
25–34	690	2.1	0.04	0.7	0.9	1.3	1.8	2.6	3.5	4.2	1.0
35–50	2079	2.1	0.03	0.7	0.9	1.3	1.8	2.6	3.7	4.5	1.0
51–64	1633	2.1	0.03	0.8	0.9	1.3	1.8	2.6	3.7	4.5	1.0
65–80	1469	2.1	0.03	0.8	0.9	1.3	1.8	2.6	3.5	4.2	1.0
Women	8278	1.8	0.01	0.7	0.8	1.1	1.5	2.2	3.0	3.7	
14–18	700	1.6	0.04	0.5	0.7	0.9	1.4	1.9	2.7	3.6	1.0/0.9*
19–24	510	1.6	0.04	0.6	0.7	1.0	1.4	1.9	2.6	3.1	0.8
25–34	972	1.8	0.03	0.6	0.8	1.1	1.5	2.2	3.0	3.8	0.8
35–50	2694	1.9	0.02	0.7	0.9	1.2	1.7	2.3	3.1	3.8	0.8
51–64	1840	1.9	0.03	0.7	0.8	1.2	1.6	2.3	3.1	3.9	0.8
65–80	1562	1.7	0.02	0.7	0.8	1.1	1.5	2.1	2.9	3.5	0.8

* First value: reference value for age of 14 years/second value: reference value for age of 15–18 years.

Table A3.2. **Daily intake of retinol (mg RE day^{-1})**

Age groups	n	Mean	SE	P5	P10	P25	P50	P75	P90	P95
Men	7093	1.0	0.01	0.2	0.3	0.4	0.6	1.1	2.1	2.8
14–18	712	0.8	0.03	0.2	0.3	0.4	0.6	0.9	1.7	2.6
19–24	510	0.8	0.04	0.2	0.3	0.4	0.6	0.9	1.7	2.5
25–34	690	1.0	0.04	0.2	0.3	0.4	0.6	1.1	2.0	2.8
35–50	2079	1.0	0.02	0.2	0.3	0.4	0.6	1.2	2.0	2.9
51–64	1633	1.0	0.02	0.2	0.3	0.4	0.7	1.2	2.3	2.9
65–80	1469	1.0	0.03	0.2	0.3	0.4	0.7	1.3	2.3	2.8
Women	8278	0.6	0.01	0.17	0.2	0.3	0.4	0.7	1.3	1.8
14–18	700	0.6	0.02	0.1	0.2	0.3	0.4	0.7	1.3	1.9
19–24	510	0.5	0.02	0.2	0.2	0.3	0.4	0.6	1.0	1.3
25–34	972	0.6	0.02	0.2	0.2	0.3	0.4	0.7	1.2	1.9
35–50	2694	0.7	0.01	0.2	0.2	0.3	0.5	0.7	1.3	1.8
51–64	1840	0.7	0.02	0.2	0.2	0.3	0.5	0.8	1.3	2.0
65–80	1562	0.7	0.02	0.2	0.2	0.3	0.5	0.8	1.3	1.7



Männer – men, Frauen – women, Alkoholfr. Getränke – soft drinks, Gerichte Fleisch – meat containing dishes, Milch, Käse – milk, cheese, Fette – fat, Suppen, Eintöpfe – soups, stews, Gemüse – vegetable, Gerichte Gemuse – vegetable based dishes, Fleisch, Wurst – meat, sausages, Obst – fruit

Figure A.3.1. **Contribution of different foods to total vitamin A intake from food in men and women from the German Nutrition Survey (copy of Abb. 5.14 of the original report)**

APPENDIX 4

British LIDNS study

The recent Low Income Diet and Nutrition Survey (LIDNS) was commissioned by the UK Food Standards Agency (FSA) to investigate the eating habits in low-income families (Nelson et al., 2007). The work was carried out by a consortium of three organisations led by the Health Research Group at the National Centre for Social Research (NatCen) and including the Nutritional Sciences Research Division at King's College London, and the Department of Epidemiology and Public Health at the Royal Free and University College London Medical School. Of particular importance to this opinion, vitamin A was included as one of the many of the food components considered.

