EHPM proposal for maximum and minimum levels for vitamins and minerals

FOOD SUPPLEMENTS FOR ADULTS AND CHILDREN SOLD IN EUROPE

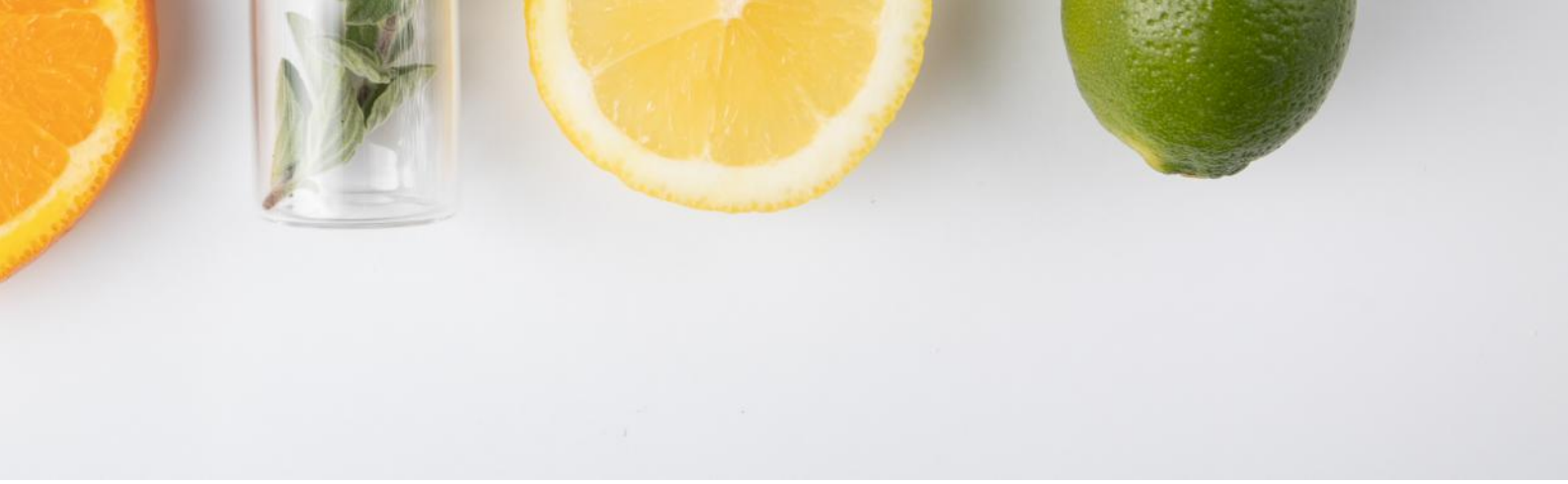
ehpm

European Federation of Associations of Health Product Manufacturers

Contents

Abbreviations and glossary

Abbreviation	Term	Glossary
AI	Adequate Intake	Estimated value when a Population Reference Intake cannot be established because an average requirement cannot be determined; Adequate Intake is the average observed daily level of intake by a population group of apparently healthy people assumed to be adequate
DRVs	Dietary Reference Values	Quantitative reference values for nutrient intakes for healthy individuals and population that may be used to assess and plan diets
EFSA	European Food Safety Authority	Independent European agency that assesses risks throughout the food chain
EHPM	European Federation of Associations of Health Product Manufacturers	European trade association representing the food supplement sector; members include National Associations from 14 European Countries, companies and service providers
ERNA	European Responsible Nutrition Alliance	Former European trade association in the food supplements sector, succeeded by Food Supplements Europe
FSAI	Food Safety Authority of Ireland	Independent statutory organisation that aims to protect consumers and raise compliance
IOM	US Institute of Medicine	Authoritative adviser on issues of health and medicine in the USA
LOAEL	Lowest observed adverse effect level	Intake that is the lowest concentration or amount of a substance shown to cause an adverse effect
MPL	Maximum permitted level of vitamin or mineral in food supplements	Highest intake determined to be safe for consumers for long-term daily intake from food supplements
MSL	Maximum safe level	Maximum safe levels of vitamins and minerals (for Ireland)
MS	Member States	Member States of the European Union



Abbreviation	Term	Glossary
NDA	EFSA Panel on Dietetic Products, Nutrition and Allergies	Expert panel advising EFSA on various aspects of the diet and food supply
NOAEL	No observed adverse effect level	Highest intake at which a substance has been shown not to cause an adverse effect
NRV	Nutrient Reference Value	EU guidance levels for labelling purposes set in legislation for 13 vitamins and 14 minerals based on daily requirements
PRI	Population Reference Intake	Daily intake of a nutrient that is adequate for 97.5% of people in a population or population group
PSI	Population Safety Index	A numerical value assigned to vitamins and minerals for allocation into categories of risk depending on the margin between the upper safe level of intake and the daily requirement
RI	Reference Intake	EU guidance levels for labelling purposes set for vitamins and minerals, macronutrients, salt, sugars, and energy based on daily requirements
RLV	Reference Label Value	Label value for nutrient requirements that preceded the NRV/RI
SCF	Scientific Committee on Food	European advisory committee that preceded EFSA
UL	[Tolerable or Safe] Upper Level	Estimate of the highest chronic daily intake that carries no appreciable risk of adverse health effects; the UL is a risk marker rather than a threshold, set for population groups, based on the available evidence in humans and animals

Acknowledgments

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Executive summary

The aim of this report is to propose a model for setting maximum permitted levels for food supplements (MPLs) that are safe for consumers, based on a robust scientific approach, and ensures informed consumer decisions. The model allows for maximum consumer choice and continued benefits for consumers once harmonised MPLs are set.

The proposals are based on:

- Recent scientific investigations of relevant parameters on which to base MPLs
- Peer reviewed publications that have undertaken in-depth investigations of data needed for the estimation of MPLs
- Learnings from previous and more recent risk management models for determining MPLs, e.g. 2020 FSAI Report and FSAI Guidance

To propose MPLs, European ULs are used as a priority. Dietary intake data are the most recent from countries with mature markets for both fortified foods and food supplements that are deemed to be of sufficient quality.

The chosen data sets, from national dietary surveys in Ireland and the Netherlands, include intake from fortified foods and provide intakes at the 95 percentile, which is judged to be sufficiently cautious as the ULs themselves are based on a precautious approach.

MPLs are proposed for adults and children aged 4-10 years.

Future food fortification is accounted for by qualitative assessment based on intelligence from EHPM's member associations. This is also supported by evidence that the trend for intakes of micronutrients is generally downwards over time.

The MPLs are based on the UL minus intake at the 95 percentile, with adjustment by rounding to practical levels and an additional qualitative assessment where the science requires.

Where scientifically justified in relation to safety, proposed MPLs for particular vitamins and minerals include an upper bound supported by consumer information and a lower bound for which the consumer information is not required.

Proposals for minimum amounts are also provided.

