Draft

Principles for deriving and applying Dietary Reference Values

Opinion of the Scientific Panel on Dietetic Products, Nutrition and Allergies

(Question No EFSA-Q-2005-015a)

(Agreed on 11 April 2008 for release for public consultation)

PANEL MEMBERS

Jean-Louis Bresson, Albert Flynn, Marina Heinonen, Karin Hulshof, Hannu Korhonen, Pagona Lagiou, Martinus Løvik, Rosangela Marchelli, Ambroise Martin, Bevan Moseley, Andreu Palou, Hildegard Przyrembel, Seppo Salminen, Sean (J.J.) Strain, Stephan Strobel, Inge Tetens, Henk van den Berg, Hendrik van Loveren and Hans Verhagen.

SUMMARY

The European Commission has requested EFSA to review the existing advice of the Scientific Committee for Food on population reference intakes for energy, nutrients and other substances with a nutritional or physiological effect. These reference values date from 1993. Since then new scientific data have become available for some of the nutrients, and scientific advisory bodies in many EU member states and in the US have reported on recommended dietary intakes.

This opinion focuses on the general principles for development and application of dietary reference values (DRV) - quantitative reference values for nutrient intakes for healthy individuals and populations which may be used for assessment and planning of diets.

Similarly to the earlier SCF report in 1993 the Panel proposes to derive the following DRV:

- *Population reference intakes (PRI):* the level of (nutrient) intake that is adequate for virtually all people in a population group.
- *Average requirement (AR)*: the level of (nutrient) intake that is adequate for half of the people in a population group, given a normal distribution of requirement.
- *Lower threshold intake (LTI):* the level of intake below which, on the basis of current knowledge, almost all individuals will be unable to maintain metabolic integrity, according to the criterion chosen for each nutrient.

In addition, the Panel also proposes to derive the following DRV:

- *Adequate Intake (AI):* the value estimated when a PRI cannot be established because an average requirement cannot be determined. An AI is the average observed daily level of intake by a population group (or groups) of apparently healthy people that is assumed to be adequate.

- *Recommended intake ranges for macronutrients (RI):* the recommended intake range for macronutrients, expressed as % of the energy intake. These apply to ranges of intakes that are adequate for maintaining health and associated with a low risk of selected chronic diseases.

The Panel will not address the *Tolerable upper intake level (UL)* as this has been assessed previously. The UL is the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans[1]

Some of the DRV - the AR, PRI and LTI - relate to nutrient requirements that are defined by specific criteria of nutrient adequacy. In defining nutrient requirement the selection of criteria to establish nutrient adequacy is an important step. For most nutrients a hierarchy of criteria for nutrient adequacy can be established, ranging from prevention of clinical deficiency to optimisation of body stores, or status. Which criterion, or combination of criteria, will be the most appropriate will be decided on a case-by-case basis.

Within any lifestage group, nutrient requirements vary between individuals and the AR, PRI and LTI represent different points on distribution individual requirements. Nutrient requirements also differ with age, sex and physiological condition, due to differences in the velocity of growth for the younger age groups, and age-related changes in nutrient absorption and body functions and/or functional capacity, such as renal function. Especially in older subjects, variability in functional capacity and in energy expenditure appears higher than in younger adults, particularly for elderly above 75 yr.

Because of this, DRV are developed for different life stage and sex groups. The panel proposes to establish DRV for the following age groups, like in the SCF reports of 1993 and 2000: *6-11 months; 1-3 years; 4-6 years; 7-10 years; 11-14 years; 15-17 years; 18-29 years; 30-59 years; 60-74 years; and ≥ 75 years.* For the age group < 6 months requirements are considered to be equal to the supply from breast-milk, except in those cases where this does not apply. Separate reference values will be established for pregnant and lactating women, taking into account the additional nutrient requirement for the formation of new tissues, or to compensate for the nutrients lost to the body in the form of human milk, respectively, and considering the physiological adaptations that occur during these conditions.

Interpolation or extrapolation between population groups will be used in instances where no data are available for defined age and sex groups. Both isometric (linear with body weight) or allometric (body weight to the power of a chosen exponent) scaling methods are being used. Which method is the most appropriate will be decided on a case-by-case basis.

Reference heights and weights are useful when more specificity about body size and nutrient requirements are needed than that provided by life stage categories. Reference weights will be the same as in the SCF report, and for children <1 year, as established by the WHO for fully breastfed infants.

Dietary reference values can be used for different purposes, such as in diet assessment and diet planning, both at the population and individual level, but also as a basis for reference values in food labelling, and in establishing food based dietary guidelines.

In *dietary assessment* of groups the AR can be used to estimate the prevalence of inadequate intakes of micronutrients (the AR cut-point method), if the distribution of nutrient intakes is normal, and intakes are independent from requirements. The PRI should not be used for this

[1] An opinion on tolerable upper intake levels for vitamins and minerals was published in February 2006 (http://www.efsa.europa.eu/en/science/nda/nda_opinions.html).

purpose as this would result in overestimation of the proportion of the group at risk of inadequacy.

For macronutrients with a defined recommended intake range for individuals, the distribution of usual intake of individuals may be assessed to ascertain what proportion of the group lies outside the recommended lower and upper limits of the range. In case of energy, the mean usual intake of energy of a defined group, relative to the average requirement, may be used in assessing the adequacy.

For assessment of adequacy of nutrient intakes in individuals dietary reference values are of limited use. Usual intakes below the AR are likely inadequate, and below the LTI very probably inadequate, while chronic intakes above the UL may be associated with an increased risk of adverse effects. For a valid assessment of the adequacy of an individual's usual intake, combined information with clinical, biochemical (status), and anthropometric data, are needed.

In *dietary planning* for groups the usual intake *distribution* should be between the AR and UL to avoid inadequate, respectively excessive intakes. For nutrients such as vitamins, minerals, and protein, the PRI can be a practical starting point. However, target median intakes higher than the PRI might be considered, especially in case of a skewed intake distribution.

For macronutrients the distribution of usual intake of individuals should be such as to minimize the proportion of the group that lies outside the recommended lower and upper limits of the range. For energy, the reference intake (estimated average energy requirement) of the group based on sex, age, height, weight, and physical activity level of the group may be used as a planning goal.

Key words

Dietary reference values (DRV), Population reference intakes (PRI), Recommended intake ranges for macronutrients (RI).

TABLE OF CONTENTS

BACKGROUND AS PROVIDED BY EC

The scientific advice on nutrient intakes is important as the basis of Community action in the field of nutrition, for example such advice has in the past been used as the basis of nutrition labelling. The Scientific Committee for Food (SCF) report on nutrient and energy intakes for the European Community dates from 1993. There is a need to review and if necessary to update these earlier recommendations to ensure that the Community action in the area of nutrition is underpinned by the latest scientific advice.

In 1993, the SCF adopted an opinion on the nutrient and energy intakes for the European Community[2]. The report provided reference intakes for energy, certain macronutrients and micronutrients, but it did not include certain substances of physiological importance, for example dietary fibre.

Since then new scientific data have become available for some of the nutrients, and scientific advisory bodies in many EU member states and in the US have reported on recommended dietary intakes. For a number of nutrients these newly established (national) recommendations differ from the reference intakes in the SCF (1993) report. Although there is considerable consensus between these newly derived (national) recommendations, differing opinions remain on some of the recommendations. Therefore, there is a need to review the existing EU reference intakes in the light of new scientific evidence, and taking into account the more recently reported national recommendations. There is also a need to include dietary components that were not covered in the SCF opinion of 1993, such as dietary fibre, and to consider whether it might be appropriate to establish reference intakes for other (essential) substances with a physiological effect.

In this context the EFSA is requested to consider the existing population reference intakes for energy, micro- and macronutrients and certain other dietary components, to review and complete the SCF recommendations, in the light of new evidence, and in addition advise on a population reference intake for dietary fibre.

For communication of nutrition and healthy eating messages to the public, it is generally more appropriate to express recommendations for the intake of individual nutrients or substances in food-based terms. In this context the EFSA is asked to provide assistance on the translation of nutrient based recommendations for a healthy diet into food based recommendations intended for the population as a whole.

TERMS OF REFERENCE AS PROVIDED BY EC

In accordance with Article 29 (1)(a) and Article 31 of Regulation (EC) No. 178/2002, the Commission requests EFSA to review the existing advice of the Scientific Committee for Food on population reference intakes for energy, nutrients and other substances with a nutritional or physiological effect in the context of a balanced diet which, when part of an overall healthy lifestyle, contribute to good health through optimal nutrition.