The sample consisted of 25818 families, from the same number of addresses, in 528 electorate units (wards) spread over the UK, with over-representation of financially deprived areas. Screening of suitability, in terms of financial and material deprivation, was carried out by door-step questionnaire. From each selected household with two or more residents, two respondents were then randomly chosen to participate in the study. If children were present, one adult and one child were selected. Both adults were selected where there were no children. The overall response rate for fully productive individuals was 55 %, giving a sample size of 3728 individuals with complete records. The low income population sample contained proportionally more women (60 %) than men (40 %). Overall, it also comprised proportionally more children (32 %) and people aged 65 years and over (21 %) compared with the general population. The data set was weighed to correct for over-sampling in Scotland, Northern Ireland, and Wales and also for category bias in non-respondents. Eating habits were assessed by four 24-h recalls of diet on random days (including at least one weekend day) within a ten-day period. Data collection was carried out from November 2003 to January 2005.

Because the LIDNS was commissioned to look at nutritional deficiencies as related to economic and material deprivation, the data are primarily presented from this point of view. However, it does provide useful data about the upper range of vitamin A intake in the UK population as well as relatively detailed information on the major sources for vitamin A intake in the average consumer. The LIDNS does not report the sources of vitamin A among high consumers of vitamin A.

Table A4.1. **Total vitamin A intake from food (animal and plant sources) expressed as retinol equivalents (µg RE day^{-1}) in UK cohorts of different age-groups**

	Males			Females		
Age group	**mean ***	**97.5th percentile**	**SD**	**mean ***	**97.5th percentile**	**SD**
2–10	733	6489	1438	527	1484	510
11–18	625	2071	384	568	1337	583
19–34	795	1927	901	677	1636	773
35–49	824	2701	1211	809	3438	1259
50–64	1342	9995	2089	982	4082	1363
> 65	1144	5832	1475	1096	5157	1484

* The average intake of vitamin A was estimated by summing the average intakes from all food sources.

The LIDNS Report uses Lower Recommended Nutrient Intake (LRNI, about 40 % of the RDA) to define the minimum supply of vitamin A that must be provided. Between 7 % (men and women, > 65) and 18 % (men, 19–35 years old) of the subjects in the study had vitamin A intakes below the LRNI.

Table A4.2. **Intake of preformed vitamin A (µg RE day^{-1}) from foods of animal origin in UK cohorts of different age groups**

	Males			Females		
Age group	**mean***	**97.5th percentile**	**SD**	**mean***	**97.5th percentile**	**SD**
2–10	475	5475	1377	269	790	400
11–18	300	759	162	278	718	510
19–34	421	1251	814	296	721	676
35–49	475	2091	1165	423	1735	1147
50–64	852	9025	1979	498	3604	1262
> 65	661	5262	1398	620	4951	1401

* The average intake of pre-formed retinol was estimated by summing the average intakes from all food sources of animal origin.