Introduction

Over recent years consumption of products containing additional vitamins and minerals to those naturally present in foods has increased in many people's diets. To ensure that the total intakes of vitamins and minerals from all sources on the market do not endanger health, regulatory authorities have deemed it necessary to set harmonised maximum amounts in Europe. Maximum permitted levels for fortified foods are foreseen under Regulation 1925/2006 (EC, 2006), and harmonised maximum permitted levels for food supplements (MPLs) are foreseen under Directive 2002/46/EC (EC, 2002) along with minimum amounts for use in food supplements. This Directive also establishes lists of permitted sources of vitamins and minerals that have been assessed for safety.

As harmonised MPLs across Europe have not yet been agreed, many Member States (MS) have set national levels for various vitamins and minerals. This creates challenges for the industry, particularly companies that sell products across Europe, as divergent national rules hinder the free circulation of products within the European market.

In 2021, DG SANTÉ resumed work on harmonised maximum and minimum levels in food supplements, and maximum levels in fortified foods. The European Food Safety Authority (EFSA) has been requested to review previous opinions on the Tolerable/Safe Upper Levels (ULs) issued by the Scientific Committee on Food (SCF) and the EFSA Dietetic Products, Nutrition and Allergies (NDA) Panel, and to take account of recent scientific developments and evidence, for eight micronutrients:

- Vitamin A
- Folic acid/ folate
- Vitamin D
- Vitamin E
- Vitamin B6
- Iron
- Manganese
- β-Carotene

Where the data are insufficient to establish a UL, EFSA has been asked to indicate the highest level at which there is reasonable confidence for the absence of adverse effects.

DG SANTÉ has also established a Task Force of Member States to work on scientific aspects of maximum and minimum levels and will consult stakeholders at various timepoints during the process. An impact assessment will be launched at an early stage, with consultations in the second quarter of 2023 and on the draft Regulation. The timeline to complete the work is by the end of the EC's mandate in 2024.

SETTING MAXIMUM LEVELS

Directive 2002/46/EC (EC, 2002) and Regulation 1925/2006 (EC, 2006) set out parameters to be taken into account when setting MPLs for food supplements (EC, 2002), and maximum amounts for micronutrients added to foods (EC, 2006). These are:

- Upper safe levels of vitamins and minerals established by scientific risk assessment based on generally accepted scientific data, taking into account, as appropriate, the varying degrees of sensitivity of different consumer groups
- Intake of vitamins and minerals from other dietary sources
- When the maximum levels are set due account shall also be taken of reference intakes[1] of vitamins and minerals for the population
- When setting maximum amounts for micronutrients added to foods, the contribution of individual products to the overall diet of the population or sub-groups, and the nutrient profile of the food product concerned will also be considered

[1] Population Reference Intake (PRI) or Adequate Intake (AI)

Based on these requirements, a Commission Discussion paper (EC, 2006a) identified various issues that need to be considered. These include:

- Which ULs to use where these are not set for Europe
- Whether maximum levels should be set for vitamins and minerals that show a low risk of adverse effects even at very high intakes
- Whether maximum levels should be set separately for food supplements and fortified foods
- Whether dietary survey data from individual Member States can be used to set maximum levels across Europe, or whether adjustments are needed
- Whether intakes from different population groups should be taken into account
- The extent to which Dietary Reference Values (DRVs) such as the Population Reference Intakes (PRIs) need to be taken into account
- Whether different minimum amounts to the significant amount required for a claim or label declaration on foods should be set for certain nutrients in specific foods or categories of foods, and if so on what basis
- Whether the minimum amounts in food supplements should be linked to the significant amount present for labelling in foods or whether they should be set in a different way

Many of these issues allude to the incomplete numerical parameters and incomplete data sets on which maximum levels are to be based. The key parameters are the ULs and dietary intake data.

In most cases the UL is set for the total daily intake of a nutrient that is safe over the long-term, although the research on which the ULs are based has generally considered test intakes in addition to the usual diet.

As studies of safety have not been systematic, the SCF scientific opinions (issued up to April 2003) and EFSA scientific opinions (issued May 2003 to 2005) could not establish ULs for all micronutrients. Due to gaps in the evidence, ULs were not established for phosphorus, chloride, iron, manganese, nickel, potassium, sodium, tin, vanadium and vitamin C (though it was commented that 1g/day total intake is not a cause for concern).

For other micronutrients, a UL could not be established for all population groups e.g. a UL for calcium was established for adults including pregnant and lactating women, but could not be established for children and adolescents.

In other cases, the data show that even at very high intakes there is no evidence of harm (vitamins B1, B2, B12, biotin, pantothenic acid, vitamin K and chromium).

In most cases where a UL was established a lack of evidence in different population groups, particularly younger age groups, meant that ULs needed to be extrapolated based on scaling according to body surface area to allow for differences in basal metabolic rate or on body weight differences.

Measuring dietary intake is also fraught with challenges. The Commission discussion paper (EC 2006a) recognised the lack of uniform dietary survey data across Europe, and the many limitations of existing data sets. It is generally recognised that these limitations include inaccuracies inherent in the various ways of collecting intake data, the challenges of assessing quantities of food eaten, particularly in home-cooked recipes and accounting for ingredients in manufactured foods, representation of specific population groups, accounting for food waste, and the frequency with which surveys are conducted regarding their ability to reflect current intakes of vitamins and minerals.

Compromise will therefore be essential to proximate suitable measures of intake to determine harmonised MPLs.

Another consideration is the point along the range of population intakes that should be used. Intakes for different population groups are determined at various points across the intake range including the mean, median, and more extreme upper and lower bounds including 97.5% and 2.5%, and/or 95% and 5%.

Dietary surveys can also be used to identify micronutrients for which intakes are low in particular population groups, and those for which intakes at the upper end of the range approach or even exceed the UL, and these factors can also be taken into account when making a qualitative assessment of the overall data.

Effects of exceeding the UL vary for different micronutrients and depend on the amount of excess, the severity of the adverse effect and the dose response relation for nutrient intake. However, a recent analysis of dietary intake data in Ireland found that the 95 percentile intake of selected vitamins and minerals in adults aged 18-64 years and children aged 7-10 years were well below the ULs, even when overages of 25% were taken into account, indicating in current markets little risk of adverse health effects associated with excessive intakes (Flynn et al., 2017).

It is important that MPLs are set according to accepted risk management procedures, i.e. that the risks should be precisely identified and addressed in context, are scientifically assessed, and the outcomes systematically evaluated according to the severity of the risk and the likelihood of it occurring. Any control measures should be proportionate to the risk, and should take into account the overall implications for stakeholders including potential negative impacts of the control measures themselves.

Examples of risk management models assessing MPLs

Since the publication of Directive 2002/46/EC (EC, 2002) and Regulation 1925/2006 (EC, 2006), relevant issues for setting maximum levels have been researched, and numerous scientific bodies and stakeholders have proposed risk management models for establishing MPLs.

ERNA/EHPM MODEL 2004

EHPM's previous contribution to the debate on setting MPLs was published jointly with the European Responsible Nutrition Alliance (ERNA) in 2004 (ERNA/EHPM, 2004). The paper proposed a methodology for setting MPLs, based on quantitative and/or qualitative assessment of the data and included a number of precautionary measures. The ULs used were those set by SCF/EFSA or, when absent, by the US Institute of Medicine (IOM).