In the first instance the EFSA is asked to provide advice on energy, macronutrients and dietary fibre. Specifically advice is requested on the following dietary components:

- Carbohydrates, including sugars;

[2] Scientific Committee for Food, Nutrient and energy intakes for the European Community, Reports of the Scientific Committee for Food 31st series, Office for Official Publication of the European Communities, Luxembourg, 1993.

- Fats, including saturated fatty acids, poly-unsaturated fatty acids and mono-unsaturated fatty acids, *trans* fatty acids;
- Protein;
- Dietary fibre[3].

Following on from the first part of the task, the EFSA is asked to advise on population reference intakes of micronutrients in the diet and, if considered appropriate, other essential substances with a nutritional or physiological effect in the context of a balanced diet which, when part of an overall healthy lifestyle, contribute to good health through optimal nutrition.

Finally, the EFSA is asked to provide guidance on the translation of nutrient based dietary advice into guidance, intended for the European population as a whole, on the contribution of different foods or categories of foods to an overall diet that would help to maintain good health through optimal nutrition (food-based dietary guidelines).

ACKNOWLEDGEMENT

The European Food Safety Authority wishes to thank the members of the Working Group for the preparation of this opinion: Alan A. Jackson, Wulf Becker, Jean-Louis Bresson, Albert Flynn, Karin Hulshof, Martinus Løvik, Ambroise Martin, Andreu Palou, Hildegard Przyrembel, Sean (J.J.) Strain, Inge Tetens and Henk van den Berg.

ASSESSMENT

1. Introduction

Acknowledging the magnitude of the task involved for this request and considering the resource implication and time-constraint, the Panel decided on the following approach:

- To lay down the general principles for the basis of deriving and applying dietary reference values (DRV).
- DRV comprise both nutrient recommendations and reference intake levels.

For each nutrient/dietary component:

- to review existing DRV and relevant related scientific publications;
- to identify criteria (endpoints), and key evidence / data on which to base the DRV; and
- based on the above, to give a critical and independent judgement on the appropriate DRV.

The main objective for nutrition recommendations is to ensure a diet that provides energy and nutrients for optimal growth, development, function and health during the whole life. Nutrient requirements can be deduced from physiological needs and metabolic demand. There is also increasing evidence that nutrients and diet composition influence the risk of chronic diseases (WHO, 2003). In more recent editions of (national) nutrient recommendations, epidemiological and other data on disease risk have therefore been used, if available, as an additional criterion in estimating nutrient requirements, such as for calcium and vitamin D, but also in establishing recommendations for safe and adequate intake ranges for macronutrients.

[3] There is no harmonised definition of dietary fibre at the European Community level.
At the international level the recent meeting of the Codex Committee on Nutrition and Foods for Special Dietary Uses made a recommendation for the definition of dietary fibre for nutrition labelling purposes but a definition has not yet been adopted.
(see Alinorm 05/28/26 Appendix III - http://www.codexalimentarius.net/web/reports.jsp?lang=en)

In this task, the Panel will focus on establishing dietary reference values for energy and nutrients. The Panel assumes that, in general, for any given population group, physiological requirements will not vary across populations in Europe and therefore allow defining a common set of dietary reference values for the European population.

2. General principles for deriving dietary reference values

As nutrients are consumed as foods, nutrient requirements need translation into recommended nutrient intakes and finally into food-based dietary guidelines to help consumers to meet recommended intakes (FAO/WHO, 1998; Eurodiet, 2000; USDA, 2005). In setting dietary (nutrient) recommendations, the following four separate steps can be identified:

2.1. Estimating the physiological requirement and metabolic demand

Metabolism embraces the processes through which life is maintained, and there are on-going needs for energy and nutrients to support these processes. The rate at which a nutrient has to be provided to the body to support metabolism and maintain function represents the physiological requirement or metabolic demand for that nutrient. The physiological requirement varies between individuals dependent upon genetic and epigenetic differences, age, sex, physiological state such as pregnancy, and also varies in the same individual in response to environmental stress such as infection, trauma, behavioural or social stressors. For a group of people of similar age, sex and state, the variation in the requirement for a nutrient has been presumed to approximate a normal distribution which can be characterised by its central tendency (mean), and its distribution (standard deviation). The metabolism is tightly regulated and its adaptation, by modifications of absorption, elimination, recycling, degradation, constitution or mobilization of body stores, allows individuals to cope with the large variations of day to day intakes, in the short- and medium term. This metabolic adaptation should be taken into account, if appropriate, when setting recommendations for populations.

2.2. Establishing the dietary requirement of nutrients

Some nutrients need to be provided in the diet, and for others metabolism can contribute to their formation and availability to the body. The amount of a nutrient which has to be provided preformed in the diet, or the amount of the precursor which has to be taken in the diet in order to meet the physiological requirement is known as the dietary requirement. The dietary requirement has been identified as that amount of a nutrient which must be consumed on a regular basis to maintain health in an otherwise healthy individual, on the assumption that the requirements for energy and all other nutrients have already been satisfied. The dietary requirement will differ from the physiological requirement depending on a range of factors, such as the efficiency or effectiveness of absorption and utilisation of the nutrient, or the extent to which the nutrient can be formed as a part of metabolic interchange. The requirement is a characteristic of an individual and the magnitude of the dietary requirement varies amongst individuals of similar age, sex and physiological state. This variation has been presumed to approximate a normal distribution which can be characterised by its central tendency (mean), and its distribution (standard deviation).

2.3 Establishing recommendations for nutrient intakes

A number of different terms have been used to characterise a habitual level of intake of a nutrient which will satisfy the needs of most of the members of a population group. For a number of purposes it is desirable to be able to identify this level of intake. For nutrients for which an average dietary requirement can be established, this level of intake has been set as the mean plus two standard deviations of the average requirement. The assumption is that if the intake of all members of the group were at this level, the risk of an inadequate intake for any member of the group would be small (<2.5%).

The definition of the dietary reference values has found great practical utility in the planning of food provisions and the characterisation of the nutritional status of populations.

Recommendations on nutrient intakes include the adequate intake (AI), the population reference intake (PRI), and the recommended intake ranges (RI) used for macronutrients.

When no average requirement can be established, adequate intake levels, and recommended intake ranges can be used. Recommendations for energy are derived on a different basis than recommended intakes for nutrients.

2.4. Food-based dietary guidelines

Food-based dietary guidelines represent the form in which advice is provided to people to assist them in selecting a diet to meet their needs for health.

Nutrients are consumed as food. A wide range of foodstuffs together comprise the diet of the individual, group or population. Advice to people about selecting foods based on their nutritional composition is not helpful without giving advice on how to select a suitable mix of foods to meet their nutritional requirements on the basis of foods. Increasingly it is being found that particular patterns of food consumption appear to confer health benefits that cannot simply be ascribed to their containing an adequate mix of individual nutrients, suggesting that there are unidentified factors which may contribute to the health benefit conferred.

3. Terminology and definitions

Wide range of terminologies have been used by different national Agencies. In 2007, an expert group from WHO/FAO discussed the concept of nutrient based dietary standards. They proposed a harmonization of terminology used by national and international groups, and to limit the number of nutrient intake values (King et al., 2007). The Panel decided to derive a set of dietary reference values following on from an earlier report (SCF, 1993) and using the same definitions:

Dietary reference values (DRV): the complete set of nutrient recommendations and reference values such as the adequate intake level, the lower threshold and upper intake levels.

Population reference intakes (PRI): the level of (nutrient) intake that is enough for virtually all healthy people in a group.

Average requirement (AR): the level of (nutrient) intake that is enough for half of the people in a healthy group, given a normal distribution of requirement.

Lower threshold intake (LTI): the level of intake below which, on the basis of current knowledge, almost all individuals will be unlikely to maintain metabolic integrity, according to the criterion chosen for each nutrient.

In addition to these values defined by the SCF (1993), the Panel will also use the following:

Adequate Intake (AI): it is the value estimated when a PRI cannot be established because an average requirement cannot be determined.

Recommended intake ranges for macronutrients (RI): the recommended intake range for macronutrients, expressed as % of the daily energy intake.

Tolerable upper intake level (UL): the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans.