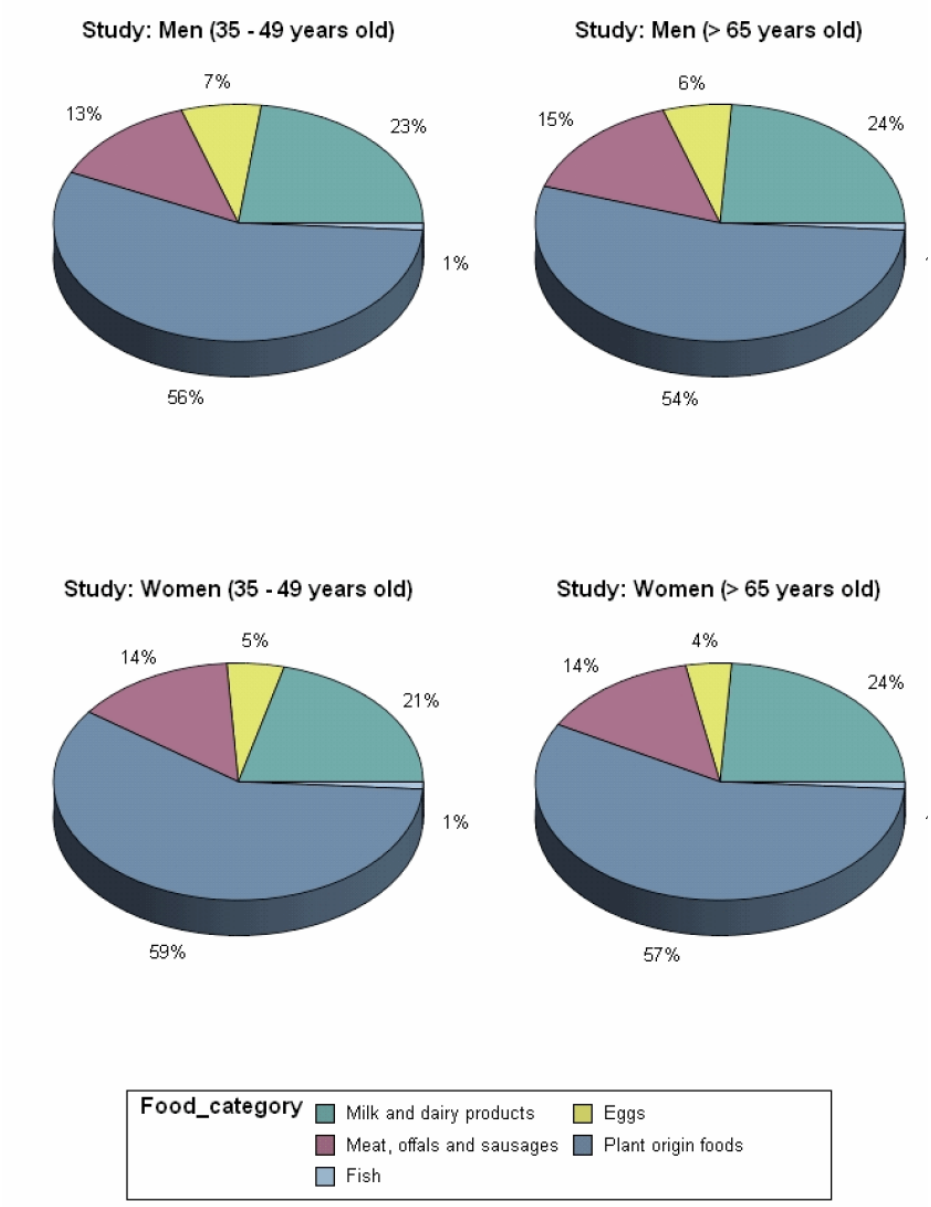


Figure A4.1. **Contribution of major food sources to the total vitamin A intake of people of 35–49 and > 65 years of age**

Carotenoids from plant products contributed to 53–64 % of the total vitamin A intake in the people with average vitamin A intake included in the LIDNS (Figure A4.1). There were no substantial differences between cohorts in sources of vitamin A. Vegetables were the largest source, providing 24–34 % of the total vitamin A intake. Adults consumed more vegetables than children and women ate slightly more vegetables than men. Fat spreads was another major source, which constituted 9–16 % of the total vitamin A intake. Men tended to get slightly more vitamin A than did women, while this source contributed about equally to the intake in boys and girls (2–18 years old). Cereal products seem to provide more vitamin A for children (12 %) than for adults, including the elderly (6–8 %). It should be noted that estimates of the contribution of carotenoids to the total vitamin A intake, as retinol equivalents, is complicated since the conversion rate of carotenoids to retinol is regulated by and inversely related to retinol intake. Total vitamin A intake may therefore be overestimated in people with high intake of preformed retinol.