The approach was to assign micronutrients into categories of risk based on the calculated Population Safety Index (PSI) which essentially determines the available "space" for intake from supplements, relative to reference intakes[2]. In this model, the PSI was determined by subtracting from the UL the upper end of the dietary intake range (97.5%) for food sources (excluding intake from supplements)[3], with allowance for intake of minerals from water, and dividing the result by the Reference Label Value (RLV). Where no UL has been set a qualitative assessment was undertaken. Vitamins and minerals were categorised into 3 groups:

- **Group 1**: No Risk Micronutrients (no UL set on the basis of lack of adverse effects at high intakes)
- **Group 2**: Low Risk Micronutrients
- **Group 3**: Higher Risk Micronutrients

The cut-off between Groups 2 and 3 was a PSI of 1.5

[2] The Population Safety Index (PSI) is calculated as the UL less male 97.5 percentile intake relative to the Reference Intake; 97.5 percentile intake data were from the UK, Netherlands, Ireland and Italy and the EU/IOM ULs were used; the cut-offs are >1.5 for Group 2, and <1.5 for Group 3.

[3] Intake data from surveys conducted in Ireland, Italy, the Netherlands and the UK

Assignment of micronutrients to risk groups

Group 1	Group 2	Group 3
No evidence of risk at levels currently consumed: No UL from which to calculate the MPL as adverse effects are not typically observed even at very high intakes; therefore no MPL is required as a risk management measure	**Low risk of exceeding UL**: MPL required for risk management and can be calculated from the UL and dietary intake data	**Higher risk of exceeding UL**: MPL required for risk management; further to calculation from the UL and dietary intake data additional qualitative assessment may be needed
Vitamin B1	Nicotinamide	Preformed retinol
Vitamin B2	Vitamin B6	Calcium
Biotin	Folic acid	Copper
Vitamin B12	Vitamin C	Fluoride
Pantothenic acid	Vitamin D	Iodine
Vitamin K	Vitamin E	Iron
Chromium	Magnesium	Manganese
	Molybdenum	Zinc
	Phosphorus	β-Carotene
	Selenium	

To propose MPLs for Groups 2 and 3, the following measures were subtracted from the UL:

- Habitual dietary intake at the upper end of the intake range (97.5 percentile) for food sources only....
- An allowance for future food fortification and changing dietary patterns (50% of intake at the 97.5 percentile for vitamins and 10% of intake at the 97.5 percentile for minerals)
- Intake of minerals from water

For Group 3 nutrients a qualitative assessment of the data was also undertaken.

The model was updated by Food Supplements Europe (FSE, 2014) to include MPLs for children aged 4-10 years and more recent dietary intake data. It has been further updated in 2021 (FSE, 2021).

The latter report provides a more recent reassessment of the PSIs. This has confirmed that the original grouping of micronutrients is still valid, with the addition of potassium to Group 2, and the omission of fluoride from group 3 on the grounds that MPLs for fluoride should be set in a local context depending on water fluoridation policies.

FOOD SAFETY AUTHORITY OF IRELAND MODEL, 2020

Guidance issued by the Food Safety Authority of Ireland (FSAI) to ensure that food supplements are safe for consumers and to establish clear rules for business (FSAI, 2020), is based on a report of the FSAI Scientific Committee (FSAI, 2020a). The report first considered assessments of the highest level of long-term intakes of micronutrients from all sources (food, fortified food and food supplements) and concluded that current levels of intake are unlikely to cause a risk to health.

The report also set Irish ULs, based on published values and determined an approach to assessing Maximum Safe Levels (MSLs) for supplements. This is straightforward, based on a general calculation on a case-by-case basis:

Maximum Safe Level (MSL) in food supplements = Tolerable Upper Intake (UL) minus intake from food sources in the diet at the 95 percentile intake (i.e. top 5% of consumers)

Risk management measures are applied to the resulting value as necessary. To date, MSLs have been proposed for seven nutrients for adults and for children aged 4-10 years: vitamins A, B6, C, D, folic acid, β-carotene and magnesium. A separate MSL is proposed for vitamin A for teenagers (11-17 years). Key factors for the assessment were:

- European ULs are used as a priority; where these have not been set the ULs used are those set by the IOM
- The reference bodyweight used for the ULs is 70 kg rather than 60 kg used by EFSA
- No risk categorisation is proposed and an extremely cautious approach is taken to all micronutrients with no UL
- Micronutrients for which no ULs have been recommended for Ireland are: β-carotene, vitamin K, thiamin, riboflavin, vitamin B12, biotin, pantothenic acid, phosphorus, potassium, chromium and silicon; the guidance advises that intake should only be from foods
- Dietary intake data are taken from the latest Irish National Nutrition Surveys[4]
- Potential changes due to future food fortification were assessed on a case-by-case basis
- There is no additional allowance for intake of minerals from water
- Label declarations of nutrient intake are used in the calculations in preference to the measured value.

[4] Irish Universities Nutrition Alliance, National Children's Food Survey, 2019; Irish Universities Nutrition Alliance, National Teen's Food Survey, 2008; Irish Universities Nutrition Alliance, National Adult Food Survey, 2011

Approach adopted by EHPM 2021

The primary aim of EHPM is to propose a model for setting MPLs that are safe for consumers, based on a robust scientific approach that maximises consumer choice and ensures continued benefits of supplementation for consumers taking particular products once harmonised MPLs are set. Minimum levels are also proposed.

EHPM has revisited the 2004 model, taking account of more recent investigations of relevant parameters on which to base MPLs and the data needed for their estimation (Flynn et al., 2017), and more recent models for calculating MPLs, such as the FSAI Scientific Committee Report and FSAI Guidance (FSAI 2020, FSAI 2020a). Some elements of the 2004 model have been refined to simplify the model in the light of these more recent publications.

Summary of EHPM's 2021 model

- Micronutrients are assigned into categories of risk, which is consistent with the need for control measures to be proportionate to the risk
- European ULs are used as a priority; where these have not been set the ULs used are those set by the IOM
- Further missing ULs have been considered by qualitative assessment
- Dietary intake data used are the most recent from countries with mature markets for both fortified foods and food supplements and deemed to be of sufficient quality; these are from National dietary surveys in Ireland and the Netherlands and include intake from fortified foods
- Intake data is for the 95 percentile, i.e. representing the 5% of consumers with the highest intakes, as the ULs themselves include a considerable level of precaution
- Future food fortification is accounted for by a qualitative assessment (based on intelligence from EHPM's member associations)
- In view of the wide variation in likely intake of minerals from water due to variations in local water supplies, challenges of measuring intakes and amounts consumed, and because many of the studies investigating adverse effects have not accounted for intake from water separately, intake from this source is not included in the current model
- Hence, the basic calculation to estimate the MPL is based on the underlying approach of the FSAI (UL minus intake at the 95 percentile)
- Where scientifically justified in relation to safety, proposed MPLs for particular vitamins and minerals include an upper bound supported by consumer information and a lower bound for which the consumer information is not required.
- Proposals for MPLs for children aged 4-10 years are based on ULs for 4-6 year-olds and averaged intake data for boys and girls at the 95 percentile for ages 4-13 (Dutch data) and 5-12 years (Irish data), which builds in additional precautionary measures
- Proposals for minimum amounts

Apart from pre-formed retinol, separate MPLs are not generally proposed for teenagers as the adult MPL is deemed to be suitable. Teenage years are characterised by rapid growth and increase in body size. The age at which the growth spurt occurs is variable, as is the rate of growth, and at this time nutritional needs are closer to adult requirements. Adult ULs ensure safety over the long term, whereas teenage years are a finite period, which also builds in a precautionary measure.