Similar recommendations and definitions are being used by other authorities and in other countries, although the terminology may vary (Table 1).

Table 1. **Terminology used for dietary reference values used by different bodies.**

This report	Population reference intake (PRI)	Average requirement (AR)	Lower threshold intake (LTI)	Adequate intake (AI)	Recommended intake range (RI)	Tolerable upper intake level (UL)
UK (DoH, 1991)	Recommended intakes (RI)	Average requirement	Lower level of intake			
SCF, 1993	Population reference intake	Average requirement	Lower threshold intake (LTI)	Adequate intake	-	-
United States (IoM 1997, IoM 1998, IoM 2002)	Recommended dietary allowance (RDA)	Estimated average requirement (EAR)	-	Adequate Intake	Acceptable macronutrient distribution ranges (AMDR)	Tolerable upper intake level
Germany, Austria, Switzerland (D-A-CH, (2000)	Empfohlene Zufuhr	-	-	Schätzwerte Richtwerte	-	-
The Netherlands (GR, 2000)	Aanbevolen dagelijkse hoeveelheid (ADH)	Gemiddelde behoefte	-	Adequate inneming	-	Aanvaardbare bovengrens
France (AFSSA, 2001)	Apport nutritionel conseillé (ANC)	Besoin nutritionnel moyen	-	Apport nutritionel conseillé (ANC)	Apport nutritionel conseillé (ANC)	Limite de sécurité
Nordic countries (NNR, 2004)	Recommended intakes (RI)	Average requirement	Lower limit of intake (LI)	-		Upper intake level (UL)

4. CONCEPTUAL BASIS FOR DERIVATION OF DIETARY REFERENCE VALUES

PRI

The PRI is derived from the average requirement (AR) of a defined group of individuals in an attempt to take into account the variation of requirements between individuals, as well as other factors affecting the requirement.

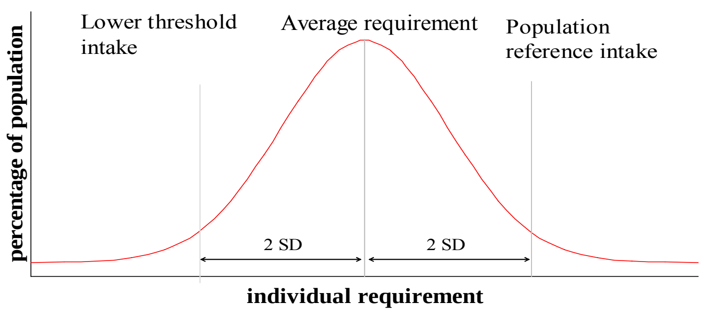


Figure 1. **Population reference intakes (PRI) and average requirement (AR), if the requirement has a normal distribution and the inter-individual variation is known**

By convention and on the assumption that the individual requirement for a nutrient is normally distributed and the inter-individual variation is known, the PRI is calculated on the basis of the AR plus twice its standard deviation (SD) (Figure 1). This will meet the requirements of 97.5% of the individuals in the population. When the distribution of the requirement among individuals is not normal, data may be transformed to normality. The magnitude of the PRI in relation to the AR depends on the estimated variation between individuals.

However, data on inter-individual variation in requirements are limited to a few nutrients. For nutrients for which the variation in requirement is unknown, a default coefficient of variation (CV) of 10% to 20% is used assuming a normal distribution (IoM: 10%; AFSSA: 15%; GR: 10-20%). Depending on the CV used the PRI is set at 1.2 (CV=10%), 1.3 (CV=15%), or 1.4 (CV=20%) times the estimated AR. In this task, the coefficient of variation will be decided on a case-by case basis.

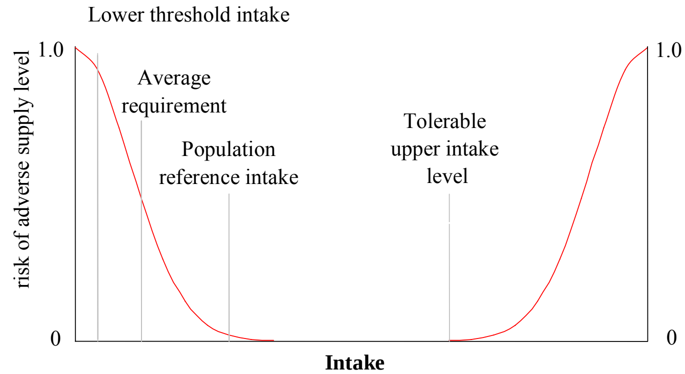
PRI are expressed on a daily basis, but are applied to usual intakes averaged over longer periods of time e.g. one week or longer.

<u>AR</u>

The average requirement is the level of intake of a defined group of individuals estimated to satisfy the physiological requirement or metabolic demand, as defined by the specified criterion for adequacy for that nutrient, in half of the healthy individuals in a life stage or sex group, on the assumption that the supply of other nutrients and energy is adequate.

<u>LTI</u>

The LTI is the lowest estimate of the requirement from the normal distribution curve, and is generally calculated on the basis of the AR minus twice its SD (Figure 1). This will meet the requirements of only 2.5% of the individuals in the population. When the distribution of the requirement among individuals is not normal, data may be transformed to normality.



From: Health and Welfare, Canada, 1983; as adapted by Netherlands Health Council, 2000

Figure 2. **Relationship between individual intake and risk of adverse effects due to insufficient or excessive intake**

<u>AI</u>

An AI is the average (median) daily level of intake based on observed, or experimentally determined approximations or estimates of nutrient intake, by a group (or groups) of apparently healthy people that is assumed to be adequate. The practical implication of an AI is similar to that of a PRI, i.e. to describe the level of intake that is considered adequate for health reasons. The terminological distinction relates to a difference in the way in which these values are derived and to the resultant difference in the 'firmness' of the value.

<u>RI</u>

For some energy-yielding macronutrients, recommended intakes are expressed as the proportion (percentage) of energy derived from that macronutrient. These are usually derived from data on intake in healthy populations and on data on risk of chronic disease and apply to ranges of intakes that are adequate for maintaining health and associated with a low risk of selected chronic diseases.

<u>UL</u>

The tolerable upper intake level (UL) is the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans[4].

<u>Energy</u>

Recommendations for energy have a different basis than those for other nutrients. The energy intake should balance total energy expenditure to avoid under- or overweight, and it is generally presented as estimated average requirement for a defined group with a specified mean height and weight, and a specified age, sex and activity level.

[4] An opinion on tolerable upper intake levels for vitamins and minerals was published in February 2006 (http://www.efsa.europa.eu/en/science/nda/nda_opinions.html). In this task, therefore, only UL's for macronutrients will be established, if appropriate.

5. Methods for determining dietary reference values – types of data used

A variety of data and methods can in principle be used in deriving estimates on (average) nutrient requirements and establishing nutrient-diet-health relationships. These may vary between *in vitro* studies, animal studies, human experimental nutrition studies, and epidemiological studies. Which methods and data are most appropriate depends on the criterion or criteria chosen.

5.1. Criteria for assessment of nutrient requirement

In defining nutrient requirement the selection of criteria to establish nutrient adequacy is an important step. An obvious criterion would be the risk of deficiency, i.e. the amount of a nutrient needed to prevent, or reverse clinical deficiency symptoms. This criterion has been used in earlier recommendations, as well as criteria based upon functional competence, i.e. the amount needed to maintain a critical nutrient-related function, biochemical or physiological, such as maintenance of a desirable plasma level or nutrient-dependent enzyme activity over a certain time period, in otherwise healthy people. Maintenance of cell (organ) integrity or data on body composition, nutrient body stores or pool size, are other typical criteria that can be used. In the more recently published recommendations, epidemiological and clinical data on health outcome, such as disease risk reduction in relation to the nutrient intake pattern and/or diet composition, are also taken into consideration, if available. Although clinical endpoints, e.g. data on morbidity or mortality, are considered the most relevant, surrogate markers of health outcome can provide useful information (IoM 1997, 1998, and 2002; Diplock et al., 1999; Asp et al., 2003 & 2004).

For most nutrients a hierarchy in criteria for nutrient adequacy can be established, ranging from prevention of clinical deficiency to optimisation of body stores or status, to minimising chronic disease risk.

Which criterion, or combination of criteria, is the most appropriate remains a matter of scientific judgement, taking into account all available data and weighing of the evidence, and should be decided on a case-by-case basis.