Table A4.3. **Main sources of vitamin A intake from animal products in average consumers from UK low income families by sex and age**

		Main sources of vitamin A from animal products - Average consumers (% of total vitamin A intake)								Contribution to total intake
		Meat*	Poultry meat	Butter	Cheese	Milk products**	Eggs	Fish	Offal	
		%	%	%	%	%	%	%	%	%
2–18	Males	4	2	4	6	18	3	1	1	39
	Females	4	2	3	6	15	4	1	1	36
19–34	Males	5	4	3	9	9	8	1	1	40
	Females	7	3	4	6	10	5	1	1	37
35–49	Males	5	4	4	7	12	7	1	2	42
	Females	5	4	4	5	12	5	1	2	38
50–64	Males	7	3	4	6	11	7	1	8	47
	Females	6	2	5	6	10	5	1	4	39
> 65	Males	5	3	8	6	10	6	1	6	45
	Females	5	2	9	4	11	4	1	6	42

* Meat includes: Beef, calf, lamb, and pork meat
** All dairy products other than butter and cheese (milk, cream, yoghurt, dairy desserts)

Table A4.4. **Main sources of preformed vitamin A intake in average consumers, expressed in percentage of total in the LIDNS Study**

		Main sources of pre-formed retinol - Average consumers							
		Meat *	Poultry meat	Butter	Cheese	Milk products **	Eggs	Fish	Offal
		%	%	%	%	%	%	%	%
2–18	Males	10	5	10	15	46	8	3	3
	Females	11	6	8	17	42	11	3	3
19–34	Males	13	10	8	23	23	20	3	3
	Females	19	8	11	16	27	14	3	3
35–49	Males	12	10	10	17	29	17	2	5
	Females	13	11	11	13	32	13	3	5
50–64	Males	15	6	9	13	23	15	2	17
	Females	15	5	13	15	26	13	3	10
> 65	Males	11	7	18	13	22	13	2	13
	Females	12	5	21	10	26	10	2	14

* Meat includes: Beef, calf, lamb, and pork meat
** All dairy products other than butter and cheese (milk, cream, yoghurt, dairy desserts)

APPENDIX 5

German EsKiMo study (children and adolescents)

The EsKiMo study was performed on request of the German Ministry of Nutrition, Agriculture and Consumer Protection, by the Robert Koch Institute and the University of Paderborn. The survey was conducted between January 2006 and the end of December 2006 among children and youth aged between six and 17 years. In 150 sample points distributed all over Germany, the participants (and their parents) were randomly selected from the register of residents.

From 2506 participants (49.8 % boys, 50.2 % girls), workable data were received. These include 1234 children between six and 11 years old and 1272 youth between 12 and 17 years old. Approximately 100 boys and 100 girls per age group of each year were included.

The methods for collecting the consumption data depended on the age of the participants. The data of the 6–11-year-old children were raised by a nutrition diary, conducted by the parents over three days. The questioning of the 12 to 17 years old was performed in a personal nutrition interview (DISHES, dietary interview software for health).

The intake of total vitamin A, given in RE per day from all sources, is shown in Table A5.1.

Table A5.1. **Daily intake of total vitamin A (mg RE day^{-1})**

	Mean	Median	5th percentile	95th percentile
Boys 6–11 years	1.0	0.8	0.4	2.1
Girls 6–11 years	0.9	0.7	0.3	1.7
Boys 12–17 years	1.6	1.4	0.6	3.3
Girls 12–17 years	1.5	1.3	0.6	3.1

Comparing these data with the RDA values of D-A-CH (2001), it can be concluded that girls between six and 11 take less (median 0.7 mg RE) than the RDA (0.8 mg RE), while boys at the same age consume the recommended amount of vitamin A. Boys and girls between 12 and 17 take more than the D-A-CH recommendation.

The relative contribution of different food sources to the mean total vitamin A intake of children and adolescents is shown in figure A5.1.