MICRONUTRIENT RISK GROUPS

The categorisation to risk groups remains the same as that of 2004, with the addition of potassium to group 2 and boron to group 3.

Group 1	Group 2	Group 3
No risk identified: No MPL proposed	**Low risk**: MPL proposed	**Higher risk for particular groups**: MPL proposed
Vitamin B1	Nicotinamide	Preformed retinol
Vitamin B2	Vitamin B6	Calcium
Biotin	Folic acid	Copper
Vitamin B12	Vitamin C	Fluoride
Pantothenic acid	Vitamin D	Iodine
Vitamin K	Vitamin E	Iron
Chromium	Magnesium	Manganese
	Molybdenum	Zinc
	Phosphorus	β-Carotene
	Selenium	Boron
	Potassium	

ULs USED

Annex 1 lists the ULs used in the assessment; PRIs or Adequate intakes (AIs) are included for context.

DIETARY INTAKE DATA USED

Annex 2 provides the dietary intakes used to calculate the MPLs. The 95 percentile intake data used are an average of those from recent dietary surveys in Ireland[5] and The Netherlands[6]. This combination allows a wider assessment of the range of intakes at the 95 percentile level and helps to

[5] Irish Universities Nutrition Alliance, National Children's Food Survey, 2019; Irish Universities Nutrition Alliance, National Teen's Food Survey, 2008; Irish Universities Nutrition Alliance, National Adult Food Survey, 2011

[6] The Netherlands: Dutch Dietary Survey 2012-2016: data for boys and girls aged 4-8 years, and for adults aged 19-79 years

mitigate the cross sectional nature of the data as intakes change longitudinally over time for various reasons.

DERIVATION OF MPLs

Group 1 micronutrients

No MPL is necessary as no UL has been set from which to calculate the MPL, due to low risk of adverse effects at high intakes.

Group 2 and Group 3 micronutrients

For the majority of Group 2 micronutrients, the MPL has been derived based on the following calculation:

MPL = Upper Safe Level less dietary intake at the 95 percentile

Group 3 is also estimated by calculation in most cases, with additional qualitative measures as necessary.

In cases where the calculation results in a negative MPL (i.e. for children for zinc and manganese) the MPLs have been based on a pragmatic approach of the DRV for children aged 4-6 years.

For some micronutrients, the UL is set specifically for food supplements, such that no calculation is required, e.g. magnesium.

OTHER RELEVANT FACTORS

Future food fortification

For most micronutrients no indications or intelligence concerning official proposals for future food fortification were identified by Member Associations across the EU. Additionally, the trend for intakes of micronutrients is generally downwards over time (PHE, 2020).

An analysis of the nutritional impact of changes in voluntary fortification practices in adults aged 18-64 years in Ireland over time found that, although the supply of fortified foods increased between 1997/8 and 2008/10 resulting in higher proportion of adults consuming fortified foods (from 67% to 82%) this did not contribute to an increased risk of intakes exceeding the UL for any micronutrients, and therefore did not contribute to an increased risk of adverse effects (Hennessy et al., 2015).

In view of current interest in vitamin D an allowance has been made for future food fortification, similar to the Irish approach.

This is because of high rates of deficiency in some European countries, coupled with the positive role of vitamin D for the immune system, which may result in higher levels of fortification in response to the Covid-19 pandemic.

OVERCOMING GAPS IN THE DATA

ULs for micronutrients with no published UL have been determined as follows:

- **Phosphorus**: As no UL was set by EFSA the EFSA opinion has been interpreted to proximate a UL of 750 mg/day for intake from supplements only, based on evidence that adverse gastrointestinal effects are observed in some individuals exposed to high supplemental intakes of >750 mg/day. For children, this is divided by 3 to give a proximate UL of 250 mg/day.

- **Potassium**: Again, as no UL was set by EFSA or by IOM, the EFSA opinion has been interpreted to proximate a UL. EFSA commented in its scientific opinion that a long-term intake of potassium supplements as potassium chloride of about 3g/day in addition to intake from foods has been shown not to have adverse effects. Though gastrointestinal symptoms have been seen in healthy subjects taking some forms of potassium supplements at doses ranging from 0.9 to 4.7 grams/day incidents appear to depend on the formulation rather than the dose. In this case a UL of 1000 mg/day for supplements only excluding potassium from the diet has been used. For children, this is divided by 3 to give a proximate UL of 350 mg/day.

- **Silicon**: Both EFSA and IOM were unable to set a UL for silicon due to a lack of suitable dose-response data. EFSA commented that typical dietary intakes of 20-50 mg/day are unlikely to cause adverse effects. IOM stated that the available toxicity data suggest that typical levels of intake have no risk of inducing adverse effects for the general population. However, the UK EVM (EVM, 2003) established a UL of 700 mg/day for a 60 kg adult based on an animal study with safety factors applied of 10 for interspecies variation and 10 for interindividual variation. 700 mg has therefore been taken as the UL.

Micronutrients for which there was no intake data in surveys have been calculated as follows:

- **Boron**: Intake data from the dietary survey for German adults (cited in Rainey & Nyquist, 1998), and data for school children from the USA (NHANES III) (cited in NIH Health Professionals Fact Sheet[7]).

- **Fluoride**: Intake data referenced in the EFSA DRV Opinion (EFSA, 2013), i.e. highest adult intake (but not 95 percentile) from food sources only in France, and data for German children aged 3-6 years from food sources (mean + SD).

- **Manganese**: Intake data referenced in the EFSA DRV Opinion (EFSA, 2013a), i.e. UK data for adults at 97.5 percentile intake, and German data for children aged 6-11 years at the 95 percentile intake.

- **Molybdenum**: Intake data referenced in the EFSA DRV Opinion (EFSA, 2013b) based on a calculated average of French data for adults at the 95 percentile intake, Denmark maximum intake for adults and Belgium maximum intake for adults, and French data for children at the 95 percentile intake.

[7] https://ods.od.nih.gov/factsheets/Boron-HealthProfessional/

Proposed MPLs

Annex 3 details proposed MPLs resulting from the EHPM risk management model.

Annex 4 provides the raw calculations behind the values prior to any rounding for reasons of practical consideration, or further qualitative assessment.

Specific cases: Lower and Upper bounds for MPLs with Consumer Information

Providing consumer information is an accepted approach for informing particular consumers and population groups about potential food risks that affect only some consumers. They afford the opportunity to protect consumers that might be affected while continuing to maximise consumer choice for those not affected. Examples of more general use of advisory statements include allergy labelling, information about food-drug interactions (e.g. grapefruit and statins), and advising non-suitability of food products for particular age groups, or pregnant women, e.g. particular types of cheese.

For specific micronutrients, providing additional consumer information will enable higher safe MPLs to be set for some food supplements, particularly when taken for short periods of time or taken by population groups at less risk of the adverse effect on which the ULs are based. This approach ensures that consumer safety is addressed as a priority and improves credibility of the industry.