5.2. Methods for establishing nutrient requirements

Experimental feeding studies in humans, such as depletion-repletion and nutrient balance studies, are classical approaches for assessing the basic (average) requirement for a nutrient. Due to the limited time of observation they may not reflect the steady state and they may underestimate the possibility of adaptation to lower intakes.

In balance studies under- or overestimation of excretory losses and/or retention are a problem due to incomplete collection of urine and faeces, and/or through the skin, depending on the level of intake. This is especially true for nutrients that are highly conserved in the body, such as iron and calcium. Balance studies indicated higher iron retentions than observed in the more reliable radio isotope studies (Green, 1968). In case of calcium apparent nutrient balance has been observed, even at relatively high intakes (around 2 g/day), and this approach likely overestimates actual requirements (Heaney, 1977; Matkovic, 1990).

For some B-vitamins, metabolic conversion (or synthesis) by the intestinal bacteria might complicate balance studies. Results from depletion-repletions studies tend to overestimate requirements, most likely due to incomplete equilibration, as was shown for vitamin B-6 (see IoM report, 1998)

Biochemical markers of the nutritional (nutrient) status, or combinations of different markers, are widely used to assess nutritional adequacy.

Data on the dose response between nutrient intake and status indicators, such as the nutrient (or metabolite) blood or tissue level, enzyme activity, are useful, but also data on physiological (functional) response measures, such as immune competence, nerve conduction velocity, or physical or cognitive performance, etc. are potentially valuable but are difficult to standardise.

For some nutrients, the so-called factorial method is used in establishing nutrient needs, which involves adding up the various factors that determine the requirement for maintenance of a defined plasma level or body store, and that is associated with the absence of adverse health effects, respectively normal tissue or body function. This needs measuring of the amounts of nutrients that leave the body via the faeces, urine and skin, either unchanged or as metabolites and also estimating the amounts that are required for growth, pregnancy or lactation. State of the art isotope techniques now enable accurate estimation of nutrient kinetics, i.e. nutrient fluxes and measurement of 'true' absorption and retention rates.

The extra requirement during growth and pregnancy is due to the amounts of nutrients that become incorporated into newly formed tissues, an effect which is referred to as 'retention'.

During pregnancy body weight increases by 10-15 kg, with a stage-specific rate, which is low in the first half, highest in the second trimester and slightly lower in the third trimester (0,15-0,69 kg/wk during wks 13-20; 0,31 – 0.65 kg/wk during wks 20 – 30, and 0,18 – 0,61 kg/wk during wks 30- 36, respectively) (IoM, 1990). The total weight gain includes the weight of the foetus (ca 25%), the placenta (ca 5%) and the amniotic fluid (6%). In setting recommendations for growing children and pregnant women consideration is also given to the many physiological adaptations that occur during these conditions, such as an increased absorption, and/or greater nutrient retention or losses.

Extra requirements during lactation are determined in part by the amounts of nutrients lost to the body in the form of human milk.

For infants during the first half of the first year of life (0 to 6 months) the nutrient intake of healthy well-growing exclusively (fully) breast-fed infants is generally considered to be adequate and, therefore, to correspond to the requirement for nutrients The average measured concentration of the nutrient in milk obtained from a representative sample of adequately nourished women is multiplied by the average intake volume of breast-fed infants over the first six months of life and regarded to be the AI over this period.

Exceptions to this rule are vitamin D and K, the intake of which is generally insufficient with human milk feeding. It is, moreover, important to ascertain the adequacy of the nutritional status of the lactating woman providing milk samples, especially with respect to those nutrients whose contents in milk depend on the dietary intake of the mother (i.e., iodine, selenium, vitamin A, vitamin B6, vitamin B12).

For older infants between 7 and 11 months a combination of the nutrient intake from human milk plus the intake from typical complementary food can be used, if no other data are available.

Basic research in animal models can produce valuable knowledge on mechanisms and/or dose-response relationship. However, due to inter-species differences, extrapolation from animal models to humans is subject to considerable uncertainties and data from animal models are rarely used in the setting of DRV, e.g. in case of ULs, when data from human studies are insufficient.

5.3. Diet and health relationship: risk of chronic disease

In addition to data on basic nutrient requirements based on maintenance of body stores and function, evidence is accumulating on the relationship between dietary intake and risk of chronic disease and obesity (WHO, 2003). For some nutrients such as sodium, calcium and vitamin D, but especially for the energy-yielding macronutrients such as fatty acids, data from clinical and epidemiological studies are now used in deriving nutritional recommendations.

Observational epidemiological studies can provide valuable data on the association between dietary nutrient intake and health effects, such as disease risk or mortality, in free-living subjects, but by themselves cannot prove causal relationships. Additional pieces of evidence are therefore needed to establish causality. Other limitations include confounding and systematic bias in nutrient and energy intake estimates from self-reporting.

Randomised, controlled intervention studies with 'hard' clinical endpoints, such as morbidity and mortality, are considered as the most reliable, and to have the highest strength of evidence.

However, also intervention trials have their limitations. Representativity of the data and extrapolation of the results to the general population can be a problem, as intervention studies are often done in selected subgroups, such as persons with an already increased disease risk or history of disease. Follow-up periods are relatively short compared to the long periods of disease development, especially in chronic disease, such as cancers. Intervention with relatively high dosages and using isolated or purified nutrients will also affect the outcome, and represent a different situation as in studies with complete diets and nutrients consumed as food at usual intake level.

Judgement should therefore be based on the consistency, strength and quality of the studies, and take into account all the available evidence obtained with the various methods, including knowledge on the mechanism linking nutrient intake and the occurrence of chronic disease.

5.4. Interpolation or extrapolation between population groups

Interpolation or extrapolation will be used in instances where no data are available for defined age and sex groups which permit proceeding according to Sections 4.1 to 4.3. Interpolation between different population groups, whether isometric (linear with body weight) or allometric (body weight to the power of a chosen exponent), has limitations and will be made according to scientific judgement on a case-by-case basis (see Appendix I).

Because of the assumptions made in interpolation or extrapolation, due to lack of knowledge on the proportionality of nutrient requirements with parameters such as body or metabolic weight during growth, reference values for the age groups between 6 months and 18 years, might have a higher uncertainty than those for adults. Metabolic weight has been defined as 0.75 power of body mass (weight), and is also used as the preferred method by some authorities to adjust for metabolic differences between age groups (see Appendix I).

5.5. Factors that affect nutrient requirements

Nutrient requirements vary between individuals due to differences in absorption and utilization of nutrients from the diet. This may be related to the food matrix, i.e. liberation of nutrients from the food matrix in the course of the digestive process, as well as to diet composition and interactions with other diet-related factors.

Bio-availability has been defined as the fraction of an ingested nutrient which is absorbed from the gastro-intestinal tract and utilised for normal physiological function or storage (Jackson, 1997). Host-related factors may play a role, such as stomach acidity, and in some cases nutrient status, but food/diet composition and food preparation are the main determinants of nutrient bio-availability. Iron in the form of haem-iron is much better available than non-haem iron due to a different absorption mechanism. The absorption of iron also depends on the size of the body iron store. Calcium from e.g. dairy products is in general better absorbed than that from vegetable sources.

Nutrient-nutrient interactions may result from competition at the level of absorption, such as between copper and zinc. Vitamin C enhances the absorption of non-haem iron through formation of a soluble complex with ferrous iron in the stomach.

Dietary protein requirements depend on the protein quality of the diet, and present another example of a food-related factor affecting dietary requirements (Millward and Jackson, 2003). Dietary protein requirements may be slightly higher for groups consuming mainly vegetable proteins, e.g. vegans.

5.6. Lifestage and sex

In this task, the reference weights for different age and sex groups from the SCF reports (1993 and 2000) will be considered (Table 2). Reference weight are used in interpolation, or extrapolation of nutrient requirements for population (sub)groups for which insufficient or no data are available to set a reference value. Reference weights are also used in calculation of the average energy requirements. The Panel recognizes that the reference weights used in the SCF report were based upon pooling of national data from a limited number of EU member states. These data are relatively old and not necessarily representative for the newer EU member states, but will be used until more recent and representative data will become available. The Panel would recommend the development of a database with reference weights and heights representative for the total European population.