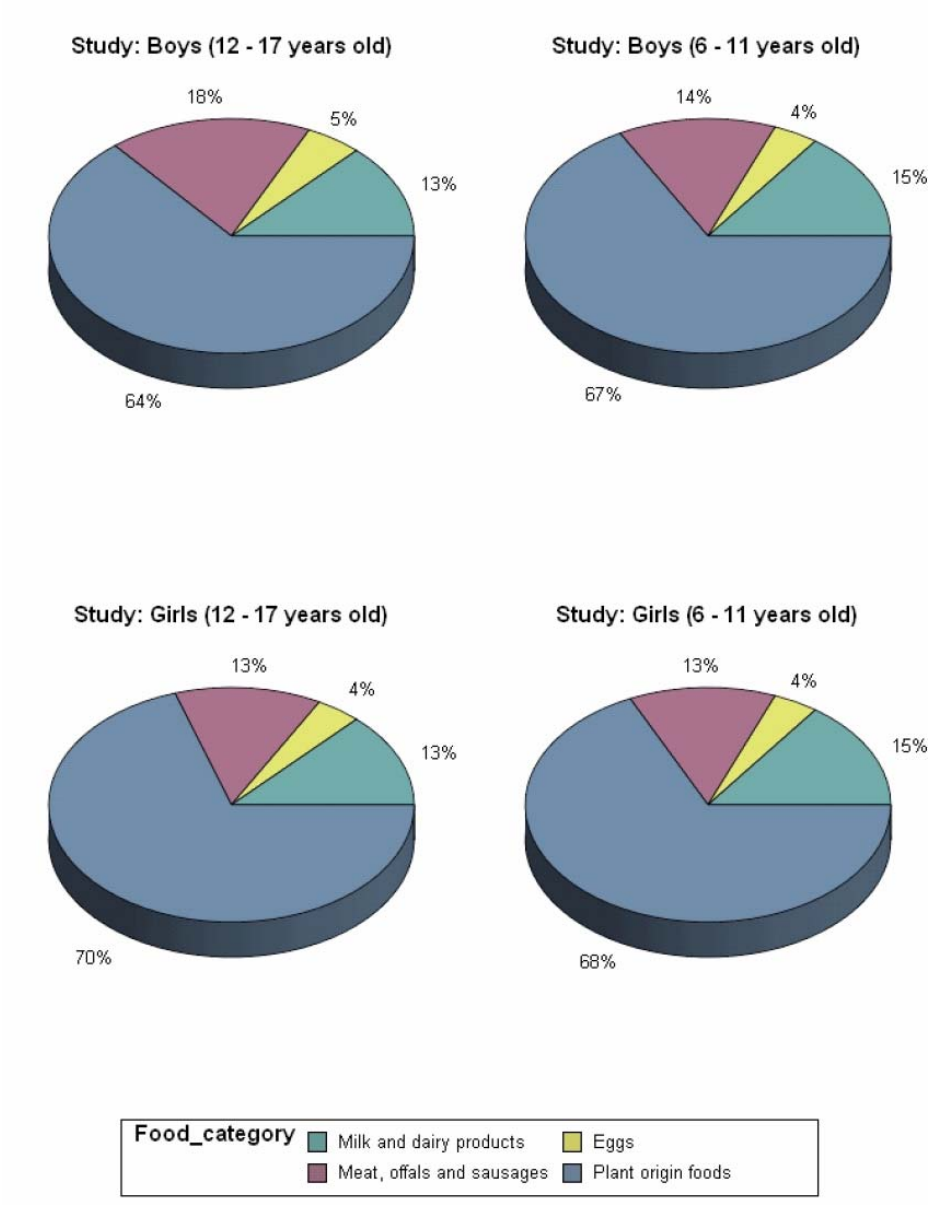


Figure A5.1. **Relative contribution of major food sources to the mean total vitamin A intake of children (6–11 years old) and adolescents (12–17 years old)**

APPENDIX 6

Intake of preformed vitamin A in the Netherlands

Kloosterman and Ocké (2007) calculated the human intake of preformed vitamin A in the Netherlands by using the most recent Food Consumption Survey for the total population (Dutch National Food Consumption Survey 3: DNFCS-3) executed in 1997-1998.

The participants (6250 persons aged 1–97 years old from 2564 households) recorded their food intake over two consecutive days (equally distributed over seasons and the days of the week). Nutrient intake from food was calculated using an extended Dutch food composition database. The intake of kidney, liver, poultry, foie gras, pâté de foie de porc, fish, milk, dairy products, cheese and eggs were recorded and the consumed retinol was calculated. For each subject, the mean over the two days was calculated and the 50^{th}, 75^{th} and 90^{th} percentiles were calculated per age group for the total group and for consumers only.