It also enables informed consumer decisions and maximises consumer choice.

The scientific justifications this approach in specific cases include:

- The adverse effect used to set the UL is mild, transient and reversible without associated clinical effects, and has not been uniformly reported in studies; the consumer is aware of such effects and though the risk varies from person to person, the effects do not occur in most individuals at the given dose, only in sensitive individuals; examples of minor and reversible effects include mild stomach upset (e.g., laxative effect), nausea, and skin flushes.
- The lowest observed adverse effect level (LOAEL) is set on the basis of sensitive consumers and the adverse effect is not generally observed.
- ULs represent the maximum level of total chronic daily intake over the long term that is unlikely to pose a risk of adverse health; hence in certain cases excursions above the UL can be tolerated for short periods without adverse effects because ULs incorporate a considerable degree of precaution; they are not a threshold for which intake above a “cut-off” is inherently unsafe. Where higher levels are intended for short term use this is stated on the label and in product information.

Taking this into account, EHPM proposals for the MPLs for specific micronutrients include an upper bound supported by consumer information and a lower bound for which the consumer information is not required (Annex 5).

Consumer information is also important to inform certain population groups about intakes of food supplements where these may differ from the general population, and these are also included in Annex 5.

Proposals for minimum amounts

The Food Supplements Directive (EC, 2002) makes provision for setting minimum amounts as well as maximum amounts for food supplements.

Article 5.3: To ensure that significant amounts of vitamins and minerals are present in food supplements, minimum amounts per daily portion of consumption as recommended by the manufacturer shall be set, as appropriate.

As harmonised minimum amounts have not yet been set in the EU, DG SANTÉ is addressing this also. In principle, if a nutrition or health claim is not made, there is no minimum amount for inclusion of a vitamin or mineral in a food supplement or for declaration on the label.

Food supplements are defined in The Food Supplements Directive (EC, 2002) as "concentrated sources of nutrients…". Though no minimum content has been defined the presence of too small an amount would not offer a benefit to consumers and could be misleading. However, the content that constitutes a "concentrated" source for inclusion, or a "significant" level for declaration on a label when no claim is made is debatable.

The Commission Discussion paper (EC, 2006) suggested that minimum amounts for vitamins and minerals in food supplements could be linked to the significant amounts required for labelling purposes [i.e. 15% of the (then) label RLV]. However the EC consulted stakeholders as to whether they should be set in a different way.

If minimum amounts are set too high particularly for multivitamins/minerals, some manufacturers might leave out lower intakes of important minerals. This is not in the best interests of public health as even small intakes can have a nutritional benefits and make a useful contribution to the diets of some consumers.

Additionally, for technological reasons, adding higher amounts of some minerals, such as calcium and magnesium for example, would result in an oversized tablet or capsule, particularly in the case of multivitamins/minerals which would be difficult to swallow, or would necessitate taking multiple tablets/capsules to achieve the daily dose. This would be undesirable for consumers. EHPM therefore proposes:

- A minimum amount for inclusion in a single nutrient food supplement of 15% RI/NRV
- A minimum amount of calcium for inclusion in a multi-nutrient food supplement of 6% RI/NRV and for declaration on the label
- A minimum amount of magnesium for inclusion in a multi-nutrient food supplement of 6% RI/NRV and for declaration on the label
- A minimum amount of boron, for which there is no NRV, for inclusion in a food supplement and for declaration on the label of 0.23mg

Summary

The aims of the EHPM risk management model are to enable setting MPLs that are safe for consumers, based on a robust scientific approach and to ensure informed consumer decisions. The model allows for maximum consumer choice and for continued benefits of supplementation for consumers once harmonised MPLs are set.

The EHPM model takes account of:

- Recent scientific investigations of relevant parameters on which to base MPLs
- Peer reviewed publications that have undertaken in-depth investigations of data needed for their estimation
- Learnings from previous and more recent models for determining MPLs, e.g. 2020 FSAI Report and FSAI Guidance

European ULs are used as a priority. ULs set by the IOM are used where EU ULs have not been set. Missing ULs have been considered by qualitative assessment.

Dietary intake data used are the most recent from countries with mature markets for both fortified foods and food supplements deemed to be of sufficient quality. The chosen data sets are from national dietary surveys in Ireland and the Netherlands. These surveys include intake from fortified foods and provide intakes at the 95 percentile, which is judged to be sufficiently cautious as the ULs themselves are based on a precautious approach.

The model includes proposals for MPLs for adults and children aged 4-10 years.

Future food fortification is accounted for by qualitative assessment based on intelligence from EHPM's member associations. This is also supported by evidence that the trend for intakes of micronutrients is generally downwards over time.

The calculation to estimate the MPL is based on the UL minus intake at the 95 percentile, with adjustment by rounding to practical levels and an additional qualitative assessment where the science requires.

Where scientifically justified in relation to safety, proposed MPLs for specific vitamins and minerals include an upper bound supported by consumer information and a lower bound for which the consumer information is not required.

Proposals for minimum amounts are also provided.

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Annex 1: ULs used in the EHPM 2021 model and Population Reference Intakes

Adults 18+ years				Source of UL	
Nutrient	**Unit**	**European PRI / AI***	**EFSA/SCF**	**IOM**	**Other**
Vitamin A	µg	750	3000		
β-Carotene	mg	Not set	< 15		
Vitamin D	µg	15	100		
Vitamin E	mg	13	300		
Vitamin K	µg	70	Not established		
Thiamin (B1)	mg	0.1	No limit set		
Riboflavin (B2)	mg	1.6	No limit set		
Nicotinamide	mg	1.6 niacin	900		
Nicotinic acid	mg	1.6 niacin	10		
Pyridoxine (B6)	mg	1.7	25		
Vitamin B12	µg	4.0	No limit set		
Folic acid	µg	330†	1000 + dietary folate		
Biotin	µg	40	No limit set		
Pantothenic acid	mg	5	No limit set		

Adults 18+ years				Source of UL	
Nutrient	**Unit**	**European PRI / AI***	**EFSA/SCF**	**IOM**	**Other**
Vitamin C	mg	110	Not established	2000	
Calcium	mg	950††	2500		
Phosphorus	mg	550	Not established		750‡‡
Magnesium	mg	350	250		
Chromium	mg	Not set	Not established		
Copper	mg	1.6	5		
Fluoride	mg	3.4	8‡		
Iodine	µg	150	600		
Iron	mg	11	Not established	45	
Manganese	mg	3.0	Not established	11	
Molybdenum	µg	65	700‡		
Potassium	mg	3500	Not established		1000‡‡
Selenium	µg	70	300		
Zinc	mg	16.3	25		
Boron	mg	Not set	11‡		
Chloride	mg	Not set	Not established		
Nickel	µg	Not set	Not established		
Silicon	mg	Not set	Not established		

Adults 18+ years				Source of UL	
Nutrient	**Unit**	**European PRI / AI***	**EFSA/SCF**	**IOM**	**Other**
Sodium	mg	Not set	Not established		
Tin	mg	Not set	Not established		
Vanadium	µg	Not set	Not established		