The age group < 6 months will not be considered given that requirements will refer to amounts of nutrients provided by breast-milk, except on a case-by-case basis where this does not apply. The choice of life stage groups is based upon differences in requirements related to velocity of growth, change in endocrine status, such as in puberty, and age-related changes in nutrient absorption and body functions and/or functional capacity, such as renal function. In older subjects, especially in elderly above 75 yr, variability in functional capacity and in energy expenditure appears higher than in younger adults. Separate recommendations will be made for pregnant and lactating women.

The age ranges used in this report slightly differ from those used in some of the national reports. The differentiation between the younger age groups between 4 and 18 years is the same as used in the earlier SCF report, while in the IoM and other (national) reports, this group is split in 4-8, 9-13, and 14-18 years, respectively, but the actual choice of age ranges remains somewhat arbitrary. The differentiation between young adulthood (18-29 yr) and middle age (30-59 yr) relates to the observed decrease in the mean energy expenditure and the achievement of an optimal peak bone mass, which affect requirements for some of the nutrients. In case of the elderly, the differentiation between 60-74 yr and >75 yr is based upon observed differences in functional and physiological capacity, and in energy expenditure.

Table 2. **Reference weights of population groups in Europe (source: SCF, 1993 and 2000)**

Age (yr)	Reference weight (kg)[1]	
	Males	Females
0-6 months	6.0	5.5
7-11 months	9.0	8.3
1-3	13.0	12.5
4-6	20.0	19.0
7-10	28.5	29.0
11-14	44.5	45.0
15-17	61.5	53.5
18-29	74.6	62.1
30-59	74.6	62.1
60-74	73.5	66.1
≥75	73.5	66.1

1 Based upon median weights of European men and women from various studies (for references see SCF, 1993). Weights for the age groups up to 1 year are based upon median values from the WHO Multicentre Growth Reference Study (WHO, 2006).

6. Application of dietary reference values for nutrients

Applications of dietary reference values fall into the two interrelated general categories, i.e. diet assessment and diet planning. Both can be done for individuals or for population(s) (groups). Dietary reference values are also applied as the basis for reference values in food labelling.

Diet assessment applications involve determining the probable (in)adequacy or excess of observed intakes. Diet planning applications involve using dietary reference values to develop recommendations for what food intakes should be in order to achieve nutritional balance. Rather than focussing on a fixed recommended or advised intake level, the distribution of nutrient intakes among the population is now considered of more importance. For that purpose a set of dietary reference values is derived that can be used both for diet assessment and planning.

6.1. Assessment of (in)adequacy of nutrient intake

6.1.1. Assessment of (in)adequacy of nutrient intake in populations

Intakes of individuals vary from day-to-day, and thus many days of intake are needed to estimate a person's usual intake. Because it is seldom practical to collect data for many days, statistical methods are available to remove the effect of day-to-day variation from the intake distribution for a group. This general approach was proposed by NRC (1986), was further developed by Nusser et al. (1996) and shown to be robust (Hofmann et al., 2002). It can also be adapted to take into account the effects of age (Waijers et al., 2006). To adjust intake distributions it is necessary to have at least two independent days of dietary intake data for a representative subsample of individuals in the group (IoM, 2000).

Most dietary assessment methods result in some underreporting of food (and nutrient) intakes at the group level, and the methods of removing day-to-day variation do not remove this negative effect. Therefore, the prevalence of inadequacy in populations may be overestimated for some nutrients (Murphy et al., 2006).

The proportion of the population with an inadequate intake may be estimated using the AR cut-point method, originally proposed by Beaton (1994) and adopted by the US Food and Nutrition Board (IoM, 2000). This method requires knowledge of the AR and the distribution of habitual nutrient intakes and has been shown to be effective in obtaining a realistic estimate of the prevalence of dietary inadequacy (Carriquiry, 1999). The percentage of the population with a habitual daily nutrient intake that is lower than the AR is taken as an estimate of the percentage of the population with probable inadequate intakes. For example, at a median intake equal to the AR, 50% of a population group will have intakes that may be inadequate for the chosen criterion of nutritional status. At a median intake level around the PRI, intakes are considered adequate for 97,5% of the population group. Higher intakes usually convey no additional health benefit. For nutrients for which a UL has been established intakes above the UL may be associated with increased prevalence of adverse effects in the population.

The AR cut-point method only holds if the distribution of nutrient intakes is normal and requirements and intakes are independent. It is generally assumed that the average daily intakes of vitamins and minerals are not related to requirements, and that the average requirements for vitamins and minerals, except iron, are symmetrically distributed (SCF, 1993; IoM, 1997). However, in the case of skewed distributions, such as in the case of iron, use of the cut-point method would lead to an underestimate of the prevalence of inadequacy in menstruating women (SCF, 1993; IoM, 2000). The SD of the habitual daily intakes of vitamins and minerals are generally greater than 30% of the mean (O'Brien *et al*., 2001; Hannon *et al*., 2001) and are almost always more than twice the commonly assumed variance of requirement of 10–15% of the mean

Energy and protein maintenance requirements are correlated with energy expenditure and body protein mass, respectively, and energy and protein intakes, together with energy and protein requirements may therefore behave collinear. Actually, this relationship may involve other nutrients, because their intakes are often correlated (Day et al., 2001 and 2004).

In these cases, application of the AR cut-point method may result in an overestimation of risks of inadequacy.

Probabilistic methods, which take into account both the intake and requirement variability might be a useful alternative for the AR cut-point method, and give a better estimation of the real prevalence of inadequacy (de Lauzon et al., 2004).

The PRI is an intake level that covers the requirement of 97-98% of all individuals when requirements of the group have a normal distribution. The PRI should therefore not be used as a cut-point for assessing nutrient intakes of groups because a certain overestimation of the proportion of the group at risk of inadequacy would result.

The prevalence of inadequacy of intake of a nutrient in a population cannot be estimated using as comparator the less precise estimates of recommended intake, e.g. nutrients with "adequate intake" (IoM, 1997), 'acceptable range of intakes' (SCF, 1993) or "safe and adequate intake" (DoH, 1991), because the relationship of such reference values to the requirement for the nutrient is not known. Groups with mean intakes at or above the AI can be assumed to have a low prevalence of inadequate intakes for the defined criterion of nutritional status.

For macronutrients which have a recommended intake range for individuals, the distribution of usual intake of individuals may be assessed to ascertain what proportion of the group lies outside the recommended lower and upper limits of the range.

Recommended intakes of energy for groups is based on estimated average energy expenditure associated with the sex, age, height, weight, and physical activity level of the group. Mean usual intake of energy relative to the average requirement may be used in assessing the adequacy of energy intakes of groups. Because there is a high correlation between energy intake and energy expenditure (requirement), median intake of food energy should be close to the requirement for there to be low risk of inadequate or excessive intake. However, because of an expected correlation between energy intakes and energy needs at the group level, it is not possible to generate an unbiased estimate of the prevalence of inadequate or excessive intakes.

6.1.2. Assessment of (in)adequacy of nutrient intake in individuals

Usual nutrient intakes of individuals may be compared with specific dietary reference values, even though dietary intake data alone cannot be used to ascertain an individual's nutritional status. However, such comparisons are of limited use because of inherent problems in the validity of the assessment of usual dietary intake in individuals. Ideally, usual intake data should be combined with clinical, biochemical, and anthropometric information to provide a valid assessment of an individual's nutritional status.

For nutrients with an AI (i.e. without an AR), if an individual’s usual intake equals or exceeds the AI, it can be concluded that the diet is almost certainly adequate. If, however, an individual’s intake falls below the AI, no quantitative (or qualitative) estimate can be made of the probability of nutrient inadequacy (IoM, 2000).

Observed intakes below the LTI have a very high probability of inadequacy.

Observed intakes of an individual below the AR very likely are inadequate because the probability of inadequacy is up to 50 percent, and an intake between the AR and the PRI may be adequate because the probability of adequacy is higher than 50 percent. For nutrients for which a UL has been established chronic intakes above the UL may be associated with an increased risk of adverse effects, and should therefore be avoided.

For macronutrients which have a recommended intake range for individuals, usual intake of individuals may be assessed to ascertain whether it lies between the recommended lower and upper limits of the range.

Recommended intakes of energy for individuals is based on estimated average energy expenditure associated with an individual’s sex, age, height, weight, and physical activity level. As such, it exceeds the needs of half the individuals with specified characteristics, and is below the needs of the other half. Because it is difficult to determine energy balance, even from several days of intake, recent weight history is used as an indicator of the likely adequacy of energy intake.