APPENDIX 7

FEEDAP calculations on the basis of the EPIC data

The food consumption survey carried out within the European Prospective Investigation into Cancer and Nutrition (EPIC) project offers the opportunity to study the diversity of food habits in Europe because it includes 35 955 subjects (22 924 women and 13 031 men) who participated in the EPIC calibration study between 1995 and 1998 (except Norway: 1999–2000), from 27 study centres in ten European countries (France, Italy, Spain, Greece, the Netherlands, the UK, Germany, Denmark, Sweden and Norway). The age of the participants ranged from 35 to 74 years at recruitment. All consumption data were collected within this study with the same protocol: one 24-hour recall.

The average and Standard Error of the Mean (SEM) consumption of the following food products were used to estimate the intake of preformed vitamin A: beef meat, chicken meat, offal, pork meat, veal meat (Linseisen et al., 2002), butter, cheese, milk, yoghurt (Hjartåker et al., 2002) eggs (Slimani et al., 2002) and fatty fish (Welch et al., 2002). Because liver data was not available in the above studies, offal was assumed to consist of 90 % liver.

Country specific data of the concentrations of preformed vitamin A in the above-mentioned foodstuffs were extracted from Section 4. For countries where those data were not available, average values were calculated and used. Retinol concentration in liver was set to the calculated average of all species, except poultry.

The Lognormal distribution was used to estimate the high consumption levels (95^{th} percentile) of each food product and for each centre by using the corresponding average, SEM and number of subjects reported in the EPIC publication.

Table A7.1. **Main sources of preformed vitamin A intake (µg RE day^{-1}) in average consumers, expressed in percentage of total (EPIC)**

		Main sources of preformed vitamin A Average consumers							
		All meat*	Butter	Cheese	Eggs	Fatty fish	Milk	Offal	Yoghurt
		%	%	%	%	%	%	%	%
Denmark	**Men**	2	11	19	7	1	21	36	2
	Women	2	7	18	11	0	18	41	3
France	**Women**	1	7	18	4	0	4	63	2
Germany	**Men**	1	21	22	4	0	12	38	1
	Women	1	16	24	6	0	15	36	1
Greece	**Men**	1	0	15	2	0	4	77	1
	Women	1	1	21	6	0	9	61	1
Italy	**Men**	1	2	12	2	0	5	77	0
	Women	1	3	17	5	0	8	65	1
Norway	**Women**	1	8	35	10	1	17	26	2
Spain	**Men**	1	0	5	5	1	9	79	1
	Women	1	1	5	8	1	16	68	1
Sweden	**Men**	2	6	19	7	1	28	32	5
	Women	2	4	20	12	1	23	34	5
The Netherlands	**Men**	3	10	21	5	0	15	45	2
	Women	2	12	26	11	0	22	23	4
United Kingdom	**Men**	2	12	9	4	1	22	49	1
	Women	2	11	11	8	1	25	42	2

* All meat includes: Beef meat, Chicken meat, Pork meat and Veal meat

Table A7.2. **Main sources of preformed vitamin A intake (µg RE day^{-1}) in high consumers, expressed in percentage of total (EPIC)**

		Main sources of preformed vitamin A High consumers							
		All meat*	Butter	Cheese	Eggs	Fatty fish	Milk	Offal	Yoghurt
		%	%	%	%	%	%	%	%
Denmark	**Men**	3	13	20	9	1	20	32	3
	Women	2	8	18	13	1	16	39	3
France	**Women**	1	6	12	4	0	4	70	1
Germany	**Men**	2	18	21	4	0	15	38	1
	Women	1	12	23	8	0	17	37	2
Greece	**Men**	1	0	11	2	0	4	81	1
	Women	1	1	19	6	0	10	62	1
Italy	**Men**	1	2	10	2	0	4	80	0
	Women	1	3	15	6	0	7	67	1
Norway	**Women**	1	10	35	12	1	16	23	2
Spain	**Men**	1	0	5	4	1	7	82	1
	Women	1	1	6	6	1	10	75	1
Sweden	**Men**	2	8	21	9	1	25	29	5
	Women	2	4	21	15	1	21	31	5
The Netherlands	**Men**	3	12	20	6	0	15	41	2
	Women	3	14	26	13	0	19	20	4
United Kingdom	**Men**	2	14	11	5	1	18	49	1
	Women	2	13	13	9	1	20	40	2