Children (4-6 years)**				Source of UL	
Nutrient	**Unit**	**European PRI / AI***	**EFSA/SCF**	**IOM**	**Other**
Vitamin A	µg	300	1100		
			Teens: 2600		
β-Carotene	mg	Not set	< 15		
Vitamin D	µg	15	50		
Vitamin E	mg	9¶	120**		
Vitamin K	µg	20	Not established		
Thiamin (B1)	mg	0.1	No limit set		
Riboflavin (B2)	mg	0.7	No limit set		
Nicotinamide	mg	1.6 niacin	220		
Nicotinic acid	mg	1.6 niacin	3		
Pyridoxine (B6)	mg	0.7	7		

Children (4-6 years)**				Source of UL	
Nutrient	**Unit**	**European PRI / AI***	**EFSA/SCF**	**IOM**	**Other**
Vitamin B12	µg	1.5	No limit set		
Folic acid	µg	140†	300 + dietary folate		
Biotin	µg	25	No limit set		
Pantothenic acid	mg	4	No limit set		
Vitamin C	mg	30	Not established	650	
Calcium	mg	800	Not established	2500	
Phosphorus	mg	440	Not established		250‡‡
Magnesium	mg	230	250		
Chromium	mg	Not set	Not established		
Copper	mg	1.0	2		
Fluoride	mg	1.0	2.5		
Iodine	µg	90	250		
Iron	mg	7	Not established	40	
Manganese	mg	1.0	Not established	3	
Molybdenum	µg	20	200		
Potassium	mg	1100	Not established		350‡‡
Selenium	µg	20	90		

Children (4-6 years)**				Source of UL	
Nutrient	**Unit**	**European PRI / AI***	**EFSA/SCF**	**IOM**	**Other**
Zinc	mg	5.5	10		
Boron	mg	Not set	4		
Chloride	mg	Not set	Not established		
Nickel	µg	Not set	Not established		
Silicon	mg	Not set	Not established		
Sodium	mg	Not set	Not established		
Tin	mg	Not set	Not established		
Vanadium	µg	Not set	Not established		

* for males 18 years and above;
** for boys 4-6 years;
¶ age 3-9 years;
† for folate; †† 25 years and above;
‡Based on 70 kg body weight;
‡‡UL proximated from evidence cited in EFSA UL opinion.

Annex 2: Dietary intake data used in the EHPM 2021 model

95 Percentile Intake

		All Adults (18+ years)			Children (boys and girls) 4-12/13 years		
Nutrient	**Units**	**Dutch Data**	**Irish Data**	**Average**	**Dutch Data 4-13 y**	**Irish Data 5-12 y**	**Average**
Retinol	mcg	1239	1022	1131	929	426	678
β-Carotene	mcg	n/a	10019	10019	n/a	5478	5478
Vitamin D	mcg	5.9	8.7	7.3	4.5	7.0	5.8
Vitamin E	mg	20.4	18.2	19.3	16.7	9.5	13.1
Vitamin C	mg	173	183	178	154	116	135
Vitamin B1	mg	1.8	2.8	2.3	1.3	2.0	1.7
Vitamin B2	mg	2.3	3.3	2.8	1.9	2.4	2.2
Vitamin B3	mg	31.0	41.2	36.1	19.9	24.8	22.4
Vitamin B6	mg	2.6	4.8	3.7	1.9	2.0	2.0
Folate*	mcg	367	246	307	250	160	205
Vitamin B12	mcg	7.7	11.0	9.4	5.7	7.2	6.5
Biotin	mcg	n/a	66.0	66.0	n/a	34.6	34.6
Pantothenate	mg	n/a	9.8	9.8	n/a	7.7	7.7
Potassium	mg	4578	4634	4606	3269	2890	3080

95 Percentile Intake

Nutrient	Units	All Adults (18+ years) Dutch Data	Irish Data	Average	Children (boys and girls) 4-12/13 years Dutch Data 4-13 y	Irish Data 5-12 y	Average
Calcium	mg	1575	1569	1572	1267	1219	1243
Phosphorus	mg	2095	2199	2147	1585	1467	1526
Magnesium	mg	488	449	468.5	242	276	259
Iron	mg	14.9	20.3	17.6	11.1	12.7	11.9
Zinc	mg	15.2	14.9	15.1	10.9	10.5	10.7
Copper	mg	2.0	2.2	2.1	1.5	1.1	1.3
Iodine	mcg	249	304	277	191	n/a	191
Selenium	mcg	77.0	n/a	77.0	50.3	n/a	50.3

Nutrient	Units	Adolescents Dutch Data 14-18 y	Irish Data 13-17 y	Average
Retinol	mcg	965	715	840

n/a: Not available;
*Data for total folates

Annex 3: Proposed MPLs with rounding and qualitative assessment

Group 1: No evidence of risk at current intakes

Micronutrient	Adults proposed MPL / MPL range with consumer information	Children (4-10 years) proposed MPL / MPL range with consumer information
Vitamin B1 (mg) Thiamin	N/A	N/A
Vitamin B2 (mg) Riboflavin	N/A	N/A
Vitamin B12 (µg) Cobalamin	N/A	N/A
Biotin (µg)	N/A	N/A
Pantothenic acid (mg)	N/A	N/A
Vitamin K (µg)	N/A	N/A
Chromium III (mg)	N/A	N/A

Group 2: Low risk of exceeding UL

Micronutrient	Adults proposed MPL / MPL range with consumer information	Children (4-10 years) proposed MPL / MPL range with consumer information
β-Carotene (mg)	8† - 15	8†
Nicotinamide (mg)	900‡	200‡
Nicotinic acid (mg)	10* - 30	3*
Vitamin B6 (mg)	20‡ - 100	5
Folic acid (µg)	700‡	100‡

Group 2: Low risk of exceeding UL

Micronutrient	Adults proposed MPL / MPL range with consumer information	Children (4-10 years) proposed MPL / MPL range with consumer information
Vitamin C (mg)	1800‡	500‡
Vitamin D (µg)	85¶	45
Vitamin E (mg)	300‡	100‡
Magnesium (mg) (dissociable salts)	250 - 450††	250*
Molybdenum (µg)	400	70
Phosphorus (mg)	750* - 1600††	250*
Potassium (mg)	1000* - 6000††	350* - 600
Selenium (µg)	225	40

Group 3: Higher risk of exceeding UL

Micronutrient	Adults proposed MPL / MPL range with consumer information	Children (4-10 years) proposed MPL / MPL range with consumer information
Vitamin A (pre-formed retinol) (µg)	1875‡	425 **11-17 years:** 1750
Boron (mg)	9	3
Calcium (mg)	1000-1600‡††	1250‡
Copper (mg)	3	0.7
Fluoride (mg)	6	2‡
Iodine (µg)	325	60

Group 3: Higher risk of exceeding UL

Micronutrient	Adults proposed MPL / MPL range with consumer information	Children (4-10 years) proposed MPL / MPL range with consumer information
Iron (mg)	27.5 - 45††	25
Manganese (mg)	4	1**
Zinc (mg)	10 - 25	5***
Silicon (mg)	700	140

n/a: Not applicable;
†Based on qualitative assessment;
‡Subject to rounding (see Annex 4 for calculated values);
†† Based on a recent assessment by the Belgian Authorities;
¶Allows for future food fortification;
*Based on UL or evidence specific to intake from supplements;
**Equivalent to EU AI for 4-6 years;
*** Equivalent to EU PRI for 4-6 years