6.2 Dietary planning

6.2.1. Dietary planning for groups

Planning diets for groups may include institutional food planning, military food and nutrition planning, planning for food assistance programs, food fortification, and assuring food safety.

For groups, the goal of planning is to determine a usual intake *distribution* that results in a low prevalence of intakes that are inadequate (i.e. less than the AR) or at risk of being excessive (i.e. greater than the UL). For nutrients such as vitamins, minerals, and protein, the PRI could be a practical starting point. However, target median intakes higher than the PRI might be considered, especially in case of a skewed intake distribution (WHO, 2006). The AI may be used as an appropriate target average when no AR has been established. For macronutrients which have a recommended intake range for individuals, the distribution of usual intakes of individuals should be such as to minimize the proportion of the group whose intake lies outside the recommended lower and upper limits of the range. For energy, the recommended intake (average energy requirement) of the group based on sex, age, height, weight, and physical activity level of the group may be used as a planning goal (IoM, 2003).

6.2.2. Dietary planning for individuals

Planning diets for individuals may include: (1) providing guidance to healthy individuals to assist them in meeting their nutrient needs, (2) counseling those with special lifestyle considerations (e.g., athletes and vegetarians) or those requiring therapeutic diets, (3) formulating diets for research purposes, (4) developing food-based dietary guidance for individuals. In addition, providing consumer information on food and supplement labels can assist consumers in planning their own diets.

The goal of planning diets for individuals is to have a low probability of inadequacy while minimizing potential risk of excess for each nutrient. For energy, the recommended intake (average energy requirement) based on an individual's sex, age, height, weight, and physical activity level may be used as an initial planning goal; however, body weight must be monitored and intake adjusted as appropriate (IoM, 2003). For macronutrients which have a recommended intake range for individuals, the usual intake of individuals should be between the recommended lower and upper limits of the range. For nutrients such as vitamins, minerals, and protein, this is done by ensuring that the usual intake meets the PRI or AI while not exceeding the UL. PRIs would be an overestimation for most individuals.

6.3. Reference values for labelling

Dietary reference values are used for nutrition information on food and dietary supplements so that consumers can compare products and see how a food fits into their overall daily diet. In the SCF opinion on the revision of reference values for nutrition labelling (2003), the PRI was suggested as a basis for reference labelling values (RLV). An 'overall' PRI was extracted, based upon PRI- (RDA-) values for adults taken from a number of European countries, as well as values from the US and FAO/WHO.

Also the population-weighted mean of the AR has been suggested for use in nutrition labelling as this lower value might be a better statistical approximation of the nutrient requirement for any one individual in the population (IoM; 2003; Tarasuk, 2006; Yates, 2007). Accepting the lower AR values rather than the PRI as a basis for RLV will affect the use of nutrient content claims on foods that are linked to RLVs, and therefore the number of foods that might claim that the product is 'source' or 'high' in a certain nutrient.

However, the substantial differences in the RLVs derived by taking the AR as the basic value, compared to the existing RLVs, which are closer to existing RDAs/PRIs, might be confusing for the consumer, and for that reason, the SCF Committee accepted the RDA/PRI as the basis for the RLV. Which value to take is not a scientific decision, but a management decision after careful consideration of all implications.

6.4. Food-based dietary guidelines

As diets are composed of foods, food-based dietary guidelines (FBDG) are the form in which advice is provided to the consumer. FBDG are generally based upon scientific evidence on the relationship between diet and chronic disease risk, taking into account nutrient recommendations (WHO 2003). The FBDG are intended for use by individual members of the general public, and as a tool for use by policymakers, nutritionists, nutrition educators and healthcare providers, to help consumers in planning an overall healthy diet, while achieving an adequate nutrient intake.

CONCLUSIONS

This opinion focuses on the general principles for development and application of dietary reference values (DRV) - quantitative reference values for nutrient intakes for healthy individuals and populations which may be used for assessment and planning of diets.

Similarly to the earlier SCF report in 1993 the Panel proposes to derive the following DRV:

- *Population reference intakes (PRI):* the level of (nutrient) intake that is adequate for virtually all people in a population group.
- *Average requirement (AR):* the level of (nutrient) intake that is adequate for half of the people in a population group, given a normal distribution of requirement.
- *Lower threshold intake (LTI):* the level of intake below which, on the basis of current knowledge, almost all individuals will be unable to maintain metabolic integrity, according to the criterion chosen for each nutrient.

In addition, the Panel also proposes to derive the following DRV:

- *Adequate Intake (AI):* the value estimated when a PRI cannot be established because an average requirement cannot be determined. An AI is the average observed daily level of intake by a population group (or groups) of apparently healthy people that is assumed to be adequate.
- *Recommended intake ranges for macronutrients (RI):* the recommended intake range for macronutrients, expressed as % of the energy intake. These apply to ranges of intakes that are adequate for maintaining health and associated with a low risk of selected chronic diseases.

The Panel will not address the *Tolerable upper intake level (UL)* as this has been assessed previously. The UL is the maximum level of total chronic daily intake of a nutrient (from all sources) judged to be unlikely to pose a risk of adverse health effects to humans[5]

Some of the DRV - the AR, PRI and LTI - relate to nutrient requirements that are defined by specific criteria of nutrient adequacy. In defining nutrient requirement the selection of criteria to establish nutrient adequacy is an important step. For most nutrients a hierarchy of criteria for nutrient adequacy can be established, ranging from prevention of clinical deficiency to optimisation of body stores, or status. Which criterion, or combination of criteria, will be the most appropriate will be decided on a case-by-case basis.

Within any lifestage group nutrient requirements vary between individuals and the AR, PRI and LTI represent different points on distribution individual requirements. Nutrient requirements also differ with age, sex and physiological condition, due to differences in the

[5] An opinion on tolerable upper intake levels for vitamins and minerals was published in February 2006 (http://www.efsa.europa.eu/en/science/nda/nda_opinions.html).

velocity of growth for the younger age groups, and age-related changes in nutrient absorption and body functions and/or functional capacity, such as renal function. Especially in older subjects, variability in functional capacity and in energy expenditure appears higher than in younger adults, particularly for elderly above 75 yr.

Because of this, DRV are developed for different life stage and sex groups. The panel proposes to establish DRV for the following age groups, like in the SCF reports of 1993 and 2000: *6-11 months; 1-3 years; 4-6 years; 7-10 years; 11-14 years; 15-17 years; 18-29 years; 30-59 years; 60-74 years; and ≥75 years.* For the age group < 6 months requirements are considered to be equal to the supply from breast-milk, except in those cases where this does not apply. Separate reference values will be established for pregnant and lactating women, taking into account the additional nutrient requirement for the formation of new tissues, or to compensate for the nutrients lost to the body in the form of human milk, respectively, and considering the physiological adaptations that occur during these conditions.

Interpolation or extrapolation between population groups will be used in instances where no data are available for defined age and sex groups. Both isometric (linear with body weight) or allometric (body weight to the power of a chosen exponent) scaling methods are being used. Which method is the most appropriate will be decided on a case-by-case basis.

Reference heights and weights are useful when more specificity about body size and nutrient requirements are needed than that provided by life stage categories. Reference weights will be the same as in the SCF report, and for children <1 year, as established by the WHO for fully breastfed infants.

Dietary reference values can be used for different purposes, such as in diet assessment and diet planning, both at the population and individual level, but also as a basis for reference values in food labelling, and in establishing food based dietary guidelines.

In *dietary assessment* of groups the AR can be used to estimate the prevalence of inadequate intakes of micronutrients (the AR cut-point method), if the distribution of nutrient intakes is normal, and intakes are independent from requirements. The PRI should not be used for this purpose as this would result in overestimation of the proportion of the group at risk of inadequacy.

For macronutrients with a defined recommended intake range for individuals, the distribution of usual intake of individuals may be assessed to ascertain what proportion of the group lies outside the recommended lower and upper limits of the range. In case of energy, the mean usual intake of energy of a defined group, relative to the average requirement, may be used in assessing the adequacy.

For assessment of adequacy of nutrient intakes in individuals dietary reference values are of limited use. Usual intakes below the AR are likely inadequate, and below the LTI very probably inadequate, while chronic intakes above the UL may be associated with an increased risk of adverse effects. For a valid assessment of the adequacy of an individual's usual intake, combined information with clinical, biochemical (status), and anthropometric data, are needed.