* All meat includes: Beef meat, Chicken meat, Pork meat and Veal meat

APPENDIX 8

Retinol intake from liver

For the preparation of this opinion, EFSA requested information on human intake of vitamin A from different sources in different age groups in Europe. The data were requested in the form of questionnaires which were sent to Member States, the EU Network on food consumption database managers. Responses were received from twelve Countries (Belgium, Bulgaria, Croatia, Czech Republic, Finland, Germany, Ireland, Italy, the Netherlands, Poland, Sweden and the UK). Adequate information with scientific background was provided by Italy (Turrini et al., 2001), Germany (Mensink and Beitz, 2004), Ireland (Harrington et al., 2001) and the Netherlands (Kloosterman and Ocké, 2007). From the first three studies, data on the consumption among adults of liver of different origins (for the total population and consumers only and for average and high consumers) were used to estimate the intake of preformed vitamin A. Country-specific data of the concentration of preformed vitamin A in liver of different origin were extracted from Section 4. In the cases where those data were not available, average values were calculated and used.

Table A8.1. **Intake of preformed vitamin A from different sources of liver in Germany, Italy and Ireland**

			Adults - Total population			Adults - Consumers only		
			Liver consumption			Liver consumption		
		% consumers	Mean (g day^{-1})	95th percentile (g day^{-1})	VIT A mean intake (µg RE)	Mean (g day^{-1})	95th percentile (g day^{-1})	VIT A mean intake (µg RE)
Germany	Pork, liver	0.04 %	0.0	0.0	2	37.0	71.4	4695
	- in liver-products	50.72 %	1.7	6.9	221	3.4	9.8	435
	- in Leberkäse[1]	21.81 %	0.1	0.4	14	0.5	1.3	62
	Lamb, liver	0.04 %	0.0	0.0	0	8.9	8.9	848
	Calf, liver	0.08 %	0.0	0.0	1	4.1	4.5	1188
	- in liver-products	0.13 %	0.0	0.0	2	4.7	11.1	1357
	Chicken, liver	13.07 %	0.2	1.2	28	1.4	3.5	215
	Duck, liver	0.59 %	0.0	0.0	0	0.6	4.5	84
	Goose, liver	0.09 %	0.0	0.0	0	2.7	5.4	415
	- in liver-products	0.06 %	0.0	0.0	0	1.3	1.6	191
	Beef, liver	4.67 %	0.3	0.0	54	6.3	12.5	1162
Italy	Pork	0.70 %	0.14	0	23	21.13	61.3	3444
	Lamb	0.40 %	0.04	9.8	6	11.61	22.8	1742
	Calf	5.20 %	1.27	0	368	24.19	43.9	7015
	Poultry	0.40 %	0.06	0	9	15.51	34.5	2342
	Beef	0.00 %	0	0	0	0	0	0
Ireland	Pork	0.15 %	0.01	0.00	2	7.14	7.14	1243
	Lamb	2.90 %	0.47	0.00	81	16.16	35.21	2796
	Calf	0.07 %	0.01	0.00	2	15.43		2901
	Poultry	0.15 %	0.01	0.00	1	8.57	11.43	831
	Beef	0.00 %	0.00	0	0	0.00	0	0

[1] meat loaf (typical Bavarian dish)

Basic data from: Mensink and Beitz, 2004; Turrini et al., 2001; Harrington et al., 2001.

APPENDIX 9

Persons taking supplements

Data on vitamin intakes from supplements and fortified food in German children and adolescents were published by Sichert-Hellert et al. in 2006. The calculations were based on the Dortmund Nutritional and Anthropometric Longitudinally Designed (DONALD) Study, involving 5990 three-day weighed dietary records from 931 German subjects (452 males, 479 females, 2–18 years of age) between 1986 and 2003. In 451 records, 133 different vitamin-containing supplements were identified. Slightly more boys (8 %) than girls (7.1 %) consumed supplements. The intake of vitamin A from usual and fortified food already reached 80 % of the RDA in all age groups.