Annex 4: Calculated MPLs from EHPM 2021 model

	Adults			Children		
Nutrient	**UL**	**95 Percentile Intake**	**Calculated MPL**	**UL**	**95 Percentile Intake**	**Calculated MPL**
Retinol mcg	3000	1131	**1869**	1100	678	**422**
β-Carotene mcg	15000	10019	**4981**	15000	5478	**9522**
Vitamin D mcg	100	7.3	**92.7**	50	5.8	**44.2**
Vitamin E mg	300	19.3	**280.7**	120	13.1	**106.9**
Vitamin C mg	2000	178	**1822**	650	135	**515**
Vitamin B3 (niacin) mg	900	36.1	**863.9**	220	22.4	**197.6**
Vitamin B6 mg	25	3.7	**21.3**	7	2	**5**
Folic acid mcg	1000	307‡	**693**	300	205	**95**
Potassium* mg	1000	[4606]	**1000**	350**	[3080]	**350**
Calcium mg	2500	1572	**928**	2500	1243	**1257**
Phosphorus*mg	750	2147	**750**	250**	1526	**250**
Magnesium* (salts) mg	250	469	**250**	250	259	**250**
Iron mg	45	17.6	**27.4**	40	11.9	**28.1**
Zinc mg	25	15.1	**9.9**	10	10.7	**0**
Copper mg	5	2.1	**2.9**	2	1.3	**0.7**

Nutrient	Adults			Children		
	UL	95 Percentile Intake	Calculated MPL	UL	95 Percentile Intake	Calculated MPL
Iodine mcg	600	277	**323**	250	191	**59**
Selenium mcg	300	77	**223**	90	50.3	**39.7**
Boron mg	11	1.72	**9.28**	4	1	**3**
Manganese mg	11	6.83	**4.17**	3	6.1	**0**
Molybdenum mcg	700	300	**400**	200	130	**70**
Fluoride mg	8	2	**6**	2.5	0.3	**2.2**

Nutrient	Teens		
	UL	95 Percentile Intake	Calculated MPL
Retinol mcg	965	715	**840**

‡For total folates;
*UL set/proximated for supplementation;
**Based on adult UL adjusted for body weight (/3)

Annex 5: Supporting label information to the consumer

Adults

Nutrient	Information to be provided to the consumer via the product label	Daily intake range requiring consumer information	Associated adverse effect
Retinol	Not suitable for pregnant women or women planning a pregnancy	All products containing retinol >750 mcg	Adverse effects on developing foetus (at 3000 mcg/day total intake)
	Over-50s and postmenopausal women: restrict total retinol intake to 1500 mcg/ day; avoid other supplements containing retinol	All products containing retinol >1500 mcg	Potential adverse effect on bone density in over 50s, particularly postmenopausal women
β-Carotene	Not to be taken by heavy smokers	>8 – 15 mg	Possible link with cancer enhancement in heavy smokers
Nicotinic acid	May cause skin flushes in sensitive people	>10-30 mg	Reversible skin flushing
Vitamin B6	For short-term use: long term intake may lead to mild tingling and numbness	>20 mg – 100 mg	Reversible neuronal (nerve) effects leading to sensory and motor effects such as mild tingling and numbness; neurotoxicity not reported at doses of 100 mg/day when consumed for a few months
Vitamin K	Not recommended if taking anticoagulants	All doses	Antagonistic effects
Calcium	For short-term use	>1000 – 1600* mg	Hypercalciuria
Iron	For short-term use	>27.5 – 45* mg	Gastrointestinal effects (constipation)
Magnesium	May result in mild digestive disturbance in sensitive people	>250 – 450* mg	Transitory gastrointestinal effects

Adults

Nutrient	Information to be provided to the consumer via the product label	Daily intake range requiring consumer information	Associated adverse effect
Phosphorus	May result in mild digestive disturbance in sensitive people	>750 – 1600* mg	Mild gastrointestinal effects such as laxative effect, and nausea
Potassium	May result in mild digestive disturbance in sensitive people	>1000 – 6000* mg	Mild gastrointestinal effects
Zinc	Take with 1 mg of copper daily	>10 – 25 mg zinc, if product does not contain 1mg copper/ day	Adverse effects of zinc on copper metabolism, copper balance and copper status

* Based on a recent assessment by the Belgian Authorities

Children

Nutrient	Information to be provided to the consumer via the product label	Daily intake range requiring consumer information	Associated adverse effect
Potassium	May result in mild digestive disturbance in sensitive children	>350 – 600 mg	Transitory gastrointestinal effects

Annex 6: Individual micronutrient assessments

β-Carotene

No UL has been set either by SCF/EFSA or by the IOM.

In 2012 EFSA re-evaluated the use of mixed carotenes and β-carotene as a food additive. EFSA concluded that use of synthetic β-carotene and mixed carotenes obtained from palm fruit oil, carrots and algae used as a food colouring is not a safety concern provided that intake from use as a food additive and as a food supplement is not more than the amount likely to be ingested from the regular consumption of foods in which they occur naturally, estimated to be 5-10 mg/day[8]. This is to ensure that intake from all sources (i.e. naturally occurring, additives, fortified foods and supplements) does not exceed 15 mg/day.

[8] EFSA 2012. Scientific opinion on the re-evaluation of mixed carotenes (E 160a(i)) and beta-carotene (E 160a (ii)) as a food additive. EFSA Journal 10(3):2593.

EFSA also published a statement concerning the risk of cancer enhancement with β-carotene in heavy smokers[9]. EFSA concluded that exposure to β-carotene used as a food additive and as a food supplement below 15 mg/day does not give rise to health concerns in the general population including heavy smokers, i.e. the level at which epidemiological studies do not show increased cancer risk with β-Carotene supplementation. The 15 mg/day value is a NOAEL and has not been adjusted for uncertainty since an Acceptable Daily Intake for use as an additive could not be set.

[9] EFSA, 2012. Statement on the safety of β-carotene use in heavy smokers. EFSA Journal 10(12):2953.

However, there is uncertainty around the true intake of beta-carotene, e.g. intake from food additives and use as a supplement is unclear, but EFSA estimated that the maximum level would be around 10 mg/day excluding intakes from use as a colouring in food. Irish intake data show that consumption of β-carotene at the 95 percentile intake is about 5 mg/day for adults and 10 mg/day for children. As intake from use as an additive is unknown it is not possible to determine the MPL for β-carotene by calculation.

Based on the EFSA opinions and estimated intakes, the proposed MPL for β-carotene is 8 mg /day for both adults and children. An upper MPL of 15 mg may be justified for adults, subject to provision of consumer information on products containing 8-15 mg/day that they are not to be taken by smokers.