In *dietary planning* for groups the usual intake *distribution* should be between the AR and UL to avoid inadequate, respectively excessive intakes. For nutrients such as vitamins, minerals, and protein, the PRI can be a practical starting point. However, target median intakes higher than the PRI might be considered, especially in case of a skewed intake distribution.

For macronutrients the distribution of usual intake of individuals should be such as to minimize the proportion of the group that lies outside the recommended lower and upper limits of the range. For energy, the reference intake (estimated average energy requirement) of the group based on sex, age, height, weight, and physical activity level of the group may be used as a planning goal.

REFERENCES

AFSSA (Agence Française de Sécurité Sanitaire des Aliments), 2001. Apport nutritionnels conseillés pour la population Française. Paris, Lavoisier Tec et Doc.

Agutter PS and Wheatley DN (2004). Metabolic scaling: consensus or controversy? *Theoret Biol Med Modelling* 1:13.

Asp NG, Cummings JH, Mensink RP, Prentice A, Richardson DP, Saris WHM (2003). Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM); Phase one: preparing the way. *Eur J Nutr* 42 (suppl. 1), 1-113.

Asp NG, Cummings JH, Howlett J, Rafter J, Riccardi R, Westenhoefer J (2004). Process for the Assessment of Scientific Support for Claims on Foods (PASSCLAIM); Phase two: moving forward. *Eur J Nutr* 43 (suppl. 2), 1-133.

Beaton GH (1994). Criteria of an adequate diet. In: Shils, M.E., Olson, J.A., Shike, M. (Eds.),

Bingham SA, Cassidy A, Cole T, Welch A, Runswich S, Black D, Thurnham D, Bates CE, Khaw KT, Day NE (1995). Validation of weighed records and other methods of dietary assessment using the 24hr urine technique and other biological markers. *Br J Nutr* 73: 531–550.

Carriquiry AL (1999). Assessing the prevalence of nutrient inadequacy. *Public Health Nutr* 2: 23–33.

D-A-CH (2000). Referenzwerte für die Naehrstoffzufuhr. Umschau/Braus Frankfurt/M..

De Lauzon B, Volatier JL, Martin A (2004). A Monte Carlo simulation to validate the EAR cut-poiny method form assessing the prevalence of nutrient adequacy at the population level. *Publ Health Nutr* 7: 893-900.

DoH (Department of Health), 1991. Dietary reference values for food energy and nutrients for the United Kingdom. Report of the Panel on Dietary Reference Values of the Committee on Medical Aspects of Food Policy, HM Stationary Office, London.

Diplock AT, Aggett PJ, Ashwell M, Bornet F, Fern EB, Roberfroid MB (1999). Functional Food Science in Europe (FUFOSE): Consensus document. Br J Nutr 81 (suppl. 1): S1-S27.

Eurodiet Core Report (2000). Nutrition & diet for healthy lifestyles in Europe. Science and policy implications. Commission of the European Communities, Directorate of health and Consumer protection. Office for Official Publications of the European Communities, Luxembourg.

FAO/WHO (1985). Energy and protein requirements. Technical Report Series 724: World Health Organization, Geneva.

FAO/WHO (1998). Preparation and use of food-based dietary guidelines. WHO Technical Report Series, No. 880. World Health Organization, Geneva.

Feldman HA and McMahon TA (1983). The ¾ mass exponent for energy metabolism is not a statistical artifact. *Respiration Physiol* 52: 149-163.

GR (Gezondheidsraad) (2001). Dietary Reference Intakes: energy, proteins, fats and digestible carbohydrates. The Hague: Health Council of the Netherlands, 2001; publication no. 2001/19R (corrected edition: June 2002).

Green R, Charton R, Seftel H, et al.(1968) Body iron excretion in man. *Am J Med* 45:336-353.

Hannon EM, Kiely M, Harrington KE, Robson PJ, Strain JJ, Flynn A (2001). The North/South Ireland Food Consumption Survey: mineral intakes in 18–64-year-old adults. *Public Health Nutr* 4: 1081–1088.

Heaney RP, Recker RR, Saville PD (1977). Calcium balance and calcium requirements in middle-aged women. *Am J Clin Nutr* 30:1603-11.

Hoffmann K, Boeing H, Dufour A, Volatier JL, Telman J, Virtanen M, Becker W, De Henauw S for the Efcosum group. Estimating the distribution of usual dietary intake by short-term measurements (2002). *Eur J Clin Nutr*, 56; S2 : 553-562.

IoM (Institute of Medicine), National Academy of Sciences (1990). Nutrition during pregnancy. National Academy Press, Washington, DC.

IoM (Institute of Medicine), National Academy of Sciences (1997). Dietary Reference Intakes: Calcium, Phosphorus, Magnesium, Vitamin D, and Fluoride. National Academy Press, Washington, DC.

IoM (Institute of Medicine), National Academy of Sciences (1998). Dietary reference intakes for thiamin, riboflavin, niacin, vitamin B_6, folate, vitamin B_{12}, pantothenic acid, biotin, and choline. National Academy Press, Washington, DC.

IoM (Institute of Medicine), National Academy of Sciences (2000). Dietary Reference Intakes: Applications in Dietary Assessment. National Academy Press, Washington, DC.

IoM (Institute of Medicine), National Academy of Sciences (2002). Dietary Reference Intakes for Energy, Carbohydrates, Fiber, Fat, Protein and Amino Acids (Macronutrients). National Academy Press, Washington, DC.

IoM (Institute of Medicine), National Academy of Sciences (2003). Dietary Reference Intakes: Applications in Dietary Planning. National Academy Press, Washington, DC.

IoM (Institute of Medicine), National Academy of Sciences (2003). Dietary Reference Intakes: Guiding principles for nutrition labelling and fortification. National Academy Press, Washington, DC.

Jackson MJ (1997). The assessment of bioavailability of micronutrients: Introduction. *Eur J Clin Nutr* 51 (suppl 1): S1-S2.

King JC and Garza A (2007) Harmonization of nutrient intake values. *Food and Nutr Bull* 28 (supll. 1): S3-S12.

Kleiber M (1932). Body size and metabolism. *Hilgardia* 6: 315-353

Kleiber M (1947). Body size and metabolic rate. *Physiol Rev* 27: 511-541.

Matkovic V, Montana D, Tominac C, et al. (1990). A study of calcium balance and the inheritance of bone mass in adolescent females. *Am J Clin Nutr* 52: 878-88.

Martin A (2001). Nutritional recommendations for the French population. *Sci. Alim*. 21(4): 309-458.

Millward DJ and Jackson AA (2003). Protein/energy ratios of current diets in developed and developing countries compared with a safe protein/energy ratio: implications for recommended protein and amino acid intakes. *Public Health Nutr* 7: 387-405.

MurphySP, Guenther PM, Kretsch MJ (2006). Using the Dietary Reference Intakes to assess intakes of groups: pitfalls to avoid. *J Am Diet Assoc* 106:1550-1553.

Modern Nutrition in Health and Disease, ninth ed. Williams & Wilkins, Baltimore, pp. 1705–1725.

NNR (Nordic Nutrition Recommendations) 4th edition (2004). Copenhagen, Nordic Council of Ministers.

NRC (National Research Council), 1986. Nutrient Adequacy. Assessment Using Food Consumption Surveys. Washington DC, National Academic Press.

Nusser SM, Carriquiry AL, Dodd KW, Fuller WA (1996). A semi-parametric transformation approach to estimating usual daily intake distributions. *J Am Stat Assoc* 91:1440-1449.

O'Brien MM, Kiely M, Harrington KE, Robson PJ, Strain JJ, Flynn A (2001). The North/South Ireland Food Consumption Survey: vitamin intakes in 18–64-year-old adults. *Public Health Nutr* 4: 1069–1080.

Rubner M (1883). Über den Einfluss der Körpergröße auf Stoff- und Kraftwechsel. *Zschr Biol* 19: 535-562.

SCF (Scientific Committee on Food), 1993. Nutrient and Energy Intakes for the European Community. Commission of the European Communities, Directorate General Industry. Office for Official Publications of the European Communities, Luxembourg.

SCF (Scientific Committee on Food), 2000. Opinion on guidelines for the development of tolerable upper intake levels for vitamins and minerals.