Table A9.1. **LIDNS: Contribution of vitamin supplements to the total intake of retinol in subjects 19 years and older**

	Men			Women		
	Supplement takers		Non-supplement takers	Supplement takers		Non-supplement takers
	Total	Food	Food	Total	Food	Food
Retinol (µg RE day^{-1})						
Mean	1264	566	608	1311	634	428
Median	987	316	317	980	266	248
SD	1147	1004	1447	1897	1789	980

APPENDIX 10

Table A10.1. **Vitamin A supplementation of compound feed (IU kg^{-1} complete feed) — A European survey**

	1994 [1]		2007 [2]			
Diet type	**Minimum[3]**	**Maximum[4]**	**Minimum[3]**	**Maximum [4]**	**Recommendation[5]**	**Allowance[6]**
Piglet						
Starter I	3300	40000	8000	31000	10000–16000	4000
Starter II	3300	25000	7000	22000	10000–16000	4000
Pig						
Grower	3300	25000	4500	15000	5000–10000	2200
Finisher	3300	11650	4000	13500	5000–10000	2200
Sows						
Gestation	5500	25000	4000	31000	10000–15000	2300
Lactating	2200	30000	5000	31000	10000–15000	4000
Poultry						
Starter	6000	20000	10000	20000	12000–16000	2500
Replacement	7500	15000	8000	15000	8000–10000	1000
Chicken for fattening						
Starter/Grower	10000	18000	8000	17000	8000–12000	2500
Finisher	6500	15000	8000	13500	8000–12000	2500
Layer	8300	14000	8000	17000	8000–12000	4500
Turkey						
Starter	8000	30000	10000	17000	12000–16000	5000
Grower	8000	20000	8000	17000	8000–12000	5000
Finisher	8000	14000	6000	15000	8000–12000	5000
Breeder	12000	25000	6000	15000	12000–16000	(5000)
Duck Grower/Finisher			8000	15000		
Calf						
Milk replacer			10000	75000		10000*
Concentrate			8000	40000		
Cattle						
Concentrate			5000	30000		2500
Dairy Cow						
Complementary feed			8000	30000		
Complete feed						5000**
Rabbit						
Grower/Finisher			10000	16000		
Breeder			8000	12000		

(1) Belgium, Denmark, Germany, Italy, the Netherlands, Portugal, Spain, the United Kingdom (Gropp, 1994)
(2) Austria, Belgium, Croatia, Cyprus, Czech Republic, Denmark, Finland, Germany, Portugal
(3) Lowest minimum reported country
(4) Highest maximum reported country
(5) Arbeitsgemeinschaft für Wirkstoffe in der Tierernährung, Germany
(6) Pig: Allowances (total amount), Society for Nutrition Physiology, 2006
Chicken: Allowances (total amount), Society for Nutrition Physiology, 1999
Turkey: Allowances (total amount), Society for Nutrition Physiology, 2004
Ruminants: Allowances (total amount), Society for Nutrition Physiology, 2001
* Flachowsky (2001), constant liver store as endpoint
** lactating, dry: 10000

APPENDIX 11

AFSSA Report on vitamin A

Table A11.1. **Number of liver samplings per animal species and results of vitamin A levels determined in animal livers under the French monitoring plan in 2002**

Species	No of samples	Average	Standard deviation	Minimum	Maximum
		IU vitamin A 100 g liver^{-1}			
Calf (suckled)	21	32479	27696	10672	106150
Calf (battery)	17	44725	19800	21498	96680
Heifer	18	21034	21484	827	82876
Pig	24	34433	18441	10064	92154
Poultry	20	41755	25168	10821	92066
Lamb	18	21344	13303	5891	52343
Rabbit	18	21439	10972	7589	47702
Seabass (wild)	2	10952	1315	10239	11664
Tuna	2	214662	138237	95239	334085
Seabream	2	35200	5729	30433	39967
Cod	4	37200	16329	17016	59889