Nicotinic acid

The EFSA ULs of 10 mg for adults and 3 mg for children have been taken as the MPLs as adverse effects are generally related to acute bolus intakes of free nicotinic acid rather than more sustained exposure from ingestion via food. Free nicotinic acid levels in food are low. 30 mg is the LOAEL for skin

flushing to which EFSA applied a safety factor to obtain the UL of 10 mg for adults. As the adverse effect (reversible skin flushing) is not harmful per se, levels from >10 mg - 30 mg can be used with provision of consumer information that such doses may result in skin flushes in sensitive people.

Vitamin B6

EFSA concluded that no adverse effects have been associated with high intakes of vitamin B6 from food sources. However, the UL applies to total intakes. EFSA set the UL for adults at 25 mg/day, based on evidence of neuronal (nerve) damage with sensory and motor effects at doses of 500 mg/day or more, and minor neurological symptoms apparent at doses of 100 mg/day or more when consumed for long periods. The UL was determined by applying a safety factor of 2 to 100 mg/day to take account of long-term intake, and a further safety factor of 2 to allow for deficiencies in the database. Assessment of the dose-response relationship was difficult because of the apparent inverse relationship between the duration of exposure and doses that can be tolerated without adverse effects.

The EFSA/SCF risk assessment concludes “minor neurological symptoms may be apparent at doses of 100 mg/day or more if consumed for long periods” and the assessment states that neurotoxicity has not been reported at doses of 100 mg/day when consumed for a period of up to a few months. Notwithstanding the slow development of symptoms at high doses and the inverse relationship between dosage and the onset of symptoms, as intakes of vitamin B6 up to 100 mg/day taken for short periods are not associated with toxicity, it is proposed that levels from >10 mg - 100 mg can be used with provision of consumer information that the product is for short-term use only.

Calcium

EFSA was unable to set a UL for infants, children or adolescents in view of a lack of data. EFSA nevertheless stated that no risk has been identified for the highest current levels of calcium intake in these age groups. EFSA set a UL for adults, including pregnant and lactating women on the basis that total intakes of 2500 mg/day are well tolerated without adverse effects. IOM based the UL for children aged 1-8 years of 2500 mg/day on the IOM UL for adults. Allowing for dietary intakes at the 95 percentile EHPM proposes a lower bound for the MPL of 1000 mg for adults. A higher bound for short term intakes of 1600 mg/day is proposed accompanied by relevant consumer information, as EFSA concluded that intakes of 2500 mg calcium per day from both diet and supplements are well tolerated without adverse effects.

Magnesium

The UL was set for children from 4 years and upwards. As the adverse effect and the UL are specific to magnesium supplements, calculations subtracting intake from food from the UL are not relevant for this nutrient and the UL is taken as the lower bound of the MPL.

EFSA established a NOAEL of 250 mg/day, based on pharmaceutical type dosages taken in addition to magnesium from the diet and intake from water. An uncertainty factor of 1.0 was applied because data were available from many studies from a spectrum of population groups including children, and pregnant and lactating women as well as adults. The adverse effects were considered to be mild and transient without pathological sequelae, and to be readily revisable for which adaptation can develop within days.. In view of the mild and transitory nature of the adverse effect in sensitive consumers, an upper bound for the MPL of 450 mg magnesium/day is proposed, with provision of consumer information about the potential for transitory gastrointestinal (laxative) effects.

Manganese

Subtraction of intake from food sources (German data for children aged 6-11 years) at the 95 percentile intake would give no allowance for children. Hence a different approach is taken. As a precautionary measure, the proposed USLs are therefore based on the EU AI for age 4-6 years.

Potassium

EFSA did not set a UL for potassium on the basis of insufficient data. However, EFSA stated that adverse gastrointestinal effects are associated with supplementation and not with dietary intake. The lowest intakes referred to in the EFSA opinion that were associated with gastrointestinal effects were doses ranging from 0.9 to 4.7g/day or more, with incidence and severity depending more on the formulation rather than the dose. Intake from supplements only of 1000 mg /day is therefore approximated as the UL and is divided by ~3 for children based on body size. For adults 1000 mg is proposed as the lower bound for the MPL and, as the UL is conservative and the range of lowest intakes at which the adverse effect has been reported is particularly wide, an upper bound supported by consumer information is proposed for adults of 6000 mg/day accompanied by consumer information about the potential for gastrointestinal (laxative) effects. Ideally potassium supplements should be taken in smaller doses 2-3 times a day.

Phosphorus

EFSA concluded that adverse gastrointestinal effects observed in some individuals exposed to high supplemental intakes of >750 mg/day were not a suitable basis to establish a UL for all sources of phosphorus. For supplement sources only, this intake has been approximated as the UL, which for children is divided by 3 to give a UL of 250 mg/day. For adults, 750 mg/day is proposed as the lower bound for the MPL, with 1600 mg/day taken as the upper bound, noting that the proximated UL is

conservative and EFSA's conclusion that normal healthy individuals can tolerate phosphorus intakes up to at least 3000 mg per day without adverse systemic effects. Consumer information is to be provided to support the upper bound level advising of the potential for mild gastrointestinal effects.

Zinc

SCF/EFSA based the UL on adverse effects of zinc on copper metabolism, copper balance and copper status. The opinion states that overt adverse effects relating to copper deficiency (arising from chronic zinc toxicity) are only evident after supplementary zinc in excess of 150 mg/day over long periods. However, it is more difficult to assess the critical effect of excess zinc at intakes below 100-150 mg/day. SCF/EFSA established 50 mg total intake as the NOAEL. An uncertainty factor of 2 was applied to allow for the small numbers of subjects and the relatively short-term nature of the studies, to give a UL of 25 mg zinc/day for total intake. Key studies in which total zinc intake was tightly controlled demonstrated that positive copper balance can be maintained at 53 mg total zinc/day for 90 days with adequate copper intakes (Davis et al., 2000; Milne et al., 2001), and that 40 mg total zinc intakes had no effect on putative indices of copper status. In view of the margin of safety if copper intake is adequate, an upper MPL of 25 mg zinc/day is proposed with provision of consumer information on products that don't also contain 1 mg copper/day.

EFSA commented that there is a lack of data for adverse effects of zinc in children and there are no data to indicate that they are more susceptible to adverse effects of zinc than adults. Hence ULs for children were developed by extrapolation of the adult UL on the basis of body surface area (body weight to the power of 0.75). However, subtraction of intake from food sources at the 95 percentile would give no allowance from supplements for children. Hence a different approach is taken. As a precautionary measure, the proposed USLs are therefore based on the EU PRI for 4-6 years.

Iron

EFSA concluded there were insufficient data on which to set a UL for iron. However, the IOM set a UL of 45 mg for adults on the basis of gastrointestinal effects (constipation) and noted that the risk of adverse effects from dietary sources is low. Specific groups at risk of adverse effects from iron include those with hereditary haemochromatosis, people with alcoholic cirrhosis and other liver diseases, and potentially older men and women. Allowing for dietary intakes at the 95 percentile EHPM proposes a lower bound for the MPL of 27.5mg/day. A higher bound for short term intakes of 45 mg/day is also proposed accompanied by relevant consumer information.

Silicon

The UL set by the UK EVM of 700 mg/day for a 60 kg adult is taken as the proposed MPL for supplements, as dietary intakes per se are not associated with adverse effects. A precautionary level for children is set at 140 mg/day.

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