SCF (Scientific Committee on Food), 2003. Opinion on the revision of reference values for nutrition labelling.

Solomons NW and Allen LH (1983). The functional assessment of nutritional status: principles, practice and potential. *Nutr Reviews* 41: 33-50.

Tarasuk V (2006). Use of population-weighted estimated average requirements as a basis for daily values on food labels. *Am J Clin Nutr* 83: 1217S-1222S.

USDA (United States Department of Agriculture), 2005. Dietary guidelines for Americans.. Internet:
<http://www.health.gov/dietaryguidelines/dga2005/document> (accessed 2 February 2007).

Waijers PMCM, Dekkers ALM, Boer JMA, Boshuizen HC, van Rossum CTM. The potential of Age Mode, an age-dependent model, to estimate usual intakes and prevalence of inadequate intakes in a population. *J Nutr* 2006, 136: 2916-2920.

West GB and Brown JH (2005). The origin of allometric scaling laws in biology from genomes to ecosystems: towards a quantitative unifying theory of biological structure and organisation.
J Eper Biol 208: 1575-1592

White CR and Seymour RS (2003). Mammalian basal metabolic rate is proportional to body mass2/3. PNAS 100:4046-4049.

White CR and Seymour RS (2005). Allometric scaling of mammalian metabolism. *J Exper Biol* 208: 1611-1619.

WHO (World Health Organization), 2003. Diet, nutrition and the prevention of chronic diseases. WHO Technical Report. Series 916. Geneva: World Health Organization

WHO (World Health Organization), 2006. Multicentre Growth Reference Study Group. WHO Child Growth Standards based on length/height, weight and age. *Acta Paediatr. Suppl.* 450:76-85.

WHO (World Health Organization), (2006). Guidelines on food fortification with micronutrients (L. Allen, de Benoist B, Dary O & Hurrell R, Eds).

Yates AA (2007). Which Dietary Reference Intake is best suited to serve as a basis for nutrition labelling for daily values. *J Nutr* 136:2457-62**.** .

GLOSSARY / ABBREVIATIONS

ADI	Acceptable Daily Intake
AFSSA	Agence Française de Sécurité Sanitaire des Aliments
AMDR	Acceptable macronutrient distribution ranges
AI	Adequate Intake
AR	Average Requirement
D-A-CH	Nutrition Recommendations for Germany, Austria and Switzerland
DoH	Department of Health (United Kingdom)
EAR	Estimated Average Requirement
EC	European Commission
EFSA	European Food Safety Authority
EU	European Union
FAO	Food and Agriculture Organisation
FNB	U.S. Food and Nutrition Board
GR	Gezondheidsraad (The Netherlands Health Council)
IoM	Institute of Medicine (United States)
LTI	Lower threshold intake
NNR	Nordic Nutrition Recommendations
PRI	Population Reference Intakes
RI	Recommended intake ranges for macronutrients
SCF	Scientific Committee for Food
SD	Standard Deviation
UL	Tolerable upper intake level
US	United States
USDA	United States Department of Agriculture
WHO	World Health Organisation

Appendix I - Interpolation and Extrapolation

Interpolation will be used in instances where no data are available for defined age and sex groups which permit proceeding according to Sections 4.1 to 4.3. Interpolation between different population groups is the least reliable method to determine the nutrient requirement. Extrapolation from the known AR or AI of one population group to other groups for which no specific data exist can be performed based on differences in typical body weights or on differences in energy requirement. Extrapolation should be performed sex-specific if differences in nutrient requirement according to sex are known. The typical body weights for age groups are listed in table 1 of Section 4.6.

Depending on whether the requirement for the nutrient under consideration is associated with the metabolic rate or is not associated with the metabolic rate allometric or isometric scaling is performed.

In *isometric scaling* the AI or AR for the population group X under consideration is derived by multiplication of the known and sex-specific AI or AR of group Y with the quotient between the typical weight of group X and the weight of group Y:

[*Formula 1*]: AI (or AR)$_X$ = AI (or AR)$_Y$ x (body weight$_X$/body weight$_Y$).

An example for this type of isometric scaling is magnesium and fluoride.

Allometric scaling reflects that the metabolic rate of an organism is an exponential function of body mass (weight). The original finding that the metabolic rate of humans and animals was linearly related to body surface area (Rubner, 1883) and therefore, roughly to body weight $^{2/3}$ was modified by Kleiber (1932 and 1947), who demonstrated that the logarithm of the basal metabolic rate of ten different mammalian species was linearly related to the logarithm of the body weight with a slope of 0.75. He coined the term *metabolic body size* for body weight $^{0.75}$ and predicted that the requirement for nutrients should be proportional to the metabolic body weight if their rate of "destruction" or excretion was found to be proportional to metabolic rate. However, this rule only applied to mature organisms at indifferent environmental temperature and at rest. Although this rule has never directly been proven to be correct with respect to nutrient requirements and although the discussion whether the mass exponent between different species is the same as within a species and whether it is nearer 0.67 or nearer 0.75 has not yet been conclusively resolved (Feldman and McMahon, 1983; Agutter and Wheatley, 2004; White and Seymour, 2003 and 2005; West and Brown, 2005), scaling as the 0.75 power of body mass (weight) has been widely accepted in nutritional science. Compared to isometric scaling allometric scaling from a higher to a lower body weight gives higher values, whereas allometric scaling from a lower to a higher body weight results in lower values.

[*Formula 2*]: AI (or AR)$_X$ = AI (or AR)$_Y$ x (weight$_X$/weight$_Y$) $^{0.75}$

When scaling down from an adult AI or AR to children corrections for growth requirements have to be made in order to account for the nutrient amount required to be incorporated into newly formed tissue. One way to do this is to add an age specific growth factor based on the proportional increase in protein requirements for growth (as calculated from Tables 33 and 34 in the FAO/WHO/UNU report, 1985) to both the formula 1 and 2:

[*Formula 3*]: AI (or AR)$_X$ = AI (or AR)$_Y$ x (weight$_X$/weight$_Y$) x (1 + growth factor)

[*Formual 4*]: AI (or AR)$_X$ = AI (or AR)$_Y$ x (weight$_X$/weight$_Y$)$^{0.75}$ x (1 + growth factor).

The following growth factors have been applied (IoM, 1998; FAO/WHO, 2004):

Age	Growth factor
7 months – 3 years	0.30
4 – 8 years	0.15
9 – 13 years	0.15
14 – 18 years males	0.15
14 – 18 years females	0.00

Another method of interpolation has been proposed and assumes that the nutrient requirement after the age of 0-5 months until the age of 18 years increases linearly with age and that the requirement between the age of 14 and 18 years is the same as that of persons 19-50 years old. Additionally the following age correction factors (AF) are applied:

6-11 months	0.03
1- 3 years	0.14
4-8 years	0.38
9-13 years	0.69

Adequate intake or the population reference intake are then calculated as follows:

$$AI = AI_{[0\text{-}5\ months]} + [\ AF\ x\ (AI_{[>14\ \mathrm{year}]} - AI_{[0\text{-}5\ month]})]$$

or

$$PRI = \mathrm{PRI}_{[0\text{-}5\ months]} + [\ AF\ x\ (PRI_{[>14\ \mathrm{year}]} - \mathrm{PRI}_{[0\text{-}5\ month]})]$$

In this formula, 'AI' stands for adequate intake and 'PRI' for population reference intake (Gezondheidsraad NL, 2002).

Extrapolation was used by the French expert Committee (Martin, 2001) as an alternative approach to interpolation in order to calculate reference values of vitamins for children. This approach assumes that both nutritional reference values at the ends of the range are valid. Acceptable Intakes for newborns derived from the supply by maternal milk and Population Reference Intakes for adults. Various representative parameters for children aged 0-18 years, provided by the National Institute of statistics, were used for extrapolation: weight, height, body mass index, square height (representative of lean body mass) energy intake (as a marker of metabolic rates), and body surface area were tested. For each vitamin, only one parameter appeared to allow satisfactory extrapolation in both sexes, either starting from the adult values to reach newborn values and starting from newborn values to reach adult values: square height (for Vitamins, B6, B12, thiamine, biotin, folic acid) and energy intake (for vitamins C, A, E, riboflavin, pantothenic acid, niacin). This methodology does not require any a priori judgement on what could be the best equation for the derivation of values for children.